

**A study of the appropriateness of prescriptions for mental  
health disorders or pain among users of a specialist  
treatment service for substance use disorders**

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# Abstract

**Background:** People with substance use disorders (SUDs) often have co-existing physical and/or mental health conditions and are prescribed a large number of medications which may or may not be justified. Among this population, psychiatric medications and opioids are often involved in adverse events. There is, however, a lack of research on the quality of prescribing of these medications. In this thesis, the appropriateness of these medications is explored, as well as the response of prescribers in a specialist addiction service (SAS) to their inappropriate prescribing.

**Methods:** A mixed methods design was utilised. A descriptive quantitative study using routinely available data was conducted to describe the scale of prescribing for service users. A second quantitative component involving questionnaires was carried out to assess the appropriateness of psychiatric medications and opioids in a sample of service users by SAS prescribers. Qualitative interviews were conducted with service users to explore their perspectives on the appropriateness of these medications while prescriber interviews explored how they responded to inappropriate prescribing.

**Results:** The descriptive study showed that 27% of service users were prescribed four or more medications with almost half of them receiving antidepressants. The second study showed that nearly half of service users had at least one inappropriate psychiatric medication or opioid. Interviews with service users revealed that most of them benefited from these medications but that their use often involved making a compromise between risks and benefits. Benefits/risks of medications, prescriber expertise, nature of addiction and communication with service users and prescribers were considered by SAS prescribers before responding to inappropriate prescribing. It appears the need to maintain service users' stability and well-being may lead to a greater focus on these issues when assessing the appropriateness of prescribing decisions.

**Conclusion:** The quality of prescribing of opioids and psychiatric medications to service users referred to this SAS appeared to present room for improvement. Further research is required with the availability of a more mixed economy of service providers in the alcohol and drug treatment sector to establish if these findings are applicable.

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## Author's declaration

I declare that I am responsible for the work submitted in this thesis. This work has not previously been submitted for any other award. Edited versions of some findings in this thesis have been published in a peer-reviewed journal. The publication is shown in appendix 4.7. To the best of my knowledge, this thesis contains no other previously published material, except where due reference is made within the text. All sources are acknowledged as references.

# Chapter 1: Introduction

The use of substances such as alcohol and illegal drugs has been linked with diverse problems among people who use them, their families and the wider society. In particular, mental and physical health problems are common in people with substance use disorders (hereafter SUDs) and medications are often required in their management. Given the extent of prescribing for this patient group, it is important to consider whether prescribed medications are appropriate for safety reasons, optimal benefit and also for cost-effective prescribing. This thesis therefore considers the appropriateness of opioids and psychiatric medications among people with SUDs (except nicotine use disorders) while also exploring how prescribers in a specialist addiction service (hereafter SAS) respond to inappropriate prescribing. Appropriateness in this thesis encompasses consideration of effectiveness, safety, cost, patients' preferences and outcomes as well as prescribers' perspectives. This introduction section will focus on the rationale for this thesis, definition and prevalence of SUDs, the concept of appropriateness, comorbidities associated with SUDs and their pharmacotherapeutic management, medication adherence as well as UK prescribing models.

## **1.1. Thesis rationale**

People with SUDs often have co-existing physical and/or mental health problems (McLellan, 2009). In particular, high levels of mental health problems (Delgadillo et al., 2012; Grant et al., 2004; Mortlock, Deane and Crowe, 2011; Regier et al., 1990) and pain (Jamison, Kauffman and Katz, 2000; Peles et al., 2005; Rosenblum et al., 2003) are prevalent in this population, with life expectancy being shorter than that of the general population (Chang et al., 2011; Hannerz, Borga and Borritz, 2001; Oppenheimer et al., 1994). Potential reasons for these high levels of morbidity and mortality include the toxicity of substances (Lieber, 1995; Stein, 1999), the adverse effects of some medications such as antipsychotics, benzodiazepines and opioids (Leslie and Rosenheck, 2004; Roose, 2000) used in treating these comorbid conditions as well as poor quality of medical care (Bjorkenstam et al., 2012). These reasons underscore the need for careful monitoring of the effect of substances and medications prescribed for people with SUDs, especially those with co-occurring mental disorders and pain.

People with comorbid mental disorders and SUDs usually have complex needs comprising health, social and economic needs (Hughes, 2006), require more resources and are challenging to manage (Department of Health, 2004). Similarly, people with comorbid pain and SUDs are more likely to have health problems, mental health symptoms and less social support when compared to those without pain (Jamison et al., 2000; Rosenblum et al., 2003). The management of comorbid pain in people with SUDs also presents a clinical challenge as there is the risk of compounding an existing SUD or even fatality through overdose if opioid analgesics are prescribed for pain relief (Action on Addiction, 2013). Furthermore, these patients are often stigmatised by healthcare professionals due to their substance use and difficult behaviour (Link et al., 1997; Lloyd, 2010) and may therefore receive suboptimal healthcare (Henderson, Stacey and Dohan, 2008), including prescribing.

Given the high levels of comorbid conditions (Arora and Kaur, 2012; Caldeiro et al., 2008; Delgadillo et al., 2012; Kidorf et al., 2004; Peles et al., 2005; Rosenblum et al., 2003; Weaver et al., 2003) and prescribing (McManus et al., 2009; Oluyase et al., 2013) among substance users who access treatment, there is the need for scrutiny of prescribing practice in this group, especially, as the quality of healthcare has been identified as a priority by the UK Government (Department of Health, 2013a). Consequently, this research explores two important aspects concerning the care for this population: the appropriateness of psychiatric medications and opioids prescribed for people with SUDs and SAS prescribers' responses to inappropriate prescribing.

Medications used in the treatment of mental disorders (for example, benzodiazepines and antidepressants) and pain (for example, opioids) have been implicated in the occurrence of adverse events including overdose and mortality in patients with SUDs (Darke, Duflou and Torok, 2011; Darke and Hall, 2003; Darke and Ross, 2000). Benzodiazepines and alcohol have often been found to be used in combination with opioids such as dihydrocodeine and oxycodone in opioid-related overdose and fatalities (Darke, Duflou and Torok, 2011; Zamparutti et al., 2011). Zamparutti et al. (2011) found that in 96% of accidental deaths involving dihydrocodeine among opiate misusers, dihydrocodeine was used in combination with other substances such as hypnotics/sedatives and other opiates (methadone, heroin and morphine). Almost half (45%) of victims who accidentally overdosed on dihydrocodeine had been prescribed it.

Antidepressant prescriptions, especially tricyclic antidepressants (hereafter TCAs), have also been linked to heroin overdose (Darke and Hall, 2003; Darke and Ross, 2000). When used in combination with heroin, TCAs significantly increase the risk of respiratory depression, coma and cardiac arrest (Darke and Ross, 2000).

In the UK, 1.5 million people are believed to be dependent on prescription drugs, surpassing the number of people in treatment for illicit drug use (Home Affairs Committee, 2013). In particular, the rise in opioid prescriptions for pain has been accompanied by an increase in its non-medical use and additional risk of morbidity and mortality (Bohnert et al., 2011; Dasgupta, 2006; Dunn et al., 2010), with a history of SUDs being a risk factor for such use (Chou, 2009; Sehgal, Manchikanti and Smith, 2012; Solanki et al., 2011). Fatal overdose involving prescription opioids more than tripled in USA between 1999 and 2002 (Paulozzi, Budnitz and Xi, 2006). These studies imply that the risk of overdose may be affected by prescribed medications taken by people with SUDs and underscore the need to assess the appropriateness of medications prescribed for this group.

There has been limited research on the appropriateness of opioids and psychiatric medications among people with SUDs. A comprehensive search of the literature conducted as part of this thesis found only eight studies (Baca-Garcia et al., 2009; Clark, Xie and Brunette, 2004; Leslie and Rosenheck, 2001; Morasco, Duckart and Dobscha, 2011; Morrison et al., 1994; Thirion et al., 2002; Walkup et al., 2000; Weinmann, Janssen and Gaebel, 2005) that assessed the appropriateness of psychiatric medications and opioids prescribed for people with co-existing mental disorders or chronic pain and SUDs. While some of these studies found that doses and duration of opioids and psychiatric medications sometimes exceeded guideline recommendations, two studies (Baca-Garcia et al., 2009; Leslie and Rosenheck, 2001) found that there was sometimes underdosing.

Britten et al. (2003) have advocated a holistic view of appropriateness encompassing patient and prescriber perspectives. The perspectives of patients and prescribers may well differ concerning prescribing appropriateness. Attempts to measure appropriateness that incorporates both perspectives will lead to a deeper understanding of the complex process of prescribing (Britten et al., 2003). Patients' perspectives could assist in

understanding their views on prescribing appropriateness, how they influence prescribing, their beliefs and concerns about medications and the possible influence of these on medication adherence. Prescribers' perspectives could assist in determining the necessity of medications and the reasons prescribing may sometimes not follow recommended standards while also providing insight into the process of clinical decision-making that prescribers go through in order to assess the appropriateness of prescribed medications. The above perspectives are however not the only criteria for evaluating prescribing. There is a need to further consider the interest of those around the patient, including the wider society, as prescribing may lead to benefit or harm for others (Cribb and Barber, 1997). For instance, there is the need to consider the impact prescribing could make on social issues associated with substance use such as crime and violence. Judgment on the appropriateness of prescribing is therefore complex and would entail consideration of these different aspects for optimal decision-making.

This thesis adds to knowledge on the clinical management of people with SUDs by assessing the appropriateness of medications prescribed for them from two perspectives (patient and prescriber<sup>1</sup>) with a particular focus on psychiatric medications and opioids while also assessing how prescribers addressed inappropriate prescribing. This study used a mixed method design and is the first to the best of my knowledge that has explored the appropriateness of prescribing of psychiatric medications and opioids from the above perspectives.

## **1.2. Thesis aims and structure**

### **1.2.1. Aims**

The aims of this thesis were:

- To investigate the level and nature of appropriateness of current medications for service users in a specialist addiction service (SAS);
- To explore prescribers' responses to inappropriate prescribing in a SAS.

The fact that prescribing appropriateness is a complex and under-researched area, and the need to understand the scale and nature of prescribing for people with SUDs

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<sup>1</sup> Prescriber perspectives include their ratings of medication appropriateness on the study questionnaires as well as the perspectives they expressed in their interviews.

necessitated the adoption of multiple methods. In addition, mixing quantitative and qualitative methods allowed for a more holistic picture on prescribing appropriateness. Quantitative methods were used to provide an overview of the different classes of medications taken by service users during their first assessment at the SAS and to enable the estimation of the magnitude of inappropriate prescribing (including medication omissions or failure to prescribe needed medications) using questionnaires. The questionnaires used include an adapted version of the Medication Appropriateness Index (hereafter MAI) and a questionnaire designed for assessing medication omissions (hereafter medication omissions questionnaire). Qualitative methods were used to provide an in-depth understanding of the appropriateness of prescribing from the service users' perspectives in addition to allowing exploration of prescribers' responses to inappropriate prescribing. It was also intended that the evidence obtained from this research would assist in making recommendations for the development of better practice in relation to prescribing of psychiatric medications and opioids for this group of people.

### **1.2.2. Thesis structure**

The rest of chapter one provides the backdrop to the study in terms of the definition and prevalence of SUDs, the concept of appropriateness, comorbidities associated with SUDs and their pharmacotherapeutic management, medication adherence and UK prescribing models. Chapter two reviews published research exploring the appropriateness of prescribing of psychiatric medications and opioids among people with SUDs. Chapter three provides an overview of the methodology adopted for this thesis and the rationale for the mixed methods design. Chapter four presents the first study carried out. It is a descriptive study detailing the different classes of medications taken by service users who were newly referred to the SAS. This study involved analysis of routinely collected data obtained from the SAS electronic database. Chapter five comprises the second study. It is a cohort study involving assessment of the appropriateness of service users' prescribed psychiatric medications and opioids by prescribers working at the SAS. Chapters six and seven present the methodology, result and discussion of the qualitative interview studies carried out with SAS service users and SAS prescribers respectively. Chapter eight offers an integration and discussion of the findings of this thesis with a focus on its practice implications, directions for future research and conclusions.

### **1.3. Substance use disorders (SUDs)**

This thesis focuses on the medications prescribed for people with SUDs and as a result, it is pertinent to understand how SUDs have been classified by the diagnostic manual used in the UK (including the SAS) for mental disorders: the International Classification of Diseases, tenth edition (ICD-10) published by the World Health Organisation (World Health Organisation, 1992). The ICD-10 classifies SUDs into harmful use and dependence. Harmful use is defined as “a pattern of psychoactive substance use that is causing damage to health” (World Health Organisation, 1992).

Dependence is defined as:

A cluster of behavioural, cognitive, and physiological phenomena that develop after repeated substance use and that typically include a strong desire to take the substance, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal state (World Health Organisation, 1992).

In order to diagnose dependence, at least three criteria occurring at any time in the same 12-month period are required among those stated above (Hasin et al., 2006). Diagnosis of dependence is further specified by the following:

- Currently abstinent;
- Currently abstinent, but in a protected environment (e.g. in hospital);
- Currently on a clinically supervised maintenance or replacement regime (e.g. with methadone);
- Currently abstinent, but receiving treatment with aversive or blocking drugs (e.g. naltrexone);
- Currently using the substance;
- Continuous use;
- Episodic use.

The American Psychiatric Association’s (hereafter APA) Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) is another manual that was

commonly used in clinical practice during the period this research was carried out. It classified SUDs into abuse<sup>2</sup> and dependence unlike the ICD-10 which classified SUDs into harmful use and dependence. The diagnostic criteria for dependence are however similar between DSM-IV and ICD-10 (Hasin et al., 2006). The DSM-IV criteria for abuse and dependence have recently been updated in the DSM-5 with abuse and dependence combined into one disorder (American Psychiatric Association, 2013).

### **1.3.1. Prevalence of SUDs**

Accurate measurement of the prevalence of SUDs is challenging because people may underestimate or deny usage to avoid being stigmatised because of their illicit status or due to the surreptitious nature of activities used in obtaining them (Hay et al., 2006; Somers et al., 2004), and are likely to be absent from many of the survey methods used to measure prevalence. People with severe SUDs are often not captured in surveys because they may be homeless or transient (Somers et al., 2004). Furthermore, studies use different definitions for SUDs which may range from frequent use to the use of formal diagnostic criteria such as ICD-10 as discussed in the previous section.

The most recent adult Psychiatric Morbidity Survey (hereafter PMS) (McManus et al., 2009) carried out in 2007, assessed the prevalence of alcohol use disorders (hereafter AUDs) in people aged 16 and above in private households in the UK. Three categories were specified for AUDs: hazardous drinking, harmful drinking and alcohol dependence. Hazardous drinking was defined as a pattern of drinking that could lead to harmful consequences whereas harmful drinking represents a type of drinking that has already resulted in harm (McManus et al., 2009). Harm may be physical or psychological. Alcohol dependence was defined as a cluster of behavioural, cognitive, and physiological phenomena that typically include a strong desire to consume alcohol, and difficulties in controlling drinking. Hazardous and harmful drinking were identified using the Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al., 1993), and alcohol dependence was assessed using the Severity of Alcohol Dependence Questionnaire, Community Version (SADQ-C) (Stockwell et al., 1994). The prevalence of hazardous/harmful drinking was 24.2% (33.2% of men, 15.7% of women) with harmful drinking involving 3.8% of adults (5.8% of men, 1.9% of women). The

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<sup>2</sup> Abuse is diagnosed by the presence of one of the following four criteria which must cause clinically significant impairment or distress: hazardous use, legal problems, neglect of major roles due to substance use and social/interpersonal problems related to use.

prevalence of alcohol dependence was found to be 5.9% (8.7% of men, 3.3% of women). This survey showed a slight decrease in the prevalence of alcohol dependence compared to the previous PMS carried out in year 2000 (Singleton et al., 2001).

The prevalence of drug misuse and dependence was also reported in the adult PMS in 2007. Drug misuse was defined according to the WHO criteria as the use of a substance for purposes not consistent with legal or medical guidelines, for example the non-medical use of prescription medications or the recreational use of illegal drugs (World Health Organisation, 1994). Although drug misuse is not necessarily problematic, it could escalate to problematic levels (Advisory Council on the Misuse of Drugs, 2008). The prevalence of illicit drug use in the past year was 9.2% (12.0% of men, 6.7% of women) with lifetime illicit use being 25.8% (29.9% of men and 21.8% of women). Dependence was defined as the presence of one of five symptoms of dependence stated in ICD-10 in the past year and its prevalence was estimated to be 3.4% (4.5% of men, 2.3% of women). This survey found a similar prevalence of drug dependence when compared to the previous PMS (Singleton et al., 2001). Similar prevalence (8.8%) for illicit drug use was reported in the 2013/14 Crime Survey for England and Wales among people aged 16 to 59 years while that for lifetime use was higher (35.6%) (Home Office, 2014).

Other methods such as the capture-recapture method and the multiple indicator method have been used to estimate the prevalence of problematic drug use in the UK. Both are indirect methods of assessment of the prevalence of drug use (Hay et al., 2010). Accurate assessment of the numbers of people involved in covert activities such as opioid or cocaine use is difficult and surveys tend to underestimate their prevalence (Hay, Rael dos Santos and Worsley, 2013). Capture-recapture method uses information on the overlap between data sources that are available at the local level to provide estimates of the size of the hidden population: that is, problem drug users not identified from any data source (Hay et al., 2006). The capture-recapture method uses multiple data sources such as drug treatment data, probation, police and prison data for calculating prevalence estimates of substances (Hay et al., 2010). Overlap between data sources are determined by comparison of initials, date of birth and gender. Statistical modelling techniques are used to examine this overlap and to produce prevalence estimates (Hay et al., 2010). The multiple indicator method models the relationship

between the capture-recapture estimates and readily available indicator data such as aggregate number of drug users in treatment or committing drug-related crimes in an area (Hay et al., 2006). It uses this relationship to provide prevalence estimates in areas where capture-recapture estimates are not available (Hay et al., 2006).

These two methods were used to estimate the prevalence of problem drug use, defined as opiate (heroin, methadone, other opiate drugs) and/or crack cocaine use, in England. The estimated prevalence of problem drug use among people between 15 and 64 years was found to be 8.4 (95% CI: 8.3 to 8.6) per 1000 population between 2011 and 2012 (Hay, Rael dos Santos and Worsley, 2013). This was similar to the reported prevalence in the survey carried out between 2010 and 2011 (Hay, Rael dos Santos and Millar, 2012). Overall, the reported prevalence of SUDs is likely to be underestimated. The next section provides a brief description of service users in structured treatment in the UK.

### **1.3.2. Service users with SUDs in structured treatment**

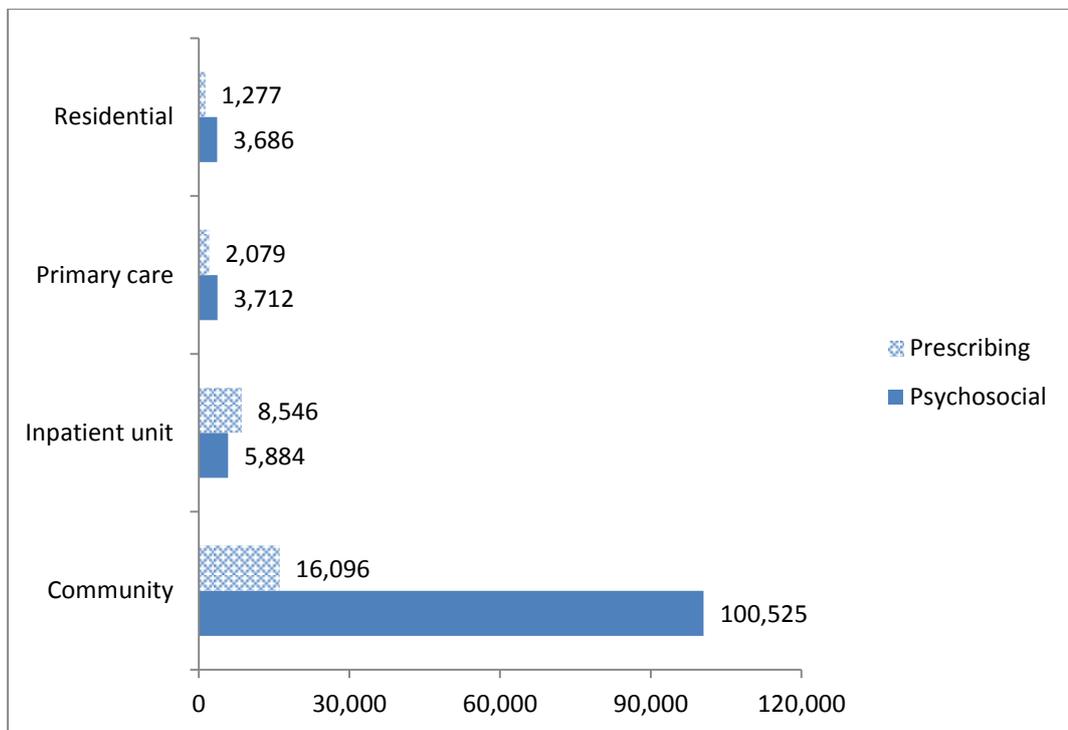
Despite the problems associated with dependence, only a minority of UK adults who are alcohol dependent and two-thirds of those dependent on drugs receive treatment annually (National Institute for Health and Clinical Excellence, 2011a; The Centre for Social Justice, 2013). Possible explanations for this include inadequate numbers of specialist treatment services, long intervals between dependence and seeking help, and the under-recognition of dependence by healthcare professionals (National Institute for Health and Clinical Excellence, 2011a).

Recent statistics concerning those in structured treatment in England show that 114,920 service users aged 18 to 75 years cited alcohol as their primary problematic substance between 2013 and 2014 while 193,198 clients were in treatment for drug dependence (Public Health England, 2014a; Public Health England, 2014b). A further 34,237 service users cited problematic alcohol use as being concurrent with other primary substances. The numbers in treatment for alcohol have increased over the last three years with a 5% increase occurring between 2012/13 and 2013/14 (Public Health England, 2013a). However, the numbers in treatment for drug dependence were similar to that of the previous year (Public Health England, 2013b). Almost 80% of those in treatment for drug dependence between 2013 and 2014 were opiate users. These data probably

represent an underestimation of the numbers in treatment due to data quality issues such as incomplete reporting (Department of Health, 2012b).

Service users in structured treatment may receive different types of interventions ranging from prescribing to psychosocial interventions in different settings. Data obtained between 2013 and 2014 shows that among those in treatment for alcohol, psychosocial interventions were more common in the community, primary care, residential and recovery houses<sup>3</sup> (Public Health England, 2014a) compared to prescribing. Prescribing was however more prevalent in in-patient units. Figure 1.1 shows the interventions received by service users in structured treatment for alcohol in different settings between 2013 and 2014.

Figure 1.1: Interventions received by service users in alcohol treatment in 2013/14



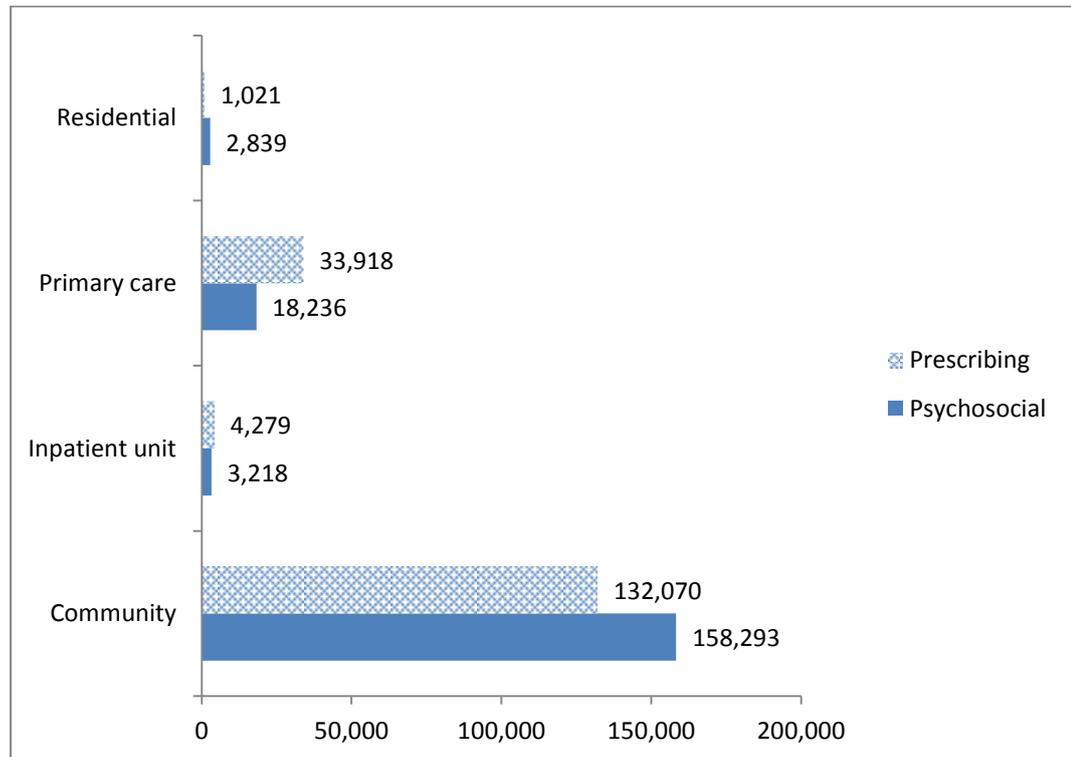
Note: Interventions received in recovery houses were not shown due to small numbers: 170 service users received psychosocial interventions while <5 service users received prescribing interventions.

Adapted from Public Health England (2014a)

<sup>3</sup>A recovery house is a residential living environment that provides integrated peer support and/or integrated recovery support. It usually requires less staffing and the care provided is less intensive than a residential rehabilitation service. Care Quality Commission. (2014). A fresh start for the regulation and inspection of substance misuse services: working together to change how we regulate, inspect and monitor specialist substance misuse services. [Online]. Available at: [http://www.cqc.org.uk/sites/default/files/20140919\\_cqc\\_a\\_fresh\\_start\\_substance\\_misuse\\_final\\_low\\_res.pdf](http://www.cqc.org.uk/sites/default/files/20140919_cqc_a_fresh_start_substance_misuse_final_low_res.pdf) [Accessed 7 March 2015].

Among those in treatment for drug dependence, prescribing was more common in inpatient units and primary care (Public Health England, 2014b). Figure 1.2 shows the interventions received by those in structured treatment for drug dependence between 2013 and 2014.

Figure 1.2: Interventions received by service users in drug treatment in 2013/14



Note: Interventions received in recovery houses were not shown due to small numbers: 237 service users received psychosocial interventions while 61 service users received prescribing interventions.

Adapted from Public Health England (2014b)

The median age of those who reported alcohol and drugs as their primary problematic substances were 43 and 36 years, respectively. A total of 64% of those with alcohol as their primary problematic substance were males while almost three-quarters (74%) of those in treatment for drug dependence were also males. Over 80% of service users in treatment for alcohol and drug dependence were white British. A total of 14% of people in treatment for alcohol reported housing problems. Almost one quarter of those in treatment for drugs had housing problems. Among those in treatment for alcohol, over 40% were self-referrals. Similar proportions were reported for those in treatment for drugs. Almost half of those exiting treatment for drug dependence and 60% of those exiting treatment for alcohol in 2013/14 were no longer dependent.

## **1.4. The appropriateness concept in prescribing**

A central aim of this thesis is to explore the appropriateness of prescribing of psychiatric medications and opioids for people with SUDs. This section therefore explores the concept of appropriateness in wider healthcare and how it relates to prescribing with a particular focus on SUDs.

### **1.4.1. Definition of appropriateness in healthcare**

Appropriateness in healthcare is a complex concept with no generally accepted definition (Bowling, 2002). The *Oxford Dictionary* defines appropriateness as the quality of being suitable or proper in the circumstances (Oxford Dictionaries, 2016a).

Donald Berwick in the USA further refers to appropriateness as the provision and use of “what works” (Berwick, 1989). This definition however makes no attempt to define “what works” (Buetow et al., 1997). A definition of appropriate care that originated from Australia by Roy Harvey considers it as:

that strategy of action which maximises the potential health benefits valued by informed individuals or populations after considering the likely outcomes, their probabilities and their costs, for each of the separate components of the strategy, and that healthcare professionals are willing to provide (Harvey, 1991, p.79).

This definition considers appropriate care to involve making a decision from different available options about alternative use of resources. The Health Services Utilisation Study (HSUS) of the USA RAND Corporation, by comparison, includes judgments on the benefit and risk of care. It states that appropriate care means that “the expected health benefit exceeds the negative consequences by a sufficiently wide margin that the procedure is worth doing” (Kahn et al., 1988, p.418).

This definition was developed after much research and takes a medical perspective by weighing risk against benefit. However, it has been criticised because it ignores the individuality of patients and does not take their needs and preferences into consideration (Buetow et al., 1997). It also does not specify the nature and size of the expected risk and benefit (Hicks, 1994) or clarify when the benefit of the procedure becomes sufficiently large that it is therefore worth doing. Further, there is no consideration of the financial implications of care (Buetow et al., 1997). In the UK, appropriate care has been

defined alternatively as the selection “of the intervention that is most likely to produce the outcomes desired by the individual patient” (Working group for the Director of Research and Development of the NHS Management Executive, 1993, p.117).

This definition clearly includes the patient’s perspective but again, does not encompass the cost-effectiveness implications (Buetow et al., 1997). In general, definitions of appropriateness in healthcare tend to include one or more of the following: provision of care that is effective, evidence-based, cost-effective, and consistent with the ethical principles and preferences of the individual or society (World Health Organisation, 2000). Appropriateness in healthcare is a judgment across these different dimensions. These dimensions are also relevant when considering appropriate prescribing. For instance, Lexchin (1998) has described appropriate prescribing as ‘trying to maximise effectiveness, minimise risks and costs, and respecting patients’ choice. An earlier publication by Barber (1995) stated that prescribers should try to achieve the above aims highlighted by Lexchin (1998) in order to ensure good prescribing.

Whether a medication is seen as effective, safe (including risks) and sometimes cost-effective has been referred to as pharmacological appropriateness (Spinewine et al., 2007). Effectiveness, risks, costs and patient choice are discussed in sections 1.4.2 to 1.4.5, followed by a discussion of another definition of appropriate prescribing (outcome-focused prescribing) by Buetow et al. (1997) in section 1.4.6.

### **1.4.2. Effectiveness**

The definition of effect is usually based on the biomedical model of disease (Barber, 1995). It involves the use of objective measurements to assess effect: for example, blood pressure lowering below a certain point. The effectiveness of treatments including medications, is usually established in clinical trials, especially, randomised controlled trials (hereafter RCTs) which are considered as the gold standard in clinical research (Dale, 2005; Lomas and Haynes, 1988; Tucker and Roth, 2006). RCTs from multiple studies are synthesized in systematic reviews and meta-analyses in order to provide a quantitative estimate of net benefit aggregated over all the included studies (Crombie, 2009; Naylor, 1995). Where available, these reviews are usually the foundation for guidelines that establish the standards for best practices in healthcare (Tucker and Roth,

2006). Guidelines may also be based on expert opinions where there is no evidence from clinical trials or observational studies (Geleris and Boudoulas, 2011).

Most of the evidence from clinical trials concerning psychiatric medications and opioids for chronic pain do not include people with SUDs (Furlan et al., 2006; Ostacher, 2011; Samet and Walley, 2008). Intervention studies targeted at individuals with both SUDs and chronic pain or mental health problems are rare. People with SUDs are particularly difficult to recruit into studies due to issues of trust between people with SUDs and recruiters since substance use is a sensitive topic and may sometimes be illegal (Ompad et al., 2008; Oransky et al., 2009). Perceived risk of research participation including concerns about personal risk, discomfort and inconvenience have also been identified as barriers to research participation among this group (Barratt, Norman and Fry, 2007).

Where people with SUDs are included in research, it usually involves the use of restricted samples that do not mirror the heterogeneous and often complex group of people with SUDs who are likely to be encountered in real-life settings (Blanco et al., 2008; Tucker and Roth, 2006). In RCTs involving people with SUDs, it is common for investigators to exclude those with complicating comorbidities and circumstances (Hoertel et al., 2014; Humphreys et al., 2005). The complex problems of this client group include co-existing physical and mental health problems (Hoertel et al., 2014; McLellan, 2009), use of multiple medications (Oluyase et al., 2013), cognitive impairments, family disruptions, social as well as economic deprivation (Lloyd, 1998). Consequently, they present with problems that lie outside the remit of guidelines which are usually focused on 'normal' populations. Guidelines based on studies excluding people with SUDs or those focused on homogeneous populations with SUDs may therefore not be appropriate for this patient population as their findings cannot be directly extrapolated to the heterogeneous population of people with SUDs. Prescribing in such situations may need to be outside guideline recommendations or regulatory approval (off-label prescribing) (Ali and Ajmal, 2012).

The psychopathology of addiction also adds to the complexity of managing people with SUDs. Chronic exposure to substances usually leads to changes in the neurochemistry of reward pathways in the brain (The British Pain Society, 2007). This leads to the development of tolerance and eventually withdrawal symptoms if the substance is

stopped (Action on Addiction, 2013). Tolerance occurs when identical doses of a drug induce decreasing levels of effect or higher doses are needed to produce the same level of effect (The British Pain Society, 2007). Tolerance may have implications for some aspects of medication use such as dosing. For instance, tolerance to opioids makes the usual opioid doses inadequate (Gershwin and Hamilton, 1998), and higher doses that exceed that used in the general population will be needed. Similarly, tolerance to the effects of psychiatric medications such as benzodiazepines may lead to the need for higher doses to achieve the same effect (Willems et al., 2013). Furthermore, opioid tolerance in people with SUDs may be complicated by the need for further dose escalation during opioid therapy as a result of opioid-induced abnormal pain sensitivity (opioid-induced hyperalgesia) which manifests as increased pain (Ballantyne and Mao, 2003).

Overall, the definition of effectiveness applicable to populations with mental disorders and chronic pain is not directly applicable to people with SUDs who have these comorbidities because most of the evidence on which effectiveness is based does not include them. Where they include SUDs patients, they focus on a restricted sample that does not adequately represent this heterogeneous population who often have complex needs. This implies that effectiveness is limited when considering the appropriateness of prescribing for people with SUDs. Changes in the brain following chronic substance use further imply that prescribing for SUD patients may sometimes need to exceed that of the general population.

### **1.4.3. Minimising risk**

Risk has been defined as the probability of an untoward happening resulting from drug treatment (Barber, 1995). All medications including prescribed ones carry the potential for harm in addition to their benefits (Barber et al., 2005). Further, individual medications for specific diseases may be less beneficial or even harmful when used along with other medications (Tinetti, Bogardus and Agostini, 2004) or substances in people with SUDs. People with SUDs are highly susceptible to medication-related risks due to their use of multiple substances with medications. Medications such as benzodiazepines, antidepressants and opioids have been implicated in adverse events including overdose and mortality in patients with SUDs (Darke, Dufrou and Torok, 2011; Darke and Hall, 2003; Darke and Ross, 2000). The need to sometimes treat people

with SUDs outside the confines of guidelines also carries its own risks. Before prescribing off-label, the General Medical Council's Good Practice guidelines (General Medical Council, 2013) recommend that the prescriber should either be satisfied that sufficient evidence exists or they should have sufficient experience of using the medication to ensure safety and effectiveness. However, most off-label prescribing have not been evaluated for their safety and effectiveness (Chen et al., 2006). Prescribing off-label therefore places greater professional responsibility and liability on prescribers (General Medical Council, 2013).

Substance use may further contribute to the intensity of adverse effects experienced by people with SUDs. For example, SUD patients may have higher levels of side effects and toxicity with limited clinical benefits when compared to those without SUDs. Among schizophrenic patients treated with antipsychotics, higher levels of extrapyramidal symptoms have been reported among patients with comorbid SUDs than those without SUDs (Potvin et al., 2006). Treating persistent pain with higher opioid doses in people with SUDs may be counterproductive due to opioid-induced hyperalgesia as analgesia may never be achieved and the potential for opioid toxicity is greatly increased (Ballantyne and Mao, 2003).

Although prescribers try to achieve clinical benefit with minimal risk of harm, there is sometimes conflict between balancing effectiveness and risk (Barber, 1995). Besides the possibility of toxicity, the need for high doses of psychiatric medications or opioids may also expose the patient to the risk of dependence on those with dependence potential such as benzodiazepines and opioids. In addition, people with SUDs may exceed the recommended doses of these medications with the potential for overdosing (Action on Addiction, 2013; Edlund and Harris, 2006). A key feature of dependence is loss of ability to regulate and control behaviour (Griffiths, 2013). There will therefore be need to set boundaries, behavioural rules as well as monitoring and follow-up (Action on Addiction, 2013; Gershwin and Hamilton, 1998). Patients on repeat prescriptions of these medications will also need to be monitored regularly to ensure that their medications are still needed and to resolve any drug-therapy problem.

There is need for caution when prescribing medications with dependence potential such as benzodiazepines and opioids for abstinent people with a history of SUDs because they

may be prone to relapse. Prolonged abstinence from protracted substance use is usually accompanied by craving, high stress responsiveness and negative emotional state, all of which makes the patient prone to relapse when exposed to the same substance or another substance (including medication) with dependence potential (Action on Addiction, 2013). In people with a history of SUDs, any reinforcing drug including those from another class can lead to craving and relapse (Savage, 2002). The neuroplastic changes caused by substances are not fully reversible and may explain the risk of relapse in people who have a history of SUDs (Action on Addiction, 2013). The potential for medication-related risk may be higher in people with SUDs. Appropriate prescribing would therefore involve minimising risk as much as possible while ensuring optimal benefit from medications.

#### **1.4.4. Minimising costs**

Relevant costs include medication costs, costs associated with the need for medication monitoring, administration (for example by a nurse) and dispensing costs (Barber, 1995). In particular, prescription items cost the National Health Service (hereafter NHS) £13.3 billion in 2012 with 62.2% and 36.5% of this cost attributable to primary care and hospital use respectively (Health and Social Care Information Centre, 2013). The cost of medications is of particular relevance because it can be managed by prescribers through cost-effective prescribing. In the UK, there is a strong push for prescribing of generic medications wherever possible because they are cheaper than branded products, with no difference in their efficacy for most medications (Meadows, 2005). It is an NHS directive for prescribers to prescribe generic drugs unless there is clinical justification for branded prescribing (Williamson et al., 2010). The NHS is publicly funded and reducing medication cost allows for the availability of more funds for other areas of healthcare (Barber, 1995).

As described in section 1.4.2, people with SUDs present a myriad of health and life problems and they may require more medications than that used in the general population in order to maintain their stability and functioning. Consequently, a dimension of cost that needs to be considered among people with SUDs is the cost of relapse to substances for them and the society if there are not prescribed medications that meet their needs. This sort of prescribing may well include prescribing that is outside guideline recommendations. Although prescribing outwith guidelines carries its own risk

(Sugarman et al., 2013), dosage or duration that exceeds guideline recommendations may be clinically justifiable if it promotes the patient's stability and prevents relapse to a substance-using lifestyle. For instance, illicit drug use is associated with great societal cost. This includes cost to the individual in terms of premature death and drug-related illnesses (BMA Board of Science, 2013). Other societal costs include the costs of drug-related crime or violence as well as damage to marital/family relationships (BMA Board of Science, 2013). The economic and social costs of drug use including heroin, crack, cocaine, ecstasy, methadone, LSD and psilocybin (magic mushrooms), in 2003-2004 in England and Wales were estimated by a Home Office report to be £15.4 billion (Singleton, Murray and Tinsley, 2006).

Appropriate prescribing in this population therefore involves cost-effective prescribing among equally potent alternatives as well as consideration of the consequences that may result from not prescribing medications or prescribing inadequate medications. It could be argued that it is cheaper to prescribe more medications (than that used in the general population) if this will contribute to the service user's stability and optimal functioning and therefore prevent relapse.

#### **1.4.5. Patient choice**

Patient involvement in their own care has gained momentum over the past decades and now represents a core value in the medical profession (General Medical Council., 2009). Ethical and practical reasons have also been advanced on the need for the inclusion of patient's choice, particularly informed choice in prescribing (Barber, 1995). It is the patient who bears the immediate burden of illness and prescribing should assist the patient in alleviating this burden (Cribb and Barber, 1997). Furthermore, as discussed in section 1.4.3, prescribing often carries its own risk. It is therefore pertinent that clinical decisions integrate patient's preferences and the trade-off patients are willing to make in terms of the risk of various health outcomes (Tinetti, Bogardus and Agostini, 2004). This may include a choice of not having medications prescribed (Barber et al., 2005).

The generalisability of results from studies that exclude people with SUDs or that includes only homogeneous SUDs populations is unknown. The lack of a solid evidence base often leads to uncertainty about prescribing and the best approach for clinical management. Patients in particular have an important role to play in determining the best

course of action when such uncertainties exist (Evans et al., 2011). It could be argued people with SUDs should be more involved with prescribing decisions than the general population due to these uncertainties. They should therefore be provided adequate information (including treatment risks and benefits) that will allow them make an informed choice concerning their management (Towle et al., 2006). They should be able to express their expectations and preferences; there should be effective communication between the prescriber and patient as well as partnership for the best decision to be arrived at (Little et al., 2001). There is a need to tailor therapy to meet the needs of individual patients according to their unique attributes as patients may differ in their illness presentation, their understanding and acceptance of treatment, preferences as well as their responses (Dale, 2005; Sullivan and MacNaughton, 1996).

Patients have been found to influence prescribers in primary care (Britten and Ukoumunne, 1997; Cockburn and Pit, 1997), and secondary care settings (Lewis and Tully, 2011; Merrill et al., 2002). Previous studies have described patient pressure or request for medications as one of the reasons for prescribing. A study carried out in general practice settings in England reported that doctors described being very pressured by patients to prescribe in 3% of consultations (Britten et al., 2003). Cockburn and Pit (1997) explored patients' expectations and GP's perception of patients' expectations on prescribing in general practice settings in Australia and found that patients who expect medications were three times more likely to receive them and when general practitioners (hereafter GPs) thought that the patient expected medications, such patients were ten times more likely to receive them.

The tendency for doctors to prescribe due to patient pressure has been described as a means of avoiding spending time with patients (Harris, Heywood and Clayden, 1990). Prescribing could be used as a means of terminating difficult consultations (Britten, 1995). This may be more common among patient groups such as those with SUDs. There is evidence that consultations with SUD patients may be difficult because they may withhold information (Action on Addiction, 2013) or may be manipulative (Conway, 2000; McGillion et al., 2000; McKeown, Matheson and Bond, 2003). This may lead to some of these patients receiving inappropriate medications or those with little or no pharmacological benefits but with the potential for side effects (Ashworth, Clement and Wright, 2002; Lewis and Tully, 2011). Some prescriptions are thought to

be unnecessary by those who prescribed them (Britten et al., 2003; Macfarlane et al., 1997). Patient involvement may therefore present a problem when considering prescribing appropriateness (Schwartz, Soumerai and Avorn, 1989; Young and Ward, 2001). Complying with a patient's choice could be problematic and unethical as they may request medications that are not clinically justifiable (Barber, 1995). This may take the form of request for a drug of abuse or request for a medication for its euphoric effects. People with SUDs may be more likely to demand medications they do not need because of their impaired control over drug use (Action on Addiction, 2013). This could lead to conflicts between the prescriber's assessment of the patient's needs and the patient's preferences and there is no simple means of resolving the question of how far the goals of therapy should be determined by patient's wants rather than professionally-assessed need (Cribb and Barber, 1997).

Furthermore, during periods of active dependence, clinicians may lose access to one of the most fundamental tools in medicine: the patient's self-report (Bailey, Hurley and Gold, 2010). Patients with SUDs may not be open about the substances and medications they use. Some have been described as difficult, aggressive, manipulative and rude (Conway, 2000; McGillion et al., 2000; McKeown, Matheson and Bond, 2003) and consequently challenging to treat. The weight therefore accorded to patient's choice would need to be carefully considered to minimise medication-related risk. In addiction medicine, these issues are sometimes faced by clinicians and have led to the introduction of 'safeguards' such as limit setting, regular urine testing, supervision of drug administration and regular review of health and functioning (Action on Addiction, 2013).

People with SUDs can also experience stigma and discrimination in healthcare settings which can hinder care-seeking and also result in poor quality of care by healthcare professionals (Ahern, Stuber and Galea, 2007; Link et al., 1997). For example, a study where doctors and problem drug users who had been admitted to a hospital in the USA were interviewed found that doctors described concerns about being deceived by patients with opioid use disorders (hereafter OUDs) particularly where opiate pain relief was needed or requested (Merrill et al., 2002). The patients in this study also expressed concerns about receiving poor medical care as they described being intentionally mistreated due to their addiction. The doctors further expressed fear of being

manipulated into inappropriately prescribing opiates. These concerns by doctors may ultimately result in denying patients needed medications. Henderson et al. (2008) in a study that examined care delivery to substance users in a hospital emergency department in USA also expressed concerns around drug-seeking behaviour by substance users. This study concluded that care had a different tone or quality when patients had alcohol or drug problems and clinical decisions were sometimes influenced by providers' adverse social judgments.

This thesis provides a means to further explore the complexities around the quality of medical care, in particular, medications provided to this underserved and often stigmatised population in a SAS in the UK. This thesis goes a step further than previous studies by considering psychiatric medications as well as opioids while also including the patient and prescriber perspectives on prescribing. The patient's perspective explored their views on the appropriateness of prescribing of psychiatric medications and opioids. The prescriber perspective involved assessment of the appropriateness of psychiatric medications and opioids using questionnaires and also exploring how they responded to inappropriate prescribing in a SAS.

#### **1.4.6. Outcome-focused prescribing**

Another definition by Buetow et al. (1997, p.261) considers appropriate prescribing to be "the outcome of a process of decision-making that maximizes net individual health gains within society's available resources".

This definition is focused on the outcome of prescribing. It is particularly important because prescribing for people with co-existing mental disorders or chronic pain and SUDs may need to be outside guideline recommendations because of their often complex presentation and circumstances. As described in section 1.4.2, people with SUDs are often excluded from the evidence on which guidelines are based and they present with issues that are not addressed in guidelines. There is generally lack of a solid evidence base for the management of individuals with these comorbidities. The outcomes of these patients therefore play a pivotal role in assessing the appropriateness of prescribing.

Buetow et al. (1997) have argued that it is possible for prescribing to follow the right or 'rational' decision-making process that involves considering effectiveness, risk and cost and still result in poor outcomes. This may happen when correct reasoning is not applied to the patient's individual circumstance. The definition by Buetow et al. (1997) suggests that appropriate prescribing takes into consideration the needs of individual patients within population-centred constraints. Poor outcomes may result if patients' preferences are not elicited or if the patient is treated as a condition rather than a person (Barber et al., 2005). Buetow's definition therefore extends beyond mere pharmacological appropriateness to include the outcome of the prescribing process. If the outcome of prescribing is good for an individual, then this definition suggests that is appropriate prescribing.

Furthermore, it is pertinent to state that the targeted outcome of prescribing may be non-medical. Reduced social functioning of people who are dependent on substances may lead to harm for both the user and people around them (Strategy Unit Drugs Report, 2003). Substance use reduces capacity for work, may lead to breakdown of family relationships, violence and crime (Choi and Pope, 1994; Miller, Maguin and Downs, 1997; Sinha and Easton, 1999; Strategy Unit Drugs Report, 2003). The need for crime reduction has been identified as one of the reasons for substitute prescribing among people who are dependent on opiates (Coid et al., 2000). For instance, the increase in methadone prescribing in the UK was not only aimed at reducing opiate use but also crime (Coid et al., 2000).

Generally, a strong association between SUDs and crime has been reported in the literature (Hammersley, Forsyth and Lavelle, 1990; Reuter and Stevens, 2008; Sinha and Easton, 1999). There is however continued debate concerning the causal pathway between substance use and crime with suggestions that the use of substances causes crime because users may need to commit crime in order to finance their drug habits while others have argued that crime often precedes substance use (Coid et al., 2000). The former suggestion implies that a supply of substances on prescription such as opioid substitute prescribing may well reduce the need to commit crime in order to finance drug use (Coid et al., 2000).

Patients have reported that psychiatric medications such as antidepressants have assisted them in returning to normal functioning including fulfilling their social roles and regaining control (Malpass et al., 2009). Benzodiazepines have also been reported to assist patients in dealing with daily stress (Cook et al., 2007) and patients have often described their reliance on them (Iliffe et al., 2004; Cook et al., 2007). These findings suggest that prescribing of psychiatric medications have profound effects on patients as they assist them in living normal lives, with the potential for benefits for those around the patient. It could be argued that benefits accruing from these medications contribute to maintaining equilibrium in the lives of these patients, many of whom have complex life problems, while also assisting in preventing relapse to a substance-using lifestyle and its associated consequences such as crime described above.

There is the need to consider the impact of prescribing on those around the patient since prescribing may lead to benefit or harm for others (Cribb and Barber, 1997). For instance, concerns have been raised that the prescription of opioids for chronic non-cancer pain may lead to an increase in their non-medical use in the community (Collett, 2001). A decision to prescribe should therefore include consideration of the impact of prescribing within society as well.

In this thesis, the term appropriate prescribing encompasses both the process of decision-making as well as the outcome of this process.

#### **1.4.7. Measures for assessing prescribing appropriateness**

In this thesis, identification of the measures used in assessing prescribing appropriateness involved a systematic approach. The review published by Spinewine et al. (2007) on different instruments that are available to measure prescribing appropriateness in the elderly was the starting point. This was followed by a systematic search of Medline database for other measures.

Two of the most important set of values in judging appropriateness are what the patient wants or prefers and the scientific rationalisation (pharmacological appropriateness) (Cribb and Barber, 1997). Most of the published research on this topic have focused on assessment of pharmacological appropriateness (Barber et al., 2005). However, Barber et al. (2005) found that judgments on appropriateness that included patient's preferences

and contextual factors sometimes led to better conclusions when compared with those based solely on pharmacological criteria. Two studies were found that assessed patients' wants or preferences and these were incorporated into decision-making when judging prescribing appropriateness (Barber et al., 2005; Britten et al., 2003). In the study by Barber et al. (2005) patient perspectives were obtained through in-depth interviews while Britten et al. (2003) used questionnaire surveys. By contrast, pharmacological appropriateness has been assessed using different measures. This section will discuss the measures that have been used in assessing pharmacological appropriateness due to its predominance in the literature. They include explicit (criterion-based) or implicit (judgment-based) measures.

#### **1.4.7.1. Explicit or criterion-based measures**

Explicit measures are usually developed from expert opinions, published reviews and consensus methods (Spinewine et al., 2007). Generally, explicit measures focus on narrow categories of medications or are disease-oriented and require little or no clinical judgment to be applied (Buetow et al., 1997). They do not tend to take into consideration factors such as comorbidities and patients' choices (Boyd et al., 2005; Tinetti, Bogardus and Agostini, 2004). Moreover, in prescribing research, evidence of validity and reliability of consensus methods are usually lacking (Buetow et al., 1997). Despite these shortcomings, explicit measures are time-saving when compared with other methods for assessing prescribing appropriateness as they can be applied to large databases. Examples of explicit measures are the Beers criteria (Beers et al., 1991) and its derivatives<sup>4</sup> (Dimitrow et al., 2011), Assessing Care of the Vulnerable Elder (hereafter ACOVE) criteria (Wenger and Shekelle, 2001), START (Screening Tool to Alert to Right Treatment) criteria (Barry et al., 2007) and STOPP (Screening Tool of Older Persons' Prescriptions) criteria (Gallagher et al., 2008).

Beers criteria consist of a list of drugs to avoid as well as doses that should not be exceeded in the elderly whereas ACOVE criteria include indicators for appropriate treatment, prevention, monitoring, education and documentation for the elderly (Wenger and Shekelle, 2001; Beers et al., 1991). START consist of criteria for the detection of prescribing omissions in the elderly whereas STOPP was developed to identify potentially inappropriate drugs in the elderly population. Other examples of explicit

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<sup>4</sup> Derivatives of the Beers criteria include the Norwegian General Practice Criteria (NORGEP) criteria, Improving Prescribing in the Elderly tool, McLeod's criteria, Zhan's criteria and the French criteria.

measures include manufacturers' recommendations, defined daily dose (hereafter DDD)<sup>5</sup> such as diazepam milligram equivalents for benzodiazepines and treatment guidelines. Explicit measures have been used to detect overprescribing (prescribing more medications than clinically needed) and underprescribing (defined as failure to prescribe needed medications or medication omission) (Briesacher et al., 2005; Osborne et al., 2002; Strothers et al., 2005; Unutzer et al., 2004). They are however limited because they do not consider patients' perspective of prescribing (Hanlon and Schmader, 2013).

#### **1.4.7.2. Implicit or judgment-based measures**

Implicit measures are judgment-based measures which usually utilise information collected from patients and published evidence to arrive at a clinical decision (Spinewine et al., 2007). Although implicit measures are sensitive and usually consider patients' preferences, they depend on clinicians' knowledge, are time-consuming and have low reliability (ibid). They are usually neither reproducible nor generalisable and can be highly subjective (Spinewine et al., 2007).

These shortcomings can be addressed by developing a standardised data collection tool that will improve reliability and validity such as the Medication Appropriateness Index (hereafter MAI) (Hanlon et al., 1992; Samsa et al., 1994), Prescribing Appropriateness Index (hereafter PAI) (Cantrill, Sibbald and Buetow, 1998) and the Assessment of Underutilisation of Medication index (hereafter AOU) (Jeffery et al., 1999). The PAI was developed to assess long-term prescribing in general practice in the UK and is restricted to the British National Formulary (hereafter BNF) while the MAI was developed to address multiple elements of drug prescribing and is applicable to various medications and conditions. The AOU is used to assess underprescribing of medications (Spinewine et al., 2007). It requires that a health professional matches a list of medical disorders to prescribed medications in order to establish if there is an omission of a needed medication. The MAI will be further discussed below because it was adapted for use in this thesis.

#### The Medication Appropriateness Index (MAI)

The MAI has been used in diverse types of studies to assess prescribing appropriateness by different healthcare professionals (Crotty et al., 2004; Hanlon et al., 1992; Schmader et al., 1994; Schmader et al., 2004). It was developed by American healthcare

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<sup>5</sup> The DDD is the *assumed average maintenance dose per day for a drug used for its main indication in adults*.

professionals and measures 10 dimensions of prescribing, namely: indication, effectiveness, dosage, correct directions, drug-drug interactions, drug-disease interactions, practical directions, expense, duplication and duration (Hanlon et al., 1992). The dimensions on the index are based on a review of the literature and the clinical experience of the developers. Despite the fact that clinical judgment is needed in rating some MAI dimensions, it has operational definitions and instructions that assist in standardising the process (Hanlon et al., 1992; Spinewine et al., 2007). The different MAI dimensions are rated as appropriate, marginally appropriate and inappropriate for each medication that is being used by the patient. If additional information is needed to answer a question on the MAI, a rating of 'don't know' may be given. The MAI has a section for comments after each question.

Weights ranging from 0 to 3 are assigned to each dimension which can be summated to give a total score ranging from 0 to 18 (Samsa et al., 1994). Indication and effectiveness have the highest weight of 3 as they are considered to be the most important dimensions. Dosage, correct directions, drug-drug- interactions and drug-disease interactions are given equal weights of 2 whilst practical directions, expense, duplication and duration are each given weights of 1. A score of 0 indicates there are no inappropriate dimensions while a score of 18 indicates that all dimensions for the medication are inappropriate. If the patient is taking multiple medications, the score for each medication could be summed up to obtain a score for the patient. Thus, either the patient or the medication could be used as the unit of analysis.

In this thesis, the MAI was adapted for use by prescribers in the assessment of the appropriateness of psychiatric medications and opioids because it allows for clinical judgment and also focuses on the patient (O'Connor, Gallagher and O'Mahony, 2012). It allows the patient's perspective to be considered and is applicable to any medication or clinical condition in any setting (O'Connor, Gallagher and O'Mahony, 2012). An alternative measure such as the PAI is restricted to medications in the BNF and also has a focus on hypertension. Although both the MAI and PAI have a standardised format, the MAI has the advantage of having instructions for its use, specific definitions of each dimension, instructions on how to answer each of the 10 questions and examples of appropriate, marginally appropriate and inappropriate ratings (Hanlon and Schmader,

2013). The MAI is also the commonly used implicit measure for assessing prescribing appropriateness (O'Connor, Gallagher and O'Mahony, 2012).

For the MAI to be used, the minimal requirements are the patient's current medical history problem list and the medication list. The validity and reliability of the MAI have been widely tested and good inter-rater and intra-rater reliability has been found. Hanlon et al. (1992) evaluated the reliability of MAI ratings between a clinical pharmacist and a geriatrician using ambulatory elderly male patients. Independent assessments of the appropriateness of chronic medications taken by these patients were made by the clinical pharmacist and geriatrician and agreement was assessed using kappa statistic, a statistical measure that indicates the proportion of agreement beyond that expected by chance (Cohen, 1960; Cohen, 1968). The kappa statistic was found to be 0.83 for inter-rater agreement and 0.92 for intra-rater agreement. Inter-rater reliability assesses the agreement between ratings made by two or more clinicians whereas intra-rater reliability measures agreement between ratings made by the same clinician on at least two occasions (Sim and Wright, 2005). A kappa statistic of 0 means that agreement is not better than that expected by chance.

Landis and Koch (1977) have suggested that kappa coefficients of 0.41 to 0.60 represent moderate strength of agreement, 0.61 to 0.80 represent substantial agreement whereas  $\geq 0.81$  represent very good agreement (Landis and Koch, 1977). The values of kappa ranges from -1 to 1, with -1 indicating agreement is worse than that expected by chance and 1 indicating perfect agreement (Sim and Wright, 2005). Additionally, inter-rater agreement was also assessed between two clinical pharmacists and the kappa statistic found to be 0.59.

Content validity, in particular item suitability and weighting have also been assessed in a previous study which found that healthcare professionals (geriatricians, internists, clinical pharmacists) considered MAI dimensions to be 'definitely' important or 'moderately' important measures of prescribing appropriateness (Samsa et al., 1994). Moreover, the healthcare professionals surveyed were able to distinguish the relative importance of the different MAI dimensions with the development of a weighting scheme which can be combined to get a single summated score as described above. In the study by Samsa et al. (1994), the summated MAI also demonstrated descriptive

validity as the heterogeneity in prescribing appropriateness among patients was reflected in the distribution of the MAI scores. For instance, one quarter (25.5%) of medications had a score of 0 which implies that there were no ‘inappropriate’ MAI dimensions; 38.5% had scores of 1 to 2 and 36% had scores of  $\geq 3$ . The validity and reliability of the MAI has however not been assessed among people with SUDs. Despite the utility of the MAI, it does not address the issue of adherence, adverse drug reactions and drug allergy (Spinewine et al., 2006). It has the potential to be time-consuming and does not assess underprescribing (Bergkvist et al., 2009).

#### **1.4.8. Summary: Appropriateness concept in prescribing**

Appropriate prescribing is a complex concept involving a judgment across a number of factors such as effectiveness, risk, cost, patients’ choices, patients’ outcomes as well as the societal impact of prescribing. It often entails making a complex trade-off between conflicting aims (Barber, 1995). Effectiveness will need to be balanced against risk. Patient preferences will also need to be weighed against effectiveness, safety and the general good of the society. The applicability of effectiveness is however somewhat limited when considering people with comorbid mental disorders or chronic pain and SUDs because SUDs is usually an exclusionary criterion in studies assessing medications for these comorbidities. Furthermore, studies that include SUD patients do not include those with complex comorbidities and circumstances. In practice, the consultation between a patient with a SUD and her prescriber is an active process in which the prescriber deals with the individual and her complex needs (Sullivan and MacNaughton, 1996). Decision-making on the appropriateness of prescribing for a SUD patient will inevitably involve consideration of the evidence-base, clinical judgment, the patient’s perspective and outcomes, unique circumstances of the patient (Straus et al., 2011; Sullivan and MacNaughton, 1996) and the societal impact of prescribing.

Most of the measures that have been used in assessing prescribing appropriateness have focused solely on pharmacological appropriateness (effectiveness, safety and cost) using explicit or implicit measures while neglecting patients’ wants or preferences. However, the few studies that have included patients’ preferences have come to a more robust conclusion when compared with those based solely on pharmacological criteria. The consideration of patients’ views in this thesis provides a way to explore appropriateness from their perspective. Prescribers assessed pharmacological appropriateness using an

adapted version of the MAI and a questionnaire designed in this research for medication omissions (medication omissions questionnaires). Interviews were carried out with them to explore how they responded to inappropriate prescribing. These different perspectives provided a more holistic picture on this complex subject.

## **1.5. Comorbidities in people with SUDs**

More than half of people with SUDs have been found to have co-existing physical and/or mental health problems (McLellan, 2009), making their healthcare needs complex. The presence of these comorbidities and the medications used in treating them may lead to poor outcomes such as serious drug interactions and overdose (Darke and Ross, 2000; Zamparutti et al., 2011). Some of these health conditions may be consequences of SUDs or may be exacerbated by SUDs (Crome et al., 2009). A causal relationship has been found between alcohol and over sixty diseases with the presence of most comorbidities having a relationship with the volume and pattern of alcohol consumption (Rehm et al., 2003). Drug use disorders (hereafter DUDs) have also been associated with adverse health outcomes. For instance, intravenous drug users (hereafter IDUs) are vulnerable to thrombosis, abscesses and blood borne diseases particularly HIV, hepatitis B and C (Mehta et al., 2011; National Institute for Health and Clinical Excellence, 2007; Stein, 1990).

Many people with SUDs also have poor mental health and vice versa (McManus et al., 2009). Comorbidity in these patients have been associated with reduced life expectancy (Chang et al., 2011; Cosci and Fava, 2011), lower quality of life (Donovan et al., 2005; Smith and Larson, 2003), medication non-adherence (Drake and Mueser, 2000; Owen et al., 1996), more physical health problems (Batki et al., 2009; Phillips and Labrow, 2000) and increased length of hospitalisation (Lyketsos et al., 2002). In addition, the cost of caring for comorbid patients is much higher than for those with single conditions due to the need for greater service utilisation including emergency service (Hoff and Rosenheck, 1998; Hoff and Rosenheck, 1999; Teesson, Slade and Mills, 2009).

Another prevalent comorbid condition with SUDs is chronic pain. Chronic pain is usually defined as pain of more than three months duration (Martell et al., 2007; Rosenblum et al., 2003). Opioids are one of the groups of medications commonly used in chronic pain management (Fishbain et al., 2008). However, some patients being

treated with opioids may develop OUDs including dependence (Fishbain et al., 2008; Portenoy, 1996). A strong predictor of OUDs is a history of SUDs. The next section further examines comorbid chronic pain and mental health conditions in people with SUDs.

### **1.5.1. Co-existing chronic pain and SUDs**

Chronic pain (pain of more than three months duration) has been reported to be a prevalent comorbidity in people with SUDs and vice versa (Caldeiro et al., 2008; Jamison et al., 2000; Kouyanou, Pither and Wessely, 1997; Martell et al., 2007; Peles et al., 2005; Rosenblum et al., 2003). Studies relevant to this thesis have focused on the prevalence of chronic pain in people with SUDs who are in treatment. Three studies (Jamison et al., 2000; Peles et al., 2005; Rosenblum et al., 2003) were found that assessed the prevalence of chronic pain among opioid dependent patients in methadone maintenance treatment programmes (hereafter MMTPs). These studies all reported higher prevalence of chronic pain when compared to other studies that assessed chronic pain in people using other substances besides opioids (Caldeiro et al., 2008) or a mixed population that included both those using opioids and other substances (Larson et al., 2007).

Rosenblum et al. (2003) also reported on the prevalence of chronic pain among opioid dependent patients in inpatient residential treatment programmes (hereafter RTPs) for alcohol or cocaine dependence. Caldeiro et al. (2008) assessed chronic pain among SUD patients in an outpatient addiction centre who are dependent on other substances besides opioids while Larson et al. (2007) assessed chronic pain among SUD patients in a residential detoxification programme. Patients were included in the study by Larson et al. (2007) if heroin, cocaine or alcohol were their first or second drug of choice. These studies have all been non-UK studies and have reported the prevalence of chronic pain to be between 16% and 61%. No UK study was found that has reported on the prevalence of chronic pain among people with SUDs in treatment. Table 1.1 provides a description of the percentage of people with SUDs in treatment who have chronic pain.

Table 1.1: Percentage of chronic pain among people with SUDs in treatment

<b>Author and country</b>	<b>Population studied</b>	<b>How pain was measured</b>	<b>% with chronic pain</b>
Jamison et al. 2000 (USA)	Opioid dependent patients in MMTPs	Questionnaire developed for study	61.3% with pain of $\geq$ 4 months
Rosenblum et al. 2003 (USA)	Opioid dependent patients in MMTPs and alcohol or cocaine dependent patients in RTPs	Numeric scale adapted from the Brief Pain Inventory	61% and 48% with pain of $\geq$ 6 months in MMTPs and inpatient RTPs respectively
Peles et al. 2005 (Israel)	Opioid dependent patients in MMTPs	Ordinal scale	55.3% with pain of $\geq$ 6 months
Larson et al. 2007 (USA)	Patients receiving residential substance abuse detoxification from heroin, alcohol or cocaine	Pain section of the 36-item Short-Form Health Survey (SF-36)	16% with pain over a two-year period
Caldeiro et al. 2008 (USA)	Veterans attending outpatient addiction centres who are dependent on other drugs besides opioids	Pain section of the 36-item Short-Form Health Survey (SF-36)	33.2% with pain over a year period

Where MMTPs = methadone maintenance treatment programmes and RTPs = residential treatment programmes

In USA, Rosenblum et al. (2003) found that 61% of opioid dependent patients in MMTP and 48% of people in inpatient RTPs for alcohol or cocaine dependence had pain of at least six months duration. The prevalence of chronic severe pain defined as pain of more than six months duration and of moderate to severe intensity (intensity assessed on a numeric scale adapted from the Brief Pain Inventory) or that interfered with daily activities was found to be 37% in MMTPs and 24% in inpatient RTPs. A similar prevalence for chronic pain (61.3%) among opioid dependent patients in MMTPs was reported by another USA study (Jamison et al., 2000) which assessed pain of at least four months duration. Another study carried out by Peles et al. (2005) found the prevalence of chronic pain of any intensity defined as current pain lasting at least six months to be 55.3% among patients in MMTPs in Israel. The prevalence of chronic moderate to very severe pain assessed on an ordinal scale between 1 (mild) and 4 (very severe) was found to be 48.2%. Most patients reported having pain for over ten years

and that pain significantly interfered with their level of activity. Caldeiro et al. (2008) in another USA study found the prevalence of chronic pain of over one year duration among veterans attending outpatient addiction centres who were dependent on other substances besides opioids to be 33.2%. Chronic pain was considered to be pain of moderate to very severe intensity at all times. Larson et al. (2007) found the prevalence of chronic pain defined as moderate or a higher level of pain over a two-year period to be 16% among patients in a residential detoxification programme for heroin, alcohol or cocaine (Larson et al., 2007).

Besides the studies by Rosenblum et al. (2003) and Jamison et al. (2000) which reported similar prevalence for chronic pain, the prevalence reported by other studies differed. The difference in the prevalence rates reported may have resulted from the diverse definitions of chronic pain used and the populations assessed. Some studies assessed pain of at least six months duration while others assessed pain of one or two-year duration in different populations. Furthermore, most used different scales for assessing chronic pain.

Increased pain sensitivity (opioid-induced hyperalgesia) due to long-term use of opioids may be a possible explanation for the higher prevalence of pain among opioid dependent patients in MMTPs (Alford, Compton and Samet, 2006; Scimeca et al., 2000). Available evidence suggests long-term opioid use may intensify rather than ameliorate chronic pain (Carroll, Angst and Clark, 2004; Rapp, Ready and Nessly, 1995), leaving clinicians with very limited options for its treatment.

Possible explanations for the frequent co-occurrence between chronic pain and SUDs include a shared common pathway between chronic pain and SUDs since both disorders have many shared neurophysiological patterns such as abnormal neural processing in the central nervous system (Centre for Substance Abuse Treatment, 2012), the use of substances to self-medicate or decrease the physical experience of pain (Rosenblum et al., 2003), or the development of pain as a result of injuries secondary to the risky lifestyle associated with prolonged SUDs (Compton, Darakjian and Miotto, 1998; Karasz et al., 2004). Furthermore, chronic pain (Bair et al., 2003; Manchikanti et al., 2007) and SUDs (Boden and Fergusson, 2011; Strathdee et al., 2002) have been associated with mental disorders such as depression and anxiety. The comorbidity

between mental disorders and SUDs is further considered in the next section. The risk of mental disorders such as depression have been found to increase with worsening pain (Bair et al., 2003). Unrecognised and untreated mental disorders may exacerbate pain intensity and disability (Manchikanti et al., 2007).

### **1.5.2. Co-existing mental disorders and SUDs**

Mental disorders commonly co-exist with SUDs (Boden and Fergusson, 2011; Grant et al., 2004; Mortlock et al., 2011; Regier et al., 1990; Weaver et al., 2003). This co-existence is often referred to as dual diagnosis (Carter, Fisher and Isaac, 2013; Crome et al., 2009; Gafoor and Rassool, 1998). Other terms that have been used interchangeably with dual diagnosis include dual disorders and SUD comorbidity (Drake and Mueser, 2000; Gilder et al., 2007). The term dual diagnosis is however preferred in the UK (Department of Health, 2002; Department of Health, 2006a). The definition of dual diagnosis remains controversial (Carter et al., 2013), as it may also refer to a heterogeneous group of individuals with more than just two illnesses (Cosci and Fava, 2011; Drake et al., 2001).

Different models or hypotheses have been proposed to explain the frequent co-occurrence between mental disorders and SUDs. These models have proposed a shared, causal or bidirectional pathway (Merikangas et al., 1998; Mueser, Drake and Wallach, 1998). The common factor model posits that one or more factors independently increase the risk of both mental disorders and SUDs (Bierut et al., 1998; Boden and Fergusson, 2011; Kendler, Gruenberg and Kinney, 1994; McLaughlin et al., 2012; Mueser et al., 1998). The bidirectional model proposes that interactional effects between mental disorders and SUDs are responsible for increased co-occurrence of these disorders (Mueser et al., 1998). The secondary psychiatric disorder model proposes that SUDs lead to or trigger mental disorders that otherwise would not have developed (Mueser et al., 1998; Torrens, Martin-Santos and Samet, 2006) while the secondary substance use disorder posits that mental disorders lead to SUDs (Mueser et al., 1998).

In the UK, the prevalence of co-existing mental disorders and SUDs was found to be almost 30% across a range of treatment services (Strathdee et al., 2002). The highest rates were in substance misuse services (83%), followed by a forensic service with 56%. A rate of 43% was reported in an inpatient mental health service, with 20% in a

community mental health teams. The lowest rate (8%) was reported in a primary care sample. Generally, the prevalence reported in clinical populations is higher than that reported in general population samples (Grant et al., 2004; Kenneson, Funderburk and Maisto, 2013; Merikangas et al., 1998; Regier et al., 1990). This may be because people with multiple disorders are more likely to seek treatment resulting in the detection of higher rates of comorbid conditions in clinical populations (Bennett, Peer and Gjonbalaj-Marovic, 2011; Grant, 1997). This greater treatment-seeking behaviour among people with comorbidity is usually referred to as Berkson's bias (Berkson, 1946).

Due to the wide variety of different combinations of mental disorders and SUDs that can co-occur (Compton et al., 2007; Crawford, Crome and Clancy, 2003; Lenzenweger et al., 2007), as well as the focus of this thesis on prescribing in a SAS, this section will concentrate only on the overlap between SUDs and the more prevalent mental disorders namely mood, anxiety and psychotic disorders in clinical populations. There have been many studies carried out on these comorbidities in the UK and they will be the focus of the subsequent sections.

#### **1.5.2.1. Mood and anxiety disorders**

Studies carried out in clinical populations in the UK have reported a high prevalence of mood and anxiety disorders (Delgadillo et al., 2012; Marsden et al., 2000; Strathdee et al., 2002; Virgo et al., 2001; Walsh and Copello, 2014; Weaver et al., 2003) among people with SUDs. The prevalence of depression among this population have been reported to be between 22.3% and 66% while that of anxiety disorders have been between 29% and 55%. Comorbid mood and/or anxiety disorders have been reported to be between 68% and 81% among this population. Table 1.2 below provides a description of the prevalence of comorbid mood and anxiety disorders among UK clinical populations with SUDs.

Table 1.2: Prevalence of comorbid mood and anxiety disorders among UK clinical populations with SUDs

<b>Author</b>	<b>Population studied</b>	<b>How mood and anxiety disorders were assessed</b>	<b>% with comorbidity</b>
Marsden et al. 2000	Dependent drug users in treatment <sup>a</sup>	Mental disorders were assessed using the Brief Symptom Inventory	22.3% had depression and 24.9% had anxiety disorders
Virgo et al. 2001	Patients attending addiction services comprising community drug and alcohol teams, a rehabilitation ward and a day treatment unit	Mental disorders assessed using the Department of Health's Building Bridges report criteria <sup>b</sup>	66% had depression, 29% had anxiety and 5% had bipolar disorder
Strathdee et al. 2002	Clients in different services comprising substance misuse services, forensic service, inpatient mental health service, community mental health teams and primary care.	45-60 mins dual diagnosis assessment	55% had generalised anxiety disorder, 43% had agoraphobia and 41% had depression
Weaver et al. 2003 <sup>c</sup>	Clients in substance misuse settings <sup>d</sup>	The Comprehensive Psychopathological Rating Scale and its subscales for rating depression and anxiety disorders	68% of drug service patients had a comorbid mood and/or anxiety disorder. 81% of alcohol service patients had a comorbid mood and/or anxiety disorder
Delgadillo et al. 2012 <sup>e</sup>	Patients accessing a community drug treatment service	Mental health diagnosis was established using the Revised Clinical Interview Schedule	70% of patients had current depressive and/or anxiety disorders
Walsh and Copello, 2014	Patients within statutory and non-statutory teams of a UK substance misuse treatment partnership	Diagnosis recorded by keyworker <sup>f</sup>	31.9% had major depression and 11.6% had bipolar disorder

<sup>a</sup>Includes those from inpatient units, rehabilitation units, methadone maintenance clinics and methadone reduction programs.

<sup>b</sup>This definition includes any axis I disorder as a severe mental illness depending on the patient's diagnosis and level of disability, vulnerability, risk and need for care.

<sup>c</sup>The mood disorders assessed were mild and severe depression while only severe anxiety was assessed.

<sup>d</sup>The drug and alcohol services assessed were statutory providers that offered structured appointment-based services within nurse-led clinics.

<sup>e</sup>In addition to depression, the other disorders considered in this study include generalised anxiety disorder, panic disorder, social phobia, non-specified mild neurotic disorder, agoraphobia, other specific phobias, obsessive compulsive disorder, mixed anxiety and depressive disorders.

<sup>f</sup>Diagnosis recorded for a patient was either that documented in the case note by a psychiatrist or that identified by a client's keyworker using a set of standard criteria.

The prevalence of comorbid mood and anxiety disorders among UK clinical populations varied. The differences in prevalence rates may have resulted from the diverse definitions of comorbidity used. For instance, while some studies included mild forms of mood and anxiety disorders, others did not. Furthermore, how comorbidity was assessed and the type of setting in which the study was carried out may also contribute to differences in reported prevalence rates.

High rates of mood and anxiety disorders have also been reported among patients in treatment for SUDs in other countries, such as USA (Kidorf et al., 2004) and India (Arora and Kaur, 2012). Besides Arora and Kaur (2012), the other studies did not attempt to distinguish between substance-induced and independent disorders. Making this distinction is important because intoxication and withdrawal symptoms of alcohol and other substances often resemble those of anxiety and depressive disorders (Grant et al., 2004; Raimo and Schuckit, 1998). These symptoms can sometimes be severe and usually resolve within two to four weeks of abstinence. While pharmacotherapy may be necessary for the management of an independent mood or anxiety disorder, it may not be needed for a substance-induced disorder (Schuckit, 2006). The study by Arora and Kaur (2012) found the prevalence of substance-induced depression and anxiety disorders to be 29% and 28%, respectively, among outpatients with OUDs in India. This study used the research version of the Structured Clinical Interview for DSM-IV Axis I Disorders in assessing diagnosis.

### **1.5.2.2. Psychotic disorders**

The prevalence of psychotic disorders reported among clinical populations with SUDs in the UK differs. This is mainly due to differences in how psychotic disorders are defined. Prevalence rates between 7% and 56% have been reported in the UK. Table 1.3 provides a description of the prevalence of comorbid psychotic disorders among UK clinical populations with SUDs.

Table 1.3: Prevalence of comorbid psychotic disorders among UK clinical populations with SUDs

Author	Population studied	How psychotic disorders were assessed	% with comorbidity
Virgo et al. 2001	Patients attending addiction services comprising community drug and alcohol teams, a rehabilitation ward and a day treatment unit	Mental disorders assessed using the Department of Health's Building Bridges report criteria <sup>a</sup>	13% had psychotic disorders (5% had schizophrenia, 5% had schizoaffective disorder and 3% had psychotic episodes).
Weaver et al. 2003 <sup>b</sup>	Clients in substance misuse settings <sup>c</sup>	Psychiatrists assessed patients with SUDs for psychotic disorders using the Operational Checklist for Psychiatric Disorders	7.4% of drug service patients had non-substance-induced psychotic disorders (hereafter NSIPD) and 14.5% of alcohol service patients had NSIPD.
Walsh and Copello, 2014 <sup>d</sup>	Patients within statutory and non-statutory teams of a UK substance misuse treatment partnership	Diagnosis recorded by keyworker <sup>e</sup>	56.6% had psychotic disorders

<sup>a</sup>This definition includes any axis I disorder as a severe mental illness depending on the patient's diagnosis and level of disability, vulnerability, risk and need for care.

<sup>b</sup>Psychotic disorders considered include schizophrenia and non-specific psychosis.

<sup>c</sup>The drug and alcohol services assessed were statutory providers that offered structured appointment-based services within nurse-led clinics.

<sup>d</sup>Psychotic disorders assessed were schizophrenia, psychosis, schizoaffective and delusional disorders.

<sup>e</sup>Diagnosis recorded for a patient was either that documented in the case notes by a psychiatrist or that identified by the client's keyworker using a set of standard criteria. None of the keyworkers were doctors. They were nurses (including community psychiatric nurses), social workers, drug workers and alcohol practitioners.

Weaver et al. (2003) found the prevalence of non-substance-induced psychotic disorders to be 7.4% among drug service patients and 14.5% among alcohol service patients. Virgo et al. (2001) reported a prevalence of 13% among patients attending addiction services while Walsh and Copello (2014) reported the prevalence of psychotic disorders to be 56.6% among patients within statutory and non-statutory teams of a UK substance misuse treatment partnership. The difference in prevalence rates reported might be due to how these disorders were defined and identified. Walsh and Copello (2014) who reported the highest prevalence classified patients as having psychotic disorders using either of two ways: if they have been previously diagnosed by a psychiatrist or for those

without formal diagnosis (one-third of patients), psychotic disorders were identified by the patient's keyworker using a set of standard criteria. None of the keyworkers were psychiatrists. Identification of psychotic disorders by keyworkers who are not psychiatrists may have led to the overestimation of its prevalence. Furthermore, this study included more categories of disorders under the broad group of psychotic disorders it considered.

A study carried out in Spain by Torrens et al. (2011) explored the prevalence of independent and substance-induced psychotic disorders among illicit drug users recruited from treatment and non-treatment settings. The treatment settings were an inpatient detoxification unit of a hospital and outpatient methadone maintenance programs. Nineteen (6.3%) of the 304 illicit drug users recruited from treatment settings had psychotic disorders, of which 10 (3.3%) were substance-induced. The psychotic disorders examined include schizophrenia, schizoaffective disorders and psychotic disorder not otherwise specified (NOS). The Spanish version of the Psychiatric Research Interview for Substance and Mental Disorders (PRISM) (Torrens et al., 2004) was used in assessing DSM-IV psychiatric diagnoses.

### **1.5.3. Summary: Comorbidities in people with SUDs**

The evidence from the literature indicates that mental disorders and chronic pain commonly co-exist with SUDs among treatment populations. Consequently, clinicians will often encounter service users with this comorbidity. In the SAS where the research presented in this thesis was carried out, the presence of comorbid chronic pain and mental disorders among substance users is likely to be the norm rather than the exception. Some mental disorders could be substance-induced and may not respond adequately to pharmacotherapy (Schuckit, 2006). It may therefore be appropriate for such patients not to be prescribed medications.

## **1.6. Pharmacotherapies for comorbidities**

While pharmacotherapy for mental disorders such as depression (National Institute for Clinical Excellence, 2009), anxiety disorders (National Institute for Health and Clinical Excellence, 2011b), bipolar disorder (National Institute for Health and Clinical Excellence, 2006) and pain (The British Pain Society, 2010) have been described and

their benefits demonstrated in the general population, the literature concerning management in people with SUDs have been less extensive. The only guideline published by the National Institute for Health and Clinical Excellence (hereafter NICE) that is specific to this population is that relating to the management of psychosis co-existing with SUDs (National Institute for Health and Clinical Excellence, 2011c). NICE has no published guidelines on the management of pain in people with SUDs.

Besides the NICE guideline on the management of psychosis co-existing with SUDs, other published guidelines on the management of mental disorders in people with SUDs include those published by the British Association for Psychopharmacology (hereafter BAP) (Lingford-Hughes et al., 2012). The British Pain Society has published a guideline on pain management in people with SUDs (The British Pain Society, 2007). There is also a publication on this issue commissioned by Action on Addiction (Action on Addiction, 2013). This section briefly highlights the medications recommended in these guidelines for the management of comorbid mental disorders and pain among people with SUDs.

### **1.6.1. Pharmacotherapies for co-existing mental disorders and SUDs**

There is generally a paucity of evidence to effectively guide the pharmacological management of co-existing mental disorders and SUDs (Edlund and Harris, 2006; Kranzler and Rosenthal, 2003; Ostacher, 2011). A systematic review on the pharmacological and psychological treatment of comorbid mental disorders and SUDs reported limited numbers of RCTs, and did not find treatments that were equally efficacious for both SUDs and mental disorders (Tiet and Mausbach, 2007). The review suggested that existing efficacious treatment for mental disorders and SUDs also tend to work in patients with this comorbidity. A more recent review by Kelly, Daley and Douaihy (2012) suggests that the most effective treatments for comorbid patients may be multi-faceted, involving combinations of different therapeutic approaches such as pharmacotherapy, psychotherapy and behavioural treatments.

Psychotherapeutic approaches that have been found to be most effective include a combination of motivational interviewing, cognitive behavioural therapy and 12-Step therapy (Kelly, Daley and Douaihy, 2012). This section will focus on pharmacotherapeutic approaches recommended in guidelines for the management of

comorbid mental disorders and SUDs in the UK during the period this research was carried out because they were the recommendations for best practice at the time of this research.

There are two types of guidelines addressing this comorbidity:

- Guidelines that were specifically written for this comorbidity;
- Guidelines written for individual mental health problems that address comorbidity as a complicating factor.

NICE has only one guideline addressing this comorbidity: Psychosis with co-existing SUDs (National Institute for Health and Clinical Excellence, 2011c). The BAP has published a number of guidelines on different comorbid mental disorders and SUDs. Recommendations from these guidelines and guidelines for individual mental disorders are highlighted below if they address management of comorbid mental disorders and SUDs.

Table 1.4: Pharmacotherapeutic approaches recommended for the management of comorbid mental disorders and SUDs

Guidelines	Guideline recommendations
NICE, 2011c	<p><b>Recommendations for the management of psychosis with co-existing SUDs</b>            Due to limited evidence from RCTs for the relative effectiveness of pharmacological treatments for people with psychosis and co-existing SUDs, NICE recommends that people with psychosis (including bipolar disorder) and co-existing SUDs be offered the same range of interventions recommended by NICE or BAP for people with a single diagnosis<sup>6</sup>.</p>
BAP guidelines (Goodwin, 2009)	<p><b>BAP recommendations for the management of bipolar disorder</b>            Established addictive problems should be independently assessed and treated, and consideration given to involving the specialist drug and alcohol team or dual diagnosis team if available.</p>
BAP guidelines (Barnes and Schizophrenia Consensus Group of the British Association for Psychopharmacology, 2011)	<p><b>BAP recommendations for schizophrenia</b>            Recommendations for patients with schizophrenia and comorbid substance use:</p> <ul style="list-style-type: none"> <li>- Antipsychotic medication should be optimized and clozapine considered in patients with persisting substance misuse.</li> <li>- Treatment focused on substance misuse should be offered. While psychosocial approaches will be the mainstay, pharmacotherapy should be considered and offered where possible, e.g. alcohol detoxification and relapse prevention.</li> </ul>
BAP (Lingford-Hughes et al., 2012)	<p><b>BAP recommendations for comorbid bipolar disorder and SUDs</b></p> <ul style="list-style-type: none"> <li>- Treat different phases of bipolar disorder as recommended in guidelines, for example NICE, BAP; however, assess contribution of substance use to hypomania or mania and consider if medically assisted withdrawal is required.</li> <li>- Review pharmacotherapy for bipolar disorder particularly if only on lithium, and consider adding sodium valproate.</li> <li>- Offer naltrexone to help patients reduce their alcohol consumption.</li> <li>- Offer acamprosate if naltrexone has not been effective to help patients remain abstinent.</li> <li>- Consider disulfiram if patient wants abstinence and acamprosate and naltrexone have failed.</li> </ul>
BAP (Lingford-Hughes et al., 2012)	<p><b>BAP recommendations for comorbid schizophrenia and SUDs</b></p> <ul style="list-style-type: none"> <li>- The negative impact of harmful substance use, abuse or dependence on patients with schizophrenia requires that their substance use is assessed and treatment is also focused on any harmful substance use, abuse or dependence.</li> <li>- Antipsychotic medication should be optimised following existing guidance, for example NICE, BAP.</li> <li>- Clozapine should be considered in patients with persisting harmful substance use, abuse or dependence, since it has been reported to reduce substance use and improve psychosis, but these data are still preliminary.</li> <li>- Medication for patients' substance misuse should be considered, such as optimising opioid substitution, use of alcohol relapse prevention such as naltrexone or acamprosate.</li> </ul>
BAP (Lingford-Hughes et al., 2012)	<p><b>BAP recommendations for comorbid depression and SUDs</b></p> <ul style="list-style-type: none"> <li>- Antidepressants may improve mood but not necessarily substance use in those who are depressed with harmful or dependent substance use. Generally mood will only improve in those with a significant depressive disorder, and use of antidepressants should be restricted to this population and then monitored.</li> </ul>

<sup>6</sup> Medications commonly used in the management of psychosis (including bipolar disorder) are antipsychotics, antidepressants and anticonvulsants.

	<ul style="list-style-type: none"> <li>- A comprehensive assessment should be carried out to determine how substance use and depression are linked.</li> <li>- Tricyclic antidepressants (TCAs) are not recommended due to potentially serious interactions between TCAs and substances, including cardiotoxicity and death in overdose. Consider using an antidepressant with mixed serotonergic/noradrenergic pharmacology since they may be better in improving mood in contrast to SSRIs, which have not shown consistent benefits in improving mood.</li> <li>- Medication for harmful substance use, abuse or dependence should be considered such as optimising opioid substitution, use of alcohol relapse prevention such as naltrexone or acamprosate.</li> </ul>
BAP (Lingford-Hughes et al., 2012)	<p><b>BAP recommendations for comorbid anxiety disorders and SUDs</b></p> <ul style="list-style-type: none"> <li>- Ideally patients should first undergo alcohol detoxification.</li> <li>- If detoxification is not possible, treatment of the anxiety disorder should still be attempted: follow guidelines to select most appropriate pharmacotherapy for management of their anxiety disorder.</li> <li>- Assessment by a specialist addiction service is recommended prior to using a benzodiazepine to treat their anxiety.</li> <li>- Medication for the patient’s harmful substance use, abuse or dependence should be considered, such as optimising opioid substitution, use of alcohol relapse prevention such as naltrexone or acamprosate.</li> </ul>

Overall, the recommendations from these guidelines are sometimes non-specific and where they recommend medications for management of comorbidity, those for individual disorders (SUDs or mental disorders) are suggested.

### 1.6.2. Pharmacotherapies for co-existing chronic pain and SUDs

The management of chronic pain in people with a history of SUDs has received limited attention in the literature (Action on Addiction, 2013). A literature review carried out in the USA found no research studies relating to the management of chronic pain in people with a history of SUDs (Chou et al., 2009). Intervention studies targeted at individuals with both SUDs and chronic pain are rare (Samet and Walley, 2008). Most of the guidelines including UK guidelines are based on expert consensus due to lack of strong evidence.

A number of guidelines have been published in the UK concerning pain management with varying degrees of recommendations concerning the management of chronic pain in people with SUDs (The British Pain Society, 2010; The British Pain Society, 2007; Action on Addiction, 2013). This section will focus on recommendations concerning use of opioids in chronic pain management because opioids are the most effective medications for the treatment of pain (McQuay, 1999; Rosenblum et al., 2008). In addition, opioid prescribing is the greatest challenge when considering pain management in people with SUDs (Action on Addiction, 2013). Table 1.5 provides the

pharmacotherapeutic approaches recommended for the management of chronic pain in people with SUDs with a particular focus on the use of opioids.

Table 1.5: Pharmacotherapeutic approaches recommended for the management of comorbid chronic pain and SUDs

Guidelines	Recommendations
<p>Pain and substance misuse: improving the patient experience (The British Pain Society, 2007)</p>	<p><b>Pain control in patients with SUDs</b>            General principles that may be applied for management of patients who have chronic pain requiring opioid therapy, and who currently exhibit aberrant behaviour which may indicate misuse or addiction, or have a history of SUDs:</p> <ul style="list-style-type: none"> <li>- The therapeutic regimen should be selected with the risk of aberrant drug-related behaviours in mind. For example, short-acting opioids (e.g. pethidine) are known to have greater abuse potential than long-acting or sustained release preparations. Also, non-sustained release tablets can be more easily crushed and injected.</li> <li>- The prescriber must communicate clearly with the patient about setting reasonable expectations or goals for therapy and about the necessity to frequently assess progress toward these goals. This must include a regular review of the prescription.</li> <li>- The process of building trust between clinician and the patient should include a candid discussion of acceptable and unacceptable behaviour. The results of such a discussion should be written down and given to the patient.</li> <li>- Be aware of the various potential presentations of drug-seeking behaviour. Refer patient to, or seek advice from, a pain specialist or substance misuse specialist at an early stage where appropriate.</li> <li>- Response to treatment including degree of pain control and progress towards agreed goals needs to be assessed frequently.</li> </ul> <p><b>Specific considerations for patients receiving methadone, buprenorphine or naltrexone</b></p> <p><b>Methadone</b>            If an opioid analgesic is appropriate, a non-methadone opioid may be co-prescribed. It is not necessary to rationalise the patient's entire opioid requirements to one drug.</p> <p><b>Buprenorphine</b>            The partial agonist action of this drug means that it should not be prescribed as an analgesic to patients receiving full agonists (e.g. methadone) as withdrawal may be precipitated.</p> <p><b>Naltrexone</b>            Naltrexone is a long-acting opioid antagonist and patients receiving it as therapy for addiction are likely to be refractory to opioid analgesia. When opioid therapy is introduced after cessation of naltrexone, careful monitoring will be required.</p> <p>It is particularly important that the substance misuse team and the patient's primary care team are kept informed of progress with pain management.</p>
<p>Opioids for persistent pain (The British Pain Society, 2010)</p>	<p><b>Prescribing for patients with a history of SUDs</b>            - Individuals with a history of SUDs are at risk of developing problems when prescribed opioids for pain relief. If opioids are the most appropriate therapy, they may be prescribed for patients as part of a multidisciplinary treatment plan. Comprehensive assessment of both pain and addiction is mandatory, and therapy should be closely monitored by professionals in both pain management and addiction medicine.</p>
<p>Managing persistent pain in secure settings (Public Health England, 2013c)</p>	<p><b>The role of opioids in managing persistent pain</b>            Methadone is suitable for managing persistent pain. Patients with long-term pain also receiving methadone for SUDs may experience pain as the dose reduces. Pain can be treated in this circumstance by maintaining an effective methadone dose. The pharmacokinetics of methadone mean that once-daily dosing is unsuitable for managing pain and it should instead be given as a twice-daily divided dose.</p>
<p>Action on addiction</p>	<p>This guideline was based on key guidelines published in English language. The recommendations and the guidelines from which they were derived are presented below:</p>

(Action on Addiction, 2013)	<p><b>Chronic pain management in recovering, abstinent addicts (Centre for Substance Abuse Treatment, 2012)</b> Goals for treating chronic non-cancer pain (hereafter CNCP) in patients who are in long-term recovery are:</p> <ul style="list-style-type: none"> <li>• Initiate opioid therapy only if the potential benefits outweigh risk and only for as long as it is unequivocally beneficial to the patient. For relapse in patients for whom opioid addiction is a serious problem, referral to an opioid treatment programme (hereafter OTP) may be the best choice.</li> </ul> <p><b>Chronic pain management in patients on Opioid Substitution Treatment (Centre for Substance Abuse Treatment, 2012)</b> Pain clinicians should work closely with the patient’s SUD treatment provider. Patients with chronic pain likely will not obtain adequate pain control through a single daily dose of methadone. Prescription of additional opioids for pain management through a medical provider may be required. Such arrangements require close communication between the OTP and the prescribing clinician. The buprenorphine dose-response curve declines as the dose is increased. To optimise analgesic efficacy, the drug should be given three times a day when pain reduction is a goal.</p> <p><b>Chronic pain management in patients currently or recently addicted (Centre for Substance Abuse Treatment, 2012)</b></p> <ul style="list-style-type: none"> <li>- Most patients addicted to prescription opioids have a prior SUD. Clinicians should adopt universal precautions in considering opioid therapy for patients who have CNCP. The presence of active addiction makes successful treatment of chronic pain improbable.</li> <li>- Identification of an active SUD indicates that the patient should be referred for formal addiction treatment. In patients who relapse to opioid addiction, referral to an OTP may be the best choice.</li> <li>- Patients who have chronic pain likely will not obtain adequate pain control through the single daily dose of methadone that can be provided through an OTP. Such programmes may be willing to collaborate in the management of patients, allowing the prescription of additional opioids for pain management through a medical provider. Such arrangements require close communication between the OTP and the prescribing clinician.</li> </ul> <p><b>Chronic pain management in patients currently or recently addicted (Macintyre et al., 2010)</b> Long-term opioids may not provide continuing effective pain relief and there is an uncertain risk of abuse of the drugs. Inadequate pain relief because of pharmacological tolerance may improve with opioid dose escalation, while improvements in analgesia in the presence of opioid-induced hyperalgesia may follow a reduction in opioid dose.</p>
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In summary, opioids are not contra-indicated for chronic pain management in individuals with SUDs or a history of SUDs. However, people with a past or current history of SUDs may be at risk of developing OUDs. Therefore, chronic pain management in this group of people may need to involve professionals working in pain medicine and addiction medicine for optimal management. Professionals working in pain medicine are more oriented towards support and are therefore trained to respond to the patient’s pain while those in addiction medicine have an orientation that is focused on structure (Action on Addiction, 2013). Structure often involves the need to set boundaries, behavioural rules, monitoring and independent corroboration of patients’ self-report (Action on Addiction, 2013).

### **1.6.3. Summary: Pharmacotherapies for comorbidities**

In general, there is a paucity of evidence for the management of comorbid mental disorders and SUDs as well as comorbid chronic pain and SUDs. Evidence for the management of comorbid mental disorders and SUDs are generally not detailed. They however recommend medications for individual disorders in the management of this comorbidity. Guidelines for chronic pain management do not oppose the use of opioids in people with a current or past history of SUDs. If the benefit of prescribing opioids outweighs the risk in this group, prescribing should involve a close-working relationship between the pain team and the addiction team. While there is need for more research to guide the pharmacological management of these comorbidities, this thesis will in the interim assess the appropriateness of medications prescribed for the management of these frequently co-occurring disorders.

## **1.7. Medication adherence**

Adherence has been defined as the extent to which a patient's behaviour coincides with medical or health advice (Mackay, Taylor and Patel, 2011). Non-adherence to prescribed medications prevents people from experiencing full benefit from them (Chapman and Horne, 2013). It represents a lost opportunity for health gains for the patient with the potential for increased morbidity and mortality if health deteriorates (Simpson et al., 2006). It also leads to waste of healthcare resources (Horne et al., 2005).

Symptoms of mental disorders such as disorganisation and lack of insight in psychotic disorders and low mood in depression may limit a patient's ability to adhere to prescribed medications (Beck et al., 2011; Mackay, Taylor and Patel, 2011). Substances use may also contribute to such behaviours. Intoxication as a result of substances and alcohol-related brain damage may have negative effects on cognitive function, thereby contributing to non-adherence (Berry et al., 1993; Horner, 1997; Schilt et al., 2008; Sullivan and Pfefferbaum, 2005). Non-adherence may be further influenced by the patient's beliefs or perceptions about the need for medications (Mackay, Taylor and Patel, 2011). Patients often have beliefs about their illness and treatment (Horne and Weinman, 1999; Weinman et al., 1996). These beliefs have been found to influence their views of their prescriptions and adherence (Brown et al., 2005; Horne and Weinman, 1999). Consequently, exploring patients' beliefs is fundamental to understanding

adherence (National Institute for Health and Clinical Excellence, 2009). Consideration of patients' beliefs could lead to improved quality of prescribing as clinicians would be able to engage patients in decision-making concerning therapy (Horne et al., 2013).

Prescribers may contribute to non-adherence by failing to explain the benefits and side effects of treatment, having a poor therapeutic relationship with patients and prescribing multiple regimens (Duerden, Avery and Payne, 2013; Gellad, Grenard and Marcum, 2011; Mackay et al., 2011). Prescribing multiple regimens (polypharmacy) increases the number of unnecessary or inappropriate medications (Goh, 2002; Nobili, Garattini and Mannucci, 2011; Rambhade et al., 2012), drug interactions and adverse events (Bourgeois et al., 2010; Duerden, Avery and Payne, 2013; Guthrie et al., 2011). Britten et al. (2003) found that patients receiving unnecessary prescriptions in general practices in England were more likely to be non-adherent.

Different methods have been used for measuring adherence. This includes direct and indirect methods (Patel and David, 2007). Direct methods include measurement of the blood levels of the drug or its metabolite while indirect methods include pill count, use of self-report, clinician report (Kemp et al., 1996), rates of prescription refill and electronic medication monitors (Patel and David, 2007). Self-report of adherence has however been identified by NICE to be appropriate for use in clinical settings generally since it is cheap, quick and easy to use when compared to other methods (Nunes et al., 2009).

Rates of non-adherence in mental health vary depending on the diagnosis, setting, type of adherence difficulty and measure used for assessing level of adherence (Mackay, Taylor and Patel, 2011). The prevalence of non-adherence has been reported to be between 40–60% for antipsychotics (Zygmunt et al., 2002), 30–97% (median 63%) for antidepressants (Pampallona et al., 2002) and 18–52% for mood stabilizers (Scott and Pope, 2002) with the presence of a SUD being a strong predictor of non-adherence (Patel and David, 2007). When compared to those without SUDs, some previous studies (Manwani et al., 2007; Owen et al., 1996; Sajatovic et al., 2006; Weiss, 2004) have found higher levels of non-adherence among those with co-occurring SUDs and mental disorders. Owen et al. (1996) found that schizophrenic patients with SUDs were significantly more likely to report non-adherence when compared to those without co-

occurring SUDs. Similarly, bipolar patients with SUDs have reported higher levels of non-adherence (Manwani et al., 2007; Sajatovic et al., 2006).

Various studies have explored the relationship between adherence and the beliefs of patients with mental health problems such as depression, schizophrenia and bipolar disorder (Brown et al., 2005; Clatworthy et al., 2009; Jonsdottir et al., 2009) and chronic pain (Nicklas, Dunbar and Wild, 2010). Generally, across these studies higher levels of adherence were associated with stronger beliefs or perceptions about the need for treatment and lower concerns about treatment. However, no study was found that examined this relationship among people with SUD comorbidity. Due to evidence of the high levels of non-adherence among people with SUDs and the fact that patients' beliefs or perceptions have been found to have an influence on adherence, this thesis assessed patients' level of adherence to their medications using a self-report questionnaire developed for this purpose (adherence questionnaire) as well as the influence of their beliefs or perceptions on their reported level of adherence.

## **1.8. Prescribing models in the UK**

This section extends the discussion of prescribing by considering the prescribing models available in the UK. In the SAS where this research was carried out, both medical and non-medical prescribers (in particular, nurses) are able to prescribe substitute and relapse prevention medications for people with SUDs. Prescribing has traditionally been a medically dominated activity but is now extended to other healthcare professionals (also known as non-medical prescribers), such as nurses, pharmacists, physiotherapists, radiographers, optometrists, chiropodists and podiatrists, in the UK as part of the NHS modernisation agenda (Hacking and Taylor, 2010).

The origin of non-medical prescribing in the UK can be traced to the Cumberlege Report which suggested that:

The Department of Health and Social Security (hereafter DHSS) should agree a list of items and simple agents which may be prescribed by nurses as part of a nursing care programme, and issue guidelines to enable nurses to control drug dosage in well-defined circumstances (DHSS, 1986).

Further, the Report of the Advisory Group on Nurse Prescribing, also called the Crown Report, recommended that health visitors and district nurses be empowered to prescribe from a limited formulary within set protocols (Department of Health, 1989). Following these recommendations, a pilot scheme for nurse prescribing that included sites in different regions of England was set up (Luker et al., 1998). Nurse prescribing subsequently became part of government policy following the success of the pilot programmes and became a national initiative in 1998 (Department of Health, 1999). Pharmacists were also subsequently given prescribing rights (Department of Health, 2006b; Department of Health, 2003). Over the years, other healthcare professionals such as physiotherapists and podiatrists have been given rights to prescribe medicines within their clinical competence and legislative frameworks (Hacking and Taylor, 2010).

Reasons for the extension of prescribing rights to other healthcare professionals include the need to provide quicker and more efficient access to medicines for patients without safety being compromised, more efficient utilisation of the skills of these healthcare professionals and less fragmentation of care (Emmerton et al., 2005; Hacking and Taylor, 2010). Non-medical prescribing for nurses and pharmacists in the UK now involves a single postgraduate independent and supplementary prescribing qualification (Cooper et al., 2008; Courtenay, Gerada and Haywood, 2011).

The non-medical prescribing course is generic and prepares practitioners to prescribe (Public Health England, 2014c). While there are no legal restrictions on the clinical conditions that may be treated, clinical areas of practice are usually defined and agreed with the employing organisation (National Prescribing Centre, 2012; Nursing and Midwifery Council., 2006). In particular, the selection of nurses and pharmacists to train as independent prescribers is usually a matter for the employing organisation. The potential prescriber should be deemed competent by their employer to undertake the prescribing training (Nursing and Midwifery Council., 2006). The clinical areas in which they will prescribe is usually that in which they have considerable expertise and this should have been defined before they begin training (Department of Health, 2006b). The two main models for non-medical prescribing in the UK are supplementary prescribing and independent prescribing (Department of Health, 1999). Each of these models is considered in sections *1.8.1* and *1.8.2*.

### **1.8.1. Supplementary prescribing**

Supplementary prescribing has been defined as a “voluntary partnership between a doctor or dentist (independent prescriber) and a supplementary prescriber to implement an agreed patient-specific clinical management plan (hereafter CMP) with the patient’s agreement” (Department of Health, 2005a). This prescribing model was introduced in the UK in 2003. It allows trained healthcare professionals to take prescribing responsibility within their clinical competence for patients according to a specific CMP (Department of Health, 2005a). A supplementary prescriber may be a specially trained nurse, pharmacist, optometrist, physiotherapist, podiatrist or radiographer (Fittock, 2010). Supplementary prescribing can be from a full medicines formulary, including controlled drugs. In the past, non-medical prescribers could only use supplementary prescribing to treat drug dependence (Public Health England, 2014c). Legislative changes have now made it possible for them to independently treat drug dependence (Public Health England, 2014c).

### **1.8.2. Independent prescribing**

Independent prescribing has been defined as “prescribing by a practitioner, responsible and accountable for the assessment of patients with diagnosed or undiagnosed conditions, and for decisions about the clinical management including prescribing” (Department of Health, 2006c). It requires an initial patient assessment, interpretation of that assessment, a decision on safe and appropriate therapy, and a process for ongoing monitoring (Joint Allied Health Professions, 2013). Independent prescribing was introduced in 2006 (Hacking and Taylor, 2010). There are two forms of independent prescribers (Fittock, 2010):

- An independent prescriber, such as a specially trained nurse, pharmacist and optometrist, who can prescribe any licensed medicine within their clinical competence.
- A community practitioner nurse prescriber, such as district nurses and health visitors who can independently prescribe from a limited formulary, the Nurse Prescribers’ Formulary for Community Practitioners in the BNF.

For SUD management, non-medical prescribing is only provided by nurses, pharmacists or midwives (Public Health England, 2014c). In 2012, legislation amendment allowed

nurses and pharmacists to assess, diagnose and independently prescribe controlled drugs for the treatment of drug dependence except diamorphine, cocaine and dipipanone which are restricted to medical practitioners licensed by the Home Office (in England and Wales) (Department of Health, 2012a; Public Health England, 2014c). Furthermore, besides medical prescribers, only nurse and pharmacist prescribers can prescribe unlicensed medicines.

The management of SUDs presents special issues because the majority of prescribing involves controlled drugs. Furthermore, the often complex needs of people with SUDs present challenges in terms of risk management (Public Health England, 2014c). Many people attending drug and alcohol services have severe comorbid mental and physical health problems. Consequently, Public Health England (2014c) has concluded that meeting these complex needs will require suitable qualified medical practitioners to work alongside non-medical prescribers in a multidisciplinary team. Options available to assist non-medical prescribers make informed and clinically appropriate decisions include clinical supervision from a medical prescriber or non-medical prescriber, managerial supervision and discussion with peer support networks (ibid).

## **1.9. Chapter summary**

This chapter has described different definitions of SUDs and health conditions that are frequently comorbid with SUDs, with a particular focus on mental disorders and chronic pain. High rates of mental disorders and chronic pain have been found in clinical populations with SUDs and there is generally a paucity of evidence on the pharmacological management of co-occurring mental disorders and chronic pain, and SUDs. This introduction chapter further showed that appropriateness is a complex concept. In relation to prescribing, it involves a judgment across a number of areas that include effectiveness, risk, cost, patients' choices, patients' outcomes as well as the societal impact of prescribing. Outcome-focused prescribing is particularly relevant among people with comorbid mental disorders or chronic pain and SUDs due to the limited nature of the evidence base for medication management. Furthermore, the benefit of prescribing among people with SUDs may not always be medical as there are important social outcomes that need to be considered among this population.

Appropriate prescribing in this population would ultimately involve consideration of a holistic assessment of the patient (including their choices, outcomes, circumstances, symptoms and comorbidities), the social impact of prescribing, the evidence base concerning the clinical pharmacology of the medication as well as clinical expertise represented by the skill and experience of the prescriber.

The different prescribing models in the UK were also presented. In the SAS where this research was carried out, both medical and non-medical prescribing (in particular, independent nurse prescribing) are utilised. The next chapter presents a scoping review that ascertains what can be learnt from the literature about the appropriateness of medications commonly used in the treatment of chronic pain and mental disorders among people with SUDs.

# Chapter 2: Appropriateness of opioids and psychiatric medications prescribed for people with SUDs: A scoping review

## **2.1. Introduction**

As described in chapter one, mental disorders and chronic pain are often comorbid with SUDs and this raises fundamental questions about prescribing practice in this group. Prescribing appropriateness involves the consideration of multiple dimensions such as effectiveness, risk, cost, preferences of individuals, their outcomes and the societal impact of prescribing. Pharmacological appropriateness encompasses medication effectiveness, safety (including risks) and cost (Spinewine et al., 2007), and has been assessed using implicit or explicit measures. Since different medications are used in treating the diverse forms of co-existing mental disorders and chronic pain, a detailed review was carried out in order to ascertain what could be learnt from the literature about the appropriateness of prescribing of medications commonly used in the treatment of these conditions: namely antidepressants, antipsychotics, anxiolytics/hypnotics, antimanic agents, anticonvulsants and opioids (excluding substitute opioids) among people with SUDs. This review includes only quantitative studies on this topic due to time constraints in this thesis. Before presenting the methods and findings of this review, the justification for the use of a scoping review rather than a systematic review is presented below.

### **2.1.1. Justification for scoping review**

This review was carried out in order to provide an overview of relevant literature concerning the appropriateness of medicines commonly prescribed for mental disorders and chronic pain. A scoping review was chosen over a systematic review for a number of reasons. Systematic reviews involve a systematic process for defining research questions, searching for studies, assessing their quality and synthesizing findings (Arksey and O'Malley, 2005; Armstrong et al., 2011). They usually focus on well-defined questions where appropriate study designs can be identified in advance. This often requires a prior understanding of the existing literature (Armstrong et al., 2011). On the contrary, a scoping study tends to address broader topics, where different study designs might be applicable (Arksey and O'Malley, 2005). A scoping review aims to

‘map’ the literature pertaining to an area of research, the sources and types of evidence available especially when the area is complex or under-researched (Mays, Roberts and Popay, 2001). This is pertinent in this thesis because the topic explored is both complex and under-researched, and there has been no previous review. Scoping reviews may also be useful for identifying gaps in the evidence base (Arksey and O'Malley, 2005), that can inform research questions and methodology. Although systematic reviews are not limited to any kind of study, most are on the effectiveness of interventions and therefore usually focus on RCTs (Levac, Colquhoun and O'Brien, 2009). Studies in this area are unlikely to be RCTs. Consequently, a scoping review methodology was employed to develop a picture of the evidence base (Armstrong et al., 2011) through the inclusion of a range of relevant study designs that address the review topic.

## **2.2. Objectives**

The purpose of this scoping review was to address the following question: What is known from the existing literature about the appropriateness of prescribing of antidepressants, antipsychotics, anxiolytics/hypnotics, antimanic agents, anticonvulsants and opioids<sup>7</sup> (excluding substitute opioids) for people with SUDs?

## **2.3. Methods**

This review utilised a rigorous and comprehensive approach in order to be transparent and thorough (Mays et al., 2001). It involved the documentation of each stage of the review process to enable it to be replicated by others (Arksey and O'Malley, 2005), thus ensuring methodological rigour (Mays et al., 2001). This section considers the following areas:

1. Types of study designs
2. Types of participants
3. Measures of appropriateness
4. Exclusion criteria
5. Outcome
6. Search strategy
7. Data collection

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<sup>7</sup> Medications grouped into any of these classes by the BNF were examined.

### **2.3.1. Types of study designs**

All available designs were included in this review with the exception of case reports. Case reports were excluded because they are usually limited to individual patients and as a result, are not generalizable (Isaacs, 2007).

### **2.3.2. Types of participants**

Studies recruiting adults aged 18 years and above with SUDs, who were also receiving opioids for chronic pain or medications for mental disorders were included in this review. Studies recruiting adults were the focus of this review because the therapeutic doses of the medications to be assessed differ between adults and children (Cella et al., 2010; Findling et al., 1998; Findling et al., 2000; Joint Formulary Committee, 2010), and the focus of this thesis is on adults. Studies including people younger than 18 years as well as adults with SUDs were considered if they separately reported prescribing appropriateness in adults. Where the age of study participants were not reported, such studies were included provided they did not explicitly refer to non-adults. This review relied on investigators' definitions of SUDs rather than providing a pre-specified definition because it was a scoping review which aimed at providing an overview of the range and extent of available evidence. This was done in order to reduce the possibility of missing relevant studies. This wide approach has been suggested for use in scoping reviews in order to increase the breadth of evidence covered (Arksey and O'Malley, 2005). Consequently, investigators' definitions of SUDs might be based on a range of measures:

1. Medical records (for example, documentation of SUDs from medical records);
2. Screening for illicit substances;
3. Self-report;
4. Responses to structured interviews such as the Diagnostic Interview Schedule (Malgady, Rogler and Tryon, 1992).

This review also relied on investigators' definitions of chronic pain and mental disorders such as mood, anxiety and psychotic disorders. There was no restriction on the setting where people with SUDs were identified.

### **2.3.3. Measures of appropriateness**

Papers were included in this review if they involved some form of assessment or measurement of appropriateness. This could include guideline adherence; manufacturers' recommendations; DDD<sup>8</sup>; validated measures such as the MAI and the PAI or any other measure specified in the study.

### **2.3.4. Exclusion criteria**

The following were the exclusion criteria for this review:

1. Studies that do not include some form of assessment or measurement of appropriateness;
2. Studies that assessed appropriateness only in people less than 18 years of age;
3. Studies that assessed the appropriateness of opioid substitute prescribing;
4. Studies in languages other than English;
5. Unpublished studies.

### **2.3.5. Outcome**

Appropriateness of prescribing defined using some form of assessment or measurement of appropriateness.

### **2.3.6. Search strategy**

Electronic databases were searched for relevant published literature. Prior to conducting a search of the databases, a researcher with experience in the systematic review methodology at the University of York was consulted in order to ensure the search strings were comprehensive. In addition to the searching of electronic databases listed below, hand-searching of the references of relevant studies was carried out. Hand-searching was necessary because electronic databases may be incomplete or vary in coverage (Arksey and O'Malley, 2005). All the six journals from which relevant studies were retrieved were also hand-searched in order to obtain any study that has been missed in database and reference list searches. The journals were hand-searched from June 1994 to November 2015 because the oldest relevant study was published in June 1994.

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<sup>8</sup> The DDD is the *assumed average maintenance dose per day for a drug used for its main indication in adults*.

Electronic databases

Three databases were searched through the Ovid SP platform on the 5<sup>th</sup> of March 2012.

The following databases were searched:

1. PsycINFO (1806 to February Week 4 2012);
2. Medline (1946 to February Week 4 2012);
3. EMBASE (1974 to 2012 March 05).

The search strings used in Medline are shown in appendix 2.1. These search strings were adapted for use in psycINFO and Embase (appendices 2.2 and 2.3 respectively). An update of the electronic databases was carried out on the 12<sup>th</sup> of November 2015.

### **2.3.7. Data collection**

Study selection

All the references identified by searching were imported into Endnote X4 and duplicates were removed. After removal of duplicates, the titles and abstracts of the remaining references were screened to identify potentially relevant studies. Copies of the full article of studies that appeared to be relevant were assessed for eligibility based on the stated inclusion/exclusion criteria. Ideally, the screening process should have been carried out by two independent reviewers in order to reduce the risk of missing out relevant studies (Edwards et al., 2002). However, the resources available prevented the inclusion of a second reviewer.

Data extraction

Data on study characteristics such as study type, setting, year of publication, country of study, participants, diagnosis assessment, sample size, measure of appropriateness and result were extracted on a standard form. Information retrieved from these studies are presented in section 2.6.2.

## **2.4. Quality assessment**

Study quality was assessed in order to reduce the possibility of bias since the quality of studies in a review can affect its overall conclusion. Studies of low quality may give misleading results (Detsky et al., 1992). Quality assessment of non-randomised studies poses some challenges due to the different types of methods that could be used.

Although there are quality assessment tools that assess the quality of these studies (Deeks et al., 2003), it is rare to find a tool that is tailored to specific topics. Deeks et al. (2003) assessed 193 tools that could be used in evaluating the quality of non-randomised studies and six of them were thought to be suitable for use in systematic reviews. Although this was not a systematic review, one of these tools was chosen for this scoping review because it allows for the assessment of individual studies in a systematic way. This ensured that the quality of relevant studies could be compared.

Of these six tools, the Quality Assessment Tool for Quantitative Studies (Thomas et al., 2004), was chosen because it covers key areas of quality and has a comprehensive guide for its completion. Furthermore, the content and construct validity of the checklist has been found to be acceptable and its test-retest reliability has been demonstrated to be good (Thomas et al., 2004). The Quality Assessment Tool for Quantitative Studies (hereafter QATQS) is designed for assessing randomised and non-randomised studies. It includes 21 items separated into eight components: selection bias, study design, confounders, blinding, data collection methods, withdrawals and dropouts, intervention integrity and analysis. After completion of the tool, ratings of ‘strong’, ‘moderate’ or ‘weak’ are given for each of the first six components in order to provide a global rating of quality. This tool was adapted for use in this study. Appendix 2.4 shows the adapted QATQS. The following items that are not relevant to the types of studies included in this review were removed (they were not taken into consideration in the global rating of study quality):

1. The ‘blinding’ questions were removed because they are not relevant to the studies in this review.
2. The ‘intervention integrity’ questions were removed because there were no interventions in the studies included in this review.
3. The ‘analysis’ questions were also removed because they were not relevant to the studies in this review.

Although the authors of the QATQS recommend that it should be used by two reviewers, quality assessment was conducted by one reviewer (A.O.) due to resource limitations. The quality assessment process was however overseen by the supervisors of this thesis.

## **2.5. Data synthesis**

The data were synthesized based on the different measures of appropriateness used in the included studies. These include guidelines, summary of product characteristics and antidepressant treatment history form. Due to the diverse nature of the medications studied, the different populations, settings and measures utilised in assessing prescribing appropriateness, a meta-analysis of the studies was not possible. In addition, the Centre for Reviews and Dissemination (CRD) Guidance for Undertaking Reviews in Health Care does not recommend the pooling of results from diverse non-randomised studies (Centre for Review and Dissemination, 2009). Consequently, a narrative synthesis of the diverse measures of prescribing appropriateness was carried out.

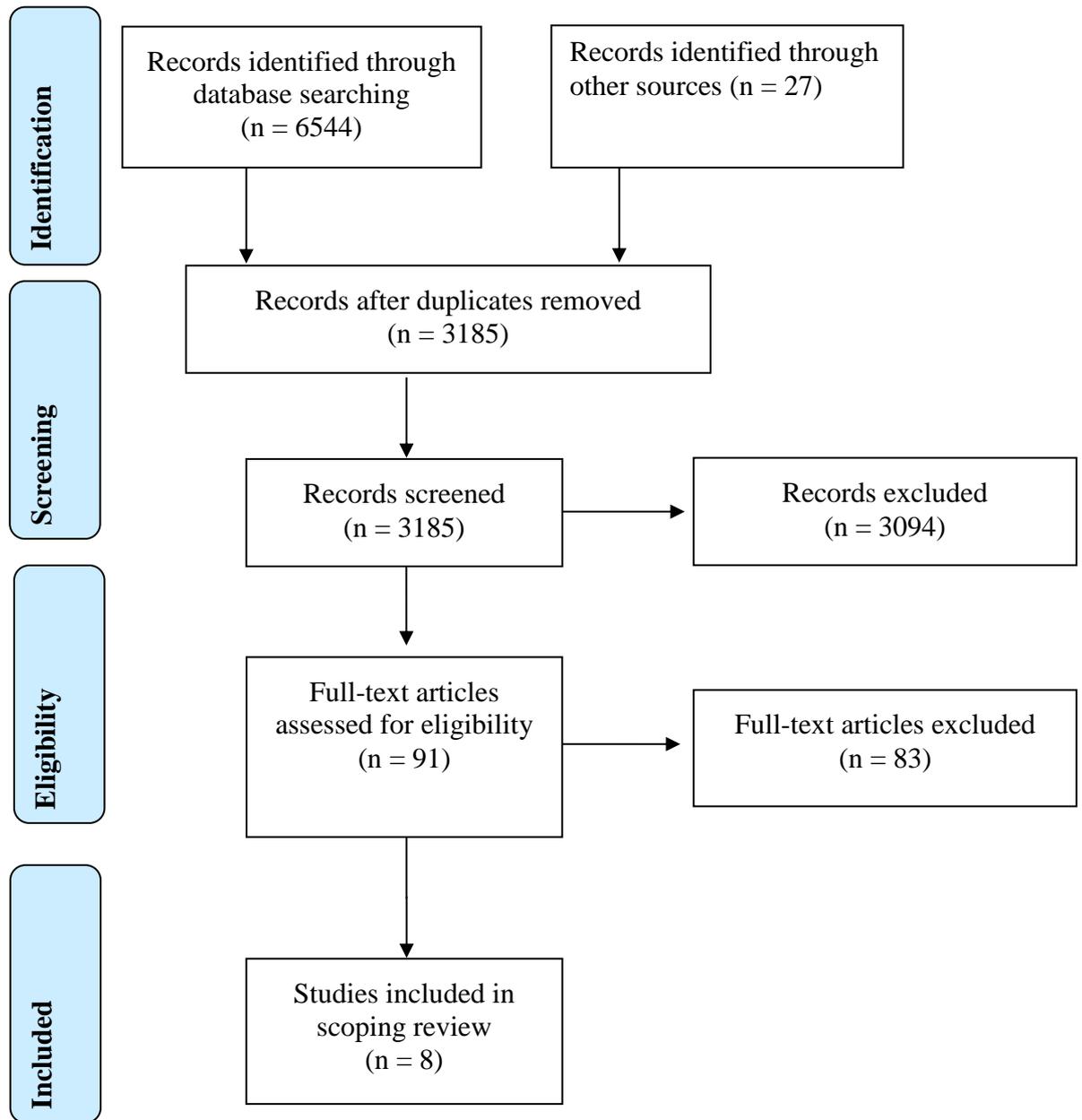
## **2.6. Results**

This section presents the results for the study selection and data extraction process. It further provides a brief description of relevant studies, quality assessment and a narrative synthesis of the measures of prescribing appropriateness.

### **2.6.1. Study selection**

There were 6,544 and 27 references identified through database searching and hand-searching, respectively. After removal of duplicates, 3,185 were screened from which 91 appeared to be potentially relevant from their retrieved abstracts. The full-text versions for the 91 studies were examined and eight were found to be relevant. Figure 2.1 shows the study selection process. Eighty three full-text versions of studies were excluded because they either did not assess prescribing appropriateness (n = 65) or state whether participants had SUDs (n=16). Other reasons for study exclusion are as follows: study did not include patients with SUDs (n = 1) and study included patients who were less than 18 years (n = 1). Appendix 2.5 displays the excluded references.

Figure 2.1: Study selection process



### 2.6.2. Description of studies

Eight articles meeting the inclusion criteria were included in this review. One study focused on antidepressants, two on benzodiazepines, three on antipsychotics and two assessed opioids. There were no studies that focused on antimanic agents and anticonvulsants. Morrison et al. (1994) assessed opioid prescribing for different types of pain. However, this study did not state how long a patient had to have pain for it to be

considered as acute or otherwise<sup>9</sup>. The majority of studies (six studies) in this review were carried out in the USA. There was one study each from France (Thirion et al., 2002) and Germany (Weinmann et al., 2005). Four studies (Clark, Xie and Brunette, 2004; Leslie and Rosenheck, 2001; Morasco, Duckart and Dobscha, 2011; Morrison et al., 1994) involved assessment of prescribing for outpatients. Weinmann et al. (2005) assessed prescribing for patients recruited in psychiatric hospitals while Baca-Garcia et al. (2009) assessed those in a university hospital. Walkup et al. (2000) assessed prescribing for inpatients recruited from general hospitals while Thirion et al. (2002) assessed prescribing from diverse settings namely GPs (accounting for 85% of prescriptions), care centres and specialists. There was no study that assessed prescribing for people in substance misuse settings. Studies utilised different measures for assessing prescribing appropriateness of which majority were guidelines. Others are the Antidepressant Treatment History Form (ATHF) and Summary of Product Characteristics (SPC). Table 2.1 shows the information retrieved from included studies.

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<sup>9</sup> A decision was taken to include it in this scoping review despite the absence of information concerning pain duration.

Table 2.1: Information retrieved from included studies

Study	Participants	Type of setting	Diagnosis assessment	Sample size	Measures used for appropriateness	Results
Baca-Garcia et al. 2009. USA. Cross-sectional study	Depressed bipolar patients with a lifetime history of AUDs and those without AUDs	University hospital	Diagnoses of AUDs (alcohol abuse or dependence) and current bipolar major depressive episode were made using SCID for DSM-III-R or DSM-IV	39 patients in the AUD group and 58 in the group without AUDs	Antidepressant treatment history form (ATHF)	Those with AUDs had higher proportion of inadequate treatment (74.3%) compared to those without AUDs (67.3%), $p = 0.03$ . Proportion of intensive antidepressant treatment is higher (ATHF rating of 4 and 5) in those without AUDs (15.5% vs 2.6%).
Leslie and Rosenheck. 2001. USA. Cross-sectional study	Department of Veterans Affairs (VA) outpatients diagnosed with schizophrenia. Some had comorbid SUDs	Outpatient	Diagnoses of SUDs (in particular, substance abuse) and schizophrenia were based on ICD-9.	34,925 patients. 21% had a comorbid SUD	The Schizophrenia Patient Outcomes Research Team (PORT) recommendations	Patients with SUDs were significantly less likely to be dosed above PORT guidelines compared to those without SUD (OR = 0.85, 95% CI: 0.78 – 0.93). There was no significant difference in likelihood of dosing below guidelines (OR = 1.01, 95% CI: 0.93 – 1.10).
Weinmann, Janssen and Gaebel. 2005. Germany. Cohort study	Patients diagnosed with a primary psychotic disorder at the time of hospital admission. Some had comorbid SUDs	Psychiatric hospital	Diagnoses of psychotic disorders were based on ICD-10. How SUDs (substance abuse and dependence) were diagnosed was not stated	508 patients. 17% had a comorbid SUD	Based on the PORT, APA guidelines and guidelines of the German Society of Psychiatry, Psychotherapy and Nervous Disease	There was no significant difference in the likelihood of receiving medication care outside guideline recommendations between those with and without SUD (OR = 0.80, 95% CI = 0.40 - 1.79).
Clark, Xie and Brunette. 2004. USA. Cross-sectional study	Medicaid beneficiaries with a range of psychiatric disorders. Some had comorbid SUDs	Outpatient	Diagnoses of psychiatric disorders and SUDs (abuse or dependence) were based on ICD-9.	9,589 patients. 36.8% had a comorbid SUD	The APA recommendations	Those with comorbid SUDs were more likely to use benzodiazepines for $\geq 4$ months ( $p < 0.0001$ ) except those with schizophrenia. Those with major depression ( $p < 0.0001$ ) or other psychiatric disorders ( $p = 0.05$ ) comorbid with SUDs were significantly more likely to use fast-acting benzodiazepines.
Thirion et al. 2002. France. Cross-sectional study	Opiate dependent patients prescribed buprenorphine maintenance therapy	Outpatient mostly GPs (85%). Others include care centres (11%) and specialists (4%)	Not stated	2,078 patients	Summary of product characteristics (SPC) for benzodiazepines	Daily doses of prescribed benzodiazepines often above that specified in the SPC but proportion of patients in which this occurred was not stated
Morrison et al. 1994. USA. Cohort study	Ambulatory HIV-infected patients. This included intravenous drug users (IDUs)	HIV clinic	Not stated	190 patients. 11% were IDUs	Published guidelines for the use of opioids in the treatment of cancer patients	IDUs were more likely to be prescribed opioids inappropriately than were men who were homosexuals ( $p < 0.001$ ) or heterosexual people ( $p = 0.01$ )

Morasco, Duckart and Dobscha. 2011. USA. Cohort study	Veterans with chronic non-cancer pain (CNCP) prescribed chronic opioid therapy. Some had comorbid SUDs	Outpatient	Patients classified as having CNCP based on electronic medical record pain numeric rating scores. SUDs (AUDs, illicit SUDs, prescription DUDs) diagnoses were based on ICD-9-CM	5,814 patients. 19.5% had a SUD diagnosis	Guidelines for the use of chronic opioid therapy published by Chou and colleagues, 2009.	Those with SUDs did not differ from those without SUDs in receipt of long acting opioids (OR = 0.94, 95% CI: 0.81 - 1.09)
Walkup et al. 2000. USA. Cohort study	Inpatients with schizophrenia or schizoaffective disorder. Some had comorbid SUDs	General hospital	Diagnoses of SUDs (in particular, substance abuse) was based on the MINI while diagnoses of schizophrenia or schizoaffective disorder was confirmed using SCID for DSM-III-R or DSM-IV	293 patients. 36.9% had a comorbid SUD	The Schizophrenia Patient Outcomes Research Team (PORT) recommendations	There was no significant difference in likelihood of excess discharge doses between patients with and without comorbid SUDs (17.6% vs 22.7%; p = 0.17).

Note: ICD-9 classifies SUDs into abuse and dependence unlike ICD-10 which classifies SUDs into harmful use and dependence

Where,

APA = American Psychiatric Association

AUD = Alcohol use disorder

DUD = Drug use disorder

SCID = Structured Clinical Interview for DSM Disorders

ICD-9 = International Classification of Diseases, 9<sup>th</sup> Revision

ICD-9-CM = International Classification of Diseases, Clinical Modification-9<sup>th</sup> Revision

ICD-10 = International Classification of Diseases, 10<sup>th</sup> Revision

MINI = Mini-International Neuropsychiatric Interview

OR = Odds ratio

### **2.6.3. Quality assessment**

Most of the studies had either ‘moderate’ or ‘strong’ global ratings using the adapted QATQS (see table 2.2). Studies were given a global rating of ‘strong’ if they had three or more strong ratings in each of the assessment components and no weak ratings. A global rating of ‘moderate’ was given if less than four strong ratings and one weak rating whereas a global rating of ‘weak’ denoted the presence of two or more weak ratings. One of the criteria ‘withdrawals and drop-outs’ was not applicable to six studies because all eligible patients were included and there were no withdrawals/drop-outs. This criterion was excluded when assessing the global rating for these six studies. While the adapted QATQS was useful in assessing the quality of studies in a systematic way, some of its components were difficult to rate due to their subjective nature. For instance, it was difficult to decide the percentage of relevant confounders controlled for. The adapted QATQS does not also state explicitly the number of confounders that will need to be taken into consideration for at least 80% of confounders to be controlled for. In this review, where studies controlled for factors known to influence prescribing such as age and comorbidities, they were given strong ratings in the ‘confounder’ component of the assessment tool.

A number of studies did not control for these confounders and may lead to flawed conclusions about the quality of prescribing for people with SUDs, especially those with co-existing mental disorders. This is particularly apposite given that people with SUDs co-existing with mental disorders may have more severe and persistent symptoms and they may be more resistant to treatment compared to those with single conditions (Volkow, 2010; Green, 2005). Consequently, they may require higher doses or need to be treated for a long duration. Further information about each quality rating category is described below.

#### **Selection bias**

Six studies were considered to be ‘strong’ in this component. Five of these studies included all the eligible patients during the period examined and analysed existing administrative databases while in one study (Weinmann et al., 2005) over 80% of those screened provided consent. In the study by Baca-Garcia et al. (2009), a ‘weak’ rating was given because participants (bipolar patients with and without SUDs) were recruited through advertising and referrals. There was no information on where adverts were placed and who referred patients. Advertising and referrals may result in self-selection as those recruited may be different from those who were not (Levin, 2006). As a self-selecting group, there may be

less ill. Hence, their willingness to take part in this study. A ‘weak’ rating was also given to the study by Walkup et al. (2000) because there was insufficient detail provided on the number and characteristics of eligible patients who agreed to participate.

### Study design

All the studies were considered to be ‘strong’ in their designs as the designs used were appropriate in addressing their objectives. The types of studies that are most likely to address the research question posed in this review are observational studies such as cross-sectional or cohort studies. Four studies (Morasco et al., 2011; Morrison et al., 1994; Walkup et al., 2000; Weinmann et al., 2005) included in this review were cohort studies while the remaining were cross-sectional studies.

### Confounders

Three of the included studies were considered ‘weak’ in this component because those with mental disorders or pain co-existing with SUDs were not compared with those without SUDs in order to determine whether there are any differences that could explain the tendency for more or less inappropriate prescribing. For instance, comorbidities such as hepatic impairment may lead to a reduction of antipsychotic doses (Kane et al., 1998). Furthermore, none of these three studies controlled for potential confounders such as age and number of comorbidities between people with and without SUDs in their analysis. This suggests that they may be biased towards overestimating the percentage of inappropriate medications.

Age and number of comorbidities may influence medication dosing (Rochon, Schmader and Sokol, 2014). People with comorbidities may need higher or lower doses depending on the type and severity of comorbidities. On the other hand, four other studies were considered to be ‘strong’ in this component because they controlled for variables such as age and comorbidities (Leslie and Rosenheck, 2001; Morasco et al., 2011; Walkup et al., 2000; Weinmann et al., 2005). One study (Thirion et al., 2002) that assessed benzodiazepine prescribing among opiate dependent patients was considered ‘weak’ as there was no comparison of those prescribed benzodiazepines with those who were not prescribed in order to determine if there are differences that could explain the reasons for doses above the SPC of benzodiazepines.

### Data collection methods

Six studies were rated as ‘moderate’ in this component because the data assessed were from existing medical records. Medical records may be subject to error due to failure to consistently document relevant information, errors in medical record abstraction, under-reporting or over-reporting of care (Chen et al., 2006). The remaining two studies (Baca-Garcia et al., 2009; Weinmann et al., 2005) were considered to be ‘strong’ because they described their data collection tools and the validity and reliability of these tools have been tested.

### Withdrawals and drop-outs

This component was not applicable to most studies because of their retrospective or cross-sectional design. Six studies assessed past medications of people. One study (Weinmann et al., 2005) was rated as ‘moderate’ because the number of patients excluded was stated and 60 to 79% of patients completed the study as recommended in the adapted quality assessment tool. Walkup et al. (2000) was given a ‘weak’ rating because it does not provide information on withdrawals/drop-outs from the study.

### Global rating of studies

Overall, the quality of the studies included in this review varied (see table 2.2). Six studies had either strong or moderate global ratings: three studies were strong and three were moderate. Two studies had weak global ratings. Table 2.2 describes the global quality rating of studies included in this review.

Table 2.2: Global quality rating of studies

Author and year	Selection bias	Study design	Confounders	Data collection methods	Withdrawals and drop-outs	Global rating
Morrison et al. 1994	Strong	Strong	Weak	Moderate	Not applicable	Moderate
Walkup et al. 2000	Weak	Strong	Strong	Moderate	Weak	Weak
Leslie and Rosenheck 2001	Strong	Strong	Strong	Moderate	Not applicable	Strong
Thirion et al. 2002	Strong	Strong	Weak	Moderate	Not applicable	Moderate
Clark, Xie and Brunette 2004	Strong	Strong	Weak	Moderate	Not applicable	Moderate
Weinmann, Janssen and Gaebel 2005	Strong	Strong	Strong	Strong	Moderate	Strong
Baca-Garcia et al. 2009	Weak	Strong	Weak	Strong	Not applicable	Weak
Morasco, Duckart and Dobscha 2011	Strong	Strong	Strong	Moderate	Not applicable	Strong

#### 2.6.4. Narrative synthesis of prescribing appropriateness

This section presents a narrative synthesis of the studies according to the measure of prescribing appropriateness used. Six studies assessed adherence to guideline recommendations while one study assessed whether recommendations in the summary of product characteristics for benzodiazepines was followed. Another study used a computer algorithm that is based on the antidepressant treatment history form to assess the appropriateness of antidepressant medications prescribed by psychiatrists. Seven studies compared prescribing appropriateness between those with and without SUDs. Thirion et al. (2002) however assessed the appropriateness of benzodiazepine dosage only in people with SUDs (opiate dependent patients on buprenorphine-maintenance treatment). The narrative syntheses of these studies are presented below.

##### 2.6.4.1. Use of guidelines as a measure of appropriateness

The narrative syntheses of studies assessing guideline adherence for prescribing of opioids and psychiatric medications are presented separately because they are different classes of medications.

### **Guideline adherence as a measure of appropriateness of psychiatric medications**

Four studies (Clark et al., 2004; Leslie and Rosenheck, 2001; Walkup et al., 2000; Weinmann et al., 2005) assessed guideline adherence in prescribing of psychiatric medications. Leslie and Rosenheck (2001) and Walkup et al. (2000) assessed adherence to the Schizophrenia Patient Outcomes Research Team (hereafter PORT) recommendations for antipsychotic prescribing while Weinmann, Janssen and Gaebel (2005) assessed adherence to recommendations for antipsychotic prescribing developed from three guidelines namely the PORT recommendations, the American Psychiatric Association (APA) guidelines and guidelines of the German Society of Psychiatry, Psychotherapy and Nervous Disease. Clark, Xie and Brunette (2004) assessed adherence to the APA guidelines for benzodiazepine prescribing.

The study by Leslie and Rosenheck (2001) was conducted in the USA and assessed whether the dose of oral antipsychotics prescribed for outpatients with schizophrenia in the Department of Veterans Affairs (hereafter VA) conformed to the PORT recommendations. Dose was defined as the total amount of medicine prescribed for the patient. In particular, administrative database comprising antipsychotic prescription drug records written between June 1999 and September 1999 for 34,925 patients was assessed (21% had a comorbid SUD). Diagnoses of schizophrenia and SUDs (in particular substance abuse) were based on the ICD-9 diagnostic codes. Schizophrenia was determined by the presence of a primary or secondary diagnosis of schizophrenia in at least two outpatient encounters in a specialty mental health outpatient clinic.

The PORT guideline recommends that the total daily chlorpromazine equivalents for all typical antipsychotics should be between 300 mg and 1000 mg while different doses are recommended for different atypical antipsychotics. Patients with substance abuse diagnosis were significantly less likely to be dosed above PORT guidelines compared to those without substance abuse diagnosis (OR = 0.85, 95% CI: 0.78 – 0.93). There was no significant difference in the likelihood of dosing below guidelines between those with and without co-existing substance abuse diagnosis (OR = 1.01, 95% CI: 0.93 – 1.10). This suggests that in people with and without co-existing substance abuse diagnosis, there was also underdosing of medications. Overall, for this group of schizophrenic patients, there was significantly less inappropriate prescribing of antipsychotics for those with a SUD.

This study adjusted for patient characteristics such as age, patient ethnicity (black or Hispanic), distance of patients' residence from the hospital, presence of primary or secondary diagnosis of mental illness in addition to schizophrenia, hospital/facility characteristics as well as days of psychiatric hospitalisation during the period considered using multivariate regression analysis. This study had a 'strong' global rating on the adapted QATQS because it was considered to be devoid of selection bias since it included all the eligible patients during the study period. Its study design was appropriate in addressing its research question and it controlled for confounders. It therefore had no weak rating in any of the components on the adapted QATQS.

The study by Walkup et al. (2000) was also conducted in the USA and assessed whether the dose of antipsychotics (oral and depot preparations) prescribed for inpatients with schizophrenia or schizoaffective disorder recruited from four general hospitals conformed to the PORT recommendations. In particular, this study assessed the antipsychotic dose prescribed for 293 patients at discharge. Over a third of these patients had a comorbid SUDs (in particular, substance abuse). Diagnoses of schizophrenia and schizoaffective disorder were confirmed using the Structured Clinical Interview for DSM-III-R or DSM-IV. Diagnosis of substance abuse was based on the Mini-International Neuropsychiatric Interview (MINI). In addition, this study required that there should be at least one indication that staff were aware of patient's substance abuse either through report of this by the primary therapist or documentation in the patient's record. This study assessed whether antipsychotic prescriptions were excessive at discharge. Excessive antipsychotic dosage was defined as dosing that exceeded the 1000mg/day recommended in the PORT guidelines. There was no significant difference in likelihood of excess discharge doses between patients with and without comorbid SUDs (17.6% vs 22.7%;  $p = 0.17$ ).

This study adjusted for patient characteristics such as age, length of stay in hospital, voluntary admission and comorbidities using logistic regression analysis. This study had a 'weak' global rating for selection bias on the adapted QATQS because the number and characteristics of eligible patients were not clearly stated. It also had a weak rating on the withdrawal/drop out component on the adapted QATQS because it did not state the number of patients that completed the study.

The study by Weinmann, Janssen and Gaebel (2005) assessed adherence to an expert panel recommendation concerning antipsychotics among inpatients with psychotic disorders

recruited from three different hospitals in Germany. The study assessed 508 patients aged between 18 and 65 years with a primary psychotic disorder according to ICD-10 between October 2000 and May 2002 at the time of hospital admission. Seventy eight percent (78%, 394) had a diagnosis of schizophrenia while 17% had a comorbid substance abuse or dependence diagnosis. How substance abuse and dependence were diagnosed was not stated. Illness severity, psychopathology symptoms, social functioning and side effects were assessed using validated instruments. After reviewing the literature for available guidelines and considering three prominent guidelines (the PORT recommendations, the APA guidelines and the guidelines of the German Society of Psychiatry, Psychotherapy and Nervous Disease), an expert panel decided on quality criteria against which patients' medications were assessed. Five measures of quality were chosen by the panel:

1. For a first psychotic episode, second generation antipsychotic (hereafter SGA) monotherapy should be prescribed at discharge
2. Antipsychotic dosage at discharge should not exceed 1000 chlorpromazine equivalents
3. Patients with severe persistent psychotic symptoms which are unchanged for more than three weeks should have a significant change of antipsychotic dosage or a switch to a different antipsychotic within three weeks
4. Patients with severe depressive symptoms for at least two weeks should receive an antidepressant medication or a change of antipsychotic medication (switch to SGA)
5. Dosage of antipsychotic should be reduced if there is severe akathisia, parkinsonian side effects, tardive dyskinesia or a different antipsychotic monotherapy should be used within 3 weeks, or medication prescribed for the side effect should be changed or clozapine or another SGA should be prescribed.

The main outcome was defined as guideline adherence without patient factors contributing. Patient factors that were considered include poor compliance which was assessed using a compliance scale consisting of 7-items, drop-out from study or escape from hospital. There was no significant difference in the likelihood of receiving medication care outside guideline recommendation between those with and without co-existing SUDs (OR = 0.80, 95% CI: 0.40 - 1.79).

This study controlled for factors such as gender, episode of treatment, number of previous hospital stays, social functioning, severity of psychotic and depressive symptoms using

logistic regression. This study had a ‘strong’ global rating on the adapted QATQS because it had no ‘weak’ rating in any of its components. Selection bias was considered to be absent because over 80% of those screened provided consent. Its study design was appropriate in addressing its research questions as it controlled for confounders and also described its data collection methods. It was given a moderate rating in one of the components on the adapted QATQS (withdrawals and drop-outs) because some patients did not complete the study.

The study by Clark et al. (2004) was conducted in the USA and assessed adherence to the APA guideline on benzodiazepine prescribing among New Hampshire Medicaid beneficiaries with psychiatric disorders between January 1995 and December 1999. The APA panel on benzodiazepine recommends the following:

1. Persons with SUDs should receive lower-risk benzodiazepines rather than those with high abuse potential such as alprazolam, estazolam and triazolam.
2. Persons with SUDs should be prescribed benzodiazepines for short duration (less than four months) due to the risk of dependence.

All Medicaid<sup>10</sup> claims for people aged 18 to 64 years were examined and those with psychiatric disorders among these patients were identified retrospectively. For people who had both Medicaid and Medicare<sup>11</sup> eligibility, psychiatric disorders and comorbid SUDs were also identified from their Medicare data. The following primary psychiatric diagnoses using ICD-9 were examined: schizophrenia, bipolar disorder and major depression. Other psychiatric disorders were grouped into a single category. People with a diagnosis of substance abuse or dependence (except tobacco) or who were treated for SUDs were defined as those with SUDs.

There were 9,589 patients who were participants in this study. Of 1552 schizophrenic patients, 614 (39.6%) had a SUD while 228 (46.4%) of 491 bipolar patients, 1195 (31.8%) of 3757 patients with major depression and 1496 (39.5%) of 3789 patients with other psychiatric disorders had SUDs as defined by the study criteria. Those with SUDs

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10 Medicaid is a health services program for people and families with low incomes in America. Centers for Medicare & Medicaid Services. (2013). *Medicaid* [Online]. <http://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Eligibility/Eligibility.html>. [Accessed 10 January 2014].

11 Medicare is a Federal health insurance program that pays for medical care for the elderly and certain disabled Americans. Centres for Medicare and Medicaid Services. (2013). *Medicare program - General information* [Online]. <http://www.cms.gov/Medicare/Medicare-General-Information/MedicareGenInfo/index.html>. [Accessed 10 January 2014].

comorbid with bipolar disorder, major depression or other psychiatric disorders were significantly more likely to be prescribed benzodiazepines for four or more months ( $p < 0.0001$ ). However, patients with co-occurring schizophrenia and SUDs were significantly less likely to be prescribed benzodiazepines ( $P < 0.0001$ ). Furthermore, those with major depression co-existing with SUDs or other psychiatric disorders co-existing with SUDs were significantly more likely to be prescribed fast acting/high potency benzodiazepines than those without SUDs (25.2% vs 14.6%,  $p < 0.0001$  and 18.2% vs 13.5%,  $p = 0.05$  respectively). There was no significant difference between patients with bipolar disorder co-existing with and without SUDs and schizophrenia co-existing with and without SUDs on the prescribing of fast acting/high potency benzodiazepines (18.5% vs 13.5%,  $p = 0.22$  and 5.3% vs 4.3%,  $p = 0.49$ , respectively). This study had a 'moderate' global rating because it had one 'weak' rating. It did not take other factors (such as comorbidities and severity of illness) that could account for longer duration of prescribing into consideration.

In summary, all the studies that used guidelines as a measure of prescribing of psychiatric medicines assessed the appropriateness of only one class of psychiatric medications. An American study of good quality by Leslie and Rosenheck (2001) found that oral antipsychotics prescribed in outpatient settings for people with co-existing schizophrenia and SUDs in the VA tended to comply with guideline recommendations though there were also instances of dosing of people with SUDs below guideline recommendations. This study recommended that there should be further research to explore the reasons for prescribing by physicians.

Another American study of poor quality by Walkup et al. (2000) found that among inpatients with schizophrenia or schizoaffective disorders from four general hospitals those with SUD comorbidity were unlikely to be prescribed antipsychotics outside guideline recommendations when compared to those without SUD comorbidity. A study of good quality carried out among inpatients with psychotic disorders recruited from three different psychiatric hospitals in Germany found that patients with SUD comorbidity were unlikely to receive medication care outside of current guideline recommendation compared to those without comorbidity. These two studies suggest that the appropriateness of antipsychotic prescribing in these settings is comparable between psychotic patients with and without SUD comorbidity.

Another American study of moderate quality found that adherence to the APA guidelines on benzodiazepine prescribing varied depending on patients' comorbid psychiatric disorders. For conditions such as comorbid SUDs and bipolar disorder, major depression or other psychiatric disorders, benzodiazepines were prescribed for longer than recommended. This may reflect a tendency for people with these comorbid conditions to exhibit anxiety, insomnia or other conditions for which benzodiazepines may be used over a period of time. It may also imply that patients are not being regularly reviewed since benzodiazepines are usually recommended for short-term use due to their dependence potential (American Psychiatric Association, 1990; Joint Formulary Committee, 2010). The effectiveness of benzodiazepines diminishes with prolonged use (Vinkers and Olivier, 2012).

### **Guideline adherence as a measure of opioid prescribing appropriateness**

Two studies (Morasco et al., 2011; Morrison et al., 1994) assessed guideline adherence in opioid prescribing. Morrison et al. (1994) assessed adherence to published guidelines for opioid prescribing among HIV patients while Morasco, Duckart and Dobscha (2011) assessed adherence to guidelines for the use of chronic opioid therapy.

Morrison et al. (1994) conducted their study in USA and assessed the appropriateness of prescribing by looking at indication. Indication has been defined by Hanlon et al. (1992) as the sign, symptom, disease or condition for which the medication is prescribed. This study was a retrospective cohort study that reviewed the appropriateness of opioid prescribing (mostly codeine or oxycodone-containing formulations) for patients in an ambulatory HIV clinic located in a public teaching hospital. The study sample were patients with HIV of which some had a history of intravenous drug use. The records of 220 patients out of which 190 were HIV positive were reviewed between 1986 and 1989. The patients' medication lists and physician notes for each visit were used for assessing opioid prescribing. This study used the guideline for the management of pain in cancer patients in an outpatient setting as the standard against which opioid prescribing was compared because of the lack of guidelines for the use of opioids in HIV patients.

Inappropriate opioid prescribing was considered to be prescribing for conditions for which the guideline stated that they were not efficacious such as muscle spasm, bone pain and vascular headache. Prescribing was also considered inappropriate if a clear indication was not documented or a prescription was refilled without it being for an appropriate

indication. The following were the percentages of various risk factors for HIV among the 190 HIV patients: 57% were homosexual/bisexual, 11% were IDUs, 18% were both homosexual/bisexual and IDUs, 7% were heterosexual and 8% fell into 'other' category. IDUs were more likely to be prescribed opioids inappropriately than heterosexual men or women ( $p = 0.013$ ) or homosexual men ( $p < 0.001$ ). Of 53 opioid prescriptions for IDUs, 48 (90.6%) of them were considered inappropriate.

The authors suggested that patients who had abused drugs previously such as the IDUs may have requested unnecessary opioid medications. It was not known to what extent prescribers thought these medications were inappropriate. Further, the guideline used was not specific to HIV but cancer and the management of these conditions differ. Thus, it may not be best practice to use a guideline for cancer to assess HIV. This study concluded that physicians should prescribe opioids appropriately and future studies should incorporate patients' views. This study had a 'moderate' global rating because it had one 'weak' rating in the confounder component of the adapted QATQS. It did not control for potential confounders such as a diagnosis of cancer.

Morasco, Duckart and Dobscha (2011) carried out a retrospective cohort study that assessed opioid guideline adherence in the management of chronic non-cancer pain (hereafter CNCP) in patients with and without SUDs. This study included veterans with CNCP receiving opioid treatment within a Veterans Affairs regional healthcare network in the Pacific Northwest (Washington, Oregon, Idaho and Alaska) in 2008. Administrative data concerning these veterans were collected from the Veterans Integrated Service Network (VISN)-20 Data Warehouse which contains data from the main clinical software packages of the national VA databases. CNCP was identified from the electronic medical record pain Numeric Rating Scores (NRS) that is routinely administered during ambulatory visit. Pain intensity was rated on a scale of 0 to 10 with 0 being no pain and 10 being worst pain imaginable. CNCP was assessed by the presence of pain scores of  $\geq 4$  on the NRS in three or more different months.

A total of 5,814 patients who had an opioid prescription for 90 or more days were included in this study. Some patients such as those with cancer diagnosis were excluded. SUDs considered in this study include all AUDs, prescription DUDs and illicit SUDs. This includes patients whose SUDs were in remission. All diagnoses were based on the ICD, clinical modification-9<sup>th</sup> revision. Opioid prescriptions were converted to their morphine

equivalents. The guideline published by Chou and colleagues (Chou et al., 2009) was used as the standard and recommends that long-acting rather than short-acting opioids should be prescribed to patients with SUDs due to their lower abuse potential. It also recommends that patients with CNCP should be prescribed antidepressants if they have major depression or dysthymia because treatment of these conditions is associated with improvement in pain.

Almost one-fifth (19.5%) of patients had a SUD diagnosis. Those with SUDs had a higher pain score than those without SUDs (6.7 (SD = 1.3) vs 6.6 (SD = 1.3),  $p < 0.001$ ). Those with SUDs did not differ from those without SUDs in receipt of short-acting (85.7% vs 87.8%) or long acting opioids (26.9% vs 26.0%). Patients with SUDs were more likely to receive concurrent antidepressant prescriptions (73% vs 61.7%). However, on controlling for age, VA facility, gender, major depression diagnosis and pain intensity using generalized estimating equations, no difference was observed between patients with SUDs and those without SUDs in the likelihood of receiving antidepressants or long-acting opioids. This study therefore found that among veterans with CNCP receiving opioid treatment within a Veterans Affairs regional healthcare network in the Pacific Northwest, there was no difference in opioid guideline adherence between those with and without SUDs. This study had a 'strong' global rating on the adapted quality assessment tool because it included all eligible patients and therefore was not biased in patient selection. Moreover, it controlled for potential confounders and had no 'weak' rating in any of the components on the adapted quality assessment tool.

#### **2.6.4.2. SPC as a measure of benzodiazepine prescribing appropriateness**

Only one study by Thirion et al. (2002) used the SPC as a measure of prescribing appropriateness. Thirion et al. (2002) assessed whether the doses of benzodiazepines prescribed for buprenorphine-maintained opiate-dependent patients in France were within the standards specified in the summary of product characteristics<sup>12</sup> (SPC) of benzodiazepines. Benzodiazepines and buprenorphine were issued in a variety of outpatient settings: GPs, care centres and specialists. The benzodiazepines assessed in this study were alprazolam, bromazepam, clorazepate, diazepam and flunitrazepam. This study did not however state the reasons for benzodiazepine prescribing. Forty-three percent (43%) of patients (total = 2078) were prescribed benzodiazepines with the most frequently prescribed being flunitrazepam (584, 28.1%) followed by bromazepam (373, 17.9%) and

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<sup>12</sup> A Summary of Product Characteristics (SPC) contains information on how to use a particular medication safely and effectively.

clorazepate (166, 8%). The daily doses of prescribed benzodiazepines were reported to be often above that specified in the SPC for benzodiazepines. However, the percentage of prescriptions in which this occurred was not stated. This study had a ‘moderate’ global rating because it had one ‘weak’ rating in the confounder component of the adapted QATQS. There was no comparison of those prescribed excessive benzodiazepine doses with those who were not prescribed to determine if there were any obvious differences that may account for this prescribing.

In summary, the study that examined benzodiazepines found that in a variety of outpatient settings in France, benzodiazepine doses among buprenorphine-maintained opiate-dependent patients were higher than recommended by guidelines. This result may reflect excessive benzodiazepine prescribing and a tendency for its abuse in this population. A previous study has reported benzodiazepine abuse among buprenorphine-maintained opiate-dependent patients (Lavie et al., 2009).

#### **2.6.4.3. ATHF as a measure of antidepressant prescribing appropriateness**

The study by Baca-Garcia et al. (2009) was conducted in the USA and compared the appropriateness of antidepressants prescribed for 39 depressed bipolar patients with a history of AUDs with those of 58 depressed bipolar patients without AUD history. A computer algorithm that is based on the Antidepressant Treatment History Form (hereafter ATHF) was used to assess antidepressant medications issued by the patients’ psychiatrist in the three months before patients were recruited into the study. The ATHF rates antidepressant treatment based on indication, dose, treatment duration and patient adherence (Oquendo et al., 2003). The ATHF assigns a score of 0 to 5. A rating of 0 indicates that no psychopharmacologic treatment was prescribed while 1 or 2 indicates inadequate treatment. Treatment receives a rating of 1 if the medication dose is less than 50% of an adequate dose. A rating of 3 or greater indicates adequacy of treatment. Scores of 1 or 2 were considered inadequate treatment whereas 3 and above were adequate treatment.

Participants were recruited via advertising/referrals and participated in mood disorders research in a hospital setting. No information was provided concerning where adverts were placed and how referrals were carried out. Diagnoses of current bipolar major depressive episode and AUDs were assessed using the Structured Clinical Interview (SCID) for DSM-III-R or DSM-IV. Symptoms of depression, mania, aggression, hostility as well as suicide history were assessed using validated instruments. Of 39 participants with a history of

AUDs, 27 patients were diagnosed with alcohol dependence (with 4 patients having current alcohol dependence, 6 patients in partial remission, 17 patients in full remission) whilst 12 (30.8%) patients had alcohol abuse (4 with current alcohol abuse and 8 in full remission).

The results showed that bipolar patients with AUDs had a higher proportion of inadequate antidepressant treatment (ATHF ratings of 1 and 2) than those without AUDs (74.3% vs 67.3%,  $p = 0.03$ ). The proportion of intensive treatment with antidepressants determined via ATHF ratings of 4 and 5 was higher in those without AUDs compared with patients with AUDs (15.5 vs 2.6%). The statistical significance was however not stated. This study had a 'weak' global rating on the adapted QATQS because it had weak ratings in each of the following: selection bias and confounders. Recruitment through advertising and referrals may result in self-selection. Consequently, those recruited may differ in notable ways from those who were not recruited (Levin, 2006). Furthermore, the study did not control for confounders such as comorbidities.

A study of poor quality found that among depressed bipolar patients prescribed antidepressants by psychiatrists in a hospital setting in America, those with AUDs were more likely to have inadequate antidepressant treatment. Given the high proportion of inadequate treatment in both groups of patients, the authors proposed that inadequate prescribing may be more related to physician factors than patient characteristics, as some psychiatrists may be reluctant to prescribe antidepressants due to the potential for antidepressant-induced mania. They also proposed that alcohol use may be a contributing factor to inadequate antidepressant treatment due to the fact that stigma associated with alcohol could lead to differential treatment of those with and without AUDs. Stigmatising attitudes towards people with SUD have been found to be common among health professionals (Lloyd, 2010).

## **2.7. Strengths and weaknesses**

This scoping review explored the range and extent of available evidence on the appropriateness of prescribing of opioids for chronic pain relief and psychiatric medications for people with SUDs. It is the first review in this area and found a paucity of evidence. Furthermore, none of the studies were carried out in a substance misuse setting. There is therefore a paucity of information on the appropriateness of prescribing of opioids for chronic pain relief and psychiatric medications for people with SUDs in a substance

misuse setting. The studies in this review were of mixed quality, with over half of them assessing adherence to a range of different guidelines. Studies that assess guideline adherence have been criticised because guidelines are usually specific to particular diseases or drugs (Cantrill et al., 1998; Tinetti, Bogardus and Agostini, 2004). Clinical guidelines do not usually take all co-existing conditions/diseases of the patient into consideration (Cantrill et al., 1998; Duerden, Avery and Payne, 2013). They assess disease management and not patient management (Shaneyfelt and Centor, 2009). This limitation was obvious in most of the studies included in this review because they could only assess the appropriateness of particular medications for specific conditions without taking into consideration the patients' comorbidities and medications for them as well as their preferences.

Comorbidities and co-prescribed medications may affect the effectiveness, dose and duration of other prescribed medications (Joint Formulary Committee, 2010). Interactions between substances and medications or between medications may further affect prescribing decisions. In addition, patient preferences play a role in decision-making when prescribing medications and should be considered when assessing appropriateness (Barber et al., 2005). As discussed in section 1.4.2, the development of tolerance to medications such as opioids and benzodiazepines may necessitate prescribing of higher doses of these medications (Gershwin and Hamilton, 1998; Willems et al., 2013). Consequently, sound judgment on the appropriateness of prescribing cannot be disconnected from the overall context of prescribing. If the context is not taken into consideration, medications may be erroneously identified to be inappropriate. This is particularly apposite among people with co-existing mental disorders or chronic pain and SUDs because their often complex health situation may necessitate deviation from guidelines in order for the best possible care to be provided (Hughes, 2011).

Studies in this review were based on individual hospitals or included outpatients in particular settings. The diverse nature of the study settings and population may also account for variation in prescribing. For instance, patients who are more complex in terms of the severity of their illness and comorbidities may more likely be treated in hospitals (Verdoux et al., 1996). This may necessitate the adjustment of medications above or below those recommended in guidelines. Such prescribing may be appropriate for these patients. However, the studies included in this review did not assess whether deviation from guidelines were appropriate for patients. On the other hand, it is possible that some

situations in which guidelines were adhered to may have been clinically inappropriate for patients based on their complex health situations. Strict adherence to guidelines may inadvertently promote inappropriate prescribing. There is therefore the need for the use of measures that allow for clinical judgment (including eliciting patient's preferences) when assessing prescribing appropriateness. An example of such measure is the MAI which allows for the use of clinical judgment with explicit instructions in rating prescribing appropriateness.

A number of studies in this review assessed single guideline areas such as dose or indication while those that assessed more than one area considered a limited number of areas. Therefore, the results of the studies in this review do not provide a holistic picture concerning all areas of prescribing appropriateness that are considered important by healthcare professionals such as indication, effectiveness, dose, drug-interactions, duration, duplication and cost (Samsa et al., 1994). More research is therefore needed to investigate multiple areas relating to prescribing appropriateness among people with SUDs in a substance misuse setting. In addition, most of the studies were conducted in the US where provision of healthcare is largely dependent on the patients' ability to pay or insurance coverage. The findings of this review cannot therefore be generalised to the UK where the healthcare system is free at the point of delivery.

It is possible that this review may have missed out relevant papers due to its focus on studies published in English and the limited number of databases searched. Some of the review studies were also limited because they did not control for confounding factors that could have influenced their outcomes. In addition, it was not possible to assess reasons for non-adherence to guidelines from prescribers' perspective due to the retrospective design of most of the studies. The perspectives of patients on the appropriateness of their medications were also not included in any of the studies despite the influence of these perspectives on the actual use of medications (adherence). Focusing only on quantitative studies further made it impossible to explore appropriateness from the perspectives of patients and prescribers. Qualitative studies are useful for exploring and describing participant's understanding and interpretation of phenomena (Ritchie, 2003). Patient and prescriber perspectives are important areas to further explore in order to provide a holistic view of appropriateness.

Chapter 5 of this thesis describes a research study which seeks to address these gaps by assessing multiple areas of prescribing appropriateness among patients with SUDs attending an outpatient addiction service. Chapters 6 and 7 also describe research studies that assess the perspectives of patients and prescribers concerning prescribing appropriateness respectively, using qualitative interview methods.

## **2.8. Summary**

Overall, these studies together suggest that there are frequently variations in prescribing of opioids for chronic pain relief and psychiatric medications across people with and without SUDs in particular contexts and settings. None of them incorporated the views of prescribers or patients concerning the appropriateness of these medications though these were suggested as areas to further explore. All the studies were undertaken outside the UK and their findings are therefore not generalizable to the UK setting. The studies were of mixed quality and over half assessed guideline adherence. Furthermore, while some of the studies assessed single areas relating to appropriateness others assessed a limited number of areas. None of the studies assessed appropriateness in a substance misuse setting. There is therefore a gap in the literature on the appropriateness of prescribing of opioids for chronic pain and psychiatric medications for substance users attending a substance misuse setting. In particular, this review highlights the need for studies assessing multiple areas of appropriateness of opioids and psychiatric medications among people with SUDs in this setting.

# Chapter 3: An overview of aims, methodology and methods

Following on from the scoping review, the aims of this thesis were two-fold. These aims and the research questions addressing them are described below. For the purposes of this thesis, patients attending the SAS will be termed ‘service users’.

## **3.1. Thesis aims**

Aim 1:

To investigate the level and nature of appropriateness of current prescribed medications for service users in a SAS.

Research questions addressing Aim 1:

1. What types and quantities of prescribed medications are taken by service users?
2. What is the level and nature of inappropriate prescribing?
3. How do service users with inappropriate medications differ from those who do not have such medications?
4. Does the appropriateness of prescribed medications change over the course of service users’ treatment?
5. How do service users perceive the appropriateness of their prescribed medications, changes to them and its impact on their quality of life?
6. To what extent do service users adhere to their medications and is this influenced by their perceptions on appropriateness?
7. What are the potential cost savings that could result from stopping or reducing the use of inappropriate medications?

Aim 2:

To explore prescribers’ responses to inappropriate prescribing in a SAS.

Research questions addressing Aim 2:

1. How do prescribers at the SAS assess the appropriateness of prescribed medications and how are changes made?
2. What factors are considered before initiating changes to service users’ medications?
3. How has the MAI impacted prescribers’ practices?

The SAS prescribers were interviewed rather than the original prescribers of service users' medications. It would have been difficult to trace the original prescribers and this was thought to be beyond the resources of this thesis. Moreover, this thesis is firmly focused on the assessment of prescribing appropriateness in a SAS, in which the evidence (Delgadillo et al., 2012; Marsden et al., 2000; Weaver et al., 2003) suggests there will be large proportions of service users with comorbid conditions. They therefore represent a particularly apposite group for exploring questions of prescribing appropriateness. The medications whose appropriateness were assessed include psychiatric medications and opioids<sup>13</sup>. The absence of these medications without justification (medication omission) was also considered to be inappropriate.

### **3.2. Specialist Addiction Service (SAS) setting**

The setting where this research was carried out is a statutory NHS specialist service that provides tier 3 level interventions to adults who misuse alcohol and/or drugs. However, almost 80% of service users attending the SAS are people who misuse alcohol (Oluyase et al., 2013). The SAS is located in Leeds, a city of West Yorkshire, with a population of 751,500 of whom 81% are white British (as of 27 March 2011) (Office of National Statistics, 2012). The SAS is part of the Leeds and York Partnership NHS Foundation Trust, a Trust that provides specialist mental health and learning disability services to people in Yorkshire. At present, the SAS no longer exists in its original form. The clinical service of the SAS has now been joined with four other services in Leeds under the banner of Forward Leeds.

Tier 3 interventions generally involve the provision of care-planned interventions following a comprehensive assessment (National Treatment Agency for Substance Misuse, 2006b). It involves community-based assessment, care planning and review, provision of evidence-based interventions (detoxification, maintenance and psychosocial interventions) including addressing of co-existing conditions such as depression and anxiety as well as liaison services for acute medical (including pregnancy), psychiatric and social care (National Treatment Agency for Substance Misuse, 2006a).

Service users coming to the SAS may self-refer or they could be referred from other sources such as general practitioners (GPs), psychiatrists, hospital, social services, drug

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<sup>13</sup>Although this thesis is concerned with opioids for chronic pain relief, SAS consultants suggested that opioids prescribed as substitutes for those with opioid use disorders should be included among medications assessed. Consequently, the appropriateness of opioids prescribed for chronic pain and substitute opioids were assessed.

services as well as the criminal justice system. Some information is usually collected about newly referred service users (such as their demographic information, health problems and medications) and included on the referral form. All newly referred service users are usually required to book an appointment before their first assessment. They are then sent a self-completion booklet to complete before their first or baseline assessment. Those who come to the clinic without their booklets are given a new copy to complete before they are assessed.

Evidence obtained from a senior SAS staff suggested that new referrals to the SAS are all screened by a nurse on the basis of their referral information in order to get more information if needed or reject the referral. If the referral is accepted, the nurse further determines which of the three teams the person should be allocated to and whether the person should be seen by a doctor. Allocation to a doctor was said to be based on complexity and in particular any prescribing issues while allocation to nurse prescribers and other therapists was decided by the SAS team organising the clinic. Evidence from this study (section 5.9.6) and that obtained by the researcher suggests the allocation system was not often implemented in practice. The researcher observed that receptionists tended to allocate service users to doctors, nurse prescribers and other therapists in all the three SAS teams on their clinic days.

The three teams are the pregnancy and parenting team, the hospital team and the dual diagnosis team. Whilst the pregnancy and parenting team manages service users who are pregnant or those with child care issues, the hospital team manages those identified and referred by hospital in-reach workers and the dual diagnosis team manages those with co-existing mental disorders and SUDs. Each team has its own clinic day in which newly referred service users are assessed. The keyworker (nurse prescriber, doctor or other therapists) carries out the baseline assessment which involves a 45- to 60- minute comprehensive assessment of the service user. Keyworkers, including prescribers, are expected to complete booklets relating to their assessment of the service user after the consultation and also fill in a care plan. They are expected to provide a summary of their assessment to the secretaries of the different teams to be typed for documentation in the service user's folder. Keyworkers may also need to attend to existing service users with whom they have scheduled appointments. Consequently, the clinic is usually busy for keyworkers. The same keyworker is often responsible for the follow-up of service users throughout their treatment at the SAS.

### 3.3. Consultation process with psychiatrists

This consultation was carried out to determine the views of the SAS consultant psychiatrists (there were three psychiatrists at the SAS) on the classes of medications that are likely to be inappropriately prescribed for people with SUDs. Information obtained from this consultation was intended to guide the selection of medications whose appropriateness will be assessed by SAS prescribers in the medication appropriateness study. Only consultant psychiatrists were involved in this process because they were the only group of doctors working at the SAS during this period. Although, there were nurse prescribers at the SAS, they were not involved because of the narrower area in which they prescribe.

All the different classes of prescribed medications which were being taken by service users in the secondary data analysis (study 1) were included in a questionnaire which was sent via email to the three consultant psychiatrists. The questionnaire asked *“how often do you think these medications are inappropriately prescribed for service users with SUDs?”* and provided four potential responses: frequently, sometimes, rarely and never. The questionnaire is shown in appendix 3.1. They were asked to complete the questionnaire and a meeting was organised to discuss their responses.

At the meeting, the consultants brought the questionnaire along and discussed the reasons for their responses to each class of medication. By the end of the meeting, there was agreement on seven classes of medications that they thought may be inappropriately prescribed for service users with SUDs, namely: opioids (including those prescribed as opioid substitution therapy), antidepressants, antipsychotics, anticonvulsants, drugs used in substance dependence (disulfiram, acamprosate, bupropion, varenicline, lofexidine and baclofen), antimanic agents and anxiolytics/hypnotics. Although this thesis is concerned with opioids for pain relief, the consultants suggested that opioids prescribed as substitution therapy for those with OUDs should be included. Consequently, the appropriateness of opioids prescribed for chronic pain and substitute opioids<sup>14</sup> were assessed in the medication appropriateness study. There were three classes of medications on which there was no agreement among the consultants, namely, antihypertensives (beta-blockers prescribed for anxiety disorders or during alcohol detoxification were included under anxiolytics), proton pump inhibitors and drugs used in asthma and COPD management. The consultants agreed on the exclusion of all the other classes of

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<sup>14</sup> Only two service users were on opioids prescribed as substitution therapy in the medication appropriateness study.

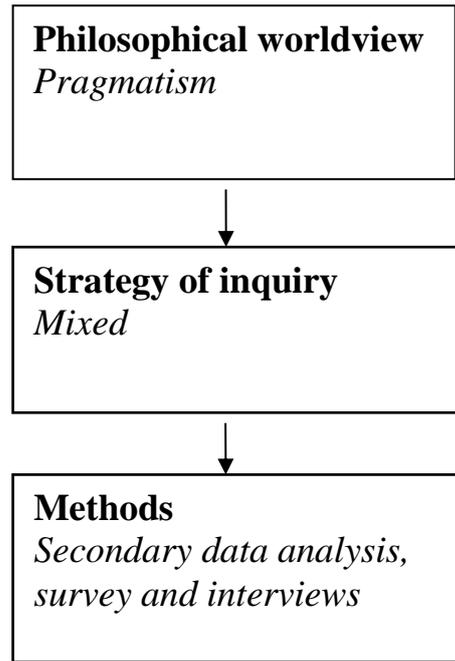
medications. Another meeting was subsequently scheduled where a final decision was taken on the medications on which there was no agreement.

Before the second meeting I sent a list including the medications on which there was agreement and those on which there was lack of agreement to the consultants for their consideration. Only two of the consultant psychiatrists were present at this second meeting. Antihypertensives (except beta-blockers prescribed for anxiety disorders or during alcohol detoxification), proton pump inhibitors and drugs used in asthma and COPD management were excluded at this meeting on the basis of lack of expertise to assess their appropriateness as they are not routinely prescribed in mental health/addiction settings. The consultant psychiatrists agreed on the seven classes of medications listed above and suggested that these medications should be considered for inclusion among those to be assessed in the medication appropriateness study.

### **3.4. Methodology**

The research methodology is important because it sets out the theoretical assumptions of the researcher and the work plan for research. Methodology has been defined as the “*science of studying how research is to be carried out*” (Rajasekar, Philominathan and Chinnathambi, 2013) and delineates the research design. According to Creswell (2009), there are three components of a research design: the philosophical worldview, strategies of inquiry and the research methods. The philosophical worldview encompasses the philosophical assumptions guiding research and it usually informs the strategies of inquiry that will be adopted. The methods refer to the techniques or procedures used for data collection and analysis and results from the strategies of inquiry chosen for research. The elements utilised in this thesis are shown in figure 3.1.

Figure 3.1: Thesis components



Adapted from Creswell (2009)

### 3.4.1. Philosophical worldview

The philosophical worldview for this thesis was pragmatism. Pragmatism became the logical worldview because it is typically associated with mixed methods research (Feilzer, 2010; Morgan, 2007; Tashakkori and Teddlie, 2003) due to its pluralistic nature (Creswell, 2009; Creswell and Plano Clark, 2011) and focus on “what works” (Patton, 1990). A pragmatic approach employs ‘what works’ in particular circumstances, with the research questions given prominence (Creswell et al., 2011; Morgan, 2007). Unlike other worldviews such as the positivist/empiricist or interpretivist/constructivist worldviews that have been associated with quantitative and qualitative methods respectively, pragmatism allows for the adoption of multiple methods. It allows for the use of pluralistic approaches to derive knowledge about the research problem (Creswell, 2009). This is pertinent in this thesis because it addresses a complex issue that demands exploration through multiple perspectives.

Pragmatism has been criticized because it does not provide a solution to philosophical disputes (Johnson and Onwuegbuzie, 2004). There have been arguments for and against mixing qualitative and quantitative methods due to their different philosophical foundations (Johnson and Onwuegbuzie, 2004; Morgan, 2007). Some authors have argued

that the philosophical foundations of quantitative (positivism/empiricism) and qualitative (interpretivism/constructivism) research are incompatible because of their different assumptions about the world and reality (Howe, 1988). Johnson and Onwuegbuzie (2004) have however argued that the aim of pragmatism is not to provide a solution to ancient disputes about different philosophical assumptions. Rather, pragmatism provides a means for the mixing of methods to address the research questions.

The pluralistic nature of pragmatism implies that multiple philosophical perspectives can be adopted for research. In particular, postpositivism and phenomenology were adopted in this thesis. The ontological and epistemological position of each method is considered below, ontology being concerned with the nature of the 'knowable' or the nature of reality (Guba, 1990), thus reflecting the researcher's 'beliefs about the nature of the social world and what can be known about it' (Bisman, 2010; Snape and Spencer, 2003). Epistemology is concerned with 'the nature of the relationship between the knower (the inquirer) and the known (or knowable)' (Guba, 1990).

#### **3.4.1.1. Postpositivism**

Postpositivism is a philosophical approach that attempts to address some of the limitations of positivism (Clark, 1998). The following are the premises upon which postpositivism is based.

##### **Ontological position**

Similar to positivism, reality is deemed to exist in postpositivism (Clark, 1998; Guba, 1990). However, unlike positivism, postpositivism holds that reality is only imperfectly apprehendable because it is impossible for reality to be perceived by imperfect human sensory and intellectual mechanisms (Guba, 1990). Consequently, postpositivism represents a shift from the 'naïve' realism position adopted in positivism to one of 'critical' realism (Guba, 1990). It is the belief in both positivism and postpositivism that science requires precision, logical reasoning and attention to evidence (Clark, 1998; Crossan, 2003). There is an emphasis on well-defined concepts or variables, controlled conditions or as close an approximation to it as possible, precise instrumentation and empirical testing (Guba and Lincoln, 1994).

##### **Epistemological position**

Unlike positivism that advocates objectivism such that the inquirer adopts a distant non-interactive posture with what is being inquired into, postpositivism advances a modified

form of objectivism since in reality objectivism cannot be truly attained (Guba, 1990). Reality is viewed by a subjective receiver and is therefore always someone's reality (Bisman, 2010; Racher and Robinson, 2003). Every part of research from identifying and operationalising the research question to data collection/analysis and report writing is influenced by the researcher. Objectivism however represents an ideal that could be achieved reasonably closely if the inquirer strives to be neutral as much as possible and also provides an account of their own predispositions and influences on that which is being inquired into (Guba, 1990). In postpositivism, claims about reality must be subjected to critical examination to facilitate apprehending it as closely as possible (Letourneau and Allen, 1999).

In this thesis, postpositivism influenced the researcher's adoption of quantitative methods of inquiry as seen in the secondary analysis of routinely collected data and medication appropriateness study. It also influenced my views on the role of the researcher and the researcher's beliefs on the research process (Clark, 1998). For instance, my background as a pharmacist has influenced aspects of the research process such as choices made in research planning and data collection/analysis. The influence of the researcher on the research process is described in section 3.5.

#### **3.4.1.2. Phenomenology**

##### Ontological position

Phenomenology is based on the assumption that reality is multiple and socially constructed through the interaction of individuals with others and the world, with individuals assigning meaning to their perceptions and experience (Guba, 1990; Racher and Robinson, 2003). Phenomenology adopts a 'relativist' ontology because there are many possible interpretations of phenomena with no foundational process by which truth or its falsity can be determined (Guba, 1990). Social facts are characterised and recognised by their meanings to individuals (Bowling, 2002). In phenomenology, the inquirer aims to discover these subjective or lived experiences of those being studied (Balls, 2009). It is the belief in phenomenology that the most interesting questions are not about the reality of the world but about peoples' interpretations of them (Green and Thorogood, 2004). Phenomenology considers how the subject relates to the experience, how he understands and also values the phenomenon (Kockelmans, 1987).

## Epistemological position

The epistemological stance of phenomenology is ‘subjectivity’ since this represents the only means of understanding the experiences of individuals (Guba, 1990). Reality is deemed to exist only in respondents’ minds and subjective interactions are the only means of discovering them. Due to its focus on drawing out individual experiences and perceptions, methods often employed in phenomenological research include interviews and observations (Lester, 1999). Just like postpositivism, it is the belief in phenomenology that the researcher and the inquiry are not detached, rather the researcher shapes the research process (Englander, 2012; Racher and Robinson, 2003).

Two approaches have been described in phenomenology namely descriptive phenomenology and interpretative phenomenology (Balls, 2009). Descriptive phenomenology is attributed to Edmund Husserl (Husserl, 1963) and seeks to describe rather than explain. It usually starts with a perspective free from preconceptions by the researcher (Lester, 1999). The researcher sheds all prior personal knowledge and preconceptions in order to engage with the lived experiences of research participants (Balls, 2009). This approach has however been criticised because it is impossible to put aside all preconceptions and knowledge, and approach what is being researched in a completely blank or neutral way (Koch, 1995; Lopez and Willis, 2004). This criticism led to the development of the interpretative phenomenology by Martin Heidegger (Creswell, 2009).

In interpretative phenomenology, it is believed that the researcher’s experience is utilised when developing research questions and shaping other peoples’ interpretations. Interpretative phenomenology was adopted in this thesis because of the view that the researcher is interpreting something in which she exists (Lopez and Willis, 2004). It is therefore impossible to have a blank or neutral standpoint (Koch, 1995). However, making preconceptions explicit and explaining how they are being used in the inquiry is part of interpretative phenomenology (Lopez and Willis, 2004). In keeping with the tenets of interpretative phenomenology, the researcher presented her own experiences, its influence on her research topic, questions and interpretation in section 3.5.

Interpretative phenomenology contributed to the exploration of service users and prescribers’ views on the appropriateness of prescribing in this thesis using an interview method. Service users are likely to construct their views on the appropriateness of

prescribing based on their experience of using their medicines. However, prescribers may assess prescribing appropriateness based on their medical training and through their experience of working with service users. It is therefore possible that how they view the appropriateness of prescribing may be different.

#### **3.4.1.3. Use of postpositivism and phenomenology in thesis**

This thesis involved the use of both postpositivism and phenomenological philosophical perspectives. The early postpositivist perspectives, focusing on the secondary data analysis and medication appropriateness study showed the limitations of these approaches for understanding a complex and multidimensional construct like 'appropriateness'. These approaches were limited because it was not possible to understand the meaning of appropriateness from the perspective of different participants. Taking a phenomenological approach in the latter part of the project allowed a better understanding of multiple perspectives and complex attributions about appropriateness.

#### **3.4.2. Strategy of inquiry**

The pragmatic approach embracing both postpositivist and phenomenological perspectives allowed a pluralistic mixed methods approach to be adopted. This section introduces mixed methods research (hereafter MMR), its use in this thesis, the particular design of MMR adopted and the integration of the different methods.

MMR has been defined as:

The type of research in which a researcher or team of researchers combine elements of qualitative and quantitative research approaches (e.g., use of qualitative and quantitative viewpoints, data collection, analysis, inference techniques) for the purposes of breadth and depth of understanding and corroboration (Johnson, Onwuegbuzie and Turner, 2007, p.123).

Johnson, Onwuegbuzie and Turner (2007) arrived at this definition after carrying out a survey of the views of experts on the definition of MMR. A total of 36 leading methodologists in MMR identified from Tashakkori's "Bridges Website" and from contributions in a special journal (*Research in the Schools*) issue on MMR were contacted and asked to respond via email. Tashakkori's Bridges Website<sup>15</sup> is a mixed methods

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<sup>15</sup>Available at <http://www.tashakkori.com/bridges.html>

network for the behavioural, social and health sciences. The above definition of MMR was reached after a cross-case analysis of the definitions provided by the experts. Although there have been arguments concerning mixing qualitative and quantitative methods as described in section 3.4.1, there are similarities that have been acknowledged between qualitative and quantitative research such as the commitment of both types of methods to the understanding of the world as well as a shared commitment to rigor and critique in the research process (Reichardt and Rallis, 1994). Casebeer and Verhoef (1997) have argued that qualitative and quantitative research are part of a continuum of research, and techniques should be selected based on the research question. MMR thus applies quantitative and qualitative research methods depending on the research questions.

MMR can be used for five broad purposes (Greene, Caracelli and Graham, 1989): triangulation, complementary, development, initiation and expansion purposes. Triangulation involves the comparison of the findings from one method against that of another method. In particular, different methods with offsetting or counteracting biases are used in investigating the same phenomenon in order to strengthen the validity of findings. Complementary purpose involves enhancing or clarifying the results from one method with another. Here, qualitative and quantitative methods are used to measure overlapping but also different facets of a phenomenon in order to produce an enriched understanding of that phenomenon. In development purpose, the result of one method informs the other method. Initiation purpose entails revealing contradictions in one method with another. Expansion on the other hand involves seeking breadth and depth of one method with another.

#### **3.4.2.1. Justification for MMR in thesis**

In this thesis, MMR was used for complementary, development and expansion purposes. The research aims argued for a mixed method strategy because the appropriateness of prescribing is a complex concept that cannot be adequately explored using only one method. The first quantitative method (secondary data analysis) provided a picture of the different classes of prescribed medications taken by service users. It assisted in understanding the scale of prescribing for service users and also informed the second study (questionnaire survey) as the medications assessed for appropriateness were selected from it.

The questionnaire survey allowed SAS prescribers to assess the level and nature of inappropriate prescribing among service users. The questionnaires used (in particular, the adapted-Medication Appropriateness Index and the Medication Omissions Questionnaire)

allowed both quantitative and qualitative data to be obtained from SAS prescribers about medication appropriateness. The qualitative data expanded on the quantitative data as it assisted in understanding the reasons for the ratings given by prescribers. Data from the questionnaire survey further informed some aspects of sampling in the service user interviews as interviewed service users were those found to be on prescribed opioids and/or psychiatric medications in the survey.

The interviews with SAS prescribers contributed to an understanding of the process of clinical decision-making that prescribers go through in order to assess the appropriateness of prescribed medications as well as how they responded to inappropriate prescribing. Service user interviews provided a means of understanding how service users perceive their prescribed medications and changes made to them. Both prescriber and service user interviews were therefore useful in exploring the complexity of decision-making without the simplification required for quantitative data collection, thereby providing a more complete picture. Finally, findings from the quantitative and qualitative methods were integrated for a more complete understanding of the topic.

#### **3.4.2.2. Design of MMR**

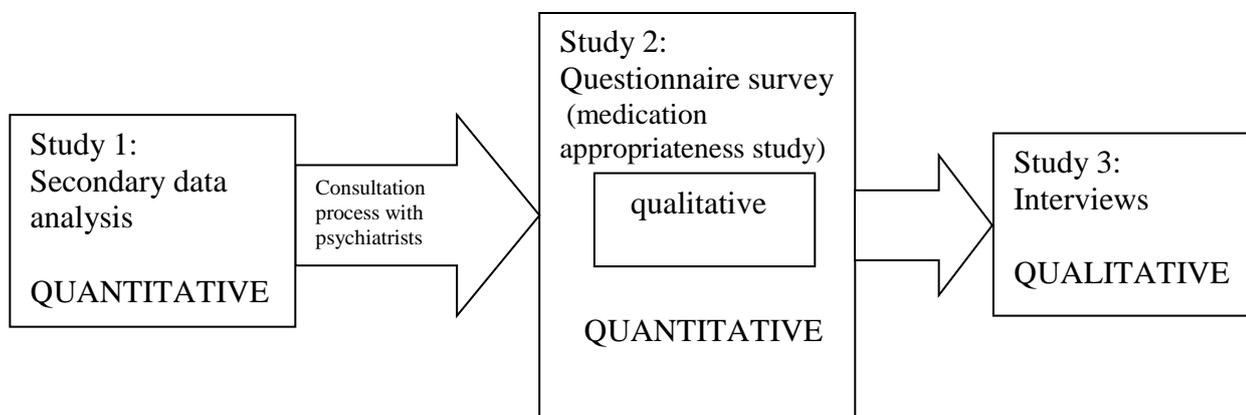
According to Creswell (2009), factors that can influence the design of MMR include timing, weighting and mixing. Timing is important because it determines whether the qualitative and quantitative methods will be sequential or concurrent. It is also possible to have a combination of sequential and concurrent timing (multiphase combination timing) over a program of study (Creswell and Plano Clark, 2011). The multiphase combination timing was used in this thesis.

Weighting considers whether priority will be given to one method or if both will be given equal weighting. The quantitative and qualitative methods were given equal weighting except in the questionnaire survey (medication appropriateness study) where the quantitative data in the adapted-Medication Appropriateness Index (hereafter A-MAI) and Medication Omissions Questionnaire (hereafter MOQ) were given priority because the qualitative data assisted in expanding on the reasons for ratings of appropriateness given by prescribers.

Mixing deals with when and how mixing of the different methods will take place. It can occur during any of the stages of research. Mixing of methods occurred in the medication

appropriateness study as well as during the interpretation of the research findings from the various methods. Figure 3.2 shows the MMR design for this thesis.

Figure 3.2: Mixed methods design



Adapted from Creswell (2009)

Note:

The consultation process with SAS consultant psychiatrists was used to inform the classes of medications whose appropriateness were later explored in study 2.

→ Indicates that data were collected sequentially.

Capitalisation in figure 3.2 indicates that weight is given to the quantitative data in study 2.

In the early stages of this study, the researcher considered the different methods that could be used in addressing the aims and research questions. She decided to use the following methods within a multiphase combination timing:

1. Study 1: Secondary data analysis involving investigation of routine clinical data. The total number of service users whose data were analysed was 1783;
2. Study 2: Questionnaire survey in the medication appropriateness study (use of the A-MAI and MOQ by SAS prescribers to assess the appropriateness of service users' medications and use of the Adherence Questionnaire (hereafter AQ) to assess service users' adherence). Sixty service users consented to participate in this study and were all assessed by SAS prescribers for the omission of opioids and/or psychiatric medications at their first SAS appointment using the MOQ. A total of 37 of these 60 service users were on prescribed opioids<sup>16</sup> and/or psychiatric medications and were assessed by SAS prescribers using the A-MAI. The 37

<sup>16</sup> Only two service users were prescribed opioids as substitution therapy, others were prescribed opioids for chronic pain.

service users were also administered the AQ. The total number of prescribed opioids and psychiatric medications taken by these 37 service users was 59.

Twenty-three of the 37 service users were available for follow-up data collection three months later and had their prescribed opioids and/or psychiatric medications assessed again at their three-month follow-up appointment by the same prescriber (except three service users) using the A-MAI. The total of prescribed opioids and/or psychiatric medications taken by these 23 service users was 33;

Study 3: Semi-structured interviews with service users and SAS prescribers. Fourteen service users were interviewed during their three-month follow-up appointment or at their next visit if this was not convenient. Interviewed service users were a sample of those whose prescribed opioids and psychiatric medications were assessed using the A-MAI at their first SAS visit. All but two SAS prescribers were interviewed either before they left the SAS if they were on short rotation or at the end of the medication appropriateness study if otherwise.

The secondary data analysis was first carried out. This was followed by a consultation process with SAS consultant psychiatrists to inform the classes of medications whose appropriateness was later explored using the A-MAI and MOQ in the medication appropriateness study. The consultation process has been described in section 3.3. The medication appropriateness study was the second to be carried out. In this study, the A-MAI and MOQ were used by prescribers to assess prescribing appropriateness. Both the A-MAI and MOQ were used to collect quantitative and qualitative data. However, the qualitative data in this context only comprised the reasons for the appropriateness ratings given by prescribers and consequently lacked sufficient depth (richness). In addition, the qualitative data were responses to closed questions and therefore did not allow exploration of prescribers' responses (O'Cathain and Thomas, 2004). Interviews were thus needed as a means for obtaining more detailed information and allowed probing of interviewees' responses (Adams et al., 2008). Interviews were the last to be carried out.

Semi-structured interviews rather than structured or unstructured interviews were employed for an in-depth understanding of the perspectives of service users on the appropriateness of prescribed medications and the responses of prescribers to inappropriate prescribing. It also provided the flexibility for issues relevant to respondents to be explored. Structured interviews, as the name implies, have a rigid set of questions and this

rigidity forecloses the exploration of important issues that may emerge during the interview that have not been pre-planned (Alshenqeeti, 2014; Berg, 2007). Unstructured interviews allow for the discussion of issues that emerge from the interview with the respondent charting the course of the interview through their response (Berg, 2007). This type of interview is very time-consuming and difficult to manage due to its lack of structure (Gill et al., 2008). Semi-structured interviews are somewhere in the middle between structured and unstructured interviews and allow for flexibility in exploration of issues not anticipated in the planning stage of research (Alshenqeeti, 2014; Berg, 2007).

It was necessary for the researcher to carry out the studies in this thesis as described in the temporal order above because the first study (secondary data analysis) not only provided an overview of prescribing in general, it gave the researcher the opportunity to know the SAS, understand how it works, how prescribers operate in this setting and subsequently plan for the other studies. Prior to this study, the researcher had no experience of working in a SAS. She was introduced to the SAS prescribing protocol, the booklets completed by service users, the roles of nurse prescribers and doctors, and she also had the opportunity to shadow prescribers during their consultations with a number of service users. Consequently, the secondary data analysis was an important starting point for subsequent studies. Starting with the interviews would have led to a loss of appreciation of the SAS setting and would have been challenging without the studies that preceded it.

#### **3.4.2.3. Integrating qualitative and quantitative results**

The linking of qualitative and quantitative results has been described as one of the most important steps in MMR (Teddlie and Tashakkori, 2009). However, many mixed methods studies have been criticized because they have failed in this respect (Bryman, 2007). Bryman (2007) has argued that the connection between qualitative and quantitative findings should always be explored in mixed designs for purposes of clarification or breadth and depth of understanding. Consequently, this section describes how the results of the quantitative and qualitative methods used in this thesis were linked.

The data obtained from the quantitative and qualitative methods were initially analysed separately because they addressed different research questions relating to appropriateness. In addition, sequential mixed studies such as the one carried out in this thesis are often analysed separately in order to support the follow-up actions (Creswell and Plano Clark, 2011). For example, the service users interviewed were those found to be taking prescribed

opioids and/or psychiatric medications in the A-MAI questionnaire survey. Thus, the A-MAI questionnaire survey informed some aspects of the service user interviews.

One strategy through which results can be integrated in MMR is the side-by-side comparison proposed by Creswell and Plano Clark (2011). Side-by-side comparison involves presenting the quantitative results and the qualitative findings together in a discussion or in a summary table so that they can be easily compared. This assists in highlighting areas where the results from each study agree (converge), are complementary or contradictory for a greater level of understanding (O'Cathain, Murphy and Nicholl, 2010). This approach was adopted in this thesis as the quantitative and qualitative studies were examined for the themes that cut across them whilst also highlighting themes that were unique to each study for a holistic picture. The results obtained from the secondary data analysis, questionnaire survey and the interviews were compared along five themes derived from these studies.

### **3.5. Reflexivity**

Reflexivity refers to sensitivity to the ways in which the researcher, their experience, beliefs and characteristics such as professional status may have shaped the research process (Mays and Pope, 2000). In qualitative research with a phenomenological perspective, reflexivity is important because the researcher is the primary instrument of data elicitation (Smith, 2004). This implies that it is important for researchers to evaluate how they have influenced research (Demi and Warren, 1995). Below the researcher presents a brief account of her characteristics, background and values, and how these might have influenced this thesis.

This research was carried out by A. O, a young female pharmacist. Prior to undertaking this Ph.D., she had gained a Bachelor's degree in Pharmacy (Nigeria) and a Master's degree in Clinical Pharmacy, International Practice and Policy (London). She practiced as a pharmacist for a year in Nigeria before studying for her Master's degree. Coming from a pharmacy background probably influenced some of the decisions she made while planning for this research. For instance, the researcher's pharmacy background made her initially more inclined to view mental disorders (including SUDs) as a brain disease and this accounted for her interest in pharmacological management. However, her engagement with service users, prescribers and the literature in the course of this research has broadened her view as she now considers mental disorders to be complex disorders with multi-level

mechanisms comprising social, psychological and behavioural factors as well (Deacon, 2013).

Furthermore, the researcher's pharmacy practice prior to starting her PhD programme had involved interaction with doctors as prescribers rather than nurses. This probably had some influence on her initial approach to nurse prescribers. For example, the consultation that informed the selection of medications she focused on in the medication appropriateness study comprised only doctors (in particular, consultant psychiatrists). Only consultant psychiatrists were involved in the consultation because they were the only group of doctors working at the SAS during this period. Although she interacted with some nurse prescribers about medications they prescribe prior to carrying out this research, having a consultation with them similar to that with doctors would have been helpful in understanding their collective perspective. This might have influenced the medications the researcher focused on in the medication appropriateness study.

The researcher developed an interest in SUDs during her undergraduate training and became particularly interested in prescribing for this group as a result of her own clinical experience while working in Nigeria. While writing up her Master's degree dissertation, she applied for the Collaboration for Leadership in Applied Health Research and Care (CLAHRC) funded studentship in research on the appropriateness of prescriptions given to people with SUDs. The inspiration for this research came from a NHS staff who raised the quality of prescribing for service users with SUDs as a potentially important issue which required investigation. The researcher subsequently commenced her Ph.D programme. Although she is not registered as a pharmacist in the UK, she gained some clinical experience through her hospital rotation during her Master's degree.

The researcher's professional background may have influenced her views about the appropriateness of medications such as its indication, side effects and drug interactions. For instance, due to her prior clinical experience, reading relevant literature and talking to a range of people, she had developed an assumption that people with SUDs may be more likely to be prescribed certain medications (for example, opioids) inappropriately. These assumptions may have influenced some aspects of this research such as the way in which data was collected and analysed. The researcher was aware of this and tried to remain open to the possibility that participants did not share this view. The researcher made effort to ensure that the questions she asked during the interviews were not leading. She also

ensured that she paid attention to competing explanations during analysis and these were reported when presenting results and discussing them. The involvement of her thesis advisory panel in the research process was also a means of ensuring an accurate representation of findings as much as possible.

In addition, it has been suggested that researchers should consider how they introduce themselves to participants since this may influence participant's views about them and the information they chose to disclose (Jack, 2008; Richards and Emslie, 2000; Schutz, 1994). For instance, Richard and Emslie (2000) found that disclosure of the professional role of the researcher to participants and participants' perceptions of that role influenced the type of information participants chose to share. For prescribing research, if the interviewer is a healthcare professional, the interviewee (for example, service users) may choose not to disclose actual information concerning their prescribed medications (for example, information concerning their adherence) for fear of being judged or having their medicines withdrawn. This may lead to the social desirability bias with service users providing the answers that they believe the researcher wants to hear (Ganster, Hennessey and Luthans, 1983). However, this possibility was off-set as service users were informed that any information shared with the researcher will not be disclosed to healthcare professionals at the SAS.

Further, in this study the researcher did not introduce herself as a pharmacist to service users but rather as a research student at the University of York. She only went further to disclose her professional identity if asked. Although no service user asked about the researcher's professional background, it is possible that some might have assumed she had a health background. This may have affected how they responded. In spite of this possibility, some service users disclosed that they were non-adherent to their medications.

Prior to conducting the interviews, the researcher was initially apprehensive about her planned interaction with service users. The researcher is a professional from a different cultural background to most service users and does not have a history of substance use. Furthermore, although she is knowledgeable about the clinical management of the comorbidities she focused on in this research, she does not have a history of being prescribed psychiatric medications for mental disorders or opioids for chronic pain. She was therefore concerned about what service users' perceptions of her would be, rapport building and how this might impact on the data she obtained from them. These

considerations made her ensure that she showed respect and empathy to service users. During the interviews the researcher ensured she listened carefully, avoided unnecessary interruptions except for purposes of clarification, and was sensitive to what participants said. It is the researcher's view that her pharmacy background and experience had given her good listening skills and a sense of empathy which she carried over into the interviewing process with participants. Contrary to her initial apprehension, she found that she was able to engage with most service users. Service users appeared at ease during the interviews though there were occasions when some of them said they could not remember information (this may be related to some form of cognitive impairment or reluctance to disclose information). The rapport she built with participants before the interviews was probably advantageous as some service users sometimes wondered aloud how she was able to get so much information from them at the end of the interview while others appreciated the opportunity to talk to someone. It is the researcher's opinion that these service users valued the opportunity to tell their stories because of the rapport she had built with them, as well as the attention and interest she showed. A study of people with a past history of SUDs reported that they sometimes described their experience of relating their stories as therapeutic (Grant, 2014).

There were however a few interviews that posed challenges for the researcher. In one of the challenging interviews, the service user's partner followed her into the interview room though the researcher had initially informed her that she would be conducting a one-on-one interview. The researcher found this interview to be difficult because she could not ask her partner to leave the interview room and the service user was also not engaging with the interview. She provided very short responses to the questions the researcher asked and within about 10 minutes the interview was over. The researcher realised that she obtained very limited information from this interview. In retrospect, the researcher's view is that she should not have proceeded with this interview since it is possible that the service user was reluctant to discuss her medical/medication history and SUD history in the presence of her partner. The second challenging interview she had was with a service user who walked out during interview because it was boring him. Again, this service user was not engaging with the interview and provided short responses. The useful information she obtained from these two interviews were very limited.

The professional background of the researcher was probably both an advantage and a disadvantage in her interviews with prescribers. It was an advantage in that she is familiar

with the medications used in the management of commonly co-existing disorders with SUDs. She could understand the technical terms used by the healthcare professionals that participated in the interviews. On the other hand, it is possible that her background influenced how prescribers responded to the interviews since they were aware of her professional background. Prescribers may have exaggerated how they assessed the appropriateness of service users' medications (social desirability effect) due to fear of admitting less than optimal practice to her. It is therefore possible that the findings of this study may differ if she had been from a different professional group.

### **3.6. Summary**

This chapter has described the methodological approach and techniques used to investigate the appropriateness of prescribing for service users as well as the responses of prescribers to inappropriate prescribing. The philosophical worldview the researcher adopted in this thesis was pragmatism. The pluralistic nature of pragmatism enabled the use of both postpositivist and phenomenological perspectives. This further allowed a mixed methods approach to be used. Furthermore, a comprehensive understanding of the appropriateness of prescribing and responses to inappropriate prescribing required the adoption of multiple methods, thus building a more holistic picture than could be obtainable using a single method. Quantitative methods were used to provide an overview of the different classes of medications taken by service users during their first assessment at the SAS in addition to allowing for the estimation of the magnitude of inappropriate prescribing. Interviews with prescribers provided a means for an understanding of their responses to inappropriate prescribing while interviews with service users aided an understanding of their perspectives on the appropriateness of medicines assessed in this study. The next chapter presents the first study carried out in this thesis: a secondary data analysis of routine clinical data obtained from the SAS electronic database and its findings.

# Chapter 4: Secondary data analysis of routine clinical data

## **4.1. Study rationale**

As discussed in chapter 3, the analysis of routinely collected data obtained from the SAS electronic database was carried out in order to provide a comprehensive overview of the different classes of medications taken by service users who are newly referred to the SAS. This was the first quantitative study in this thesis. It represents a first step towards understanding prescribing in this client group since there is a lack of research assessing the different types of medications prescribed for them. Published studies have only described particular psychiatric medications such as antidepressants (Petrakis, Leslie and Rosenheck, 2003) and benzodiazepines (Brunette et al., 2003; Clark et al., 2004) prescribed for service users. Due to the dearth of published research in this area, the types of medications prescribed for service users were studied using routinely available data in a single SAS. The research questions addressed are described below:

1. What types and quantities of prescribed medications are taken by service users?
  - a. What types of medications are service users at the SAS taking at their first treatment episode between September 2007 and January 2011?
  - b. What is the prevalence of polypharmacy (four or more medications) among service users?
  - c. What is the prevalence of psychiatric polypharmacy (four or more psychiatric medications) among service users?
  - d. What are the distinguishing profiles of service users on polypharmacy and psychiatric polypharmacy?

Polypharmacy was defined as prescribing four or more medications for the same person (Department of Health, 2001) while complex psychiatric polypharmacy was considered to be prescribing of four or more psychiatric medications for the same person. The following medications were regarded as psychiatric medications: antidepressants, anxiolytics, hypnotics, anticonvulsants, antipsychotics and mood stabilisers. Although polypharmacy is not synonymous with inappropriate prescribing, the number of unnecessary or inappropriately prescribed medications increases with polypharmacy (Goh, 2002; Nobili et al., 2011; Rambhade et al., 2012). Only the prevalence of polypharmacy was assessed in

this study because other aspects of prescribing appropriateness such as indication, dose and duration of therapy were not consistently documented on the SAS database.

## **4.2. Methods**

This section describes the method used in this study: a secondary data analysis of routine clinical data at the SAS. It also describes the inclusion and exclusion criteria, data management and analysis plan, and ethical process for this study.

### **4.2.1. Secondary data analysis of routine clinical data**

Information about service users assessed during their first treatment episode between September 2007 and January 2011 were extracted from the SAS electronic database by the information analyst. This period was selected for study in order to provide a picture of the medications prescribed for service users over a considerable period of time. As described in section 3.2, prior to visiting the SAS for their first treatment episode, service users are sent a self-completion booklet. This booklet enquires about the newly referred service user, their prescribed medications and measures considered to be key in addiction such as dependence, psychological well-being and social well-being (Raistrick, Heather and Godfrey, 2006). Dependence and psychological well-being are assessed at the SAS using the Leeds Dependence Questionnaire (hereafter LDQ) (Raistrick et al., 1994), and the Clinical Outcomes in Routine Evaluation 10-item measure (hereafter CORE-10) (Barkham et al., 2013) respectively. Social well-being is assessed using the Social Satisfaction Questionnaire (hereafter SSQ) (Raistrick et al., 2007). In addition to these three measures, a fourth measure EQ 5D (Brooks, Rabin and De Charro, 2003) is used in assessing quality of life. These measures are further described in section 4.3.1.2.

The completed booklets are collected from service users at their appointment and entered into the electronic database by secretaries of the different clinical teams, who have been trained in the use of the database. The database has been developed over the last 20 years. Data of service users attending for their first treatment episode between September 2007 and January 2011 were analysed in this study. The prescribed medications of service users were grouped into different classes using the British National Formulary (BNF), No 59, classification (Joint Formulary Committee, 2010). The BNF classification was used because it is the official formulary used by healthcare professionals in the UK. It contains information on the medications prescribed, dispensed and administered in the UK. This study informed the selection of medications whose appropriateness was subsequently

assessed in the medication appropriateness study following a consultation process with SAS psychiatrists.

#### **4.2.2. Inclusion/exclusion criteria for secondary data analysis**

Service users were eligible for inclusion in this study if they attended for their first session of a new course of treatment at the SAS between September 2007 and January 2011. People classified as newly referred service users therefore include those previously discharged but starting a new course of treatment within the specified time period. If included service users were discharged and then attended the SAS again within the time period, these later courses of treatment were excluded. This approach avoided representation of multiple episodes of the same person in this analysis.

#### **4.2.3. Data management and analysis**

This section presents how data obtained from this study were managed and analysed. Data management is first presented followed by the analysis of data.

##### Data management

Data used in this study were anonymised and extracted from the SAS electronic database by the SAS information analyst. The dataset was sent to the researcher by the information analyst through a password protected excel file via the SAS intranet as approved by the ethical committee. Data were then transferred via an encrypted memory stick to the University of York for analysis on a double password protected computer. The researcher converted the excel file to an SPSS file before analysing it. Some inaccuracies were observed in the data. For example, some medications were incorrectly spelt. Citalopram, an antidepressant, was sometimes spelt as citaolpram or citaloopram. Where the spellings of medications could not be reconciled with any known medication, they were not included in the analysis.

The researcher grouped all the medications on the database using SPSS syntax into their different classes as obtainable in BNF, No 59, including those that were incorrectly spelt. For example, different groups of antidepressants such as the tricyclic antidepressants, the selective serotonin reuptake inhibitors and monoamine oxidase inhibitors were all grouped into the antidepressant class. All medications were assigned only to one class. For instance, some antidepressants such as amitriptyline are also used for the treatment of neuropathic pain (Joint Formulary Committee, 2010). However, they were only classified as

antidepressants in this study. This was through necessity as the indications for medications were often not recorded on the database. Data were retained for five years to allow for completion of the PhD and dissemination of the results.

#### Data analysis

Data analysis was performed using SPSS (v 18) at the Department of Health Sciences, University of York. Descriptive statistics for continuous variables were expressed as means (SD) and those for categorical variables as frequencies and proportions. Median and interquartile range (Q1, Q3) were presented for variables that are not normally distributed. The independent samples t-test was used in the analysis of data comprising two independent groups that are normally distributed. The independent samples t-test is used to compare the means between two independent or unrelated groups on the same continuous, dependent variable (Peacock, 2010). Data that are not normally distributed were transformed to the logarithmic form for improvement in their distribution. However, if the logarithmic transformation did not improve the distribution, then analysis of two independent groups was carried out using a non-parametric test (Wilcoxon Rank Sum test). Wilcoxon Rank Sum test is a non-parametric test that is used to compare two independent groups when the assumption of normality is not met (Bland, 2000). Chi-squared test was used in the analysis of two or more categorical variables. Where the assumptions for it were not met, Fisher's exact test was used. For chi-squared to be used in testing for association between variables, 80% of the expected frequencies must be greater than five and all expected frequencies must be greater than one (Bland, 2000).

Binary logistic regression was used to determine whether there are any significant differences between those service users who were on polypharmacy and those who were not on them, on any of the predictor variables (age, sex, level of dependence, referral pathway, referral substance, quality of life), while simultaneously controlling for each of the other variables. Binary logistic regression is used to assess the association between predictors of a variable and the variable itself while controlling for potential confounders (Antonogeorgos et al., 2009). It is used when the dependent variable is dichotomous (in this case, presence or absence of polypharmacy).

Predictor variables were included in the model based upon theoretical justification as well as evidence from published studies for an association with the dependent variable. For instance, age has been reported to be associated with polypharmacy in previous studies (Al Ameri et al., 2014; Moen et al., 2009) while the type of referral substance and level of

dependence may be important because some substances such as alcohol have been associated with more illnesses (Gutjahr, Gmel and Rehm, 2001). This may result in the need for more medications among people who are dependent on alcohol. There may also be a tendency for the severity of illness and by extension, number of prescribed medications, to be related to levels of dependence. Some studies have reported use of more medications among women compared to men (Bjerrum et al., 1998; Venturini et al., 2011). Referral pathway may also be important because people referred from hospital may be on more medications since they may be more ill compared to those who self-referred or those referred from their GPs. Those with lower quality of life may be more ill and therefore more likely to be on more medications when compared to those with a higher quality of life.

Binary logistic regression was also used to assess if there are any significant differences between service users who were on psychiatric polypharmacy and those who were not on them on the above-mentioned predictor variables. Information relevant to statistical modelling such as the value of *R-squared* and *goodness of fit* test are not presented because the purpose of this analysis is not model building. P-values, odds ratios and 95% confidence intervals for the odds ratios are reported. An alternative method of analysis to logistic regression is discriminant analysis. However, logistic regression was preferred because it produces more accurate results when the independent variables are a combination of continuous and categorical variables (Pohar, Blas and Turk, 2004) as it is in this study. Statistical significance was at the 5% level and all reported p-values were two-sided. Where multiple testing occurred, Bonferroni adjustment (Bland and Altman, 1995) was carried out.

#### **4.2.4. Ethical considerations**

The ethical application for the secondary data analysis was first submitted for consideration by the Health Sciences Research Governance Committee (hereafter HSRGC) at the University of York before being sent via email to the NRES Committee South West Exeter on the 19<sup>th</sup> of October 2011 for proportionate review. Proportionate review is used when a study carries minimal risk to the study participants due to the absence of patient identifiable information. This study involved analysis of anonymised data extracted from the SAS electronic database and therefore carried minimal risk of identification of study participants. The NRES Committee requested the inclusion of evidence of valid insurance, confirmation of support from the University of York, clarification of research site,

confirmation of scientific critique and statistical review in their opinion letter on the 26<sup>th</sup> of October 2011 before a favourable ethical opinion would be given. A favourable ethical opinion (shown in appendix 4.1) was subsequently obtained from the NRES Committee. This was followed by approval from the Research and Development (R & D) Department of the Leeds Partnership NHS Foundation Trust (now Leeds and York Partnership NHS Foundation Trust).

## **4.3. Results**

### **4.3.1. Characteristics of newly referred service users**

This section presents a description of the sociodemographic characteristics of newly referred service users attending the SAS as well as comparison of key addiction measures obtained for service users with their normative ranges.

#### **4.3.1.1. Sociodemographic characteristics**

There were a total of 1783 newly referred service users during the period examined. Majority were males (58.3%) with a mean age of 40.5 (SD = 11.2). Most service users were of white ethnicity (86.1%) and cited alcohol (78.2%) as their primary problematic substance. Self-referral accounted for the highest number of referrals making up about one-third (31.5%), followed by referral from general practitioners (21.6%). Drug services were responsible for 13.6% of referrals, general hospital (including accident and emergency) 11.5%, psychiatrists 7.9% and others such as social services and criminal justice 13.9%. Over half (53.1%) of service users were unemployed and most of them (about 60%) lived in rented accommodation. Table 4.1 presents service users' sociodemographic characteristics.

Table 4.1: Sociodemographic characteristics of service users in the secondary data analysis study (n and % presented for all characteristics except age)

<b>Sociodemographic characteristics</b>	<b>Total sample (n)</b>	
Age (mean, SD)	1783	40.5 ± 11.2
Gender		
Male		1040 (58.3%)
Female	1783	743 (41.7%)
Ethnicity <sup>a</sup>		
White		1536 (86.1%)
Other		92 (5.2%)
Not stated	1783	155 (8.7%)
Housing status <sup>b</sup>		
Rented		1011 (59.8%)
Home owner		349 (20.7%)
Homeless		225 (13.3%)
Other	1690	105 (6.2%)
Referral substance <sup>c</sup>		
Alcohol		1395 (78.2%)
Opioids		263 (14.8%)
Other	1783	125 (7%)
Referral source <sup>d</sup>		
Self		560 (31.5%)
General hospital and A&E		205 (11.5%)
General practitioner		385 (21.6%)
Psychiatrist		141 (7.9%)
Drug services		243 (13.6%)
Other	1783	248 (13.9%)
Employment status <sup>e</sup>		
Employed		333 (19.8%)
Unemployed		894 (53.1%)
Other	1684	457 (27.1%)
Number of previous SAS episodes <sup>f</sup>	1783	1 (1, 2)
Number of prescribed medicines <sup>f</sup>	1761	2 (1, 4)

<sup>a</sup>Other ethnicity includes mixed (3.2%), Asian or Asian British (1.2%), Black or Black British (0.3%) and other ethnic groups (0.4%), <sup>b</sup>other housing status includes those living in supported housing (6%) and travellers (0.2%), <sup>c</sup>other referral substances include those referred because of sedatives (0.8%), cannabis (2.4%), stimulants (2.7%), hallucinogens (0.3%), polyuse (0.7%) and solvents (0.1%), <sup>d</sup>only 0.1% of service users were referred from hospital A & E, drug services include statutory (7%) and non-statutory drug services (6.7%) whereas other includes social services (2.4%), criminal justice (0.7%) and other referral sources (10.8%), <sup>e</sup>other employment status includes inactive people (16.9%), those who preferred not to state their status (0.8%) and others (9.4%). <sup>f</sup>data not normally distributed, therefore median and interquartile range presented. Where A & E = Accident & Emergency and SD = standard deviation.

Due to the fact that almost 8 out of every 10 service users had alcohol as their primary referral substance, their demographics were compared to the population of service users in contact with structured treatment for alcohol (primary problematic substance) in England (Public Health England, 2014a), and they were found to be similar in their age. There were however more males, more service users of white ethnicity and more self-referrals among those in structured treatment. No data were presented on employment status by Public Health England (2014a) and data on housing status were not directly comparable due to

differences in categories of housing situation used. Service users attending for their *first* new treatment episode had a median of one treatment episode in the past.

#### **4.3.1.2. Key measures of addiction used in the SAS**

As already described in section 4.2.1, dependence, psychological well-being and social well-being are considered to be key outcome measures in addiction (Raistrick, Heather and Godfrey, 2006). Dependence and psychological well-being are assessed at the SAS using the Leeds Dependence Questionnaire (hereafter LDQ) (Raistrick et al., 1994), and the Clinical Outcomes in Routine Evaluation 10-item measure (hereafter CORE-10) (Barkham et al., 2013) respectively. Social well-being is assessed using the Social Satisfaction Questionnaire (hereafter SSQ) (Raistrick et al., 2007). In addition to these measures, the EQ 5D (Brooks et al., 2003) is used in assessing quality of life.

The LDQ is a 10-item self-completion questionnaire for the assessment of the level of dependence on substances such as alcohol, illicit drugs as well as prescribed medications (Heather et al., 2001; Raistrick et al., 1994). It measures similar areas of dependence to the ICD-10 (World Health Organisation, 1993). The areas measured include pre-occupation with substance, salience of substance-related activity, compulsion to start using, planning procurement and use of substance, maximising the drug effect, narrowing of the repertoire of drug-taking behaviour, compulsion to continue use, primacy of drug effect over other aspects of substance use, constancy of drug-induced state and a cognitive set of needing to use in order to cope with everyday life. The LDQ has a score ranging from 0 to 30 with higher scores representing higher levels of dependence. The LDQ has extensive and independent validation (Heather et al., 2001; Kelly et al., 2010; Paton-Simpson and MacKinnon, 1999).

Heather et al. (2001) proposed the following normative ranges for alcohol dependence using the LDQ: mild (0 to 15), moderate (16 to 23) and severe dependence (24 to 30). Cut-offs were also proposed for mild opioid dependence (0 to 20), moderate opioid dependence (21 to 25) and severe opioid dependence (26 to 30). When compared to these normative ranges, SAS service users referred for their alcohol problems were moderately dependent ( $18.1 \pm 8.4$ ) whereas those referred for opioids were mildly dependent ( $8.2 \pm 8.9$ ). The value obtained for alcohol is similar to that previously reported by Raistrick et al. (1994) for service users who were dependent on alcohol at the SAS. However, the value for opioids is lower compared to the study by Raistrick et al. (1994).

The CORE-10 (Barkham et al., 2013) is a short version of the 34-item Clinical Outcomes in Routine Evaluation – Outcome Measure (CORE-OM) (Barkham et al., 2001; Evans et al., 2002). It is a self-reported 10-item questionnaire for assessing different domains of psychological well-being, namely, depression, anxiety, physical, trauma, general functioning, social functioning, close functioning, subjective well-being, risk to self as well as risk to others.

Each item on the CORE-10 is scored on a five point scale ranging from 0 to 4 with the lowest possible score being 0 and the highest being 40. Higher scores indicate a higher level of psychological distress. Its psychometric properties have been investigated and reported (Connell and Barkham, 2007). The clinical cut-off for psychological distress using CORE-10 is 11 (Barkham et al., 2013). Within this clinical range, a score of 11 is the lower boundary of the ‘mild’ level, 15 for the ‘moderate’ level, and 20 for the ‘moderate-to-severe’ level (Connell and Barkham, 2007). A score of 25 or more marks the ‘severe’ level. The CORE-10 score obtained for SAS service users was 21.8 (SD = 9.1), indicating the presence of ‘moderate to severe’ levels of psychological distress among this population. There has been no previous study that used the CORE-10 among substance users. However, the score obtained in this study is similar to that obtained from a clinical population ( $20.2 \pm 7.9$ ) recruited from a GP practice in the UK (Connell and Barkham, 2007).

The SSQ was developed to assess social satisfaction in people with SUDs (Raistrick et al., 2007). It is an 8-item scale adapted from a pre-existing scale, Social Problems Questionnaire (Corney and Clare, 1985). The areas assessed by the SSQ include accommodation, living arrangements, employment, financial position, amount of time you are able to go out, amount of time you see your friends, closest relationship and relationship with your family. The SSQ has a score ranging from 0 to 24 with higher scores indicating higher levels of social satisfaction. The psychometric properties of the SSQ has been investigated and reported (Raistrick et al., 2007). A score of 16 or more indicates a well-functioning population (Raistrick et al., 2014). The mean level of social satisfaction among SAS service users using the SSQ was 13.9 (SD = 5.6), and is similar to that reported in a recent study among the SAS population (Raistrick et al., 2014).

The EQ 5D assesses five domains which comprise mobility, self-care, social, pain, and psychological with three levels (no problems, some problems, extreme problems) within

each domain (Sanz et al., 2011). A person's health state can therefore be classified into one of 243 ( $3^5$ ) theoretically possible health states, each of which has been assigned a utility. These health states have been ranged as EQ 5D index scores in a large UK population sample from 0 (worst possible health state) to 1 (best possible health state) (Dolan, 1999). Some states are considered to be worse than death and given negative values. Higher values indicate better health-related quality of life. Quality of life was assessed using the EQ 5D among SAS service users and found to be 0.5 (SD = 0.4). The EQ 5D score was similar to that previously reported ( $0.4 \pm 0.4$ ) in an alcohol dependent population in an outpatient setting in the UK (Foster, Peters and Kind, 2002). The EQ 5D has been validated in clinical and non-clinical populations (Brazier, Jones and Kind, 1993; Johnson and Pickard, 2000; Schrag et al., 2000). It has also been shown to be a valid measure of quality of life among people with alcohol and heroin dependence (Gunther et al., 2007; van der Zanden et al., 2006). Table 4.2 provides a description of these measures.

Table 4.2: Key measures of addiction for service users in the SAS

Measures of addiction	Total sample (n)	
LDQ <sup>a</sup>	1745	17 (9, 24)
CORE-10	1749	21.8 $\pm$ 9.1
SSQ	1708	13.9 $\pm$ 5.6
EQ5D <sup>a</sup>	1748	0.6 (0.2, 0.8)

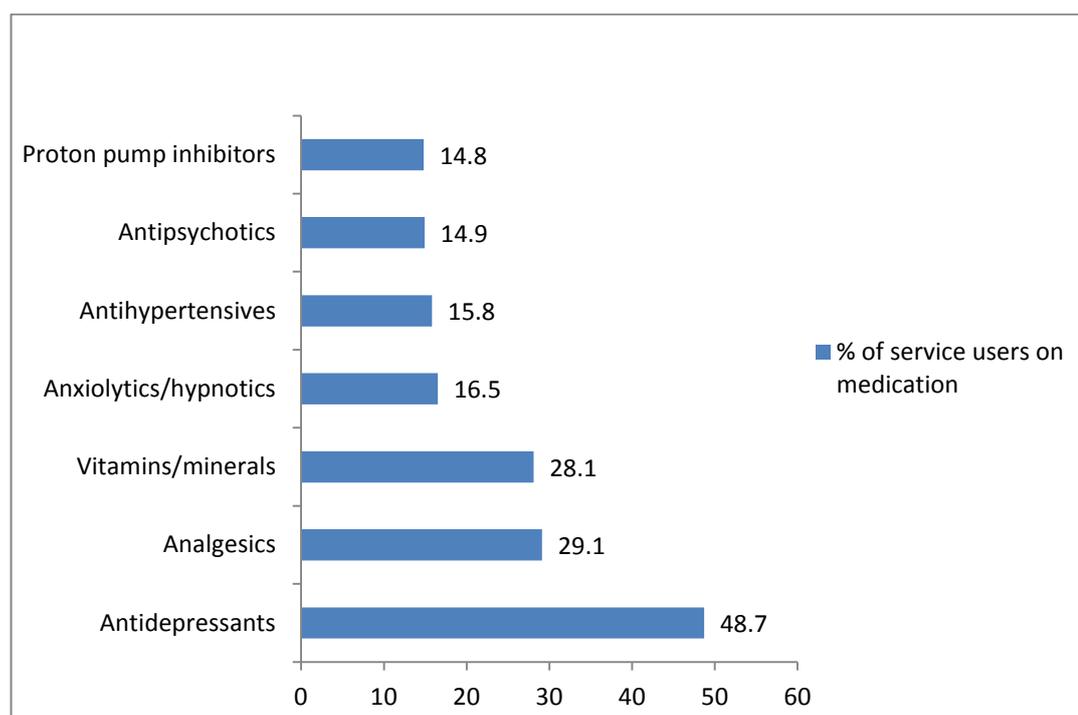
<sup>a</sup>Data not normally distributed, therefore median and interquartile range presented.

### 4.3.2. Types of medications taken at first treatment episode

Service users were prescribed a variety of medications. The three most commonly prescribed medications were antidepressants (48.7%), analgesics (29.1%) - mostly opioids- and vitamins/minerals (28.1%). Thus, nearly half of service users arriving for treatment had a prescription for antidepressants. Of the analgesics prescribed, 84.4% were opioids, with methadone, buprenorphine and suboxone<sup>17</sup> making up 60% of them. Figure 4.1 provides a description of the seven most commonly prescribed medications for SAS service users between September 2007 and January 2011. The percentage of other prescribed medications ranged from 0.2% to 6.6%. Appendix 4.2 provides a full description of the prescribed medications.

<sup>17</sup> It is unclear if these medications were prescribed as substitution therapy for opioid dependence or not due to lack of consistent documentation of indication on the SAS electronic database.

Figure 4.1: The seven most commonly prescribed medications for service users



#### 4.3.3. Prevalence of polypharmacy and psychiatric polypharmacy

Over one-quarter (27%) of service users were on polypharmacy whereas only 1.7% were on psychiatric polypharmacy.

#### 4.3.4. Profiles of service users on polypharmacy and psychiatric polypharmacy

This section presents the following results:

- Comparison of the sociodemographic characteristics of service users with and without polypharmacy and psychiatric polypharmacy
- Comparison of key measures of addiction among service users with and without polypharmacy and psychiatric polypharmacy
- Variables associated with polypharmacy and psychiatric polypharmacy using logistic regression.

##### 4.3.4.1. Sociodemographic characteristics of service users with and without polypharmacy

Service users on polypharmacy were significantly older ( $p < 0.0005$ ), differed in their referral source ( $p < 0.0005$ ), referral substance ( $p < 0.0005$ ) and employment status ( $p < 0.0005$ ). Service users with polypharmacy were more likely to be referred from general hospital, general practitioners (GPs) and psychiatrists while those without polypharmacy

had more self-referrals, referrals from drug services and others. Those on polypharmacy were more likely to have alcohol as their referral substance whereas in those without polypharmacy, opioids and ‘other’ substances were more common as referral substances. They were also more likely to be in ‘other’ employment category comprising inactive people (retirees, students, home-makers, long-term sick), those who preferred not to state their status, and any categories besides those considered to be employed or unemployed. Table 4.3 presents the significant sociodemographic differences between service users with and without polypharmacy (appendix 4.3 provides a full description of sociodemographic characteristics). The level of significance was set at 0.4% due to Bonferroni adjustment for multiple testing (Bland and Altman, 1995).

Table 4.3: Sociodemographic characteristics of service users with and without polypharmacy (n and % presented for all characteristics except age)

<b>Sociodemographic characteristics</b>	<b>Service users without polypharmacy</b>	<b>Service users with polypharmacy</b>	<b>P-values</b>
Age <sup>a</sup>	38.4 ± 10.43	46.15 ± 11.11	P < 0.0005 <sup>#</sup>
Referral source <sup>b</sup>			
Self	415 (32.3%)	138 (29%)	
General hospital	124 (9.6%)	78 (16.4%)	
General practitioner	270 (21%)	110 (23.1%)	
Psychiatrist	93 (7.2%)	48 (10.1%)	
Drug services	196 (15.3%)	44 (9.2%)	
Other	187 (14.6%)	58 (12.2%)	
Total	1285	476	P < 0.0005 <sup>+</sup>
Referral substance <sup>c</sup>			
Alcohol	948 (73.8%)	427 (89.7%)	
Opioids	238 (18.5%)	25 (5.3%)	
Other	99 (7.7%)	24 (5%)	
Total	1285	476	P < 0.0005 <sup>+</sup>
Employment status <sup>d</sup>			
Employed	266 (21.9%)	63 (14%)	
Unemployed	670 (55.2%)	215 (47.8%)	
Other	277 (22.8%)	172 (38.2%)	
Total	1213	450	P < 0.0005 <sup>+</sup>

<sup>a</sup>Mean and standard deviation presented for age, <sup>b</sup>other referral sources include social services, criminal justice and others, <sup>c</sup>other referral substances include sedatives, cannabis, stimulants, hallucinogens, solvents and polyuse, <sup>d</sup>other employment status includes inactive, not stated and others, <sup>#</sup>calculated using independent sample t-test, <sup>+</sup>calculated using chi-squared test.

#### 4.3.4.2. Key measures of addiction in service users with and without polypharmacy

Service users on polypharmacy had higher levels of psychological distress and lower quality of life measured using the CORE-10 and EQ 5D respectively (p < 0.0005). Table 4.4 shows only the CORE-10 and EQ 5D scores because there were statistically significant

differences between service users with and without polypharmacy (appendix 4.4 provides a full description of these key measures of addiction).

Table 4.4: Key measures of addiction in service users with and without polypharmacy

Measures of addiction	Service users without polypharmacy	Service users with polypharmacy	P-values
CORE-10	21.41 ± 9.27	23.07 ± 8.46	P < 0.0005
EQ 5D	0.69 (0.27, 0.85)	0.29 (0.08, 0.69)	P < 0.0005

#### 4.3.4.3. Sociodemographic characteristics of service users with and without psychiatric polypharmacy

Service users on psychiatric polypharmacy differed significantly only in their referral source from those who were not on psychiatric polypharmacy ( $p < 0.0005$ ). Those on psychiatric polypharmacy were more likely to be referred from psychiatrists while those without psychiatric polypharmacy had more self-referrals and referrals from general hospital, GPs and drug services. Appendix 4.5 provides a full description of these sociodemographic characteristics.

#### 4.3.4.4. Key measures of addiction in service users with and without psychiatric polypharmacy

There were no significant differences in the SAS key measures of addiction between those with and without psychiatric polypharmacy. Appendix 4.6 presents a description of the key measures.

#### 4.3.4.5. Variables associated with polypharmacy using logistic regression

This section presents the independent variables that are associated with polypharmacy in the logistic regression analysis (see table 4.5). The dependent variable in this analysis was dichotomous, that is the presence or absence of polypharmacy. Polypharmacy was defined as prescribing of four or more medications for the same person (Department of Health, 2001). The independent variables that were significantly associated with polypharmacy were age, level of dependence measured using the LDQ, quality of life measured using the EQ 5D, referral source, referral substance and employment status. Controlling for all other variables, the odds of polypharmacy increased as age increased ( $p < 0.0005$ ). Level of dependence and quality of life had an inverse relationship with polypharmacy and were both statistically significant. The odds of polypharmacy decreased as LDQ and EQ 5D both increased, adjusting for other variables. This means that as level of dependence increased, the odds of polypharmacy decreased. Similarly, as quality of life improved the

odds of polypharmacy decreased. The association between referral sources and polypharmacy was significant ( $p = 0.04$ ) with referrals from drug services ( $p = 0.04$ ) and self-referral (0.002) in particular being significant. Compared to those referred from general hospital, service users referred from drug services and self-referrals were significantly less likely to be on polypharmacy. The relationship of the referral substances with polypharmacy was also statistically significant ( $p < 0.0005$ ) with opioids in particular being inversely associated with polypharmacy, while ‘other’ substances were not. Controlling for other variables, the odds of polypharmacy among service users referred for opioid use was 0.3 times that among those referred for alcohol use (95% CI: 0.16 to 0.54). Employment status was significantly associated with polypharmacy ( $p = 0.004$ ). The odds of polypharmacy among inactive people were two times that among the employed population (95% CI: 1.33 to 3.10). The odds of polypharmacy among unemployed people were 1.4 times that among those who were employed (95% CI: 0.97 to 1.99). However, this was not statistically significant. Table 4.5 shows the variables associated with polypharmacy.

Table 4.5: Variables associated with polypharmacy

Predictor variables	B-coefficient	P-value	Odds ratio and 95% CI
Age	0.05	$P < 0.0005$	1.05 (1.04 to 1.06)
Gender	-0.08	$P = 0.59$	0.93 (0.70 to 1.22)
LDQ	-0.03	$P = 0.006$	0.97 (0.96 to 0.99)
CORE-10	-0.02	$P = 0.07$	0.98 (0.96 to 1.0)
EQ 5D	-2.20	$P < 0.0005$	0.11 (0.07 to 0.18)
Referral source		$P = 0.04$	
GP	-0.45	$P = 0.05$	0.64 (0.41 to 1.00)
Psychiatrist	-0.16	$P = 0.59$	0.85 (0.47 to 1.53)
Drug services	-0.57	$P = 0.04$	0.57 (0.33 to 0.98)
Self	-0.68	$P = 0.002$	0.51 (0.33 to 0.78)
Other	-0.50	$P = 0.05$	0.61 (0.37 to 1.01)
Referral substance		$P < 0.0005$	
Opioids	-1.21	$P < 0.0005$	0.30 (0.16 to 0.54)
Other	-0.40	$P = 0.19$	0.67 (0.37 to 1.22)
Employment status <sup>a</sup>		$P = 0.004$	
Unemployed	0.33	$P = 0.08$	1.39 (0.97 to 1.99)
Inactive	0.71	$P = 0.001$	2.03 (1.33 to 3.10)
Constant	-0.89	$P = 0.08$	0.41 <sup>b</sup>

Where CI = confidence intervals

<sup>a</sup>Only ‘inactive’ comprising long-term sick, retirees, students and home makers was used among ‘other’ employment status, <sup>b</sup>only odds ratio is presented.

#### 4.3.4.6. Variables associated with psychiatric polypharmacy using logistic regression

The independent variables associated with psychiatric polypharmacy were analysed using logistic regression. Psychiatric polypharmacy was defined as prescribing of four or more psychiatric medications for the same person. The dependent variable was dichotomous,

that is the presence or absence of psychiatric polypharmacy. The large number of independent variables for the dependent variable (presence or absence of psychiatric polypharmacy) prevented the calculation of the odds ratio and 95% CI for some of the variables. The minimum number of independent variables recommended for the dependent variable when using logistic regression is 10 (that is, 10 service users with psychiatric polypharmacy and 10 service users without psychiatric polypharmacy (Hosmer and Lemeshow, 2000), otherwise the estimation of the coefficients becomes unstable resulting in misleading results. The number of service users with psychiatric polypharmacy was only 30 which was small compared to the required minimum of 10 variables per independent variable. For all the eight independent variables of psychiatric polypharmacy to be used, there should be at least 80 service users with psychiatric polypharmacy and 80 without psychiatric polypharmacy. Consequently, the independent variables associated with psychiatric polypharmacy are not presented.

#### **4.4. Discussion of SAS database findings**

This section presents a discussion of the results of this study in relation to prior research.

- Types of medications and polypharmacy

There was variation in the types of medications prescribed for service users, with high levels of prescribing of antidepressants. The high prevalence of antidepressants likely reflects the high levels of mood and/or anxiety disorders among those attending the SAS since they are used in the treatment of these disorders in the UK (National Institute for Health and Clinical Excellence, 2006; 2009; 2011b). In particular, antidepressants are initially recommended only for the treatment of severe forms of depressive and anxiety disorders. Other classes of medications such as benzodiazepine anxiolytics may be used for short-term treatment of anxiety disorders or where anxiety disorders are disabling and severe (Baldwin et al., 2013).

As earlier described in section 1.5.2.1, mood and anxiety disorders commonly co-exist with SUDs, with a high prevalence occurring in treatment populations (Delgadillo et al., 2012; Weaver et al., 2003; Arora and Kaur, 2012; Cole and Sacks, 2008). Weaver et al. (2003) found that 68% and 81% of drug service and alcohol service patients, respectively, in a substance misuse setting had a comorbid mood and/or anxiety disorder. The prevalence of severe depression was found to be 27% and 34% among drug and alcohol service patients respectively. Severe anxiety was reported in 19% and 32% of drug and alcohol service patients respectively. In total, 50.3% of patients (both drug and alcohol

service patients) had either severe depressive or anxiety disorders. Delgadillo et al. (2012) reported similar prevalence of current depressive and/or anxiety disorders among people with SUDs in a UK community drug treatment service with 58% of patients having severe symptoms.

Furthermore, this study found that about 15% of service users were prescribed antipsychotics. This is within the reported prevalence of psychotic disorders (7.4% to 56.6%) (Weaver et al., 2003; Walsh and Copello, 2014) among people with SUDs in the UK. As discussed in section 1.5.2.2, differences in the prevalence rate reported in the literature may be due to how psychotic disorders were defined and identified in these studies. Weaver et al. 2003 reported on the prevalence of non-substance-induced psychotic disorders whereas it is unclear if Walsh and Copello (2014) reported only on non-substance induced psychotic disorders. Walsh and Copello (2014) who reported the highest prevalence (56.6%) considered psychotic disorders to include schizophrenia, psychosis, schizoaffective and delusional disorders while Weaver et al. (2003) who reported the lowest prevalence (7.4%) included only schizophrenia and non-specific psychosis. Furthermore, in the study by Walsh and Copello (2014), psychotic disorders were recorded if there was evidence that a psychiatrist had previously diagnosed a patient. For one-third of patients who did not have a psychiatrist's diagnosis, psychotic disorders were identified by the patient's keyworker who were neither doctors nor psychiatrists. This may have led to overestimation of the prevalence of psychotic disorders in the above study.

It has been argued that the adverse consequences of SUDs are likely to make people unhappy and anxious and may mistakenly be diagnosed as a mental disorder (Horwitz and Wakefield, 2007). Psychological distress associated with dependence is often difficult to separate from an independent mood or anxiety disorder. Intoxication and withdrawal symptoms of alcohol and other substances often resemble those of anxiety and depressive disorders and they can sometimes be severe, though resolving within two to four weeks of abstinence (Grant et al., 2004; Raimo and Schuckit, 1998). Consequently, such disorders may be unnecessarily treated with medications. There is therefore the possibility that prescribers have inappropriately prescribed psychiatric medications such as antidepressants and anxiolytics for service users. The extent to which this was the case could not be determined in the current study as information on the original prescriber's clinical decision-making processes was not available. It is also possible that these medications were prescribed for other indications. For instance, some antidepressants are also used in

the management of pain and eating disorders (Royal College of Psychiatrists, 2012; National Collaborating Centre for Mental Health, 2004). The lack of consistent documentation of indication for medication use on the electronic database made it impossible to know the actual reasons for which these medications were prescribed. The extent of prescribing argues for more research on this issue and further consideration of prescribing practice in this group of people.

Almost 30% of service users were prescribed analgesics. These comprised substitute opioids, non-substitute opioids and non-opioid analgesics. Substitute opioids such as methadone, buprenorphine and suboxone made up half of prescribed 'analgesics'. Non-substitute opioids and non-opioid analgesics were prescribed for 15% of service users, with non-substitute opioids in particular being prescribed for 10% of service users. Non-substitute opioids and non-opioid analgesics were probably prescribed for pain, since they are usually used in pain management (Fishbain et al., 2008; Juska and Balon, 2013).

Pain, including chronic pain, is a common comorbid condition in people with SUDs (Peles et al., 2005; Rosenblum et al., 2003; Jamison et al., 2000; Larson et al., 2007; Caldeiro et al., 2008). More than half of people in a residential detoxification programme for alcohol and drug use disorders (cocaine and heroin) have been reported to have moderate to very severe pain with 16% reporting persistent pain of two years duration (Larson et al., 2007). Caldeiro et al. (2008) found the prevalence of moderate to very severe pain to be almost 60% among veterans attending outpatient addiction centres who were dependent on other substances beside opioids. Over one-third of patients had chronic pain of over one year duration.

When compared to the high prevalence of pain reported among people with SUDs in other studies, the fact that only 10% of service users reported taking prescribed non-substitute opioids is surprising and may be due to a number of reasons. Firstly, it may represent a tendency to under-report prescribed opioid use. Under-reporting of opioid use may be due to fear of losing access to this medication among people who are dependent on them (Action on Addiction, 2013). Secondly, it may have resulted because of the study focus on prescribed opioids and not on opioids obtained from other sources such as over-the-counter or illicit sources. Evidence from the US and Australia shows that non-medical users of opioids frequently obtain them from friends, relatives and drug dealers (Jones, Paulozzi and Mack 2014; Nielsen et al., 2013). Thirdly, it may represent a tendency to use other

medications in pain management in this group of people. Lastly, it may be due to a tendency to undertreat pain in this population. Under-treatment of pain has been highlighted as a problem among people with SUDs, such as those maintained on methadone for OUDs (Dunn, Brooner and Clark, 2014).

The prescribing of opioids is particularly challenging in people with SUDs as prescribers must ensure that opioids are appropriately prescribed for them, that is, not withheld unjustly or overprescribed. This is due to the need to prevent opioid misuse, dependence (Fishbain et al., 2008; Portenoy, 1996; Turk, Swanson and Gatchel, 2008; Morasco et al., 2013), diversion and drug interactions (Baldacchino et al., 2010) while ensuring that pain is adequately managed.

- Prevalence of polypharmacy and psychiatric polypharmacy

The prevalence of polypharmacy and of psychiatric polypharmacy were 27% and 1.7% respectively. No previous study was found that examined polypharmacy or psychiatric polypharmacy among people with SUDs. Consequently, the prevalence reported in this study could not be compared with a SUD population. In addition, studies have tended to adopt different definitions of polypharmacy making direct comparison difficult. Polypharmacy has been defined using various cut-offs such as the use of two or more drugs for 240 days or more (Veehof et al., 2000), use of four or more medications (Bikowski, Ripsin and Lorraine, 2001) and use of five or more different prescription medications (Linjakumpu et al., 2002; Jorgensen et al., 2001). The PRACTICE study involving 15 general practice settings in England reported that 17% of patients were receiving between five and nine medications and 9.7% ten or more (Avery et al., 2012). Findings from the Health Survey for England 1998, showed that in people over 75 years approximately 36% were taking four or more prescribed drugs (Department of Health, 1998).

The prevalence of psychiatric polypharmacy is lower than that reported among psychiatric outpatients (Goldberg et al., 2009; Mojtabai and Olfson, 2010). Mojtabai and Olfson (2010) examined prescribing patterns of psychiatric medications comprising antidepressants, antipsychotics, mood stabilisers and sedative-hypnotic among psychiatric outpatients in USA and found that 33.2% of patients had three or more of these medications prescribed for them between 2005 and 2006. Goldberg et al. (2009) also examined the prescribing patterns of psychiatric medications comprising lithium,

anticonvulsants, antidepressants and antipsychotics among patients with bipolar disorder in USA and found that 18% of patients were taking four or more of these medications (Goldberg et al., 2009). Again, these studies are not directly comparable to the database study because they do not focus on people with SUDs.

The prevalence of polypharmacy found in this database study may reflect the complex health problems and comorbidities of service users (Dickey et al., 2002). Dickey et al. (2002) reported a high prevalence of medical disorders among people with comorbid SUDs and severe mental illness. Where there are multiple conditions, polypharmacy may be needed and beneficial. However, it may also be harmful as it increases the risk of drug interactions and adverse events (Duerden, Avery and Payne, 2013; Guthrie et al., 2011; Bourgeois et al., 2010). Medications such as opioids and benzodiazepines that are used in the treatment of conditions that commonly co-occur with SUDs have been implicated in the occurrence of drug overdose and mortality in patients with SUDs (Darke, Duflou and Torok, 2011; Darke and Hall, 2003; Darke and Ross, 2000; Zamparutti et al., 2011). The number of unnecessary or inappropriately prescribed medications increases with polypharmacy (Rambhade et al., 2012; Goh, 2002). It is therefore important to consider whether each medication is being prescribed appropriately, both individually and in the context of the service user's total medication exposure, risk of drug interactions and comorbidities (Hilmer, 2008; Duerden, Avery and Payne, 2013). This is particularly apposite among people with SUDs due to their comorbid conditions, need for management by different specialists and increased tendency for risky interactions between medications and substances. In this study, it was not possible to evaluate whether polypharmacy was necessary because the indication of medications were often absent from the electronic database.

#### - Variables associated with polypharmacy

The variables that were significantly associated with polypharmacy were age, level of dependence, quality of life, referral source, referral substance and employment status. The odds of polypharmacy increased as age increased. This finding is in line with previous studies (Veehof et al., 2000; Moen et al., 2009; Al Ameri et al., 2014) that have found similar associations between age and number of prescribed medications. Polypharmacy tends to increase with age due to increased comorbidities (Duerden, Avery and Payne, 2013; Olsson, Runnamo and Engfeldt, 2011). Level of dependence measured using the LDQ showed an inverse relationship with polypharmacy. In particular, as the level of

dependence on opioids increased, polypharmacy decreased ( $p = 0.01$ ) (data not shown). This association was not observed with alcohol and ‘other’ substances. This could have resulted because prescribers were wary of prescribing medications to people with more severe opioid dependence probably due to apprehension about drug interactions. The type of referral substance was also significantly associated with polypharmacy. Compared to those whose referral substance was alcohol, those who had opioids as their referral substance were less likely to be on polypharmacy. This may reflect the extensive damage that alcohol causes to the organ systems compared to opioids. Alcohol has been linked to over 60 diseases (Gutjahr et al., 2001). Given that a number of service users in this study used other substances in addition to their primary referral substance, it is not possible to disentangle the extent to which the different substances contributed to polypharmacy. For instance, some service users whose referral substance was opioids were also drinkers<sup>18</sup>.

Polypharmacy was associated with lower quality of life. The use of multiple medications may adversely affect service users’ quality of life through the possibility of side effects from the different medications. For instance, antipsychotics have been associated with weight gain, and this has been linked to lower quality of life among schizophrenic patients (Allison, Mackell and McDonnell, 2003). Similarly, the sexual side effects from antidepressants can result in lower quality of life among those taking them (Higgins, Nash and Lynch, 2010). While medications may contribute to improvement in quality of life through their beneficial effects, they may also contribute to decreasing it (Olsson et al., 2011). An alternative explanation is that those on polypharmacy were less healthy and therefore they reported lower quality of life.

When compared to service users referred from general hospital, those referred from drug services and self-referrals were significantly less likely to be on polypharmacy. This may be due to the fact that service users from these settings were less ill compared to those referred from hospital. Service users treated in hospitals are usually complex with co-occurring medical and mental health disorders (O’Toole et al., 2006).

Employment status was also significantly associated with polypharmacy although only the ‘inactive’ category was statistically significant ( $p = 0.001$ ). The odds of polypharmacy among service users in the ‘inactive’ category were two times that among employed people. The inactive group comprised those who are neither in the employed nor

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<sup>18</sup>38% of service users whose referral substance was opioids were also drinkers.

unemployed category such as those who are long-term sick, retired, students and home makers. The higher likelihood for polypharmacy among the 'inactive' category may be due to the nature of this group. Retired people are more likely to be older with more comorbid conditions (Boutayeb, Boutayeb and Boutayeb, 2013) while sick people would suffer from one or more health conditions. Consequently, they are more likely to be on polypharmacy.

There have been two major hypotheses concerning the relationship between employment and health: the social causation hypothesis proposes that employment improves health whereas the social selection hypothesis suggests that health shapes people's employment status (Adda, Chandola and Marmot, 2003; Blane, Smith and Bartley, 1993; Ross and Mirowsky, 1995). It is believed that these mechanisms may also reinforce each other (Blane, Smith and Bartley, 1993; Ross and Mirowsky, 1995), as poor health may lead to unemployment which may lead to further deterioration in health (Bartley, 1994). The fact that more people in the 'inactive' category had polypharmacy may therefore reflect the fact that they comprised people with more health problems.

Unemployed people were unlikely to be on polypharmacy when compared to those in employment. The evidence concerning the relationship between unemployment and poor health is contradictory, and physical health does not necessarily decline during unemployment (Bartley, 1988). One study even found that health may improve during unemployment (Ramsden and Smeed, 1981). Psychological health may however be diminished during unemployment as some studies have reported higher levels of depression and anxiety in this population when compared to those in employment (Khlaf, Sermet and Le Pape, 2004; Kasl and Jones, 2000). Unemployment may also lead to deterioration in health behaviours such as alcohol use leading to morbidity. However, studies have not consistently reported this finding (Cook et al., 1982; Lee et al., 1990). Cook et al. (1982) did not find any significant difference in heavy drinking between employed and unemployed British men while in another UK study by Lee et al. (1990), more unemployed people reported being non-drinkers compared with those in employment.

#### **4.5. Strengths and limitations**

The limitations of this study include the fact that it was a retrospective study of routinely collected data and therefore there were quality issues relating to missing or inaccurate data and self-report. Data entered into the self-completion booklets by service users were self-

written. This data was not collected as part of an interactive interview with a healthcare professional which may have assisted in gathering more comprehensive information regarding service users' medication history. It is possible that service users may not report some of their medications due to a perceived need to avoid disclosure or even due to cognitive impairment secondary to substance use (Simpson et al., 2004). It is therefore possible that this study underestimated the number of prescribed medications and consequently polypharmacy.

Furthermore, entry of information about service users into the database was reliant upon human input and therefore prone to errors. Data entered into the SAS electronic database were extracted from self-completion booklets by secretaries of the different clinical teams and then included on the database. Although secretaries who entered this information have been trained in the use of the database, they have limited knowledge on different types of medications and health conditions. It is therefore possible that they may have missed recording some medications on the database. Names of medications were also sometimes incorrectly spelt. For example, citalopram (an antidepressant) was sometimes spelt as citaolpram or citaloopram. Where the spellings of medications could not be reconciled with a known medication, they were not included in the analysis. Again, this study may consequently have underestimated the number of prescribed medications and polypharmacy. Poor quality data are often a problem in studies that utilise routine clinical data (Iezzoni, 1997) rather than data specifically collected for research.

It is possible that some medications that were grouped under a particular BNF class were used for other indications. For example, amitriptyline could be used as an antidepressant and also for neuropathic pain. However, it was classified only as an antidepressant in this study in order to avoid multiple counting. Furthermore, the reason for medication use was not consistently documented on the electronic database from which the data analysed in this study were obtained. It was therefore not possible to know the actual indications for medications. Other details such as dose and duration of prescribed medications were often not included on the database. This may have resulted because service users did not report these details or secretaries did not include them on the database. Despite these limitations, the use of routine clinical data represented a relatively fast and inexpensive method of research. Descriptive studies employing routinely available data are cheaper to execute and are less time consuming compared to studies that involve prospective collection of primary data.

The use of routine clinical data also hindered data collection on some important factors such as number and types of comorbidities. The lack of such information including indication, dose and duration precluded the assessment of prescribing appropriateness. If these data were available, they would have been useful in judging prescribing appropriateness. This study was however necessary due to a lack of previous research and it represents a first step in exploring this area.

A strong point of this study is the fact that it included all relevant service users during the period assessed. Consequently, it was comprehensive in describing service users' prescribed medications. One of the research questions (distinguishing profiles of those on psychiatric polypharmacy) could not be addressed because of the large numbers of independent variables in the logistic regression analysis. The minimum number of independent variables recommended for the outcome variable when using logistic regression is 10 (that is, 10 service users with psychiatric polypharmacy and 10 service users without psychiatric polypharmacy (Hosmer and Lemeshow, 2000). The number of service users with psychiatric polypharmacy was however small compared to the required minimum of 10 variables per independent variable. This prevented the calculation of the odds ratio and 95% CI for some of the variables in the logistic regression analysis. Lastly, this study was carried out in a single SAS and its findings are not generalizable to other SAS services in the NHS.

#### **4.6. Summary of key findings**

This study found that almost half of service users were on antidepressants at their first assessment at the SAS. Other classes of medications whose prevalence exceeded 10% were analgesics, vitamins/minerals, anxiolytics/hypnotics, antihypertensives, antipsychotics and proton pump inhibitors. All other classes of medications were below 10%. The prevalence of polypharmacy and psychiatric polypharmacy were 27% and 1.7% respectively. The independent variables that were significantly associated with polypharmacy were age, level of dependence measured using the LDQ, quality of life measured using the EQ5D, referral source, referral substance and employment status. A journal article reporting on aspects of this study, in particular, the psychiatric medications taken by service users with a range of SUDs has been published in *Advances in Dual Diagnosis* (Oluyase et al., 2013). The published study is shown in appendix 4.7.

# Chapter 5: Medication Appropriateness Study (MAS)

## **5.1. Study rationale**

This chapter reports on the second quantitative study in this thesis. Evidence from the scoping review showed that only limited dimensions of prescribing appropriateness have been assessed in previous studies. In addition, no study has assessed prescribing appropriateness among service users being treated in a SAS. The medication appropriateness study (hereafter MAS) therefore involved the use of the A-MAI by SAS prescribers (medical doctors and nurse prescribers) in assessing the appropriateness of current prescribed medications (in particular, opioids and psychiatric medications) for service users attending the SAS between August 2012 and April 2013. In the MAS, the MOQ was also used in assessing failure to prescribe needed psychiatric medications and opioids for SAS service users.

Service users recruited and assessed at their first SAS visit were followed up at their three-month review appointment. For instance, service users recruited and assessed at their first SAS visit in August 2012 were followed up at their three-month review appointment in November 2012. The last set of service users were recruited in December 2012 and were followed up at their three-month appointment in March 2013. Where service users did not attend their three-month review appointment but attended a subsequent one, they were followed up at this appointment until the end of data collection in April 2013.

One of the questionnaires used in assessing appropriateness, the medication omissions questionnaire (MOQ), and the adherence questionnaire (AQ) were both designed for this study and were used only at service users' first SAS visit. The MOQ was only used by SAS prescribers at service users' first SAS visit in order to ascertain if there was an omission of both psychiatric medications and opioids or either of them when service users were coming into treatment while the AQ was administered to service users to assess their level of adherence to their medications when coming into treatment. The A-MAI was however used by SAS prescribers in assessing medication appropriateness at service users' first SAS visit and at three-month follow-up review appointment. Both time periods usually involve extensive assessments of service users' medical and medication history. Assessment at service users' three-month review appointment assisted in determining if

there have been any changes in medications found to be inappropriate at first SAS visit. The research questions addressed are highlighted below:

1. What is the level and nature of inappropriate prescribing?
2. How do service users with inappropriate prescribed medications differ from those who do not have such medications?
3. Does the appropriateness of prescribed medications change over the course of service users' treatment?
4. What are the potential cost savings that could result from stopping or reducing the use of inappropriate medications?

## **5.2. Questionnaire survey as a research method in the MAS**

A survey generally refers to the selection of a sample of people from a population, asking them a set of questions and using their answers to make some inference about the wider population (Fowler, 2014). Questionnaire surveys involve the use of questionnaires to collect data (Kelley et al., 2003). There is usually no attempt to control conditions in survey research. Surveys do not involve the allocation of respondents into groups and the treatments they receive are not varied (Kelley et al., 2003). They are therefore appropriate for descriptive studies. Surveys are also well suited for analytical studies whose intention is to assess the effect of a set of variables on another variable. These may involve the use of longitudinal study designs where data are collected at more than one point in time (Kelley et al., 2003). Data may be collected from the same sample on each occasion (cohort or panel studies). In this study, while the MOQ and AQ were used to collect data on medication omissions and adherence respectively at one point in time (service users' first SAS assessment), the A-MAI was used to collect data on medication appropriateness at two time-points (service users' first SAS assessment and three-month review appointment).

## **5.3. Sampling strategy and sample size**

Service users

A purposive sampling strategy was utilised in order to recruit service users who were able to provide evidence relevant to addressing the research questions (MacNealy, 1999). This involved recruiting only those assigned to be assessed by prescribers (nurse prescribers or medical prescribers) during their new treatment episode in the study period, so that appropriateness could be rated in such service users by their SAS prescribers.

The sample size for this study was estimated from the current case load of SAS prescribers. It was estimated that the maximum number of service users that could be assessed by the seven prescribers who worked as permanent staff<sup>19</sup> at the SAS between August 2012 and December 2012 was 112 because each prescriber sees an average of one newly referred service user per week. Weaver et al. (2003) reported that 79% of drug and alcohol service clients took part in their study assessing comorbidity of SUDs and mental illness in community mental health and substance misuse services. Assuming that a similar percentage of service users would consent to take part in this study, the number of service users that could be recruited was 88. The total number of service users actually seen by prescribers was 76, and 60 of them were recruited into this study.

#### Prescribers

All prescribers (nurse prescribers and medical doctors) at the SAS were recruited into this study. Nurse prescribers were included despite their limited remit of prescribing because this study sought to understand prescribing practice in general.

### **5.4. Inclusion/exclusion criteria**

#### Inclusion criteria

- Service users who were attending the SAS for the first session of a new treatment episode during the study period;
- Service users assessed by prescribers (nurse prescribers or medical doctors) only.

#### Exclusion criteria

- Service users who were unable to be interviewed using spoken English;
- Service users who were intoxicated;
- Service users who were assessed by non-prescribers.

### **5.5. Recruitment**

#### Service users

Service users attending the SAS could self-refer or they could be referred from sources such as general practitioners (GPs), psychiatrists, hospital, social services, drug services as well as the criminal justice system. Information obtained about newly referred service users by SAS staff included their demographic information, health history and medications. This information was included on their referral form. All new referrals were

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<sup>19</sup>There were only seven prescribers at the SAS at the onset of this study. Seven other prescribers joined the SAS at various points during this study.

required to book an appointment for their first assessment at the SAS. They were also sent a self-completion booklet (hereafter SCB) to fill out before their first assessment and were asked to arrive at the SAS reception 30 mins before their appointment so that they could have a health check. Those who did not come along with their completed SCB were given another one to fill out by the receptionist.

The first point of contact for new referrals on arrival at the reception was the SAS receptionist who had a register containing all service users attending for the day. Evidence from a senior SAS staff suggested all new referrals to the SAS were screened by a nurse on the basis of their referral information before their first SAS assessment in order to determine if the referral should be accepted or declined and whether the person should be seen by a doctor as well as the team the person should be allocated to. Allocation to a doctor in any of these teams was said to be based on complexity and in particular any prescribing issues while allocation to nurse prescribers and other therapists was decided by the team whose clinic day it was<sup>20</sup>. However, evidence obtained by the researcher suggested receptionists tended to allocate service users to doctors, nurse prescribers and other therapists in the team whose clinic day it was. Allocation occurred when service users arrived at the SAS. Evidence from this study (see section 5.9.6) and that obtained by the researcher therefore suggested inadequate implementation of the allocation system described by the SAS staff in practice.

The receptionists, having been briefed by the researcher, introduced the study to service users who were to be assessed by either nurse prescribers or doctors only since these prescribers would assess the appropriateness of prescribed medications in this study. The study was not introduced to 13 service users who were to be assessed by prescribers due to intoxication (n = 1), communication problems about service users' arrival time (n = 2), prescribers were new to the SAS and they informed the researcher they wanted to get accustomed to SAS routine at their first assessment of service users (n = 10). Service users who were to be assessed by non-prescribers were excluded.

Service users who were interested in the study were referred to the researcher for further information (all service users informed about the study agreed to speak with the researcher). The researcher went through the participant information sheet (hereafter PIS) (see appendix 5.1) with all interested service users in the waiting area (it was not possible

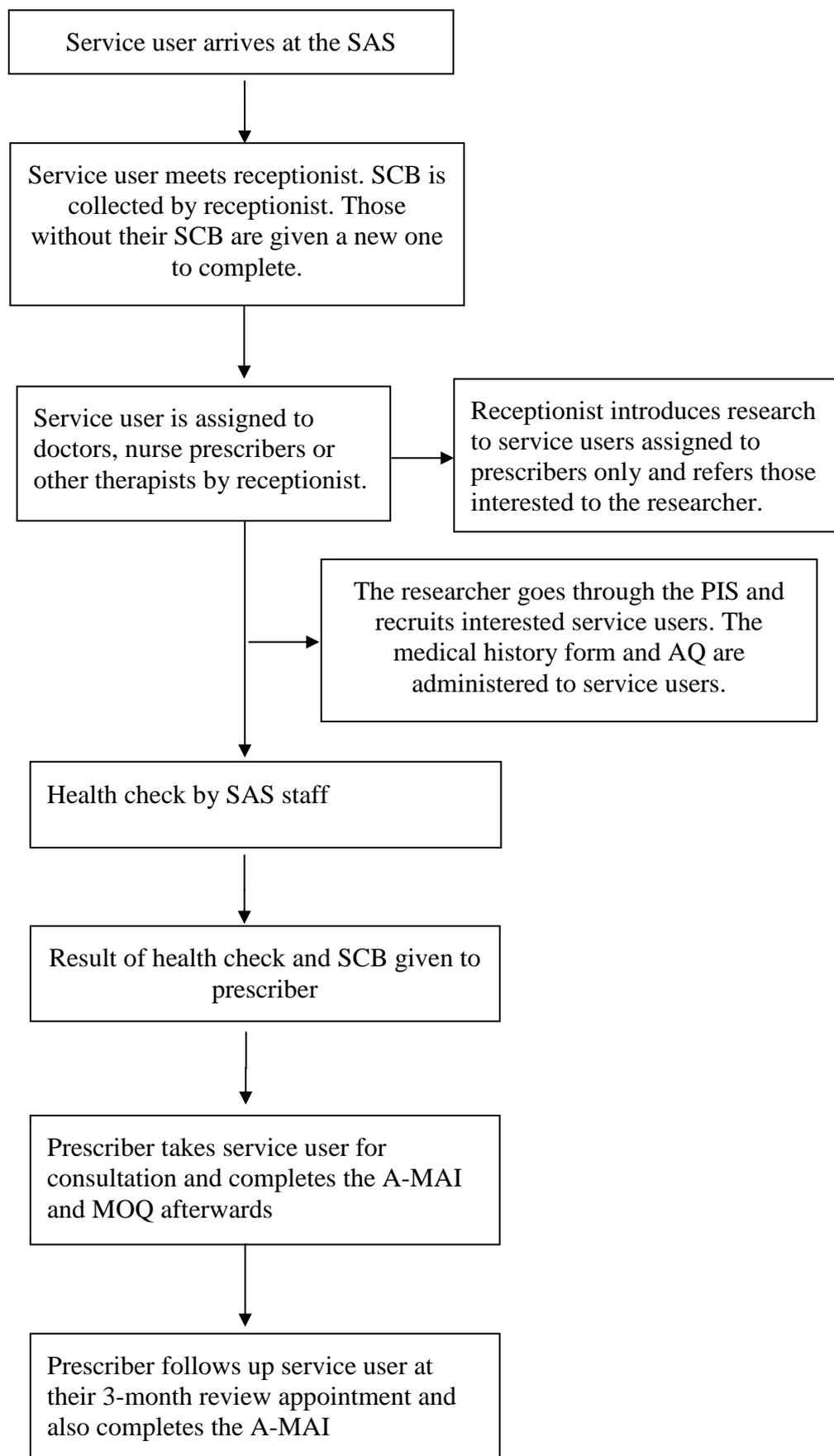
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<sup>20</sup>As described in section 3.2, the three teams are the dual diagnosis team, hospital team, and the pregnancy and parenting team. Each team has its own clinic day in which newly referred service users are assessed.

to use a private room because they were either being used by SAS staff or for other SAS activities) before their routine health check. Those who were happy to participate in the study were asked to sign a consent form (appendix 5.2) and a photocopy of this form was given to the service user as their own copy. The researcher then administered the medical/medication history form (appendix 5.3) and AQ (appendix 5.4) to service users to complete. The medical/medication history form includes information on the current prescribed medications being taken by service users, their doses, dosage interval, length and reason for use, who made diagnosis and when diagnosis was made. Where service users requested the researcher's assistance in completing the forms, she obliged them. This was followed by a routine health check, which was usually conducted by trained SAS staff after which the results of the health check and the SCB were given to the prescriber who would conduct the assessment.

Following the health check, the service user sat in the waiting area to be ushered into the consulting room by the prescriber. The prescriber (who the researcher would have given the study questionnaires: A-MAI and MOQ prior to the consultation) then came to the waiting area to take the service user to the consultation room for a 45- to 60- minute assessment. Prescribers were given flexibility concerning when to complete the study questionnaires. Generally, they either completed them at the end of each consultation or at the close of the clinic for the day. The researcher then collected the completed questionnaires back from prescribers. Recruited service users were followed up at their three-month review appointment by the same prescriber with the exception of three service users who were followed up by different prescribers because one prescriber (two service users were assessed by this prescriber) left the SAS while the other prescriber's clinical team was changed. Again, prescribers assessed the appropriateness of service users' medications using the A-MAI during their consultations with service users at their three-month follow-up review appointment. Figure 5.1 delineates the recruitment process.

Figure 5.1: The study recruitment process



## Prescribers

The researcher distributed information sheets about this study to all the SAS prescribers. She then arranged a brief meeting with each prescriber where she discussed the study in detail, including the principles of informed consent. The prescribers were each given one week to consider participating in this study after which she obtained written informed consent and collected their demographic information (see appendix 5.5, 5.6 and 5.7 for the information sheet, consent form and demographics questionnaire respectively). All the SAS prescribers agreed to take part in this study.

## **5.6. Data collection tools**

The data collection tools in this study included questionnaires for assessing appropriateness (A-MAI and MOQ) and adherence, and forms for documenting medical/medication history. The choice and adaptation of the MAI as well as the development of the MOQ, AQ and forms for documenting medical/medication history are described below.

### **5.6.1. Choice and adaptation of the MAI**

The MAI has been described in chapter 1 (section 1.4.7.2). It is a validated questionnaire that was developed to assess 10 dimensions of appropriateness, namely: indication, effectiveness, dosage, correct directions, drug-drug interactions, drug-disease interactions, practical directions, expense, duplication and duration (Hanlon et al., 1992). These dimensions are rated as A (appropriate), B (marginally appropriate), C (inappropriate) or Z (don't know) for each medication that is being used by the patient. To provide clarity for raters while also improving reliability, the MAI has general instructions for use, specific definitions of each criterion, instructions on how to answer each of the 10 questions and specific examples of 'A', 'B' and 'C' (Hanlon and Schmader, 2013).

Raters may tick Z (don't know) if they need additional information from patients' notes to rate the dimension. In this study, raters were asked to rate Z (don't know) if they cannot make a judgment on the appropriateness of the medication. The MAI has a section for comments after each question. Prescribers were asked to elaborate on the reasons why they gave a rating other than 'A' (appropriate) in the comments section. These comments aided an understanding of why a medication was marginally appropriate or inappropriate. The MAI was therefore used to collect both quantitative and qualitative data.

Weights ranging from 0 to 3 are assigned to each dimension of the MAI and these can be summated to give a total score ranging from 0 to 18 (Samsa et al., 1994). A score of 0 indicates the absence of inappropriate dimensions while a score of 18 indicates that all dimensions for the medication are inappropriate. If the patient is taking multiple medications, the score for each medication could be summed up to obtain a score for the patient. Either the patient or the medication could be used as the unit of analysis. Although Z (don't know) ratings are included on the MAI, there is no guidance in the MAI instructions on the score to be given for Z (don't know) ratings. Consequently, in this study, weightings were not used as prescribers may rate Z (don't know) for dimensions they are unsure of. Z (don't know) ratings were particularly useful in this study because of variability of knowledge among doctors and nurse prescribers regarding some of the assessed medications.

The MAI was chosen for this study because it allows for the use of clinical judgment when assessing the appropriateness of prescribing for each patient. Unlike the explicit or criterion-based measures described in section 1.4.7.1, the MAI allows the patient to be the centre of focus rather than diseases (Spinewine et al., 2007). Furthermore, the fact that SAS prescribers had contact with service users before using the adapted-MAI provided an avenue for them to elicit service users' preferences before assessing prescribing appropriateness. Decision-making concerning prescribing appropriateness could therefore incorporate service users' preferences. In addition, the MAI measures multiple dimensions of appropriateness and can be used to assess different types of medications. Its dimensions have been considered by healthcare professionals to be important in the assessment of prescribing appropriateness (Samsa et al., 1994).

The researcher sent the developer of the MAI, Prof Joseph Hanlon, an email to request a copy of the MAI and the instructions for rating it. Prof Hanlon subsequently sent a copy of the MAI (appendix 5.8) to her. She examined the MAI and its corresponding instructions and found the instructions to be based on American formularies and medication texts such as the American Hospital Formulary Service (AHFS) drug information. Consequently, she requested a version of the MAI that has been adapted for use in the UK (UK-MAI) in the Randomised Evaluation of Shared Prescribing for Elderly People in the Community over Time (RESPECT) trial (Richmond et al., 2010). Appendix 5.9 shows the UK-MAI.

Another problem with the US version of the MAI was that its instructions were not specific on how to rate the other items on it if question 1 ‘is there an indication for the drug?’ is rated as inappropriate. However, the UK-MAI provides clearer rating instructions. For example, it specifies that raters should answer other questions (questions 2, 3, 4, 5 and 9) by assuming that the service user has the diagnosis or indication for which they were prescribed the medication. This is because it is possible that a medication is not indicated and the dosage, direction and duration of use are also inappropriate.

The researcher subsequently adapted the instructions on the UK-MAI for use with the US version of the MAI in this study. The instructions on the UK-MAI were adapted for two reasons:

- Firstly, the adapted instructions provided specific examples of when medications assessed in this study (prescribed opioids and psychiatric medications) would be considered as appropriate, marginally appropriate and inappropriate;
- Secondly, the adaptation was necessary so that service users’ preferences could be incorporated into decision-making when assessing appropriateness.

In previous studies (Hanlon et al., 1992; Hanlon et al., 2004; Schmader et al., 1994; West, Cordina and Cunningham, 2012), the MAI had been rated using only the medical history problem list and the medication list of the patient without face-to-face contact with them. However, in this study, SAS prescribers had face-to-face contact with service users before using the MAI. They could therefore elicit service users’ preferences and take them into consideration when making decisions about prescribing appropriateness.

After adapting the instructions, the researcher discussed them with one of the consultant psychiatrists at the SAS and he suggested minor amendments. The adapted-MAI (A-MAI) is shown in appendix 5.10. Despite the general utility of the MAI, it does not assess medication adherence and omissions (Spinewine et al., 2007). Medication adherence and omissions were assessed using questionnaires designed for these purposes.

### **5.6.2. Pilot and training on the A-MAI**

The researcher had two different training sessions for SAS prescribers on the A-MAI. The first training session included seven prescribers (3 doctors and 4 nurse prescribers) and involved discussion of the A-MAI and its operational definitions. The researcher had

initially proposed that nurse prescribers use a different questionnaire to document any concerns they have about service users' medications because some nurse prescribers had earlier expressed reservations about assessing appropriateness due to their more limited area of expertise. Nurse prescribers' areas of expertise cover medications used in the management of SUDs such as benzodiazepines for alcohol withdrawal, vitamin supplementation in AUDs, disulfiram and acamprosate for alcohol relapse prevention, methadone and buprenorphine for opioid maintenance or detoxification. Occasionally, other opioids such as dihydrocodeine may be prescribed for opioid maintenance.

However, this study also involved assessment of the appropriateness of other psychiatric medications and opioids which are not within the scope of practice of SAS nurse prescribers. The researcher decided to include nurse prescribers despite this limitation because the focus of this thesis was on understanding prescribing practice in general. Nurse prescribers are increasingly playing key roles in addiction medicine as medical expertise is being decimated. Furthermore, the non-medical prescribing course is generic (Public Health England, 2014c) and nurse prescribers would therefore have some level of knowledge about psychiatric medications and opioids. It could also be argued that experienced nurse prescribers working with complex service users with comorbidities will sometimes identify medications that they have concerns about. For instance, there might be concerns about interactions between the medications within their expertise and other prescribed medications. This study provided an opportunity for nurse prescribers to highlight such concerns and the particular areas of prescribing they are concerned about. Where they could not reach a decision or make a judgment, they could rate Z (don't know). After discussing the A-MAI and its instructions at this meeting, the nurse prescribers decided that they would use it in their assessment of prescribing appropriateness.

The second meeting with prescribers involved discussion of a case study (appendix 5.11) comprising a service user's medical and substance history as well as prescribed psychiatric medications with all prescribers. The researcher discussed each of the operational definitions of the A-MAI using the case study and the prescribers shared their views and asked questions. For staff (seven prescribers) who joined the SAS after the start of the study and therefore missed this initial training, the researcher arranged a face-to-face meeting to discuss the A-MAI and its operational definitions so that they could also participate in the study. This however did not include discussion of the case study due to their busy schedules.

The developer of the MAI recommends that two individuals should rate the MAI in order to compare the reliability of ratings. However, it was not possible for two prescribers to have face-to-face contact with the same service user in order to assess their medications using the A-MAI. The busy workload of prescribers made this impossible. An alternative approach could have been that one prescriber has face-to-face contact with the service user and assesses their prescribed opioids and/or psychiatric medications using the A-MAI while the researcher would abstract relevant patient information such as their substance use history, medical and medication history for a second prescriber to utilise in assessing the appropriateness of these medications. However, this would have made inclusion of service users' preferences impossible by the second prescriber since he/she will not have interacted with the service user in a face-to-face discussion before assessing medication appropriateness. Consequently, service users' preferences will not be taken into consideration in the assessment of appropriateness. In this study, only one rater filled out the A-MAI. A previous study by Tobia et al. (2008) also had only one rater.

### **5.6.3. Medication omission questionnaire (MOQ) design**

Medication omissions defined as failure to prescribe needed medications (Spinewine et al., 2007) was assessed using the MOQ. Initially, an adapted version of the Assessment of Underutilisation of Medication Index (AOU) was considered but this was dropped at the pilot stage with prescribers in order to reduce the number of questionnaires to be filled out. The AOU is used in assessing underprescribing (that is, the omission of a needed medication) (Jeffery et al., 1999). Medication omission was assessed using a single question: are any of the medications of interest not being prescribed for an active condition without reason? This question had two response choices (yes or no) with a section to describe the omitted medications and actions to be taken concerning them. The MOQ is shown in appendix 5.12.

#### **5.6.3.1. Feasibility testing and face validity**

The ease of completion and face validity of the MOQ was tested with seven SAS prescribers (3 doctors and 4 nurse prescribers) prior to its use in the medication appropriateness study. They found it easy to understand and complete. They did not suggest any change to it.

#### **5.6.4. Adherence questionnaire design**

While designing this study, I considered different measures that could be used in assessing service users' adherence to their prescribed medications such as medical records, pill count and self-report. There is no 'gold standard' measure of adherence as all measures have their pros and cons (Haddad, Brain and Scott, 2014). Medical records were considered to be unsuitable because they would not be available for majority of service users attending for their first assessment. Similarly, service users are unlikely to visit the SAS with their pills. Hence, pill count was also considered to be unsuitable. Moreover, the use of medical records and pill count does not indicate actual usage of medicines (Garfield et al., 2011). Consequently, the only feasible means of assessing adherence in this study was via self-report questionnaires by service users.

Self-report is limited because it is subject to the ability of the service user to recall and patients have been reported to overestimate their levels of adherence (Horne et al., 2005). Despite these limitations, NICE guidelines have identified self-report of adherence as appropriate for use in clinical settings (Nunes et al., 2009) since it is cheap (Gagne and Godin, 2005; Hawkshead and Krousel-Wood, 2007), quick and easy to use (Miller and Hays, 2000; Paterson, Potoski and Capitano, 2002). Self-report questionnaires should be brief, generic rather than disease-specific and should be suitable for patients taking single or multiple medications for different conditions (Garfield et al., 2011). It should also reflect the varied ways in which people take medications.

The researcher considered existing adherence questionnaires such as the Medication Adherence Questionnaire (hereafter MAQ) (Morisky, Green and Levine, 1986) and Medication Adherence Rating Scale (hereafter MARS) (Thompson, Kulkarni and Sergejew, 2000) and the Brief Medication Questionnaire (hereafter BMQ) (Svarstad et al., 1999) based on these criteria but none was suitable. The MARS focuses on people with psychosis only and therefore was not suitable. The BMQ consists of three sections with multiple sub-sections. The BMQ has to be completed for each prescribed medication and therefore was considered unsuitable due to its potential to become lengthy for service users on multiple medications. The MAQ was dropped because of its limited response choices (dichotomous response categories of 'yes' and 'no') as it does not reflect the varied ways in which people take medications and also because its items are designed to focus on one specific disease state at a time (Tan, Patel and Chang, 2014). Consequently, the researcher designed a short questionnaire (AQ) (appendix 5.4) for assessing service users' adherence

to their prescribed medications. The aim was to create a questionnaire which took less than five minutes to complete.

#### **5.6.4.1. Response mode**

One response mode was used in the questionnaire design: Likert scale. This questionnaire asked service users ‘how often do you take this medication as recommended?’ and provided five potential responses in a Likert scale format: very often, often, sometimes, rarely and never. Five point Likert scale was used because it is quick to complete and allows responses to be scaled depending on service users’ level of adherence. It was administered during service users’ first assessment at the SAS.

#### **5.6.4.2. Feasibility testing and face validity**

The ease of completion and face validity of the adherence questionnaire items were tested with two ex-service users who serve as mentors for other service users at the SAS prior to its use in the medication appropriateness study. They found it easy to understand and fill out. The questionnaire took less than five minutes to complete. They did not suggest any change to it.

#### **5.6.5. Forms for documenting medical/medication history**

The form for documenting medical/medication history was piloted with seven SAS prescribers (3 doctors and 4 nurse prescribers). The prescribers suggested the inclusion on the form of the person who diagnosed a service user with a health condition and when the diagnosis was made. This form comprised name of medication, dose, frequency, length and reason for use, who made diagnosis and when diagnosis was made (see appendix 5.3).

### **5.7. Data analysis and management**

This section presents how data obtained from the medication appropriateness study were analysed and managed.

#### **5.7.1. Data analysis**

Data analysis was performed using SPSS (v 18) at the Department of Health Sciences, University of York. Descriptive statistics for continuous variables were expressed as means (SD) and those for categorical variables as frequencies and proportions. Median and interquartile range (Q1, Q3) were presented for variables that are not normally distributed.

The independent samples t-test was used in the analysis of data comprising two independent groups that are normally distributed. The independent samples t-test is used to compare the means between two independent or unrelated groups on the same continuous, dependent variable (Peacock, 2010). Data that are not normally distributed were transformed to the logarithmic form for improvement in their distribution. However, if the logarithmic transformation did not improve the distribution, then analysis of two independent groups was carried out using a non-parametric test (Wilcoxon Rank Sum test). Wilcoxon Rank Sum test is a non-parametric test that is used to compare two independent groups when the assumption of normality is not met (Bland, 2000). Chi-squared test was used in the analysis of two or more categorical variables. Where the assumptions for it were not met, Fisher's exact test was used. For chi-squared to be used in testing for association between variables, 80% of the expected frequencies must be greater than five and all expected frequencies must be greater than one (Bland, 2000).

In this thesis, A-MAI dimensions rated as A (appropriate) or B (marginally appropriate)<sup>21</sup> were considered to be appropriate while dimensions rated as C (inappropriate) were considered inappropriate. Dimensions rated as Z (don't know) were reported but not taken into consideration when analysing data<sup>22</sup>. Where a medication had no A-MAI dimension rated as C (inappropriate), it was considered to be appropriate while a medication that had one or more C (inappropriate) ratings was considered inappropriate. Analysis of appropriateness therefore involved dichotomising ratings of A-MAI dimensions into two groups: appropriate or inappropriate. While dichotomising the appropriateness ratings may lead to the loss of useful information and may be associated with greater error, it was decided to carry out the analysis as described above because it simplifies the analysis, leads to easy interpretation and presentation of results (Altman, 2006). This approach to analysis was also used by the originators of the MAI (Hanlon et al., 1992).

The number of service users with one or more inappropriate medications was reported. Among the different classes of prescribed medications, the number of medications with one or more inappropriate dimensions was also reported. For example, the number of antidepressants that had one or more inappropriate dimensions was reported.

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<sup>21</sup>Refer to appendix 5.13 for reasons cited by prescribers for marginally appropriate ratings on the A-MAI.

<sup>22</sup>None of the medications (prescribed opioids and psychiatric medications) assessed in this study had all MAI dimensions rated as Z (don't know).

Binary logistic regression was used to assess for the presence of significant differences between service users with inappropriate medications (one or more C ratings in their prescribed medications) and those without them, using number of prescribed medications as a predictor variable. Number of prescribed medications was used as a predictor variable because it has been found to be associated with the medication appropriateness in previous studies that used the MAI (Duerden, Avery and Payne, 2013; Schmader et al., 1994; Spinewine et al., 2007). Statistical information relevant to modelling such as the value of *R-squared* and *goodness of fit* test are not presented in the results section because the purpose of this analysis is not model building. Statistical significance was at the 5% level and all reported p-values were two-sided. Where multiple testing occurred, Bonferroni adjustment (Bland and Altman, 1995) was carried out.

### **5.7.2. Data management**

After consent, participants (service users and prescribers) were given a unique anonymous identification (ID) code. This code was used in all data collection forms and questionnaires. The consent forms were the only document containing identifiable information among service users' data collection forms while the demographics questionnaire and consent forms for prescribers contained identifiable information. These were kept in a locked cabinet at the SAS, separate from other data generated in this study. They would be stored for five years. Participants were only identifiable by their study ID code. Any information which could be used to identify participants was not included on the questionnaires and other data collection forms. Electronic data were stored on a double password protected computer at the SAS and were only accessible to the researcher. Electronic data were transferred via an encrypted memory stick from the SAS to a password protected computer at the University of York for analysis. Again, electronic data will be retained for five years at the University of York (except audio recording which will be retained at the SAS) to allow for completion of the PhD programme and dissemination of results.

### **5.8. Ethical considerations**

Ethical application for the MAS and the interviews with service users and prescribers were made in the same application. This section therefore reports on the ethical issues that are relevant to the MAS as well as issues relevant to both the MAS and interviews. Issues relevant to the interviews only are described in section 6.3. The ethical application was first submitted to the HSRGC. Some ethical issues relevant to both studies were considered

such as how incriminating disclosure other than those required by law would be addressed. The researcher addressed this by stating that all information provided in the course of this study would be kept confidential except there is a disclosure of risk of harm to self or others. Such disclosures will be discussed with the appropriate staff at the SAS for further action. Service users were informed about this in the participant information sheets and also before their interviews. A situation warranting disclosure did not however arise in the course of the interviews. Other suggestions by the HSRGC include the use of less technical terms on the information sheet and possibility of including non-English service users. The latter was not possible as there were no resources for this. Subsequently, all the documents were posted to the NRES Committee Yorkshire & The Humber for consideration on the 8<sup>th</sup> of June 2012. One of the researcher's supervisors and the researcher attended an interview by the NRES committee on the 27<sup>th</sup> of June 2012.

The main ethical issue relating to the MAS discussed at this meeting was the short time interval (20 mins) in which service users needed to make a decision about taking part in the study. However, the researcher stated that she would go through the information sheet with interested service users to ensure that they understand what the study is about and what it will involve. She argued that her face-to-face discussion with service users will allow a full explanation of the study and the principles of informed consent before service users sign the consent form. This is particularly apposite for service users, many of whom have low literacy levels. Furthermore, she gave service users her contact details (this was also stated on the information sheet) in case they have any further queries concerning this study. Service users were informed that consent is voluntary and they can withdraw at any time.

During the design of this study, the researcher considered the option of sending the information sheet to service users along with the SAS self-completion booklets before their first assessment so as to ensure they had adequate time to consider taking part in the study. However, this would have been a waste of resources because only service users who were assessed by prescribers were the focus of this study and not all service users attending the SAS. It would have been difficult to know which service users were to be allocated to prescribers or other therapists *a priori* because they were allocated to keyworkers at their baseline assessment.

Another ethical issue relating to both studies was the need for absolute confidentiality regarding all the information provided by the participants (service users and prescribers).

This is because the service users may be concerned that the information they provided might affect their care. For example, they may be concerned that their participation in this study may lead to the withdrawal of medications they value. Therefore, the researcher assured all service users that the information they provide will not be shared with their prescribers. Prescribers were also assured of the confidentiality of all information they provided in this study. Furthermore, all participants were assured that the information they provide would be anonymised in all publications stemming from this study. All the consent forms for service users and prescribers were stored in a locked cabinet at the SAS. The questionnaires used in this study did not contain the name or clinic identification numbers of service users rather the study identification numbers were used.

The REC gave a favourable ethical opinion of the research (appendix 5.14) based on meeting a number of conditions. The conditions that need to be met relate to the interviews and are described in section 6.3 which highlights the ethical considerations for the interviews. The conditions were met and a confirmation letter for the study was obtained from the committee. After approval by the NRES Committee Yorkshire & the Humber, some minor changes were made to the study. The A-MAI and the form for documenting service users' medical/medication history were combined into a single data collection form for ease of completion. The researcher was sent a minor amendment acknowledgement letter (appendix 5.15) on the 30<sup>th</sup> of August 2012.

## **5.9. Results**

### **5.9.1. Recruitment and response rates of participants**

A total of 76 service users were assessed by prescribers (nurse prescribers and doctors) at their first SAS visit between August 2012 and December 2012. Of these, 63 were approached<sup>23</sup> and 60 (95%) consented to participate in the MAS. These 60 service users include those who were either on target medications (psychiatric medications and/or opioids) as well as those were not on them. Information on service users' prescribed medications was obtained using the medical/medication history form. Medication appropriateness was assessed by SAS prescribers using the A-MAI and MOQ. While all 60 service users were assessed for omission of any of the target medications using the MOQ,

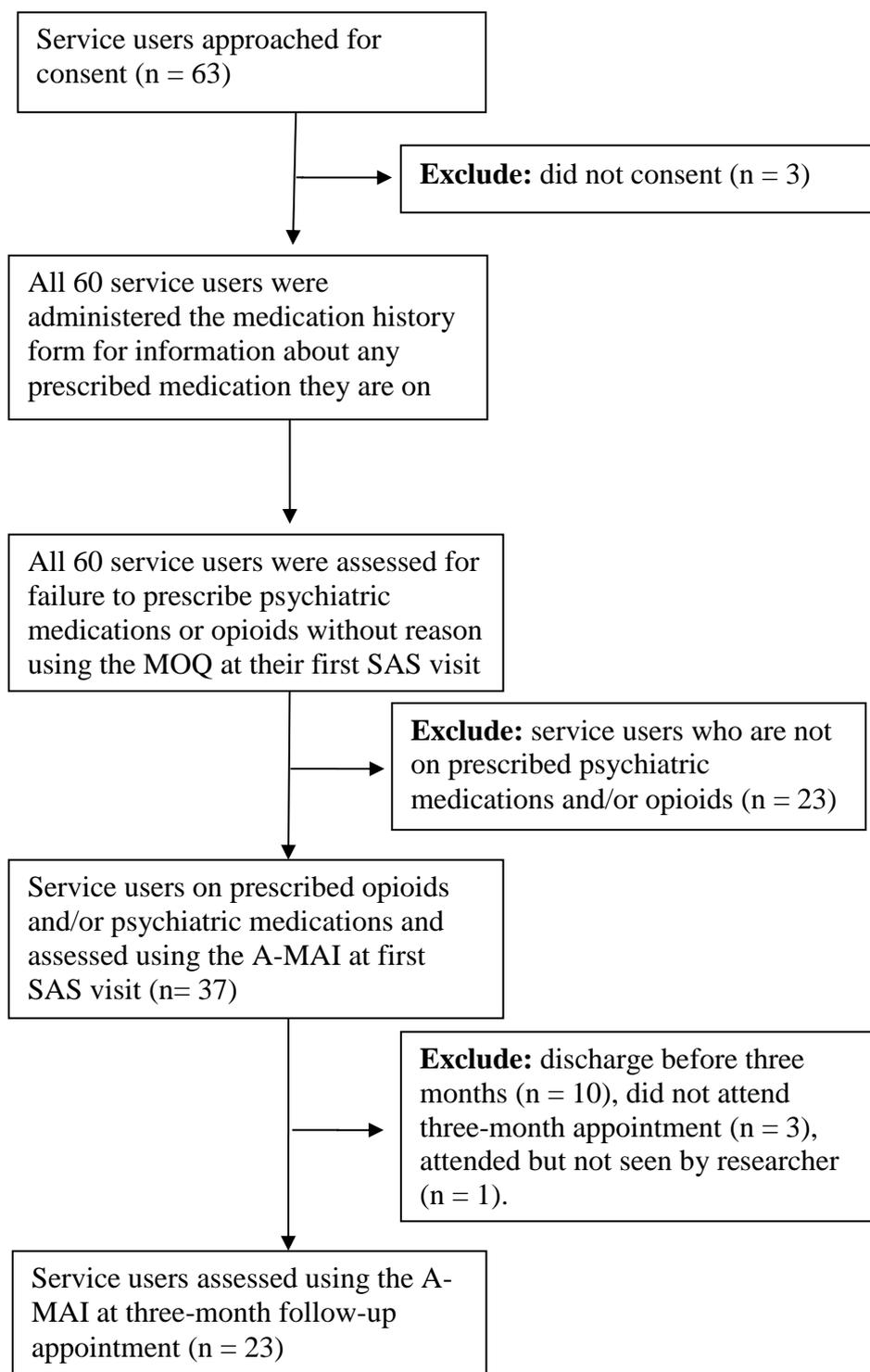
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<sup>23</sup>The reasons the 13 service users were not approached for consent includes: intoxication (n = 1), miscommunication about service users' arrival time (n = 2) and prescribers were new to the SAS and informed the researcher that they wanted to get accustomed to SAS routine at their first assessment of service users (n = 10).

only 37 service users (61.7%) who came into treatment with these target medications had them assessed for appropriateness using the A-MAI. Consequently, the denominator in the MOQ and A-MAI population were different. As described in section 5.1, the MOQ was only used at service users' first SAS visit while the A-MAI was used both at first SAS visit and three-month follow-up appointment.

Almost two-thirds (23) of the 37 (62%) service users were available for follow-up data collection three months later. They had their medications (prescribed opioids and/or psychiatric medications) assessed again at their three-month follow-up appointment by the same prescriber (except three service users) using the A-MAI. Three service users were assessed by different prescribers at first SAS visit and three-month follow-up appointment because one prescriber (two service users were assessed by this prescriber) left the SAS while the other prescriber's clinical team was changed. Of those not followed up (n = 14), 10 were discharged before their three-month visit, 3 did not attend their appointment and one attended but was not seen by the researcher. Figure 5.2 delineates the recruitment process.

Figure 5.2: Service users' recruitment and response rates



### 5.9.2. Omission of opioids and psychiatric medications

All 60 service users who consented to this study were assessed for omissions of opioids and psychiatric medications. There were however no medication omissions. The reasons for this finding were further explored in the interviews with prescribers in chapter 7 (section 7.3.6).

### **5.9.3. Sociodemographic characteristics of service users assessed using the A-MAI at first SAS visit**

Thirty-seven service users were on both psychiatric medications and opioids or either of them at their first SAS visit and therefore had their medications assessed by SAS prescribers using the A-MAI. Their mean age was 44.4 (SD: 11.4) and there were more males (59.5%) than females. The majority (81.1%) were referred for their alcohol problems. Over 90% were of white ethnicity and half (51.4%) of service users lived in rented accommodation. Self-referral accounted for over half (54.1%) of referrals and only 14% were employed.

The characteristics of the 37 service users were compared to those of service users from the SAS database analysis and they were similar in their gender distribution. There were however differences in the following characteristics: the A-MAI population were slightly older, had more whites, more alcohol and opioid referrals, more home owners and those with 'other' housing status. They also had more self- and GP-referrals and those in 'other' employment status. Statistical analysis was not carried out due to the large difference in sample size between the database population (n = 1783) and A-MAI population (n = 37). The table below compares the characteristics of these two populations.

Table 5.1: Comparison of the sociodemographic characteristics of service users assessed using the A-MAI with the SAS database population (n and % presented for all characteristics except age)

<b>Sociodemographic characteristics</b>	<b>A-MAI population (n = 37 except stated otherwise)</b>	<b>SAS database population (n = 1783 except stated otherwise)</b>
Age (Mean, SD)	44.4 ± 11.4	40.5 ± 11.2
Gender		
Males	22 (59.5%)	1040 (58.3%)
Females	15 (40.5%)	743 (41.7%)
Ethnicity		
White	33 (94.3%)	1536 (86.1%)
Non-white	2 (5.7%)	92 (5.2%)
Not stated	0	155 (8.7%)
Housing status <sup>a</sup>		
Rented	19 (51.4%)	1011 (59.8%)
Home owner	9 (24.3%)	349 (20.7%)
Other	9 (24.3%)	330 (19.5%)
Referral substance <sup>b</sup>		
Alcohol	30 (81.1%)	1395 (78.2%)
Opioids	6 (16.2%)	263 (14.8%)
Other	1 (2.7%)	125 (7%)
Referral source <sup>c</sup>		
Self	20 (54.1%)	561 (31.5%)
GP	10 (27%)	385 (21.6%)
Other	7(18.9%)	837 (47%)
Employment status <sup>d</sup>		
Employed	5 (13.9%)	333 (19.8%)
Unemployed	11 (30.6%)	894 (53.1%)
Others	20 (55.6%)	457 (27.1%)

<sup>a</sup>Other housing status comprises homeless (30%), temporary (55.6%) and hostel (11.1%) accommodation, <sup>b</sup>other referral substance for A-MAI population includes only cocaine while that for the database population includes sedatives, cannabis, stimulants and others, <sup>c</sup>other referral source comprises hospital, psychiatrist, criminal justice, drug services, community mental health team, social services and other referral sources, <sup>d</sup>other employment status includes long-term sick or disabled, student, retirees and others.

#### **5.9.4. Other characteristics of service users assessed using the A-MAI at first SAS visit**

The median level of dependence and interquartile range (hereafter IQR) measured using the LDQ was 19 (7.8, 26.8). When compared to the normative ranges for LDQ scores (Heather et al., 2001), service users referred for their alcohol problems were moderately dependent on alcohol whereas those referred for opioids were mildly dependent (data not shown). Level of psychological distress measured using the CORE-10 resulted in a mean score of 24.1 (SD = 10.7). The mean CORE-10 score of service users indicates the

presence of moderate-to-severe levels of psychological distress (Connell and Barkham, 2007). Mean quality of life score measured using the EQ 5D was 0.6 (SD = 0.3), and is slightly higher than that reported by Foster, Peters and Kind (2002) in a UK outpatient alcohol dependent population. Mean level of social satisfaction score measured using the SSQ was 12.2 (SD = 6.8), and is similar to that reported in a recent study among the SAS population (Raistrick et al., 2014). The median number and IQR of prescribed medications and previous SAS episodes were 2 (2, 5) and 1 (0, 2) respectively. Some of the above reported values were similar to that of the database population with the exception of LDQ, CORE-10 and SSQ scores. LDQ and CORE-10 scores were slightly higher among the A-MAI population while SSQ score was higher in the SAS database population. Table 5.2 shows the table comparing these characteristics in the A-MAI and database population.

Table 5.2: Comparison of other characteristics of service users assessed using the A-MAI with SAS database population

Characteristics of service users	A-MAI population	SAS database population
LDQ <sup>a</sup>	19 (7.8, 26.8)	17 (9, 24)
CORE-10 <sup>b</sup>	24.1 ± 10.7	21.8 ± 9.1
SSQ <sup>b</sup>	12.2 ± 6.8	13.9 ± 5.6
EQ 5D <sup>a</sup>	0.7 (0.4, 0.9)	0.6 (0.2, 0.8)
No of previous SAS episodes <sup>a</sup>	1 (0, 2)	1 (1, 2)
No of prescribed medicines <sup>a</sup>	2 (2, 5)	2 (1, 4)

<sup>a</sup>Median and interquartile range are presented because data are not normally distributed, <sup>b</sup>mean and standard deviation are presented because data are normally distributed.

### 5.9.5. Level and nature of inappropriate prescribing at first SAS visit

This section presents the following results:

- Number of inappropriate medications
- Inappropriate A-MAI dimensions and reasons for inappropriateness
- Factors associated with prescribing appropriateness at first SAS visit

#### 5.9.5.1. Number of inappropriate medications

This study found that almost half (n = 16) of the 37 service users on prescribed opioids and/or psychiatric medications<sup>24</sup> had one or more inappropriate ratings on the A-MAI. The total number of prescribed medications (opioids and/or psychiatric medications) for the 37 service users was 59. The total number of prescribed medications exceeds 37 because some

<sup>24</sup> 25 service users were on at least one prescribed psychiatric medication, 5 service users were on prescribed opioids while 7 service users were on both prescribed opioids and psychiatric medications.

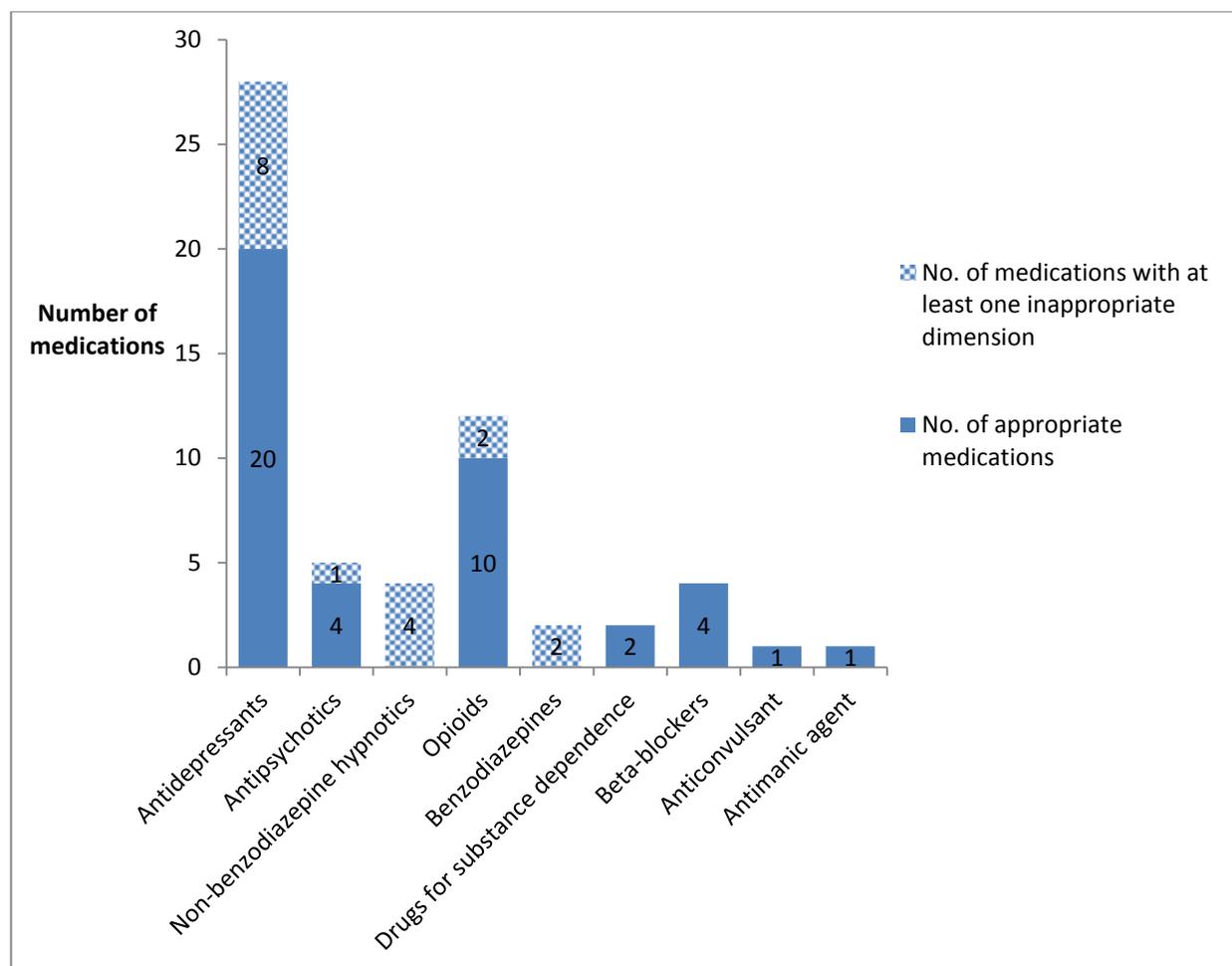
service users were prescribed two or more classes of medications concurrently. Of the 59 prescribed medications, over one-quarter (n = 17) were inappropriate on one or more MAI dimensions<sup>25</sup>. The next paragraph will describe the types of medications with inappropriate A-MAI dimensions.

One of five prescribed antipsychotics had at least one inappropriate A-MAI dimension, whereas all the four prescribed non-benzodiazepine hypnotics (all z-drugs) were deemed to be inappropriate on one or more A-MAI dimensions. Similarly, the two prescribed benzodiazepines had at least one inappropriate A-MAI dimension. Two of the twelve prescribed opioids had one or more inappropriate dimension on the A-MAI. Of the 28 prescribed antidepressants, over one-quarter (n = 8) were deemed to have at least one inappropriate A-MAI dimension. Other types of prescribed medications such as beta blockers prescribed for anxiety disorders, antimanic agents, anticonvulsants and drugs used in treating substance dependence were without inappropriate dimensions. The distribution of appropriate and inappropriate ratings across different medications is shown in figure 5.3.

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<sup>25</sup>Indications for prescribed medications are presented in appendix 5.16

Figure 5.3: Distribution of appropriate and inappropriate ratings across different medications



Note: The total number of prescribed opioids and/or psychiatric medications = 59. There were 28 antidepressants, 5 antipsychotics, 4 non-benzodiazepine hypnotics, 12 opioids, 2 benzodiazepines, 2 drugs for substance dependence, 4 beta-blockers for anxiety problems, 1 anticonvulsant and 1 antimanic agent. All beta-blockers were propranolol prescribed for anxiety problems while all non-benzodiazepine hypnotics were z-drugs prescribed for sleep problems. The anticonvulsant was pregabalin prescribed for sciatica.

### 5.9.5.2. Inappropriate A-MAI dimensions and reasons for inappropriateness

This section describes the A-MAI dimensions that were rated to be inappropriate. A-MAI dimensions rated to be marginally appropriate are presented in appendix 5.13. The A-MAI dimensions comprise indication, effectiveness, dosage, correct directions, drug-drug interactions, drug-disease interactions, practical directions, expense, duplication and duration. There were a range of inappropriate A-MAI dimensions cited for the different classes of medications except antipsychotics. The eight antidepressants that were rated inappropriate had 12 inappropriate A-MAI dimensions. The dimension with the highest percentage of inappropriateness was ‘indication’. Some of the reasons cited for inappropriateness include prescribing of antidepressants for low mood<sup>26</sup> and prescribing

<sup>26</sup> NICE (2009) does not recommend the use of antidepressants for the initial treatment of mild depression such as low mood because the risk-benefit ratio is poor.

for alcohol-related depression. Other reasons cited for inappropriateness are shown in table 5.3. Only one antipsychotic was rated inappropriate in its dosage due to prescribing above the BNF recommended limit. The two benzodiazepines had four inappropriate A-MAI dimensions with duration of therapy having the highest percentage of inappropriateness. Duration of therapy also had the highest percentage of inappropriateness for non-benzodiazepine hypnotics. Duration of benzodiazepines and non-benzodiazepine hypnotics were inappropriate due to prescribing beyond the BNF recommended period. Overall, the four non-benzodiazepine hypnotics had six inappropriate A-MAI dimensions. The two opioids that were rated inappropriate had three inappropriate A-MAI dimensions. In particular, drug-disease interactions had the highest percentage of inappropriateness due to potential interactions that could occur between opioids such as dihydrocodeine and alcohol<sup>27</sup>. Table 5.3 shows the range of reasons for inappropriate medication ratings while table 5.4 provides a description of the total number of inappropriate A-MAI dimensions for each class of medications at service users' first SAS visit.

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<sup>27</sup>Dependence on substances, including alcohol, was considered to be the disease among service users.

Table 5.3: Reasons for inappropriate medication ratings at first SAS visit

<b>Medications</b>	<b>Inappropriate A-MAI dimensions</b>	<b>Reasons cited for inappropriateness</b>
Antidepressants	Indication	Antidepressants (in particular, citalopram and sertraline) prescribed for low mood. Antidepressant (sertraline) prescribed for alcohol-related depression. Antidepressant (amitriptyline) prescribed for an unlicensed indication (sleep problems).
	Effectiveness	Service users reported lack of effectiveness from antidepressants (in particular, amitriptyline, mirtazapine and sertraline)
	Drug-drug interactions	Potential for interaction between dosulepin and tramadol
	Drug-disease interactions	Potential for interaction between dosulepin and alcohol Potential for interaction between mirtazapine and alcohol
	Duplication with other drugs	Continued co-prescribing of citalopram and venlafaxine despite improvement in depression
Antipsychotics	Dose	Antipsychotic (olanzapine 25mg daily) was prescribed at a dose above the BNF limit
Benzodiazepines	Indication	Chlordiazepoxide prescription was continued after alcohol detoxification
	Directions	Lack of clarity about temazepam use
	Duration of therapy	Benzodiazepines (in particular, chlordiazepoxide and temazepam) were prescribed beyond BNF recommended duration without review
Non-benzodiazepine hypnotics (Z-drugs)	Duration of therapy	Z-drug (zopiclone) duration beyond BNF recommendation
	Cost	Z-drugs more expensive than alternative (benzodiazepines)
Opioids	Drug-drug interaction	Potential for interaction between tramadol and dosulepin
	Drug-disease interaction	Potential for interaction between opioids (dihydrocodeine and tramadol) and alcohol

Table 5.4: Inappropriate A-MAI dimensions at service users' first SAS visit

	Number of inappropriate ratings in different A-MAI dimensions								
	Indication	Effectiveness	Dose	Direction	Drug-Drug interact*	Drug-disease interact*	Duplication	Duration	Cost
Antidepressants	4	3			1	3	1		
Antipsychotics			1						
Benzodiazepines	1			1				2	
Non-benzodiazepine hypnotics								4	2
Opioids					1	2			

Where interact\* = interaction

### 5.9.5.3. Factors associated with prescribing appropriateness at first SAS visit

Only one factor (number of prescribed medications) predicting prescribing appropriateness (proportion of service users with and without at least one inappropriate A-MAI dimension) was assessed using logistic regression due to small numbers. Sixteen service users had one or more inappropriate medications while 21 service users were without inappropriate medications at first SAS visit. The number of prescribed medications in particular was assessed because it has been found to be associated with prescribing appropriateness (Duerden, Avery and Payne, 2013; Spinewine et al., 2007). The result of the logistic regression analysis however showed that the number of prescribed medications was not a significant predictor of prescribing appropriateness ( $p = 0.59$ ) in this study. The odds ratio obtained was 0.93 (95% CI: 0.72 to 1.21). The 95% CI shows that the odds of having at least one inappropriate A-MAI dimensions could be as low as 0.72 or as high as 1.21 with every unit increase in the number of prescribed medications.

### 5.9.6. Comparison of the characteristics of service users assessed by nurse prescribers and doctors

Given that evidence obtained from a senior SAS staff (see section 3.2) suggests that service users assessed by doctors may be more likely to be complex with more prescribing issues, service users assessed by doctors and nurse prescribers were compared. This study found that service users assessed by nurse prescribers and doctors were not significantly different in any of the characteristics examined. In fact, it was found that nurse prescribers

tended to assess service users with more medications when compared with doctors. This difference was however not statistically significant. Table 5.5 compares the characteristics of service users assessed by nurse prescribers and doctors.

Table 5.5: Comparison of the characteristics of service users assessed by nurse prescribers and doctors

Characteristics of service users	Nurse prescriber assessment (n = 13)	Doctor assessment (n = 24)	P-value
Age	45.3 ± 9.8	43.9 ± 12.4	0.72 <sup>a</sup>
Gender (n, %)			
Male	8 (61.5%)	14 (58.3%)	0.85 <sup>b</sup>
Female	5 (38.5%)	10 (41.7%)	
Ethnicity (n, %)			
White	12 (100%)	21 (91.3%)	0.54 <sup>c</sup>
Non-white	0	2 (8.7%)	
Housing status (n, %)			
Rented	8 (61.5%)	11 (45.8%)	0.74 <sup>c</sup>
Home owner	2 (15.4%)	7 (29.2%)	
Other	3 (23.1%)	6 (25%)	
Referral substance (n, %)			
Alcohol	13 (100%)	17 (70.8%)	0.1 <sup>c</sup>
Opioids	0	6 (25%)	
Cocaine	0	1 (4.2%)	
Referral source (n, %)			
Self	9 (69.2%)	11 (45.8%)	0.19 <sup>c</sup>
GP	1 (7.7%)	9 (37.5%)	
Other	3 (23.1%)	4 (16.7%)	
LDQ (median, IQR)	23.5 (13.3, 27.8)	16.5 (7, 26)	0.28 <sup>d</sup>
CORE-10 (mean, SD)	26.2 ± 10.1	22.9 ± 11.1	0.38 <sup>a</sup>
EQ 5D (median, IQR)	0.7 (0.4, 0.8)	0.7 (0.4, 0.9)	0.52 <sup>d</sup>
SSQ (mean, SD)	10 ± 6.9	13.3 ± 6.7	0.2 <sup>a</sup>
Number of previous SAS episodes (median, IQR)	1 (0, 2)	0.5 (0, 1)	0.49 <sup>d</sup>
Number of substances used in past 12 months (median, IQR)	2 (1, 2)	2 (2, 4.8)	0.05 <sup>d</sup>
Number of prescribed medicines (median, IQR)	3 (3, 5.5)	2 (1.3, 3.8)	0.08 <sup>d</sup>

Note: The significance level was 0.4% due to Bonferroni adjustment for multiple testing.

<sup>a</sup>Analysed using independent samples t-test, <sup>b</sup>analysed using chi squared test, <sup>c</sup>analysed using Fisher's exact test, <sup>d</sup>analysed using Wilcoxon rank sum test.

### 5.9.7. Analysis of “don't know” ratings

Due to the fact that the prescribers in this study were reviewing medication appropriateness but were not involved in the original prescribing of these medications, and to take into account variability of knowledge among doctors and nurse prescribers regarding some aspects of medications, the “*don't know*” options in the A-MAI ratings were analysed. The

“*don’t know*” option is part of the original MAI. Raters using the original MAI may tick Z (don’t know) if they need additional information from patients’ notes to rate a dimension. In this study, raters were asked to rate Z (don’t know) if they cannot make a judgment on the appropriateness of an A-MAI dimension. There was no service user who had all medications rated as “*don’t know*” by prescribers. The “cost” dimension had the highest proportion of “*don’t know*” ratings. Table 5.6 shows the distribution of “*don’t know*” ratings among different medications.

Table 5.6: Distribution of “*don’t know*” ratings among different medications

	Number of ‘don’t know’ ratings in different A-MAI dimensions								
	Indication	Effectiveness	Dose	Direction	Drug-drug interact*	Drug-disease interact*	Duplication	Duration	Cost
Antidepressants	1	3	5	1	1			2	15
Antipsychotics									3
Benzodiazepines									2
Non-benzodiazepine hypnotics									2
Opioids	2	2	2	2	1	1	1	1	7
Beta-blocker									4
Antimanic agents									1

Where interact\* = interaction

Note: Anticonvulsants and drugs used in treating substance dependence did not have any A-MAI dimension rated as ‘don’t know’ and therefore are not displayed in the table above.

Nurse prescribers rated one or more “*don’t know*” for 9 (69.2%) of the 13 service users they assessed whereas doctors rated at least one “*don’t know*” for 16 (66.7%) of the 24 service users they assessed. There were no statistically significant differences between nurse prescribers and doctors in their ratings of “*don’t know*” (p = 1.00).

### 5.9.8. Follow-up at three months

At three-month follow-up appointment, a total of 23 service users<sup>28</sup> with 33 prescriptions of opioids and/or psychiatric medications were assessed a second time using the A-MAI.

<sup>28</sup> 14 service users were on at least one prescribed psychiatric medication, 5 service users were on prescribed opioids while 4 service users were on both prescribed opioids and psychiatric medications.

The medications include 17 antidepressants, three antipsychotics, three non-benzodiazepine hypnotics (all z-drugs), seven opioids, two beta-blockers for anxiety problems and one prescription for alcohol relapse prevention. Service users' mean age was 46.7 (SD: 10.3) and almost 70% were males. Majority (82.6%) were referred for their alcohol problem. Over 95% were of white ethnicity and slightly over half (52.2%) of service users lived in rented accommodation. Self-referral accounted for 52.2% of referrals and only 14% were employed. The characteristics of these 23 service users were compared to those of the remaining 14 who were only assessed at their first visit and they were no statistically significant differences. Table 5.7 shows the comparison of these characteristics. The findings presented in sections 5.9.8.1 to 5.9.8.3 relate to the 23 service users.

Table 5.7: Comparison of service users assessed using the A-MAI at both first visit and three-month appointment with those assessed only at first SAS visit

Characteristics of service users	Service users assessed only at first SAS visit (n= 14 except otherwise specified)	Service users assessed at both first and three-month visit (n= 23 except otherwise specified)	P-values
Age (mean, SD)	40.6± 12.6	46.7 ± 10.3	0.12 <sup>a</sup>
Gender (n, %)			
Males	6 (42.9%)	16 (69.6%)	0.11 <sup>b</sup>
Females	8 (57.1%)	7 (30.4%)	
Ethnicity (n, %)			
White	12 (92.3%)	21 (95.5%)	1.00 <sup>c</sup>
Non-white	1 (7.7%)	1 (4.5%)	
Housing status (n, %)			
Rented	7 (50.0%)	12 (52.2%)	0.37 <sup>c</sup>
Home owner	5 (35.7%)	4 (17.4%)	
Other	2 (14.3%)	7 (30.4%)	
Referral substance (n, %)			
Alcohol	11 (78.6%)	19 (82.6%)	0.79 <sup>c</sup>
Opioids	3 (21.4%)	3 (13%)	
Cocaine	0	1 (4.3%)	
Referral Source (n, %)			
Self	8 (57.1%)	12 (52.2%)	0.82 <sup>c</sup>
GP	3 (21.4%)	7 (30.4%)	
Other	3 (21.4%)	4 (17.4%)	
Employment status (n, %)			
Employed	2 (14.3%)	3 (13.6%)	1.00 <sup>c</sup>
Unemployed	4 (28.6%)	7 (30.4%)	
Other	8 (57.1%)	12 (52.2%)	
LDQ (median, IQR)	17.5 (6.5, 28.2)	20 (9.3, 26.3)	0.91 <sup>d</sup>
CORE-10 (mean, SD)	20.8± 11.9	26.1 ± 9.7	0.15 <sup>a</sup>
SSQ (mean, SD)	13.9± 7.8	11.2 ± 6.3	0.28 <sup>a</sup>
EQ 5D (median, IQR)	0.7 (0.4, 0.8)	0.7 (0.4, 0.9)	0.93 <sup>d</sup>
No of previous SAS episodes (median, IQR)	0 (0, 1.75)	1 (0, 2)	0.41 <sup>d</sup>
No of substances used in the past 12 months (median, IQR)	2 (2, 4.3)	2 (1, 3)	0.41 <sup>d</sup>
No of prescribed medicines (median, IQR)	3 (2, 3.5)	3 (1, 5)	0.86 <sup>d</sup>

Note: The significance level was 0.4% due to Bonferroni adjustment for multiple testing. <sup>a</sup>Assessed using the independent samples t-test, <sup>b</sup>assessed using chi-squared test, <sup>c</sup>assessed using Fisher's exact test, <sup>d</sup>assessed using the Wilcoxon rank sum test.

### 5.9.8.1. Inappropriate prescribing at three-month follow-up appointment

This section reports on inappropriate prescribing among the 23 followed-up service users. A total of 33 opioids and psychiatric medications were prescribed for these service users. Over one-third (8) of the 23 service users had one or more inappropriate medications. Of

the 33 medications taken at this follow-up appointment, one quarter (n = 8) had at least one inappropriate A-MAI dimension. The most common medication taken by these service users were antidepressants. The next paragraph will describe the types of medications with inappropriate A-MAI dimensions.

Of the 17 prescribed antidepressants, two had inappropriate dimensions in terms of cost. By comparison, all the three non-benzodiazepine hypnotics were inappropriate in their duration because they had been prescribed for a longer period than recommended by the BNF<sup>29</sup>. An antipsychotic had an inappropriate rating in its dosage because it exceeded the BNF limit<sup>30</sup>. Two opioid medications had inappropriate ratings due to duration and drug-disease interaction<sup>31</sup>. Table 5.8 provides more information on the reasons for inappropriate A-MAI ratings at three-month follow-up appointment while figure 5.4 shows the medications with and without inappropriate A-MAI dimensions at three-month follow-up appointment.

Table 5.8: Reasons for inappropriate A-MAI ratings at three-month appointment

<b>Medications</b>	<b>Inappropriate A-MAI dimensions</b>	<b>Reasons for inappropriateness at 3-month follow-up appointment</b>
Antidepressants (n = 17)	Cost	Venlafaxine was rated to be more expensive than alternative medications for anxiety problems. Trazodone was rated to be more expensive than alternative medications for sleep problems.
Antipsychotics (n = 3)	Dose	Olanzapine 25mg daily, prescribed for schizophrenia, exceeded the BNF recommended dose
Non-benzodiazepine hypnotic (n = 3)	Duration of therapy	Duration exceeded BNF recommendation
Opioids (n = 7)	Drug-disease interactions	Potential for interaction between dihydrocodeine and alcohol
	Duration of therapy	Co-codamol was rated to be inappropriate due to its long duration of use

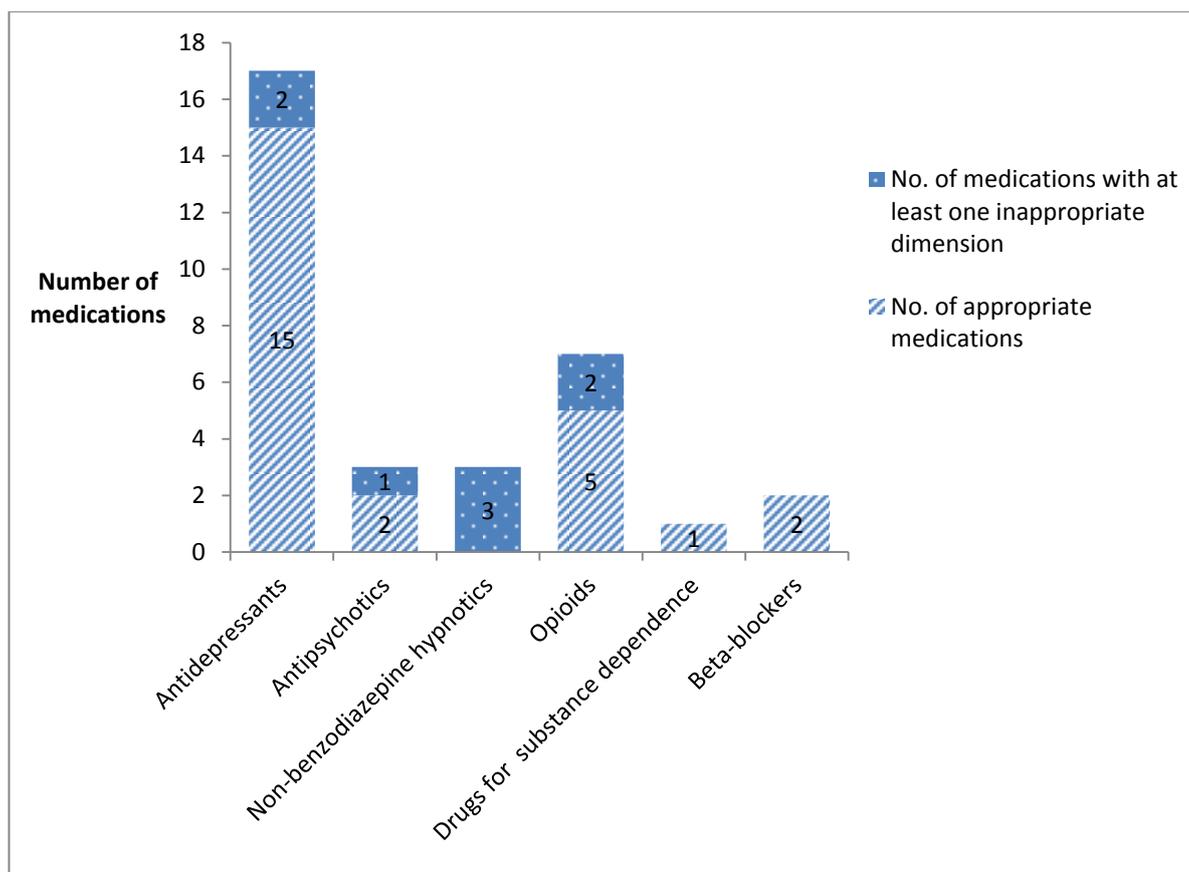
Note: Beta-blockers for anxiety problems and drugs used in treating substance dependence were without inappropriate A-MAI dimension at three-month follow-up appointment. Service users on benzodiazepines, anticonvulsants and antimanic agents at their first SAS visit were not assessed at their three-month follow-up appointment due to a number of reasons: discharge from SAS due to completion of treatment, service user did not turn up and service user was not seen at three-month follow-up.

<sup>29</sup> These three non-benzodiazepine hypnotics were also inappropriate in their duration at first SAS visit.

<sup>30</sup> The antipsychotic (olanzapine) was also inappropriate in its dose at first SAS visit.

<sup>31</sup> One opioid (dihydrocodeine) was also inappropriate due to potential interaction between it and alcohol at first SAS visit.

Figure 5.4: Medications with and without inappropriate A-MAI dimensions at three-month follow-up appointment



Note: Benzodiazepines, anticonvulsants and antimanic agents were not assessed at both first SAS and three-month follow-up appointment due to the following reasons: discharge from SAS due to completion of treatment, service user did not turn up and service user was not seen at three-month follow-up visit.

### 5.9.8.2. Changes in appropriateness of prescribed medications between first SAS visit and three-month follow-up appointment

This section further describes the changes in the appropriateness of service users' prescribed medications between first SAS visit and three-month follow-up appointment. It is of interest that none of the medications identified to be inappropriate at baseline were changed by prescribers at three-month follow-up appointment. In a further four cases, the appropriateness of individual medications changed, such that two medications formerly rated as appropriate were later rated inappropriate. This includes the venlafaxine and co-codamol described in table 5.8. An antidepressant, paroxetine prescribed for anxiety problems, was changed to venlafaxine between first SAS visit and three-month follow-up visit. Venlafaxine was rated to be more expensive at three-month follow-up visit. Co-codamol initially rated appropriate was considered to be inappropriate at three-month follow-up appointment due to its long duration of use.

Another two medications rated inappropriate at baseline were later rated appropriate.

Citalopram was rated inappropriate at first SAS visit because it was considered to have been prescribed for low mood. However, at three-month follow-up visit it was rated appropriate because the prescriber stated that it is now being prescribed for severe depression. Furthermore, the service user prescribed citalopram had reduced his alcohol use. Other reasons for a switch from inappropriate to appropriate ratings are changes in ratings given for drug-drug and drug-disease interaction for an antidepressant, dosulepin. Reasons for these changes are further described in table 5.9.

Table 5.9: Reasons for change in medication appropriateness between first and three-month visit

<b>Medications</b>	<b>A-MAI dimensions where changes occurred</b>	<b>Reasons for change in medication appropriateness</b>
Antidepressants	Indication	Citalopram was rated inappropriate at first SAS visit in an alcohol dependent service user due to prescribing for low mood. However, at three-month follow-up visit it was rated appropriate because the prescriber stated that it is now being prescribed for severe depression that is unlikely to be related to alcohol dependence.
	Drug-drug interaction	Dosulepin initially rated inappropriate due to potential drug interaction with tramadol at first SAS visit was rated to be appropriate at three-month follow-up visit because service user had stopped tramadol.
	Drug-disease interaction	Dosulepin initially rated inappropriate due to potential interaction with alcohol at first SAS visit was rated to be appropriate at three-month follow-up visit because service user had become abstinent from alcohol.
	Cost	Venlafaxine was rated to be more expensive for a service user with anxiety problems whose paroxetine was changed to venlafaxine between first SAS visit and three-month follow-up visit.
Opioids	Duration	Co-codamol initially rated appropriate at first SAS visit was rated to be inappropriate at three-month follow-up visit due to its long duration of use

### **5.9.8.3. Changes made to the medications of followed-up service users**

Eight of the 23 followed-up service users had changes made to their prescribed medications. The total number of medications that were changed among these eight service users was 10. These medications did not have inappropriate A-MAI ratings at first SAS visit. They were however changed due to the reasons described below:

- Discontinuation of acamprosate due to its use for almost a year in an alcohol abstinent service user;
- Reduction of methadone<sup>32</sup> dose at service user's directive;
- Reduction of propranolol dose due to ECG abnormality (slow and irregular heart rhythm);
- Discontinuation of prochlorperazine (prescribed for anxiety disorder) due to excessive sedation;
- Reduction of dihydrocodeine dose due to its dependence potential;
- Reduction of zopiclone dose due to its dependence potential;
- Co-codamol was stopped on completion of therapy;
- Tramadol was also stopped on completion of therapy.

The reasons for dose reduction for two medications (fluoxetine and co-codamol) could not be ascertained from service users. SAS prescribers described either carrying out or influencing the first three changes described above. Changes carried out by service users' GPs during the study duration include: discontinuation of prochlorperazine, reduction of dihydrocodeine and zopiclone doses. Information about GP-initiated reduction or discontinuation of medications was obtained from service users during their three-month follow-up visit.

### **5.9.9. Adherence to prescribed medications**

At first SAS visit, service users were given questionnaires for self-reporting of their adherence to their medications. While the majority of service users reported taking their medications very often or often, there was variation in reported adherence. Table 5.10 provides a summary of service users' levels of adherence to opioids and psychiatric medications.

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<sup>32</sup>As described in section 3.3.3, consultant psychiatrists suggested that the appropriateness of opioids prescribed as substitution therapy should be assessed in addition to other opioids.

Table 5.10: Service users' reported level of adherence at first SAS visit

Types of medicines	Number of prescribed medicines	Medicines taken very often or often (n, %)	Medicines taken sometimes (n, %)	Medicines taken rarely or never (n, %)	Medicines taken prn (n, %)
Antidepressants	28	24 (85.7%)	3 (10.7%)		1 (3.6%)
Antipsychotics	5	4 (80%)			1 (20%)
Benzodiazepines	2	1 (50%)	1 (50%)		
Non-benzodiazepine hypnotic	4	1 (25%)	1 (25%)	1 (25%)	1 (25%)
Anticonvulsant	1	1 (100%)			
Antimanic agent	1	1 (100%)			
Beta-blockers <sup>a</sup>	4	3 (75%)			1 (25%)
Drugs for substance dependence (disulfiram and acamprosate)	2	2 (100%)			
Opioids <sup>b</sup>	12	7 (77.8%)	1 (11.1%)	1 (11.1%)	

prn = as needed

<sup>a</sup>All beta-blockers presented are propranolol prescribed for anxiety disorders.

<sup>b</sup>Opioids also include combination of opioids and paracetamol (for example, co-codamol and co-dydramol). Of the 12 opioid medications, adherence was reported for only nine (9) of them. Thus, nine (9) was used as the denominator when calculating adherence percentage.

## 5.9.10. Discussion

This section presents a discussion of the findings of this study.

### - Level and nature of inappropriate prescribing

This study found that nearly half of service users had at least one inappropriate medication at their first visit to the SAS while over one-quarter of prescribed opioids and psychiatric medications have inappropriate A-MAI dimensions. The A-MAI dimensions that were assessed to be inappropriate varied across the different medications. These findings could not be directly compared with any previous studies on prescribing appropriateness among the population studied due to limited number of previous studies, use of multiple appropriateness dimensions, the assessment of a variety of medications and its setting.

Thirion et al. (2002) assessed the appropriateness of benzodiazepines among a treatment population comprising buprenorphine-maintained opioid-dependent patients and reported that prescribed doses of benzodiazepines were often above the limits specified in its SPC. The percentage of benzodiazepines in which this occurred was however not stated. One study by Baca-Garcia et al. (2009) compared the appropriateness of antidepressant medications of 39 depressed bipolar patients with a history of AUDs with those of 58

depressed bipolar patients without AUD history using the ATHF. The ATHF rates antidepressant treatment based on indication, dose, duration of treatment and adherence (Oquendo et al., 2003). It found that bipolar patients with AUDs had a higher proportion of inadequate antidepressant treatment than those without AUDs (74.3% vs 67.3%,  $p = 0.025$ ).

This study showed that a significant proportion of service users' medications were inappropriate. It was however not possible to determine whether this level of inappropriateness is higher or lower when compared to those without SUDs prescribed similar medications. The prevalence of inappropriateness might have been influenced by several factors. For instance, it is possible that the prevalence in this study was underestimated because some prescribers (especially nurse prescribers) have limited expertise in prescribing most of the classes of medications assessed. Similarly, doctors may be unable to adequately assess the appropriateness of classes of medications they prescribe less often among the medications considered.

On the other hand, inappropriateness might have been overestimated in some instances due to lack of adequate understanding of the circumstances surrounding prescribing. Barber et al. (2005) reported that their judgment of prescribing appropriateness among primary care patients in England sometimes changed depending on the amount of circumstantial evidence they had. In this study, the duration of therapy for all benzodiazepines and non-benzodiazepine hypnotics were rated inappropriate because they had been prescribed for longer than recommended by the BNF (Joint Formulary Committee, 2010) and UK guidelines (Baldwin et al., 2013). An antipsychotic dose was also rated inappropriate because it exceeded BNF recommendation. However, service users with very severe mental health symptoms and complex situations may need higher doses or longer duration of treatment than recommended in guidelines for optimal functioning. Without adequate understanding of the circumstances surrounding prescribing, such prescribing may be judged to be inappropriate.

This study attempted to incorporate service users' perspectives in the assessment of appropriateness. For example, SAS prescribers assessed some antidepressants service users reported as lacking effect to be ineffective in the 'effectiveness' dimension of the A-MAI. Several reasons have been advanced on the need for inclusion of patients' perspectives in decision-making concerning prescribing (Barber, 1995). It is the patient who bears the

immediate burden of illness and their views should therefore be incorporated when making decisions (Cribb and Barber, 1997). As discussed in section 1.4.3, prescribing is not devoid of risk. It is therefore important that decisions about prescribing incorporate patients' views and the concessions they are willing to make concerning the risk of various health outcomes (Tinetti, Bogardus and Agostini, 2004).

Prescribing outside the confines of best practice recommendations carries its own risks. For instance, the need for higher-than-usual doses of psychiatric medications and opioids may predispose the patient to high levels of side effects, toxicity and the risk of dependence on those with dependence potential. Prolonged use of opioids, benzodiazepines and non-benzodiazepine hypnotics such as the z-drugs may lead to dependence on them (Action on Addiction, 2013; Baldwin et al., 2013; Hajak et al., 2003) or exacerbation of an existing SUDs (Brunette et al., 2003). Use of benzodiazepines and non-benzodiazepine hypnotics beyond the BNF duration in this study may be an indicator of dependence on them. SUDs have been recognised as a risk factor in the development of dependence when taking these medications (Hajak et al., 2003). Long-term use of these medications may result in suboptimal benefit (Vinkers and Olivier, 2012; Willems et al., 2013) and adverse drug events.

People with SUDs may exceed the recommended doses of these medications with the potential for overdosing (Action on Addiction, 2013). Their use of substances such as alcohol and illicit drugs with their medications greatly increases this risk (Darke, Duflou and Torok, 2011; Zamparutti et al., 2011). A UK study (Zamparutti et al., 2011) assessing fatal cases involving dihydrocodeine among opiate misusers found that 96% of accidental deaths included the presence of other substances such as alcohol, hypnotics/sedatives and other opioids (heroin, morphine and methadone). Almost half (45%) of victims who accidentally overdosed on dihydrocodeine had it prescribed for them. Similarly, a previous study of oxycodone toxicity in New South Wales, Australia, reported that 70% of such oxycodone were prescribed and psychoactive substances (benzodiazepines, alcohol, other opioids, tricyclic antidepressants, antipsychotics) other than oxycodone were detected in all cases of toxicity (Darke, Duflou and Torok, 2011). While service user involvement is important, it needs to be carefully considered in this group of people for prescribing to be safe and optimal.

Depression was the most common indication in this study and antidepressants were the class of medications most commonly prescribed. This is in line with the findings of the database study which also showed high levels of prescribing of antidepressants among service users (Oluyase et al., 2013). Over one-quarter of prescribed antidepressants were rated as having at least one inappropriate A-MAI dimension: the highest dimension of inappropriateness was the ‘indication’ at service users’ first SAS visit. This reflects the fact that prescribers questioned the decision to prescribe antidepressants for people who were actively using substances. There is evidence that substance use, for example, heavy drinking may lead to depressed affect (Graham et al., 2007) and such high levels of alcohol consumption may counteract the benefits accruing from antidepressants (Ramsey, Engler and Stein, 2005).

- Characteristics of service users assessed by nurse prescribers and doctors

This study found that service users assessed by nurse prescribers did not differ from those assessed by doctors in any of the characteristics examined in this study including their “don’t know” ratings. This is despite the fact that the referral system described by the SAS staff was supposed to allow assessment of more complex service users by doctors rather than nurse prescribers. While it is possible that service users assessed by these two groups of prescribers may differ in characteristics not measured in this study, it appears that nurse prescribers and doctors were assessing service users with similar characteristics. However, nurse prescribers and doctors could not be compared in their decision-making processes concerning appropriateness because they assessed different service users. It is therefore not possible to make any assumption about similarity of decision-making concerning prescribing appropriateness.

- Adherence to prescribed medications

Adherence to prescribed medications varied in this study although most service users reported taking their medications very often or often. The regular use of medications reported by most service users is surprising given that current SUDs have been associated with non-adherence (Manwani et al., 2007; Sajatovic et al., 2006). While it is possible that service users tended to adhere to their medications, previous studies (Owen et al., 1996; Sajatovic et al., 2006; Weiss, 2004) that have assessed adherence among people with and without co-occurring mental disorders and SUDs have found higher levels of non-adherence among those with SUDs. Owen et al. (1996) assessed medication adherence between schizophrenic patients with and without SUDs and found that those with SUDs

were significantly more likely to report non-adherence to their neuroleptic medications (Owen et al., 1996). Similarly, bipolar patients with current SUDs have been found to be more likely to report non-adherence (Sajatovic et al., 2006). SUDs represent a risk factor for non-adherence among people with mental disorders (Jonsdottir et al., 2013; Montes et al., 2013). It is therefore possible that service users may have overestimated their adherence or that response was subject to recall bias (Schechter and Walker, 2002). Service users' memory may have been negatively affected by substances thus affecting their ability to recall information (Bates, Bowden and Barry, 2002; Sullivan and Pfefferbaum, 2005). They may also be insincere about their level of adherence (Chesney, 2000), and may report a high level of adherence in order to avoid embarrassment (Schechter and Walker, 2002; Tiv et al., 2012). However, the possibility of this was mitigated in this study as service users were informed that any disclosure about their medication adherence will not be shared with healthcare professionals at the SAS. Adherence was also assessed on a separate questionnaire that was not attached to the A-MAI that was rated by prescribers.

- A-MAI dimensions with “don't know” ratings

The cost dimension on the A-MAI had the highest number of “don't know”. This may reflect the fact that prescribers consider knowledge of cost a low priority. In addition, a systematic review on cost awareness among physicians that included many UK studies found that doctors were ignorant of cost (Allan, Lexchin and Wiebe, 2007). There may well be a need to support prescribers in making cost-effective prescribing decisions.

- Change in prescribing appropriateness

It is interesting to note that while almost half of service users had at least one inappropriate medication at baseline assessment, none of the medications identified to be inappropriate were changed by three-month follow-up appointment. The reason for this finding was explored during the interviews with prescribers. This finding precluded the calculation of potential cost savings accruing from stopping or reducing inappropriate medications which was initially one of the research questions.

An antidepressant that was rated to be inappropriate at first SAS visit was rated as appropriate at three-month follow-up appointment because the prescriber described the service user as having reduced his substance use, and his antidepressant as being prescribed for severe depression rather than low mood resulting from symptoms of

intoxication. Addressing SUDs may be helpful in clarifying the relationship between SUDs and depression (Miele, Trautman and Hasin, 1996). However, completely removing or reducing the contribution of substances to a mental disorder is often not achieved (Lingford-Hughes et al., 2012). In particular, this finding supports the evidence that people with substance-induced mental disorders may be later re-classified as having independent mental disorders (Magidson et al., 2013; Nunes et al., 2006; Ramsey et al., 2004). Where this occurs, withholding psychiatric medications from those with substance-induced disorders may indicate poor quality of care with the potential to predispose such service users to worse outcomes including increased severity of illness (Torrens, Martin-Santos and Samet, 2006) and suicide (Aharonovich et al., 2002; Appleby, 2000) compared to those with single disorders.

- Variability in prescribers' ratings of 'marginally appropriate' and 'inappropriate' A-MAI dimensions

The findings of this study suggest there was a degree of variability in how prescribers rated some A-MAI dimensions<sup>33</sup> (in particular, indication, drug-drug and drug-disease interactions). For instance, this study found that while some prescribers rated antidepressants to be marginally appropriate because they were prescribed for alcohol-related depression, other prescribers cited a similar reason for rating some antidepressants as inappropriate. Similarly, there was also evidence of differences in how drug-drug interactions and drug-disease interactions were rated by prescribers.

These differences may have resulted because different clinicians assessed appropriateness. The clinician evaluators were from different backgrounds and also had varying lengths of practice experience (see section 7.3.1). These differences have been suggested as possible reasons for clinical disagreements among raters (Bregnhøj et al., 2005; Stuijt et al., 2009). Stuijt et al. (2009) assessed the reliability of the MAI in a Dutch residential home using abstracted patient information and reported lower inter-rater reliability for some MAI dimensions including indication and drug interactions. Similar findings were reported in an earlier study in Denmark by Bregnhøj et al. (2005). It is a possibility that more homogeneity among the clinician evaluators could have resulted in more consistent ratings.

Furthermore, variability in the quality of information available during service users' assessments may have resulted in different appropriateness ratings. For instance, it would

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<sup>33</sup> Refer to appendix 5.13 for reasons cited by prescribers for marginally appropriate ratings on the A-MAI

be easier to make judgments on the appropriateness of prescribed medications where service users provide a comprehensive and clear history and vice versa. Decision-making may be more variable due to lack of contextual information surrounding prescribing. In this study, assessment of drug-drug and drug-disease interactions may also be affected by clinicians' judgments on the risk posed by these interactions. This judgment may differ between clinicians. The observed variability in rating may be further due to insufficient training on the use of the A-MAI. Although group training sessions involving practising the use of the A-MAI with a case study of one patient were organised with SAS prescribers, this may not have been adequate. The MAI developers recommend practising on 10 to 20 patients (Hanlon and Schmader, 2013). In addition, seven prescribers had not joined the SAS when the group training sessions took place. These prescribers joined the SAS at different periods during the course of this research. The researcher therefore had to train each of the seven prescribers individually when they joined the SAS. The training sessions involved discussion of the A-MAI and its operational instructions with each of them. Again, it is possible that the training sessions organised for these prescribers were insufficient and sometimes led to variable A-MAI ratings.

It is pertinent to say that variability of rating is expected in such a study as this because prescribers rated different service users whose clinical presentations may differ. This may also have contributed to different ratings of MAI dimensions.

### **5.9.11. Strengths and limitations**

One limitation of this study is the fact that diagnoses and associated pharmacotherapeutic management were based on self-report. These information were also self-written by service users, with the possibility that they were sometimes inaccurate. There was no independent assessment of service users' diagnoses due to the length of time needed for completion of diagnostic instruments (Anderson, Michalak and Lam, 2002; McGrady et al., 2010) in this time-pressured setting. The SAS setting has been previously described in section 3.2. Furthermore, most service users were referred from sources other than GPs and GP/referral notes were not available. Consequently, self-report represented the only feasible means for assessment of diagnosis and prescribed medications.

Self-reported diagnosis and associated pharmacotherapy may be limited because patients may not know their diagnosis and the names of their medications (Marks et al., 2010). Further, cognitive impairment from substances such as alcohol may also hinder the ability

to recall information (White, 2004) or there may be deliberate avoidance of disclosure. There is evidence that some illnesses such as depression may negatively affect self-report due to their symptomatology (Corser et al., 2008). It is therefore possible that this study underestimated the prevalence of inappropriate prescribing due to the above limitations. This study focused on exploring the appropriateness of prescribing of psychiatric medications and opioids for people with SUDs. However, it is pertinent to state that the use of prescribed medications sits alongside other non-prescribed medications such as over-the-counter (hereafter OTC) medicines, herbal medicines as well as the use of substances. Prescribers assessed for the presence of interactions between substances and prescribed opioids and psychiatric medications using the A-MAI. However, the use of OTCs and herbal medicines were not considered when assessing for interactions and prescribing appropriateness in general, though their use may impact on judgments made about appropriateness. The focus of this study on prescribed medications represents a limitation of this thesis as safe practice in prescribing would entail considering both prescribed and non-prescribed medications.

Although this study found no significant difference in the characteristics of service users assessed by nurse prescribers and doctors, it is not possible to make any inference about similarity of decision-making concerning appropriateness among both groups of prescribers because they each assessed different service users. Furthermore, it is possible that service users may differ in characteristics that were not assessed in this study. It is also possible that there were instances where prescribers did not accurately assess appropriateness since they were not present when service users' original diagnoses were made. Some medications they assessed as lacking indication or being inappropriate due to dose or duration may actually be appropriate depending on the context and service user's circumstances which prescribers may not be adequately knowledgeable about. For instance, some antidepressants were assessed as lacking indication due to the absence of depressive symptoms. An alternative explanation may be that the antidepressant has led to improvement in depressive symptoms.

Furthermore, most of the psychiatric medications and opioids assessed in this study are outside the remit of prescribing of nurse prescribers. This may have made assessment of their appropriateness challenging for nurse prescribers. While nurse prescribers could rate "don't know" where they had difficulties making a decision, there was no statistically significant difference between nurse prescribers and doctors in the number of such ratings.

However, as stated above, they assessed different service users and so no firm conclusion can be drawn from this finding. The identification of omissions of psychiatric medications and opioids would also be challenging for nurse prescribers because they are outside their scope of practice. Nurse prescribers were included despite this obvious limitation because of the need to understand prescribing practice in general as nurse prescribing proliferates and medical expertise declines in addiction medicine specialty. It could be argued that nurse prescribers working with complex service users with comorbidities will sometimes identify medications that they have concerns about or be concerned about omission of needed medications. This study provided an opportunity for nurse prescribers to highlight such issues and the particular areas of prescribing they are concerned about. In addition, where there are concerns about interactions between the medications within their scope of practice and other prescribed medications that were the focus of this thesis, this study was able to capture them. It is however acknowledged that the presence of concerns does not necessarily imply inappropriateness.

A summated score for each medication assessed using the A-MAI could not be calculated as done in some previous studies (Hanlon et al., 2004; Samsa et al., 1994; Schmader et al., 1994) because prescribers rated “don’t know” for A-MAI dimensions they could not confidently assess. Although the “don’t know” option is part of the original MAI (it was not added by the author of this thesis), it has been rarely used in previous studies. It was necessary for prescribers to utilise the ‘don’t know’ option when necessary because they are not the original prescribers of the medications they assessed and also because they may not have adequate knowledge about the circumstances of prescribing. In addition, as stated above, some groups of prescribers such as nurse prescribers have a more limited remit of prescribing compared to doctors and were allowed to rate ‘don’t know’ if they could not make a judgment on the appropriateness of prescribing decisions. A previous study (Steinman et al., 2006) that used the MAI also did not use summated scores. Steinman et al. (2006) assessed inappropriate prescribing using subscales of the MAI (indication, effectiveness and duplication) and the Beers criteria<sup>34</sup> (Beers et al., 1991).

Some research questions such as whether the appropriateness of prescribed medications changed between baseline assessment and three-month follow-up appointment could not be adequately addressed due to lack of a summated score for each medication. If this had been possible, this study could have assessed whether prescribing appropriateness improved or

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<sup>34</sup> Section 1.4.7.1 provides a very brief overview of Beers criteria.

declined using the summated score. It will also have been possible to find out factors associated with this change in appropriateness. Factors predicting prescribing appropriateness could not be adequately explored in the logistic regression analysis due to small numbers. Lack of medication omissions also meant that this area could not be explored. Despite these limitations, the use of the adapted-MAI in this study was advantageous as it allowed for clinical judgment when assessing prescribing appropriateness. Further, the sample size for this study was small and was estimated based on the maximum number of service users that could be assessed by seven prescribers who were permanent staff<sup>35</sup> at the SAS during the study period. This study estimated that the number of service users that could be recruited was 88. During the study duration, seven other prescribers joined the SAS at various points while some others left. The total number of service users seen by the 14 prescribers who took part in this study was actually 76 and 60 of them provided consent for this study. Actual recruitment was therefore less than anticipated. This resulted mainly due to non-attendance of appointments by service users.

It is possible that some instances where there were no statistically significant differences between those with and without inappropriate medications were due to the small sample size of this study. This study might have been underpowered to detect variation due to its sample size. Although this small scale exploratory study was necessary as it represents the first attempt at exploring opioid and psychiatric medication prescribing on as many appropriateness dimensions, a future study that includes a larger number of service users is needed to support or refute its findings. Sample size estimation should be carried out in order to ensure that the future study is adequately powered in order to achieve worthwhile results (McCrum-Gardner, 2010).

In addition, limited validity tests were carried out with the A-MAI and other questionnaires developed for assessing medication omissions and adherence. More studies are needed to carry out further psychometric tests. Some previous studies (Samsa et al., 1994; Schmader et al., 1994) that utilised the MAI involved the use of two raters to assess abstracted patients' data. Inter-rater and intra-rater reliability tests were carried out in these studies. Inter-rater reliability assesses the agreement between ratings made by two or more clinicians when assessing the same patient whereas intra-rater reliability measures agreement between ratings made by the same clinician on at least two occasions when assessing the same patient (Sim and Wright, 2005). While training sessions were organised

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<sup>35</sup>There were only seven prescribers at the SAS at the onset of this study. Seven other prescribers joined the SAS at various points during this study.

in this study for prescribers on how to use the A-MAI, with discussion of a case study of one patient to ensure comparable ratings, inter-rater and intra-rater reliability tests were not carried out. The limited number of training sessions may be insufficient and may have led to variability in how prescribers rated appropriateness. The originators of the MAI recommend training raters using 10 to 20 patients to ensure reliability of rating (Hanlon and Schmader, 2013).

Although testing inter-rater and intra-rater reliability before the commencement of this study would have been important to assess consistency of ratings, the applicability of these tests would have been somewhat limited in practice for the following reasons:

- Firstly, inter-rater reliability tests would have had limited applicability because prescribers assessed different service users. Assessment of different service users would most likely introduce variability;
- Secondly, intra-rater reliability tests would also be limited because improvement or deterioration in service users' health status over time has the potential to introduce variability when assessing the appropriateness of prescribed medications. For example, some medications assessed to be appropriate at first SAS visit were rated inappropriate by three-month follow-up visit and vice versa due to changes in the health of service users or medications. There were different ratings given to the same service users in these situations.

Variability of rating is expected in this type of study. Unlike previous studies that assessed appropriateness by applying the MAI to abstracted patient data, prescribers had actual contact with service users before assessing appropriateness. Each prescriber assessed different service users whose clinical presentation will most likely differ. Furthermore, prescribers' judgments on appropriateness incorporated service users' perspectives or subjective views. Consequently, two service users with the same conditions may express different views about their medications. Again, this may lead to different judgments on prescribing appropriateness.

In this study, face-to-face contact with service users was advantageous as service users' perspectives and the actual benefit they report from their medications could be taken into consideration when rating their appropriateness. This is the first study where the A-MAI was used in a clinical setting as described above, making the assessment of appropriateness service-user focused. Unlike some previous studies (see section 2.7, page 94) that focused

only on particular dimensions of prescribing appropriateness such as dose due to non-availability of information on other aspects, this study was able to assess many dimensions of prescribing appropriateness.

This study was carried out in a single SAS and its findings may not be generalizable to present-day addiction services in the UK. SAS are now rare in the UK, with a move from mainly NHS service provision to include a more mixed economy of service providers in the alcohol and drug treatment sector (Public Health England, 2014c). Furthermore, it was not possible to determine how representative service users assessed by prescribers were of those attending the SAS during the study duration because information on service users assessed by non-prescribers was not collected.

### **5.9.12. Summary of key findings**

Almost half (43.2%) of service users were found to have one or more inappropriate medications at their first SAS visit. The A-MAI dimensions that were assessed to be inappropriate varied across the different medications. Depression was the most common indication and antidepressants were the most commonly prescribed medications. Over a quarter of antidepressants prescribed were rated as having at least one inappropriate A-MAI dimension with the highest dimension of inappropriateness at first SAS visit being indication. This study also found that all benzodiazepines and non-benzodiazepine hypnotics had one or more inappropriate A-MAI dimensions, with the duration of therapy being inappropriate for all of them. They had all been prescribed for longer than recommended in the BNF. Further, while almost half of service users had at least one inappropriate medication at baseline assessment, none of the medications identified to be inappropriate were changed by their three-month follow-up appointment. Adherence to prescribed medications varied though most service users reported taking their medications very often or often. The cost dimension on the A-MAI had the highest number of 'don't know' ratings.

# Chapter 6: Qualitative interview studies with service users: methodology, results and discussion

## **6.1. Introduction to the chapter**

This chapter presents the qualitative research methodology adopted for the interviews with service users as well as the results and discussion of its findings. Qualitative research is a form of inquiry in which the researcher collects and analyses textual rather than numerical data with the aim of understanding human actions and experiences (Schwandt, 2007). Qualitative research is founded on the premise that researchers can garner a deeper understanding of phenomena than is possible with quantitative research (Silverman, 2013). Qualitative research is therefore useful for exploring complex and under-researched areas such as the topic considered in this thesis. It can also be used to answer questions around the meaning of illness and medications to patients as well as adherence to such medications (Stevenson et al., 2000).

As described in section 3.4.1.2, the phenomenological methodology adopted in this thesis aims to discover people's interpretations of their experience of the world (Green and Thorogood, 2004). A phenomenological perspective argued for the use of interviews as a research method because of the need to understand the perceptions of service users concerning the appropriateness of prescribing decisions. In particular, semi-structured interviews were utilised for an in-depth understanding of the perspectives of service users on the appropriateness of their prescribed medications. The study rationale, design, research questions addressed, sampling strategy, recruitment method and topic guide development are presented in section 6.2. The ethical process is presented in section 6.3 while the interview process, data analysis and storage plans are delineated in section 6.4.

## **6.2. Study rationale, design, research questions, sampling strategy, recruitment and topic guide development**

### **6.2.1. Study rationale**

In chapter 2 (section 2.7), the scoping review highlighted a lack of research into the views of service users with SUDs concerning prescribing decisions. This is despite increasing

calls for the involvement of patients in treatment decisions (Farrelly et al., 2015; Institute of Medicine, 2001). Patients are the single person present throughout their care and are often knowledgeable about their illness and treatment (Institute of Medicine, 2001). Their views therefore represent a valuable source of information concerning their management. In relation to this thesis, it is possible to learn about the quality of prescribing decisions by exploring the views of service users concerning the appropriateness of their medications.

### **6.2.2. Study design**

This study involved semi-structured interviews with 14 service users who were attending the SAS. All interviews were carried out at service users' three-month follow-up appointment or at their next appointment if this was more convenient. Interviews were carried out with a single service user at a time due to the sensitivity of the topic and to maintain confidentiality (McIntyre, 2012).

### **6.2.3. Research questions**

The following research questions were addressed in this study:

1. How do service users perceive the appropriateness of their prescribed medications, changes to them and its impact on their quality of life?
2. What factors do service users consider to be important in assessing if their medications are appropriate for them?
3. To what extent do service users adhere to their medications and is this influenced by their perceptions on appropriateness?

Appropriateness in the service user interviews was explored by asking service users about their need for medications, medication effectiveness, medication changes, assessment and review. Exploring appropriateness in this way was necessary because it is a complex concept that requires holistic exploration. Furthermore, ex-service users who serve as mentors for other service users did not suggest any other areas for inclusion when their views were sought concerning these different aspects of appropriateness included on the interview topic guide. The first research question was addressed by exploring service users' views about their need for medications, effectiveness, assessment and review, medication changes and impact of change on quality of life. The second question explored service users' views on factors important in assessing whether their medications are right for them. The last question dealt with service users' views on their medications and the influence of this on adherence. Semi-structured interviews were employed for an in-depth

understanding of the perspectives of service users on the appropriateness of their medications. Complex areas like appropriateness may be open to interpretation and interviews are a good way to explore their meaning.

#### **6.2.4. Sampling strategy**

Interviews were carried out with a convenience sample of service users on current prescriptions of opioids and/or psychiatric medications. All interviewed service users were a convenience sample of those who took part in the medication appropriateness study during their first SAS visit. Convenience sampling involves recruiting people who are available to take part in research (Marshall, 1996), and may not be representative of the study population (Robinson, 2014). However, the representativeness of a sample is not the goal of qualitative research (Thompson, 1999). Qualitative research and in particular phenomenology is concerned with sampling participants who have had the relevant experience (Englander, 2012), so that they can provide insight concerning the phenomenon. The impact of this sampling strategy on the transferability of study findings is further considered in chapter 7 (section 7.3.8.2).

#### **6.2.5. Recruitment**

Service users recruited into the medication appropriateness study who were still attending the SAS prior to their three-month follow-up appointment and who were on prescribed opioids and/or psychiatric medications at their first assessment were contacted by telephone to determine if they would be happy to be interviewed during their follow-up appointment. Service users who attended for their follow-up appointment and who had initially indicated interest in being interviewed were reminded of the study aims and encouraged to ask for clarification where needed. They were then given a consent form to sign. A copy of the signed consent form was given to service users before the interviews commenced.

All interviews with service users took place in a private room at the SAS. Where service users could not be interviewed during their three-month visit, another interview was scheduled for their next visit. For qualitative studies, Kvale (2007) recommends recruiting between 5 and 25 participants depending on the nature of the study, in order to reach a compromise between collecting excessive data that may be unmanageable during analysis and collecting enough data so that sufficient level of depth can be gained with meaningful conclusions. In particular, a sample size of six was recommended by Janice Morse (Morse,

1994) for phenomenological studies. A total of 14 service users were interviewed in the current study.

### **6.2.6. Developing the topic guide for interviews with service users**

The topic guide for service users (appendix 6.1) was developed from the research questions as well as discussion with my academic supervisors. It covered six major areas: service users' medical/substance use history, need for medications, effectiveness of medications, assessment and review, medication change and quality of life, and adherence. The views of ex-service users who serve as mentors for other service users at the SAS were sought about the topic guide during one of their meetings to determine if there were other areas that needed to be covered. The ex-service users did not suggest any changes to the topic guide as they considered it to be comprehensive. Before the commencement of interviews with service users, the topic guide was developed into questions to be asked. The questions were piloted with the researcher's supervisors who suggested rewording a few of the questions. The questions were then piloted with two ex-service users who did not suggest any changes.

## **6.3. Ethical considerations**

As described in section 5.8, ethical application for the medication appropriateness study and interviews with service users and prescribers were made in the same application. Section 5.8 has covered aspects of the ethical process that were common to both studies such as submission of the application to the HSRGC, issues raised at the meeting with HSRGC as well as the need for absolute confidentiality concerning information provided by study participants during the meeting with the NRES Committee Yorkshire & the Humber. This section will address the ethical issues that were specific to the interviews in general (both service user and prescriber interviews) because they were similar.

A problem that could have arisen from taking part in interviews is that lack of anonymity could lead to some participants withholding information. Service users can be concerned that the information they provide may affect their care. For example, they may be concerned that their participation in this study may lead to the withdrawal of medications they value. The researcher assured all service users that the information they provide will not be shared with their prescribers. Prescribers were also assured of the confidentiality of all information they provided in this study. Furthermore, all participants were assured that the information they provide will be anonymised in all publications stemming from this

study. The purpose of the research was explained to all participants. These steps were taken to ensure that they feel at ease during the interviews. A pertinent ethical consideration for the interview process is the potential vulnerability of service users. For instance, it is possible that some service users could feel anxious or distressed talking about their medications and medical/SUD history. This was minimised by making it clear to service users that they could stop at any point and did not have to continue with the interview. This scenario did not however occur. Service users were also informed that arrangements could be made for them to speak to one of the therapists at the SAS if they were overwhelmed during the interview. The REC gave a favourable ethical opinion of the research based on meeting the following conditions:

1. The inclusion of a clause allowing participants to consent to their interview being audio-recorded on the consent form for service users and prescribers.
2. Statement 7 (I agree to be contacted in the future concerning this study ) on the consent form for service users should be more specific about when and why service users may be contacted in the future.
3. The service user information sheet should explain that not all participants will be invited to take part in the interview stage of the study.

The changes specified by the REC were made and a confirmation letter for the study was subsequently obtained.

## **6.4. Interview process, data analysis and storage**

This section presents the process for conducting the interviews, analysing and storing them. Section 6.4.1 covers the interview process while section 6.4.2 presents the data analysis and storage plans. These processes were broadly similar for both service user and prescriber interviews. They are therefore presented together.

### **6.4.1. Interview process**

Interviewed service users had been in treatment for at least three months, were familiar with the SAS setting and had developed a level of relationship with the researcher<sup>36</sup>. Similarly, prescribers who were interviewed had all participated in the medication appropriateness study and had built a level of rapport with the researcher.

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<sup>36</sup> The researcher had recruited all service users who agreed to take part in this study and also communicated with them via the telephone before the interviews.

The setting of data collection is important in qualitative research, as interviewees are more likely to be relaxed in a comfortable and familiar environment (Stevenson et al., 2000). Service users were interviewed in a private room at the SAS which enabled them to comfortably discuss their illness and medications used in managing them. Prescribers' interviews also took place in a private room at the SAS.

The identity of the interviewer may impact on the interview (Stevenson et al., 2000). For prescribing research, if the interviewer is a healthcare professional, the interviewee (for example, service users) may not want to disclose actual information concerning their prescribed medications (for example, information concerning their adherence). They may provide answers that they feel the researcher wants to hear. Consequently, in this study the researcher did not introduce herself as a pharmacist to service users but rather as a research student at the University of York. She only went further to disclose her professional identity if asked. However, no service user asked about her professional background. She conducted all interviews in a systematic manner.

Before each interview, the purpose of the research was explained to participants in order to put them at ease about the process. Participants were informed that the interview would be audio-recorded and direct quotations from them may be used in write-ups from this thesis. Such quotations would be anonymous and any information disclosed would be kept confidential. In particular, service users were informed that exceptional disclosures which suggest that the service user or some other person is at risk of harm may be disclosed for further action to be taken. Participants were then invited to ask any questions before the interview started and then sign the consent form. A copy of the signed consent form was given to them.

The topic guides provided a rough framework for the interviews. A flexible approach to questions was taken during the interviews in order to allow the interviewer probe participants in more detail where necessary. The use of a topic guide however ensured that similar questions were asked and therefore permitted comparison of themes across each subject. Examples of questions asked during the service user interviews include "what prescribed medications are you taking?" as well as questions concerning when the medication was prescribed and by whom. More sensitive questions, for example, regarding need for medications, their effectiveness and adherence in service user interviews were

asked further into the interviews once participants felt comfortable with the process. Examples of questions asked prescribers during their interviews include “how would you define inappropriate prescribing?” and “how do you assess the appropriateness of service users’ medications?”. Where necessary, responses were reiterated to participants to check comprehension. At the end of the interview, participants were asked whether they had anything else to say. The duration of interviews with service users ranged between 10 and 104 minutes ( $45.7 \pm 30.5$ ). There were three short interviews between 10 and 17 minutes. In one of these interviews, the service user’s partner was present and this might have prevented her from engaging with the interview. She gave very short responses to the questions. Another service user requested that the interview be stopped because it was boring him. The third interview was brief because the interview room needed to be used by SAS staff. Other interviews were between 27 and 104 minutes. Interview duration with prescribers lasted between 36 and 74 minutes ( $48.1 \pm 12.5$ ). The difference in interview time was primarily because some participants spoke at length while others did not.

All interviews were audio-recorded except one in which a service user did not want to be recorded. After each interview, the researcher made brief notes on the interview experience and a critical reflection on the interview process was begun. On listening back to the audio-recording of her first service user interview, the researcher realised she did not really probe some of his responses sufficiently. She consequently made it a priority to follow-up the responses of other service users more fully when interviewing them. Questions exploring why medication omissions were absent in the medication appropriateness study were added to the topic guide for prescriber interviews.

## **6.4.2. Data analysis and storage**

### Analysis of semi-structured interviews

This section describes how interviews were transcribed and analysed and is similar for both the service user and prescriber interviews.

### Transcription

The researcher transcribed four of the interviews (all service user interviews) alongside data collection. As data collection progressed, a professional transcriber was engaged (with the assistance of my supervisors) in order to keep pace with the data collection process. Transcribing some of the interviews provided the opportunity for the researcher to familiarise herself with the data and emerging themes while also planning for other

interviews. All transcribed interviews were saved on her secured double passworded computer at the Department of Health Sciences, University of York, for analysis.

### Analysis

Initially, the researcher had proposed to use a qualitative data analysis software (Atlas.ti version 6.0) to support her analysis of the interviews. However, she decided to use Atlas.ti for data coding only (appendix 6.2a provides a screenshot of codes generated using Atlas.ti) while she undertook further data analysis in Microsoft word due to the relatively small number of interviews she carried out. Qualitative data analysis software such as Atlas.ti is particularly useful for large amounts of qualitative data (St John and Johnson, 2000). Furthermore, Coffey and Atkinson (1996) have stated that none of the qualitative data analysis softwares will perform automatic data analysis, rather they depend on the researcher defining what analytical issues are to be explored, what ideas are important and their mode of representation. All codes generated in Atlas.ti were exported to Microsoft word for further analysis.

Although there are different ways to analyse qualitative data, the *thematic framework* proposed by Miles and Huberman (1994) was used as a guide in this study. Miles and Huberman outline 13 points that make up their thematic framework analysis. They consist of:

1. Noting patterns, themes
2. Seeing plausibility
3. Clustering
4. Making metaphors
5. Counting
6. Making contrasts/comparisons
7. Partitioning variables
8. Subsuming particles into the general
9. Factoring
10. Noting relations between variables
11. Finding intervening variables
12. Building a logical chain of evidence
13. Making conceptual/theoretical coherence

Steps 1, 2 and 3 assist the researcher in seeing ‘what goes with what’. Step 4 helps in achieving more integration of the data. Step 5 shows what’s there. Step 6 sharpens understanding of data while step 7 assists in differentiating the variables. Step 7 is especially useful when coding schemes are being developed and elaborated as it assists in highlighting differences that might otherwise be blurred. Steps 8, 9, 10 and 11 help in seeing things and their relationship more abstractly. Finally, steps 12 and 13 bring about a coherent understanding of data with step 13 in particular leading to building of a more conceptual overview of the subject area (Miles and Huberman, 1994). The steps the researcher took in data analysis are described below with reference to aspects of the thematic framework used.

Firstly, the researcher read the interview transcripts several times in order to ensure that she became familiar with them. Familiarisation involves immersion in the data and is essential to gain in-depth knowledge of the nature and diversity of the data (Bradley, Curry and Devers, 2007). This ensured that she gained a holistic understanding of her interview data while constantly addressing her research questions. She became aware of key ideas and concepts and coded these themes on her interview transcripts (this refers to the first and third steps of the thematic framework analysis: *noting patterns and themes* and *clustering*). Themes are recurrent unifying ideas or statements about the subject of inquiry (Bradley, Curry and Devers, 2007). She also re-read the reflexive journals she had made during the interviews to identify if any of the themes located in the data related to her reflexive thoughts. Some of these themes were expected as the topic guide was constructed in order to explore them.

As she became immersed in her interview data, she ensured that any new themes she identified were added to her coding framework and also that they were rooted in the data (this refers to the second step of the thematic framework analysis: *plausibility*). As new themes emerged, she went over each transcript to code the data where relevant for the new themes. Consequently, her data analysis was open and inductive as the key issues and themes that were expressed by interviewees formed the basis of the coding framework. Where similar issues or views were expressed by interviewees they were clustered under the same theme. The inductive method utilised in this analysis ensured that she was immersed in the data and also had a comprehensive knowledge of it. Some of the themes at this stage were descriptive such as reasons for prescribing while others were more analytical such as antidepressants as a ‘crutch’.

This stage was followed by the stage of managing the data by combining or eliminating coded themes (this refers to the following steps of the thematic framework analysis: *making metaphors, making contrasts or comparisons, partitioning variables, subsuming particles into the general and factoring, noting relations between variables and finding intervening variables*). All codes were exported to Microsoft word where data were managed.

A metaphor is defined by the *Oxford Dictionary* as a figure of speech in which a word or phrase is applied to an object or action to which it is not literally applicable (Oxford Dictionaries, 2016b). It is also defined as a thing regarded as representative or symbolic of something else. It is used to achieve more integration of data (Miles and Huberman, 1994). A metaphor ‘medical crutch’ was used by a service user when describing his view of his antidepressant.

Making contrasts or comparisons and partitioning variables (differentiation) between the themes derived from the different cases assisted in seeing how they differ as well as their similarities. Furthermore, differentiation sometimes involved breaking up a theme into more than one theme if needed. For example, closer examination of the theme ‘benefit from medications’ from service users’ interviews showed that it also included ideas about trade-off of risks and benefits, a decision was therefore made to make trade-off of risks and benefits a theme.

*Subsuming particles into the general* and *factoring* are more than the first-level process of clustering similar themes. They involve trying to locate themes in a more abstractly defined class thereby further reducing the bulk of data and finding patterns in them. Each theme was further examined and similar ones were grouped together to form meta-themes. For example, benefit from medications, trade-off of risks and benefits, antidepressants as a ‘medical crutch’ and interference of alcohol with antidepressants were all grouped under the meta-theme ‘functional outcomes’ in service users’ interviews since they were all related to service users’ functioning. *Noting relation between variables* shows how variables relate to each other while *finding intervening variables* examines whether there are other variables that are involved in a relationship observed between two variables.

*Building a logical chain of evidence* and *making conceptual/theoretical coherence* involves putting all the information gathered from previous steps together in order to provide a holistic understanding. The process of managing the coded themes was discussed with the

researcher's academic supervisors. The feedback she obtained from her supervisors was helpful in combining or sometimes separating out themes and clarifying the reasons why different themes were placed under the overarching themes.

While some of the themes such as 'functional outcomes' related to a large proportion of participants, a few did not. For example, the theme 'entitlement to prescribed medications' was described by only four service users. This was reflected when presenting the results by counting the number of participants reporting particular themes (this refers to the fifth step of the thematic framework analysis: *counting*). Even though counting was used to reflect intensity of themes, the meaning participants have constructed concerning prescribing appropriateness was given priority in accordance with the principles of qualitative research (Merriam, 2009). Overall, the thematic framework by Miles and Huberman (1994) was useful as a guide in analysing data. However, it was not possible to follow its steps rigidly in sequence, because analysis is an ongoing iterative process in qualitative research (Bradley, Curry and Devers, 2007). Appendices 6.2b and 6.2c show samples of the coding framework for service user and prescriber interviews respectively.

## **6.5. Results and discussion**

### **6.5.1. Participants' characteristics**

Only service users taking prescribed opioids and/or psychiatric medications at both first SAS visit and before their three-month follow-up appointment were approached for interview in order to obtain their views on their current medications. Twenty three (23) service users were taking such prescribed medications at first visit and were still attending the SAS prior to their three-month review appointment. Twenty of them were contacted by telephone prior to their follow-up appointment to determine if they would consent to participate in an interview during their follow-up assessment. The remaining three service users could not be contacted before their follow-up assessment.

Four service users were not interviewed because they did not attend for their scheduled interviews whilst two service users attended but refused to be interviewed. Therefore, a total of 14 service users (of 20: 70%) were interviewed. The 14 service users did not differ from the six people who were not interviewed in their sociodemographic characteristics or level of dependence, quality of life, level of psychological distress and social satisfaction (see appendix 6.3 for table showing comparison). The mean age of those interviewed was

48.9 years (range: 26 to 66 years) and the mean number of medications they were being prescribed at their first SAS visit and three-month assessment were 3 (range: 1 to 8) and 3.4 (range: 1 to 8) respectively. The mean number of target medications (prescribed opioids and/or psychiatric medications) at first SAS visit was 1.7 (range: 1 to 3). The 14 service users comprised three females and 11 males. Alcohol was the referral substance for all but two service users who were referred for problems with heroin.

### **6.5.2. Themes highlighted by service users**

Eight themes were highlighted by service users in relation to the topics addressed in the interviews: functional outcomes, entitlement to medications, prescribing in response to stressful situations, assessment and review, discussion with clinicians, improved quality of life, adverse effect of medications and adherence. Some themes such as functional outcomes, entitlement to medications, prescribing in response to stressful situations, discussion with clinicians and adverse effect of medications were inductive themes that came out of the thematic analysis (Spencer, Ritchie and O'Connor, 2003b) while others (assessment and review, quality of life and adherence) were deductive, arising from the topic guide.

#### **6.5.2.1. Functional outcomes**

The phrase 'functional outcomes' proved a very useful and unifying theme under which to consider the views of a number of service users concerning the need for their medications and their effectiveness. This phrase has been used in the literature to describe physical, social and psychological functioning of patients (Collett, 2001). Functional outcomes came out strongly when service users discussed their need for medications and their effectiveness. All service users described their medications in relation to the effect they had on their health conditions and wider life. Some service users went on to describe the influence of substances, mainly alcohol, on the effectiveness of their medications. Four sub-themes are considered under this theme: benefit from medications, trade-off of risks and benefits, interference of alcohol with antidepressants and antidepressants as 'a medical crutch'.

#### **Benefit from medications**

Thirteen service users thought that their medications had led to some degree of improvement in their health conditions and functioning. Two service users described the positive impact of their antidepressants on their functioning:

*My Fluoxetine, yeah, I know if... I don't take it for a couple of days I... very quickly start to feel meself, you know, going ... downhill again, and start feeling low and tearful [ID 35, female, alcohol dependency].*

*...because a few months ago, I didn't take them [Citalopram] for a while and I just hit rock bottom again and then when I started back on them again, within a couple of weeks I was back to normal [ID 5, male, heroin dependency].*

Service users reporting positive effects from particular medications also sometimes described doubtful benefits from others. One service user who has a three-year history of co-codamol and citalopram use for pain and post-traumatic stress disorder (hereafter PTSD) respectively, as well as a three-month history of disulfiram use for alcohol relapse prevention, described benefits from his co-codamol and disulfiram but was uncertain about the benefit of his citalopram:

*[Co-codamol] don't take the pain fully away but it gets you to where you can get about and move around, but it does ...work... [Later, talking about disulfiram]: I've not had a drink for three... months, last time I'd gone three months without a drink I... was in me teens, I'd be... a teenager. So it, yeah, it has worked... [Later, talking about citalopram]: I don't know if it's working or not. I don't know. I can't feel any difference taking it [ID 16, male, alcohol dependency].*

Among service users who described positive effects from their medications were those who reported benefits despite being prescribed outside BNF recommendations. One elderly service user referred for his alcohol problems, with a 12-year history of olanzapine use at a dose above the BNF recommendation for long-standing paranoid schizophrenia, described the benefit he derived from his medication:

*As soon as I was put on 25mg of Olanzapine a day, at night, all slight psychotic symptoms disappeared. And I've been on those tablets for a number of years now and I find that they do very well for me psychiatrically... I haven't been mentally ill for something like oh about ten/twelve years now... thanks to the medications... I've been on the maximum dose of Olanzapine for a number of years now... but fortunately, with Olanzapine..., no side effects whatsoever; in my case that is, no side effects at all, they work very well [ID18, male, alcohol dependency].*

Another service user with a year history of zopiclone use for sleep problems described benefit from his zopiclone (the duration of zopiclone use had exceeded BNF recommendations):

*The zopiclone works because within ten, twenty minutes I'm asleep. So that does work... [ID 15, male, alcohol dependency].*

On the other hand, a service user who continued alcohol misuse despite receiving treatment at the SAS described lack of benefit from his zopiclone. Again, zopiclone duration had exceeded BNF recommendation as he has been prescribed it for six months for sleep problems:

*... I've got to... take it [zopiclone] to try and get that sleep and hope I do go to sleep and ... not wake up till morning, but it don't happen, it just doesn't happen... I've never had a full night's sleep, even with the medication I don't have a full night's sleep. Like if I take my medication tonight at about eleven/half past eleven, an hour later I'll start to go to sleep and I'll be awake for two/three o'clock (ID 27, male, alcohol dependency).*

Overall, most service users described benefits from their medications, including service users who had been prescribed medications outside guideline recommendations. It was unclear whether all those prescribed outside guideline recommendations were aware of it because the interviews did not explore this issue due to its sensitive nature. Prescribing outside guideline recommendations is common in psychiatry (Ali and Ajmal, 2012). Baldwin and Kosky (2007) reported that one of the most common types of off-label (unapproved or unlabelled) prescribing in psychiatry is prescribing higher-than-approved dosages of antipsychotics and antidepressants for patients who do not respond to the maximum approved dosages. Furthermore, while non-benzodiazepine hypnotics such as zopiclone and benzodiazepines are recommended for short-term use in insomnia (four weeks) (Joint Formulary Committee, 2010), they are commonly prescribed long-term (Baldwin and Kosky, 2007; Haw and Stubbs, 2007).

Best practice recommendations including dosing and duration recommendations are usually established in clinical trials especially RCTs and where available, they serve as the foundation for clinical guidelines (Tucker and Roth, 2006) including the BNF. Where there is no evidence from clinical trials, recommendations are based to a large extent on the

opinions of experts who make up the guideline committee (Geleris and Boudoulas, 2011). It may not be possible to directly extrapolate recommendations from guidelines on prescribing of opioids and psychiatric medications to people with SUDs because most of the evidence from RCTs exclude people with SUDs (Furlan et al., 2006; Ostacher, 2011; Samet and Walley, 2008). Where they are included, the sample does not reflect the heterogeneous group of people with SUDs who usually have multiple health problems and complex situations (Humphreys et al., 2005).

In clinical guidelines, the maximum approved dose is that which gives the best balance between the desired clinical effect and unwanted side effects (Baldwin and Kosky, 2007). This dose may not be optimal for people with SUDs and may need to be increased or decreased depending on the severity of service users' conditions and comorbidities. For example, people with co-existing SUDs and mental disorders may need higher doses or longer duration of treatment compared to those with single conditions because they may have more severe and persistent symptoms or they may be more disturbed and resistant to treatment (Green, 2005; Soyka, 2000; Soyka et al., 2001; Volkow, 2010). Conversely, the presence of hepatic impairment may lead to prescribing of lower doses of medications (Kane et al., 1998). Changes in the neurochemistry of the reward pathways of the brain secondary to chronic use of medications may also affect prescribing decisions (Gershwin and Hamilton, 1998) including dosing. Opioid doses in people with SUDs may need to be higher than in those without SUDs due to tolerance (Gershwin and Hamilton, 1998).

Generally, the effectiveness of off-label practices is often not supported by strong evidence (Baldwin and Kosky, 2007; Kane and Leucht, 2008). Naylor (1995) suggested that the patient's perspective is particularly important and should be considered where there is lack of adequate evidence or doubt about the best course of action. Continued benefit reported by patients and a lack of desire to stop treatment may be factors that fuel prescribing outside guideline recommendations (Wright, Caplan and Payne, 1994).

Furthermore, consideration of the repercussions of relapse to substance use on the individual and society may well justify the need to sometimes prescribe outside guideline recommendations in order to maintain the well-being and equilibrium of people with SUDs. Evidence from this study suggests that the appropriateness of prescribing is open to interpretation as some service users tended to view medications that improved their functioning as appropriate for them even when they were inappropriate by guideline

standards. There was therefore sometimes conflict between these two different perspectives. This study suggests that pharmacologically inappropriate prescriptions may well be appropriate in another sense if they are perceived to provide benefit by service users.

While off-label prescribing may be clinically beneficial (Ali and Ajmal, 2012) for patients with severe and complex problems such as those with SUDs, it also carries clinical risks such as adverse effects. For instance, prescribing supra-BNF doses of antipsychotics carries a greater risk of unwanted side effects such as extrapyramidal side effects (parkinsonism, akathisia, acute dystonias, tardive dyskinesia), sedation, tachycardia, weight gain, postural hypotension, seizures and hyperprolactinaemia (Royal College of Psychiatrists, 2014b).

The management of insomnia in people with SUDs requires careful consideration in order to ensure that it is not being caused by the SUDs (Royal College of Psychiatrists, 1997). Where insomnia is secondary to SUDs, there is need for management of the SUD (Baldwin et al., 2013). Long-term prescribing of non-benzodiazepine hypnotics such as zopiclone may lead to dependence especially among people with a history of SUDs (Cimolai, 2007; Hajak et al., 2003). There is therefore a need for extreme caution when prescribing off-label as well as consideration of acute and long-term benefit to patients (Ali and Ajmal, 2012). There should also be regular monitoring and follow-up throughout treatment (Baldwin et al., 2013).

Mental disorders such as PTSD reported by the service user with ID 16 may exacerbate chronic pain (Otis, Keane and Kerns, 2003; The British Pain Society, 2007), as it is associated with increased rates of psychological and physical symptoms (Otis et al., 2003; Sullivan et al., 2006). Sullivan et al. (2006) have suggested that it is possible that opioids are being used to treat an undifferentiated state of mental and physical pain. Diagnosis and treatment of mental disorders are therefore important when considering prescribing opioids. Adequate care for mental disorders may improve chronic pain (Lin et al., 2003; Sullivan et al., 2006) and also reduce the need for chronic opioid use (Sullivan et al., 2006).

Where opioids are helpful in the management of chronic pain, they should be used. However, where they do not work in adequate doses, they may need to be stopped

(Stannard, 2013). Opioids are usually prescribed for longer periods than their known efficacy in the management of chronic pain (Noble et al., 2010). Most studies have a follow-up period of less than six months (Samet and Walley, 2008), and there is limited evidence for the effectiveness of opioids over the long duration of treatment typical of chronic pain (Noble et al., 2010). Again, the patient's perspective would need to be considered for optimal decision-making. Complete symptomatic relief of chronic pain may often not be possible and an acceptable balance between improved functioning and side-effects should be seen as the goal of therapy (Department of Health (England) and the devolved administrations, 2007). Non-pharmacological treatment options such as psychological therapies (for example, cognitive behavioural therapy) may be useful alternatives or a combination of these and pharmacotherapy may need to be considered for optimal management of chronic pain (Holliday, Hayes and Dunlop, 2013) and insomnia (Baldwin et al., 2013).

### **Trade-off of risks and benefits**

Four service users described having side effects which they tolerated due to the benefits they felt they obtained. One service user with a five-year history of citalopram use for long-standing depression described sexual dysfunction resulting from citalopram but reported that it was nevertheless effective for his depression:

*Citalopram's been great. Easy to work with, you know,... easy to take, it doesn't make me drowsy... I can live a normal life on it, and I'm happy now... the only contraindication or side-effect I have from citalopram is that sometimes it prevents ejaculation. I can get to the point of climax but, ... I don't ejaculate [ID 23, male, alcohol dependency].*

Another service user with a six-month history of venlafaxine use for anxiety disorder of six-year duration described benefit from it but also acknowledged that he does not strictly follow the instructions for taking it due to the sleepiness it causes:

*... it's [Venlafaxine] made me very balanced, calm, relaxed... it has been mentioned to me that I should take two the same time, perhaps in the afternoon when I take my Disulfiram, but I don't because I don't want to be... too, too sleepy... [ID 7, male, alcohol dependency].*

One service user who described benefits from his co-codamol and disulfiram also described side effects from taking this combination of medications:

*Co-codamol and Disulfiram have been helpful... A combination of that [Disulfiram] and the Co-codamol was a concoction for me, ...it's like a sleeping tablet, cos I... tend to sleep, or drowsiness, not sleep, the drowsiness [ID 16, male, alcohol dependency].*

Service users therefore described having to make compromises due to the benefits and adverse effects they experience from their medications. Prescribing appropriateness as suggested here involves weighing the risks and benefits of medications. The fact that service users decided to continue with their prescriptions suggests that the perceived benefits outweighed the disadvantages. This finding is similar to those found in a range of different contexts (Moncrieff, Cohen and Mason, 2009; Schofield et al., 2011), and do not appear to be particularly linked to their substance use status. Moncrieff et al. (2009) in a study that assessed patients' subjective experience with antipsychotic medications found that some patients described a similar trade-off between the risk and the benefit of their medications. Comparable findings were also described by Schofield et al. (2011) in a qualitative study exploring patients' views on antidepressant use, as patients described continued antidepressant intake despite the side effects they experienced.

There was also evidence from this study that there were situations where service users did not follow the instructions for medication use in order to minimise adverse effects. They appear to have chosen to take medications or modify them according to their own beliefs of what works best for them. Section 6.5.2.7 further considers issues around medication adherence. Medications often have side effects due to the fact that most of them exert their pharmacological effects on different parts of the body simultaneously (Barsky et al., 2002). The concurrent use of multiple medications further increases the risk of side effects (Rambhade et al., 2012) especially among medications that have the potential to cause such effects on their own. Co-codamol and disulfiram both have the potential to cause drowsiness (Centre for Substance Abuse Treatment, 2009) and this may be worsened when they are taken concurrently. Given the literature and the findings of this study, judgment on the appropriateness of prescribing among service users involves balancing the risks and benefits of medications.

## **Interference of alcohol with antidepressants**

Three service users who all described some levels of benefit from their antidepressants highlighted the negative impact of alcohol on its effectiveness. One service user with a six-year history of fluoxetine use for depression described alcohol as hindering the effect of his fluoxetine:

*It does work, ... but the... drink is hindering it I think, cos obviously I'm not getting the full effect of the antidepressant because I'm getting me brain drunk, so it's interfering with that [ID 27, male, alcohol dependency].*

Another service user who was using two antidepressants for his long-standing depression described the negative effect of alcohol on his antidepressants whilst also stating that the impact of alcohol has been explained to him by his doctors:

*Well as long as I... don't drink, the Fluoxetine and the Mirtazapine work marvellously well... I've had periods of depression recently but I put that down to drinking because, from what I've had explained to me by doctors, alcohol destroys the effects of the medication. In other words, you can take as much fluoxetine and mirtazapine as you like, but if you're drinking three or four pints of beer a day that kills the effect of it, and that's why you end up depressed [ID18, male, alcohol dependency].*

The evidence that symptoms of depression could result from AUDs (Boden and Fergusson, 2011; Schuckit et al., 1997) raises the concern that alcohol misuse by depressed persons may counteract the benefits of antidepressants (Ramsey, Engler and Stein, 2005). This is in line with the findings reported by service users as they described suboptimal benefit from their antidepressants (all selective serotonin reuptake inhibitors) in the presence of alcohol. Furthermore, a recent meta-analysis found that although antidepressants such as those with noradrenergic activities are effective in treating depression in people with comorbid depression and AUDs, the selective serotonin reuptake inhibitors such as fluoxetine are not very effective (Iovieno et al., 2011). Torrens et al. (2005) in a previous meta-analysis comprising people with depression and more diverse SUDs including AUDs also reported similar findings. Overall, it appears alcohol hinders the effectiveness of antidepressants among people with SUDs and co-existing depression.

### **Antidepressants as a medical ‘crutch’**

As well as the health impact of their medications, four service users described their medications (in particular, antidepressants) as providing valuable support in their lives. One service user who had a five-year history of citalopram use for long-standing depression described the impact of his citalopram during stressful periods as follows:

*...and during a very stressful period which, my mood didn't really change that much, I used it as like a comfort blanket or a crutch to sort of like, I'm taking 40mg [Citalopram] now, so I'm bound to be all right [ID 23, male, alcohol dependency].*

Similarly, another service user with a six-month history of venlafaxine use for anxiety disorder of six-year duration described his venlafaxine as helping his decision-making in addition to its effect on his anxiety:

*...and should there be any periods of anxiety I feel very... comfortable, relaxed and... any decision making I feel, you know, I feel as though venlafaxine is helping me at that [ID 7, male, alcohol dependency].*

Other research on people's experiences with antidepressants has found that people describe them as providing valuable support in their daily lives, using terms such as ‘crutch’ or ‘cushion’ or ‘burden reliever’ (Knudsen, Hansen and Eskildsen, 2003; Knudsen, Hansen and Traulsen, 2002). While people involved in these studies sometimes described antidepressants as helping their emotional problems disappear, others described them as something that assisted them in managing their problems. This is similar to what service users in this study reported.

Furthermore, a meta-ethnography of patients' experience of antidepressants also reported that they described antidepressants as helping them return to normal functioning through fulfilling their social roles as well as carrying out their daily activities and regaining control (Malpass et al., 2009). The need to use prescribed medications such as antidepressants as a ‘medical crutch’ may well be greater among people with SUDs due to their myriad of health issues (Hoertel et al., 2014; McLellan, 2009) and life problems (Lloyd, 1998). Consequently, antidepressants may be needed to help maintain equilibrium, and thus prevent disintegration of their lives.

### 6.5.2.2. Entitlement to medications

Four service users described a sense of entitlement to being prescribed medications. One service user who had bought street zopiclone for some years before being prescribed it for sleep problems by his GP, described his awareness of the potential for addiction to zopiclone:

*I feel a lot better now, mm, and... I do appreciate that ... they [Zopiclone] are addictive... but so's smoking, so's driving really fast, so's doing a lot of other things. It's my health and I've chosen to look after it how I want and this is how I want (ID 57, male, alcohol dependency).*

Another service user went on to describe his preference for asking for what he needs from his doctor:

*Well... my personal opinion is that I think with... doctors these days, I think you have to tell them what's wrong with you or basically tell 'em what you need, rather than the sort of old school where you went to... the doctor and you spent a long time... explaining your symptoms (ID 7, male, alcohol dependency).*

This theme was also evident when one service user described how he requested an alternative to his dihydrocodeine after his GP expressed concerns about his misuse of it. He further described being addicted to his medication:

*I had said to me doctor, well when he were showing concerns about how many I was taking [Dihydrocodeine], and I says "well just stop 'em and give me summat else." And he says "No, you can't because your body is...". Basically I'm addicted to 'em even though I... don't feel addicted to 'em, but apparently me body will crave 'em if I just stop taking 'em, so [ID 29, male, alcohol dependency].*

Another service user who had deliberately taken an overdose of his prescribed antidepressant (fluoxetine) and sleeping tablet (zopiclone) in order to self-harm and had been admitted to hospital was afraid his zopiclone could be stopped by his GP but demonstrated a recognition of his right to be prescribed it:

*And the sleeper [Zopiclone], they (hospital doctors) won't prescribe it to me, so now I have to go back to my GP and hope that he'll prescribe me it again, because obvious he's gonna*

*know on... computer that I took an overdose, so he might refuse me... treatment... so I've put meself in a predicament there to try and get me medication back... but I know he can't refuse it because he's putting me physically in danger then (ID 27, male, alcohol dependency).*

Patient involvement in their own care now represents a core value in the medical profession and NHS (Department of Health, 2013b; General Medical Council., 2009). The NHS constitution states that NHS services must reflect the needs and preferences of patients (Department of Health, 2013c). Ethical and practical reasons have been advanced on the need for patient choice in prescribing as it is the patient who takes the medication (Barber, 1995). Cribb and Barber (1997) have further suggested that one aspect of good prescribing is that it does what patients want done. However, there is sometimes conflict between physician-assessed need and what patients want, and how far prescribing should be determined by either of this remains an unresolved question (Barber, 1995; Cribb and Barber, 1997).

The issue of patient choice is even more challenging in addiction medicine because patients may be less than open about the reasons for which they want medications. They may want medications in order to suspend reality or for their pleasurable effects. Craving and an impaired control over their lives (Action on Addiction, 2013) including medication use may also be factors underlying service users' request or need for certain types of medications. Furthermore, this need may be driven by the service user's desire to avoid withdrawal symptoms. It is therefore possible that the responses of some service users above (ID 57, 29 and 27) may be a consequence of these factors.

The management of risk is a particularly important issue in addiction medicine because service users may be at great risk from medications (Action on Addiction, 2013). It is therefore paramount to ensure that prescribing decisions are justified, and also prescribe with due precautions that may involve limit setting, monitoring and behavioural rules in this population (Action on Addiction, 2013). Nevertheless, prescribers may be under considerably greater pressure to respond to the self-perceived needs of substance users compared with other patient groups. People with SUDs appear to have a particularly strong sense of their own needs and seek to make their own choices about their prescriptions. This sense of empowerment may well influence prescribing decisions.

### **6.5.2.3. Prescribing in response to stressful situations**

One service user described being prescribed medication (in particular, increase in dose) in response to his situation rather than a medical issue. The service user had earlier described the valuable support he got from using his citalopram during a very stressful period in section 6.5.2.1 under the theme ‘antidepressants as a medical crutch’:

*Two days before New Year’s Eve, ... I went to see me GP, got a special appointment, and... we discussed what was happening in my life [marital problems]... and he said “Look, if you’ve made that decision that you want to leave your home you’ve gotta leave”... So he upped the dosage [of Citalopram for depression] to 40mgs and he said “You come back in a week’s time and tell me how you feel... If you’ve made the decision you’ve made it, go do it. If you can’t do it then talk with your wife, cos from a... medical point of view, it’s really not a medical issue (ID 23, male, alcohol dependency).*

Prescribing in response to life stresses rather than a clear medical indication has raised concerns about unnecessary ‘medicalisation’ of life’s challenges (Baldwin et al., 2014; Horwitz and Wakefield, 2007). There is a growing trend to use mood-altering drugs including antidepressants to treat instances of human distress or emotional unhappiness (Heath, 1999; Manninen, 2006). It is possible that prescribing in response to life’s challenges and problems may be more common among people with SUDs because of their high levels of vulnerability. Their situations are often complex with family disruptions, social and economic deprivation being prominent features (Gossop et al., 1998; Lloyd, 1998). The lifestyle of service users usually contributes to these problems and may result in demoralisation, a sense of distress and hopelessness (Action on Addiction, 2013) which prescribers may be tempted to ‘fix’ with a pill. Although this pattern of prescribing may be considered to be inappropriate in the sense that such medications are being prescribed or their doses increased in order to manage conditions for which they have no known efficacy, it may be appropriate in another sense if it provides support that assists the service user during such stressful periods.

### **6.5.2.4. Assessment and review**

This theme came out when service users were asked about the assessment and review of their medications. The following sub-themes were described by service users: medication review, addiction to medications and fear of losing medications.

## Medication review

Eleven service users described regular review of their medications. One service user with a six-month history of sertraline use for postnatal depression described the fact that her medication is regularly reviewed:

*Yeah, ... , I have reviews every, I think it's every couple of months or every few months, to see if ..., I'm still ok on the medication, so the GP knows that, ... it's working basically. I get reviews ..., ever so often. So they can know that it's doing what it's supposed to be doing [ID 61, female, alcohol dependency].*

Similarly, another service user who described a possible lack of indication for his paroxetine described regular review of his medication:

*It has been reviewed several times and, he said "I don't want you to come off it just yet." ... and it's due to be reviewed ..., so he's [GP] going to see me and review it [ID 15, male, alcohol dependency].*

One service user prescribed propranolol for anxiety disorder and dosulepin for anxiety and depression went on to describe the fact that he sometimes misses his review appointments:

*...sometimes I don't honour ... the appointments, I sometimes forget ... they're [GP] doing everything right on their side, obviously, but I'm just a bit lax with that ... I've missed a couple of appointments now, you know [ID 21, male, alcohol dependency] .*

By contrast, three service users described lack of optimal practices regarding review of their medications. One service user with a five-year history of citalopram use for long-standing depression described the fact that his citalopram is not reviewed regularly, and that he could easily obtain a repeat prescription without adequate monitoring:

*But what happens with GPs and practices, ... you just become a repeat prescription, and I can go for a year without a review when they're supposed to be every two months or every three, you know, ...you can be left to sort of float around. And I can ring the chemist up and say "I need another script". And he'll go "right, OK" and it's there two days later. You don't have to go see a GP. But that's always been the case, which is not really about*

*monitoring the effect of the drug, it's more a case of, well you're on it now, so just... keep taking it [ID 23, male, alcohol dependency].*

Similarly, another service user who has a three-year history of co-codamol use for pain described the fact that his present GP has never enquired about his medications from him and just keeps prescribing them:

*... you know, my doctor, now though, I've been transferred now, for about eighteen months maybe, she's just continued prescribing co-codamol, and I don't think she's ever asked me once why I'm on it ... Honestly, I don't think she has [ID 16, male, alcohol dependency].*

Another service user with a ten-year history of dihydrocodeine use for pain secondary to an operation on his spine described how his dihydrocodeine is rarely reviewed during his appointment for medication review with his GP:

*... you used to get review dates but very rarely they actually went through them, maybe once a year [ID 29, male, alcohol dependency].*

The standards being followed in repeat prescribing as well as its safety have been issues of concern in primary care (Garfield et al., 2009; Taylor, 1996). Repeat prescribing has the advantages of saving time, convenience and reduction in the workload of prescribers (De Smet and Dautzenberg, 2004). However, the views expressed by some service users in this study clearly suggest that their repeat prescriptions were not being regularly reviewed.

In addition, repeat dispensing (NHS Confederation Publication, 2013) where repeat prescriptions are managed by the patient's pharmacy of choice was also a problem due to lack of review by a pharmacist. Without regular review of repeat prescriptions, patients may end up being stuck on unnecessary medications and may become dependent on medications that have such tendencies. Lack of medication review could make prescribed medications become inappropriate over time. A few service users described becoming dependent on their prescribed medications. Furthermore, it is also impossible to evaluate whether patients are still taking their medications with repeat prescribing. Consequently, lack of regular review of repeat prescriptions can lead to failure to detect and resolve drug-therapy problems as well as drug wastage (Avery et al., 2000; De Smet and Dautzenberg, 2004; Saastamoinen, Enlund and Klaukka, 2008).

Swinglehurst et al. (2011) in a recent ethnographic study that was carried out in primary care settings in the UK involving observation of interactions between doctors, receptionists and administrative staff concerning repeat prescribing routines, found that when patients taking repeat prescriptions attended the clinic for medication reviews prompted by their electronic records, clinicians sometimes described the reviews as unnecessary. They tended to enter the codes for medication reviews even when there was no formal review of patients' medications during the appointment (Swinglehurst et al., 2011). As with the wider issue of communication discussed in section 6.5.2.5, this sort of behaviour by doctors may be more common towards people with SUDs and may contribute to inappropriate prescribing.

### **Addiction to prescribed medications**

Two service users described being addicted to their prescribed medications as has been touched on above and another service user expressed concerns about the possibility of addiction to his medication. Two of the quotations used here have been previously used in section 6.5.2.2. They are used here because they describe this theme aptly. One of the service users who expressed concerns about the review of his medication (dihydrocodeine at a dose of 30mg, 1 to 2 tabs qds) also described having developed addiction to it as he takes more than his prescribed dose:

*I had said to me doctor, well when he were showing concerns about how many I was taking [Dihydrocodeine], and I says "well just stop 'em and give me summat else." And he says "No, you can't because your body is...". Basically I'm addicted to 'em even though I... don't feel addicted to 'em, but apparently me body will crave 'em if I just stop taking 'em [ID 29, male, alcohol dependency].*

Another service user who had bought street zopiclone for some years before being prescribed it for sleep problems by his GP also demonstrated awareness of his addiction to zopiclone (3.75mg every other day):

*... I do appreciate that they [Zopiclone] are addictive, ... but so's smoking, so's driving really fast, so's doing a lot of other things [ID 57, male, alcohol dependency]*

There was also a service user with a six-month history of venlafaxine use for anxiety problems who expressed fear of becoming dependent on his antidepressant:

*I know, I do realise at some point that in my recovery these tablets will... eventually have to be phased out, I don't want to... become dependent on them [ID 7, male, alcohol dependency].*

This finding is supported in the literature as service users in alcohol and drug services have reported problematic use of prescription-only medicines (POM) such as opioids, benzodiazepines and non-benzodiazepine hypnotics (National Treatment Agency for Substance Misuse, 2011). The issue of addiction to prescribed medications such as opioid analgesics is a recognised public health problem in countries such as the USA (Sehgal et al., 2012). Data from the UK suggests that there is an increase in the number of people seeking help for opioid dependency (Stannard, 2013).

A contributing factor in the rise in opioid prescription misuse is the increase in opioid prescribing (Wisniewski, Purdy and Blondell, 2008). Risk factors for opioid dependence among those with chronic pain include a current or past history of dependence, type of opioid (short or long acting), dose and duration of opioids (Gourlay and Heit, 2008; Sehgal et al., 2012; Solanki et al., 2011; Sullivan et al., 2010). People with a history of SUDs have a higher risk of misusing prescription drugs (Simoni-Wastila and Strickler, 2004; Solanki et al., 2011). While people who are dependent on alcohol, who made up over 78% of service users in this SAS are unlikely to have the same drive or craving for opioids as those who are dependent on illicit opioids or those on opioid substitution therapy, there is still the possibility of misuse and dependence on prescribed opioids when used in chronic pain management (Substance Abuse and Mental Health Services Administration, 2011). High doses of opioids (greater than 120mg morphine equivalent per day) and short-acting opioids such as dihydrocodeine also increase risk of opioid misuse (Sullivan et al., 2010). Similar risk factors for dependence have been reported for non-benzodiazepine hypnotics such as zopiclone and zolpidem (Hajak et al., 2003).

The dihydrocodeine and zopiclone dependence reported in this study may reflect a combination of factors such as co-existing SUDs, high dose and long duration of use of these medications. There is need to adequately monitor the medications of people with SUDs, especially those with dependence potential as it is possible for medications that were appropriately prescribed to become inappropriate over time. In addition, for chronic pain to be managed optimally, staff in pain clinics would need a basic competence in identifying and diagnosing dependence and also access to addictions consultation while

those working in addiction clinics need a basic knowledge of chronic pain management and access to pain clinic consultations (Action on Addiction, 2013).

Fear of dependence on antidepressants has been reported among people using antidepressants with some patients believing that they could become dependent and thus altering their doses or even stopping them without involving their prescribers (Schofield et al., 2011). This implies that there is the need to address the misconceptions of service users about their medications so as to forestall unwanted outcomes such as non-adherence (Malpass et al., 2009).

### **Fear of losing medications**

Two service users expressed their fears about losing their prescribed medications. One service user had expressed concerns about the review of his dihydrocodeine, demonstrated a sense of entitlement to it and also described being addicted to it. He however did not want his medication stopped although this was the intention of his GP:

*Well only thing it [Dihydrocodeine] does is kill the pain so at least I can get on with me life like without any pain. So yeah, if I don't... take it I'd just be in constant pain.... and that's the one thing they want to take off me (ID 29, male, alcohol dependency).*

Another service user previously described in section 6.5.2.2, who had a strong sense of entitlement to zopiclone and had been treated in hospital because he deliberately overdosed on his zopiclone and antidepressant (fluoxetine), expressed fears that his GP may not continue prescribing zopiclone for him due to his overdose:

*... cos I've always just gone and explained and had me medication [Zopiclone] given... to me. I just don't know if I'm gonna get it... this time (ID 27, male, alcohol dependency).*

These quotations and their contexts highlight how difficult decision-making around service users' medications could be for prescribers. Service users wanted continued prescribing of their medications because they met their self-perceived needs while their prescribers wanted to stop these medications for other reasons. Consequently, service users and prescribers had contrasting views about the appropriateness of prescribing decisions.

Fear of the unpleasant and painful opioid withdrawal symptoms may make it difficult for people who are opioid dependent to reduce their dose or stop using them. While there may sometimes be a clear distinction between prescribing for pain and prescribing for

dependence, the difference is not always clear-cut (Action on Addiction, 2013; Rosenblum et al., 2008). For instance, it may be difficult to determine if opioids are being prescribed for pain relief, to prevent withdrawal symptoms or to satisfy craving (Action on Addiction, 2013). Furthermore, treatment with opioids may worsen pain due to rebound pain occurring during withdrawal and opioid-induced hyperalgesia may also be a contributing factor (Action on Addiction, 2013). Generalised pain is a symptom of opioid withdrawal and during such withdrawal, pain sensitivity is higher (Action on Addiction, 2013). In addition, opioid-induced hyperalgesia has been observed in patients chronically treated with high dose of opioids for chronic pain (Angst and Clark, 2006). Ironically, hyperalgesia is only reversible through opioid dose reduction or cessation of therapy (Lee et al., 2011). Again, as has been touched on under the theme ‘addiction to prescribed medications’, these pieces of evidence highlight the need for clinicians in pain management to have basic competence in addiction medicine as well as access to addiction medicine consultations for optimal management and vice versa (Action on Addiction, 2013).

The challenge in managing complex patients such as those with SUDs is therefore to effectively engage the service user (Action on Addiction, 2013). Furthermore, there may be need to set boundaries when needed to prevent harm (Action on Addiction, 2013). Although appropriate prescribing entails respecting service user choice in decision-making, this has to be balanced against safety concerns in order to prevent medication-related harm.

#### **6.5.2.5. Discussion with clinicians and adverse effect of medications**

These themes came out when service users were asked about factors they consider important in assessing if their medications are ‘right’ for them. They are considered below.

##### **Discussion with clinicians**

Six service users described discussion with clinicians as a factor they consider important in assessing if their medications are ‘right’ for them. Below are two examples of quotations from service users who described talking and listening as factors they considered important:

*Talking to me, listening to me, asking me, you know, why I was feeling the way I was, was there anything that had triggered things off, that sort of thing [ID 35, female, alcohol dependency].*

*Well like having a sit-down and talk with me doctor [ID 26, male, heroin dependency].*

Another service user with a particularly strong sense of entitlement to his medication (zopiclone) described how this process provided an opportunity for him to express his views on what he wants:

*Oh sitting down, talking to him about sleeping tablets and what I want..., it's up to me really [ID 57, male, alcohol dependency].*

On the other hand, one service user described not being listened to:

*... I could do with something better for my anxiety but I don't know what other medication I can get. I'm just taking what the doctor prescribed me. I feel like I could, it would be nice if they could give me something to help me relax more [mentions Temazepam later], you know what I mean, to calm me down but the doctor won't prescribe anything for me like that [ID 5, male, heroin dependency].*

Another service user described not being listened to and the short interval in which he was prescribed a medication:

*... So I was just telling the doctor basically what my problems were and was prescribed Paroxetine, yeah, Paroxetine, ... I don't think my GP probably listened and, yeah, listened and prescribed me a drug. I just went for a... five minute chat with my doctor ... it was just I went ... for a quick ... meeting with my GP and told him my problems and sent away with a prescription [Paroxetine]... it was just, go to the doctor and off you go, ... there's your prescription off you go [ID 7, male, alcohol dependency].*

The importance of communication in dealing with patients has been emphasized in previous studies (Hahn, 2009; Stevenson et al., 2004). Patients value being listened to, as part of a two-way communication. This helps to increase patients' understanding of their medications and allows them to seek clarification where needed (Bultman and Svarstad, 2000). It also promotes satisfaction with treatment options and improves adherence (Bultman and Svarstad, 2000; Siminoff et al., 2000). The responses of service users in this study highlighted the fact that many of them valued this two-way communication.

There were however other service users who described ineffective communication or dissatisfaction with their medications. This may be associated with challenging behaviour, suspicions concerning requests for prescribed drugs and/or wider stigmatisation of people with SUDs. People with SUDs have often been described as difficult, aggressive, manipulative and rude (Conway, 2000; McGillion et al., 2000; McKeown, Matheson and Bond, 2003) and consequently challenging to treat.

Negative attitudes towards people with SUDs may result in them receiving poor quality care. For instance, service users may be denied needed medications due to their substance using status (Ahern, Stuber and Galea, 2007; Link et al., 1997). A qualitative study of problem drug users admitted to a hospital in the USA found that patients expressed concern about receiving poor medical care and described being intentionally mistreated due to their addiction (Merrill et al., 2002). Henderson et al. (2008) in a similar study of healthcare delivery to substance users in a hospital emergency department in USA concluded that care had a different tone or quality when patients had alcohol or drug problems.

Evidence from this study shows that some service users were dissatisfied with prescribing decisions as their doctors did not listen to them. It has been suggested that prescribing may be used as a means of terminating difficult consultations (Britten, 1995). This may be more common in those with SUDs, especially in time-pressured settings such as general practice. In the UK, general practice consultations often last no more than 10 mins (Bashir, King and Ashworth, 1994). People with SUDs are known to attend GP practices more frequently than other patients and GPs have often described these patients as time-consuming to manage due to their complex problems (Deehan, Taylor and Strang, 1997; McKeown, Matheson and Bond, 2003). Time pressure is a problem in most primary care settings (McKenna, Ashton and Keeney, 2004).

A study by Tamblyn et al. (1997) showed that GPs are more likely to prescribe inappropriate medications during shorter consultations. In shorter consultations, GPs are less likely to ask questions concerning symptoms of the presenting illness, carry out less in-depth clinical examinations and are less likely to provide lifestyle advice compared to guideline recommendations (Tsigas et al., 2013). Conversely, longer consultations are associated with less prescribing and increased lifestyle advice (Wilson and Childs, 2002; Wilson et al., 1992). This suggests that where service users with SUDs do have their health

conditions reviewed, GPs may prescribe without careful assessment and prescriptions may therefore be inappropriate.

### **Adverse effect of medications**

One service user who was on two prescribed medications (six-month history of venlafaxine and five-month history of disulfiram use) described the fact that he does not want to experience adverse effects from the use of his medications:

*...Just, yeah, make sure I don't have any adverse effects... Just make sure I wouldn't have any reaction. As with any other drugs that I'm taking, like make sure, my doc, it's OK taking different drugs at,... the same time [ID 7, male, alcohol dependency].*

Adverse effects resulting from medications are a problem among patients in general. They have been implicated in 6.5% of admissions in England (Pirmohamed et al., 2004). One of the risk factors for adverse drug events is polypharmacy as it increases the potential for drug-drug interactions (Gandhi et al., 2003). Adverse effects emanating from combining medications with substances could have dire consequences for people with SUDs. Since polypharmacy may be the norm rather than the exception among service users compared to patients in the general population due to multiple comorbidities (Dickey et al., 2002), there is the need to ensure that unnecessary medications are not prescribed to foreclose the possibility of dangerous drug interactions.

### **6.5.2.6. Quality of life**

This theme arose when service users were asked about their views concerning changes made to their medications and the influence of this on their quality of life. Service users described one element: improved quality of life.

### **Improved quality of life**

All the eight service users who had medication changes described these changes as a positive event that improved their functioning. Some service users had their medications changed due to their adverse effects while others were changed due to lack of effect. One service user with a six-month history of sertraline use for postnatal depression who has had two previous antidepressants described the change to sertraline as being beneficial. Her past antidepressants were not effective for her depression:

*... I feel glad that they realised that they weren't working for me, because I didn't... feel myself when I was on, like, the Fluoxetine, and ..., I was getting wound-up with myself because I wanted to feel better but I didn't know how, which is what prompted me to go to the GP and ask if there's any other medication I can take, because I... do want to feel, I don't know if the right word is normal, but. I just wanted to feel like everybody else, and I knew that the fluoxetine, it didn't seem to be making my moods any better, and I'd see people that were out and about and happy, and..., I'd just want to be like them, which the sertraline is... doing for me, cos I do go out a lot more now than what I used to, so it seems to be working [ID 61, female, alcohol dependency].*

Another service user prescribed a supra-BNF dose of olanzapine for long-standing paranoid schizophrenia described the negative effects of his previous medication (fluphenazine decanoate) and benefits from the change of his antipsychotic from fluphenazine decanoate injection to olanzapine:

*They've been for the better. Olanzapine has been easier to cope with than carrying... hypodermic syringes of modecate [Fluphenazine decanoate injection] around ...anything was... better than the painful injections which eventually, you know, 75mgs of Fluphenazine decanoate wasn't working, the psychotic symptoms were coming through, even on 75mgs a week. But as soon as I was put on 25mgs of Olanzapine a day, at night, all slight psychotic symptoms disappeared [ID 18, male, alcohol dependency].*

Similarly, one service user described changes to her medications as a result of their untoward effects:

*I've had Citalopram, oh I can't remember the name (pause)... it was something that began with... V, but... that made me lose so much weight that they had to take me off it because it affected me in a way that I just didn't want to eat, I didn't want to do anything. They've tried several different antidepressant medications and this is the one [Fluoxetine] that I'd, seems to suit me best at the moment [ID 35, female, alcohol dependency].*

Another service user who had earlier described the benefits from his citalopram as outweighing the sexual dysfunction it causes also described the presence of side effects as the reason why his previous antidepressants were changed:

*I'd take it [Dosulepin] on an evening and it just wiped me out, and I was almost like a zombie, you know, ... I had to take it on a night to sleep, not to sleep, but I took it on a night because it made me go to sleep and, and I couldn't possibly function outside that during the day. So eventually came off that and then they put me onto things like Prozac [Fluoxetine], which was not a good drug for me. It... just, libido went up through the roof, self-control went out of the window, and that was a poor drug to be on... Citalopram's been great. Easy to work, you know, ...easy to take, it doesn't make me drowsy [ID 23, male, alcohol dependency].*

Medication changes were viewed positively by service users. Patients taking psychiatric medications often have their medications changed over the course of their illness due to factors such as side effects and lack of effectiveness (Buckley and Correll, 2008; Mitchell and Selmes, 2007a). Such changes often lead to improved functioning in patients' lives (Kartalova-O'Doherty and Doherty, 2011). The findings of this study suggest that service users' views on the appropriateness of their present medications are influenced by their previous experiences with other medications. They may be more willing to tolerate side effects from their present medications if they feel that it improves their functioning compared with previous medications. Furthermore, they may view present prescribing decisions to be appropriate if it provides benefit irrespective of whether such prescribing is outside guideline recommendations.

#### **6.5.2.7. Adherence**

Service users described different levels of adherence when discussing how their perceptions of their medications influenced their adherence.

##### **High level of adherence**

Eight service users who all described their medications to be effective also reported a high level of adherence to them. One service user with a 12-year history of olanzapine use for long-standing paranoid schizophrenia described adhering to his olanzapine in order to prevent a recurrence of his psychotic symptoms:

*So in other words, I don't want to go back to those days again... hallucinating and... having psychotic thoughts, that's why I religiously take all me medication every day [ID 18, male, alcohol dependency].*

Similarly, another service user with a six-month history of sertraline use for postnatal depression described adhering to her sertraline:

*I take them [Sertraline] every night. I take 'em all at the same time, every night. It's usually at about, between nine and ten o'clock, on a night time, so I've got into the routine of taking them all at the same time so I don't forget any [ID 61, female, alcohol dependency].*

Three service users described their medications to be suboptimally effective but still reported a high level of adherence to them. Below are examples of quotations from these service users:

*...and that's one of the reasons why I was put on paroxetine, to see if it could lift that general mood. But it hasn't and I'm just going round in a circle, every month go for me prescription, take the tablets on a daily basis [ID 15, male, alcohol dependency].*

*I've got to... take it [Zopiclone] to try and get that sleep and hope I do go to sleep and ..., not wake up till morning, but it don't happen, it just doesn't happen [ID 27, male, alcohol dependency].*

### **Variable level of adherence**

Four service users reported variable adherence to their medications. Two of them reported their medications to be effective but reported variable adherence to them. One of such service users prescribed co-codamol for pain secondary to an operation on his spine and who also described being addicted to his medication, reported going above the prescribed dose depending on the level of his pain:

*I'd say the minimum [Dihydrocodeine] would be two to three and the maximum has gone eight to ten, depending on how much pain I were in... but I might not take 'em separately, I might take two, two at a time instead of just the one, to take the pain away faster [ID 29, male, alcohol dependency].*

Another service user with a three-year history of co-codamol and citalopram use for chronic pain and PTSD respectively as well as a three-month history of disulfiram use for alcohol relapse prevention also reported variable adherence to his different medications:

high levels of adherence to the co-codamol and disulfiram because he finds them effective and variable level of adherence to *citalopram* because he is uncertain about its benefits:

*The Co-codamol I take regular, the Lansoprazole regular, the Ci-[citalopram], hit or miss with that, because I don't know if it's doing me any good, to be quite honest with you. I know the effects of the Co-codamol and the Lanso-[Lansoprazole],... I need it, so I do take it regular, very rarely miss...Is it [Citalopram], is it doing any good? I probably, personally think it isn't, I've no need to be on it,... and that's why, subconsciously, I'm not taking it regularly, if you understand what I mean, I don't think it's important [ID 16, male, alcohol dependency].*

One service user described above (ID 27, male, alcohol dependency) reported that he sometimes forgets to take his antidepressant (fluoxetine) due to his use of multiple medications and alcohol use:

*Yeah, yeah... some days ... I have forgot to take it because I'm on... that many different ones and different things, it's like, phew, and some days you... do get a bit cheesed off with 'em, cos I struggle to take 'em anyway. But some days if I've gone out, gone out and got drunk I've forgot [ID 27, male, alcohol dependency].*

For patients to benefit optimally from their medications, they need to take them as intended (Cramer, 2004). Patients' perceptions of medications have been found to influence their level of adherence (Byrne, Regan and Livingston, 2006; Chao et al., 2005; Mann et al., 2009). In the interviews carried out with service users, all those who perceived their medications to be effective described a high level of adherence to them. There was also evidence of misuse of a prescribed opioid medication as a service user who had earlier described being addicted to the medication reported going above the recommended limit.

Lack of benefit from medications may lead to non-adherence and ultimately discontinuation of treatment (Holt, 2007). However, patients who believe their medications might still help may continue treatment (Malpass et al., 2009). This was reflected in this study as a few service users continued treatment despite their suboptimal benefits. Most service users appeared to have consciously made decisions about whether to take their medications, modify their adherence or even stop taking their medications according to their beliefs about their efficacy. Although mental health conditions such as psychotic

disorders could negatively affect service users' adherence due to lack of insight and stigma (Chan et al., 2014; Higashi et al., 2013; Mitchell and Selmes, 2007a), it is possible that service users who find their medications beneficial may continue to take them to maintain their mental stability. Adherence may be negatively affected by substance use (Sajatovic et al., 2006) and polypharmacy (Murray and Kroenke, 2001). Sajatovic et al. (2006) reported that bipolar patients with a current SUD were more likely to be non-adherent compared to those without SUDs. This may be due to factors such as intoxication and poor judgment resulting from active SUDs (Sajatovic et al., 2006).

#### **6.5.2.8. Summary on service users' interviews**

Service users generally described improved functioning as a result of their medications though there was also an awareness of the adverse effects they experienced from them. Consequently, they sometimes described making compromises between the risks and benefits of their medications, with self-perceived benefits outweighing adverse effects. Lack of benefit or suboptimal benefit was sometimes described when using alcohol with antidepressants.

There was evidence that the appropriateness of prescribing is an area of conflict and depends on whose views are being represented. Service users' views often differed from the medical view represented in guidelines and those of prescribers, with improved functioning being paramount to them. The findings of this study suggest that prescribing decisions are sometimes made in response to stressful life events rather than a clear medical indication. It also appears that people with SUDs have a particularly strong sense of their own needs and seek to influence prescribing decisions. While this sense of empowerment may negatively influence decision-making leading to inappropriate prescribing, such prescribing decisions may well be appropriate in another sense if they prevent disintegration and disruption of the lives of this vulnerable group of people.

Service users described differing practices regarding the assessment and review of their medications. While some service users described regular reviews, others identified suboptimal or inadequate practices. Repeat prescribing or dispensing without adequate monitoring or review may result in poor quality care as such service users may become stuck on unnecessary medications or become dependent on those with such tendencies. Lack of regular review therefore represents a missed opportunity for identifying medication-related problems (NHS Confederation Publication, 2013).

Service users further highlighted the importance of talking and listening to them (under the theme “discussion with clinicians”) during their consultations. Some service users described not being listened to and resulting dissatisfaction with prescribing decisions. This may be associated with service users’ challenging behaviour, suspicions by prescribers or a wider stigmatisation of service users. One factor that may contribute to lack of careful assessment/review and ineffective communication in general practice is time constraint. The findings of this study revealed that a service user considered the time period in which he was prescribed an antidepressant medication in a GP consultation as “too short”. The busy workload of GPs coupled with the complexity of people with SUDs may result in situations where GPs prescribe without careful assessment, resulting in inappropriate prescribing. Time constraints may also preclude the use of non-pharmacological interventions (for example, the provision of lifestyle advice, such as alcohol abstinence and advice on sleep hygiene) in busy general practice settings though they may assist in improving symptoms of mental disorders.

Service users viewed changes to their medications positively if they led to better functioning. Most service users who derived benefit from their medications reported a high level of adherence to them compared to those who did not. While there was evidence of misuse of some prescribed medications, service users appeared to have chosen to adhere to their medications or modify their use according to their own beliefs of what works best or is appropriate for them. Chapter 7, section 7.3.8 presents the researchers’ reflections on the quality (in particular, validity and transferability) of these interviews.

# Chapter 7: Qualitative interview studies with SAS prescribers: methodology, results and discussion

## **7.1. Introduction to the chapter**

This chapter presents the qualitative research methodology adopted for interviews with SAS prescribers, the result and the discussion of its findings. The purpose of qualitative research has already been described in section 6.1. Qualitative interviews have a place in prescribing research as they can be used to illuminate the factors that influence prescribing decisions (Stevenson et al., 2000). The phenomenological perspective (Green and Thorogood, 2004) adopted in this thesis argued for the use of interviews as a research method because of the need to explore how prescribers understood and responded to inappropriate prescribing. In particular, semi-structured interviews were employed in this study.

The study rationale, design, research questions addressed, sampling strategies, recruitment methods and topic guide development are presented in section 7.2. The ethical process, interview process, data analysis and storage plans were similar for both the prescriber and service user interviews and would not be described again in order to avoid unnecessary repetition. The ethical process has been described in section 6.3 while details of the interview process, data analysis and storage plans are provided in section 6.4.

## **7.2. Interviews with prescribers: rationale, study design, research questions, sampling, recruitment and topic guide development**

### **7.2.1. Study rationale**

As shown in the scoping review in chapter 2, there has been a paucity of research into prescribers' views on the appropriateness of prescribing of psychiatric medications and opioids for people with SUDs. Furthermore, how prescribers in a SAS respond to inappropriate prescribing among the service users they treat is unknown. The evidence suggests that service users in these settings usually have comorbid conditions (Delgadillo et al., 2012; Marsden et al., 2000; Weaver et al., 2003) and are on multiple prescribed medications (Oluyase et al., 2013), with the potential for unnecessary prescribing and dangerous drug interactions. Medications such as benzodiazepines, opioids and

antidepressants have been implicated in overdose incidents and mortality in people with SUDs (Darke, Duflou and Torok, 2011; Darke and Hall, 2003; Darke and Ross, 2000). The prescribers in this setting represent a particularly apposite group for exploring questions around prescribing appropriateness due to the large number of medications their patients take.

### **7.2.2. Study design**

This study involved semi-structured interviews with 12 prescribers who were working at the SAS. Four of the interviewed prescribers were nurses while the remaining were doctors of varying seniority (see section 7.3.1). One-on-one interviews were used because it would be very difficult to get time-pressed clinicians together for a focus group discussion. Group interviews were also considered to be unnecessary since interactions within the group may be prohibitive (Crawford, 1997) to some prescribers.

### **7.2.3. Research questions**

Prescribers' interviews explored how they responded to inappropriate prescribing. The following research questions were addressed:

1. How do prescribers at the SAS assess the appropriateness of prescribed medications, and how are changes made?
2. What factors are considered before initiating changes to service users' medications?
3. How has the MAI impacted prescribers' practices?

### **7.2.4. Sampling strategy**

In line with qualitative research inquiry, the aim of the sampling strategy adopted in this study was to recruit respondents who can provide valuable insight into the topic and also to provide a broad overview of the perspectives of different prescribers (nurse prescribers and doctors). All but two prescribers working at the SAS during the study duration took part in the interviews. One prescriber was not interviewed due to time limitations while another prescriber was not invited to take part in the interviews because he left the SAS before the interview phase began. The similarities and differences between nurse prescribers and doctors in the topics explored are considered in the presentation of results and discussion.

### **7.2.5. Recruitment**

The researcher distributed participant information sheets (appendix 7.1) to all prescribers working at the SAS. It contained information about the medication appropriateness study and the interviews. All prescribers who consented and participated in the medication appropriateness study were informed that they would be subsequently interviewed. Interviews were organised with prescribers before they left the SAS if they were on short rotation or at the completion of the medication appropriateness study if they were permanent staff. All interviews were arranged to take place at a convenient time for prescribers at the SAS.

### **7.2.6. Developing the topic guide for interviews with prescribers**

The topic guide for prescribers (appendix 7.2) was designed to cover the following areas: assessment of prescribing appropriateness: types of inappropriate prescribing encountered, factors considered when assessing prescribing appropriateness, challenges encountered and interventions made concerning inappropriate medications; negotiation of medication changes with service users as well as impact of A-MAI on prescribing. The opinion of the researcher's academic supervisors and one of the consultant psychiatrists at the SAS were sought about the topic guide. Minor changes were suggested such as clarifying the reason for the interview. All areas covered were developed into questions. The questions were piloted with the researcher's academic supervisors who suggested a few changes such as re-wording and re-ordering some of the questions. The changes suggested were carried out before the researcher began interviewing prescribers.

## **7.3. Results and discussion**

### **7.3.1. Prescriber characteristics**

There were fourteen prescribers who worked at the SAS during the duration of this study consisting of four nurse prescribers and ten doctors. The doctors had different grades: one senior house officer (hereafter SHO), one locum doctor, five specialist registrars (hereafter SPR) training to be consultant psychiatrists and three consultant psychiatrists. Thirteen of the 14 prescribers were invited to take part in the interviews and all but one of those invited were interviewed. One SPR was not interviewed due to time limitations and another SPR was not invited to take part because he left the SAS before the interview

phase began. Consequently, the sample of prescribers interviewed consisted of four nurse prescribers, one SHO, one locum doctor, three SPRs and three consultant psychiatrists.

The interviews took place at the SAS and lasted between 36 and 74 minutes ( $48.1 \pm 12.5$ ). The difference in interview time was as a result of the varying length of time that prescribers spoke. The interview length was not found to be related to the number of years of experience in addiction. The topic guide was covered during all the interviews. The prescribers represented a broad range of qualifications and experience in the addiction field. Three of them had no prior experience of practicing in addiction specialty but the remaining nine prescribers had prior experience of addiction specialty ranging from 6 months to 35 years. Other characteristics of prescribers are described below:

#### Nurse prescribers

One male and three female nurse prescribers took part in the interviews. They had practiced as nurse prescribers in addiction specialty for between one and five years and as nurses in addictions for between five and twenty-two years. Their ages ranged from 34 to 55 years.

#### Doctors

Six male and two female doctors took part in the interviews. Three of the male doctors were consultant psychiatrists. While two doctors had no prior experience of working in an addiction specialty before coming to the SAS, others had between six months and thirty-five years of experience. Consultant psychiatrists in particular, had between three and 35 years of experience in addiction specialty. Doctors' clinical practice ranged from between six and 41 years. Their ages ranged from 31 to 65 years.

### **7.3.2. Assessment of the appropriateness of service users' medications**

As discussed in section 3.2, service users are referred to the SAS from different sources: namely GPs, psychiatrists, hospital, social services, drug services, community mental health teams as well as the criminal justice system. Some service users also self-refer.

Information such as the service users' demographics, health conditions and medications are obtained from all referred service users by SAS staff and are included on the referral form. All referred service users are sent a self-completion booklet where they document their demographics, health conditions and prescribed medications amongst other information

before coming to the SAS. Those who come to the clinic without the booklet are given a new copy to complete before they are assessed by keyworkers (including prescribers).

Evidence obtained from a senior SAS staff suggested that new referrals to the SAS are all screened by a nurse on the basis of their referral information, in order to assign service users to one of the three teams (hospital team, dual diagnosis team, pregnancy and parenting team) and also determine whether the person should be seen by a doctor. Allocation to a doctor was said to be based on complexity and, in particular, any prescribing issues. Where a service user is not required to be seen by a doctor, allocation to nurse prescribers and other therapists was decided by the SAS team organising the clinic. The findings of the medication appropriateness study (see section 5.9.6) and evidence obtained by the researcher suggests the allocation system described above was not always implemented. The researcher observed that receptionists tended to allocate service users to doctors, nurse prescribers and other keyworkers in all the three SAS teams on their clinic days.

Each team has its own clinic day where new referrals are assessed. The keyworker (nurse prescriber, doctor or other therapists) carries out the baseline assessment which involves a 45 to 60 minute comprehensive assessment of the service user. All keyworkers including prescribers are expected to complete booklets relating to their assessment of the service user (including filling in a care plan) after the consultation. Keyworkers also provide a summary of their assessment to the secretary of their team who has the responsibility of typing and documenting it in the service user's folder. Keyworkers will also need to attend to existing service users who they have scheduled appointments with. The clinic is therefore usually busy for keyworkers and participation in this research made extra demands on their already tight schedule. Service users are usually followed up by the same prescriber throughout the duration of their treatment.

Depending on the referral source, prescribers have varying levels of information when assessing service users. With the exception of service users referred from GPs, the information available is usually only that documented in the self-completion booklet and the referral information. Prescribers may also seek clarification directly from the service user or contact service users' GPs if considered necessary. Service users referred by their GPs usually have a GP summary in addition to their completed booklet. The summary usually includes a brief outline of the medical and medication history of the service user.

Interviews with prescribers provided an exploration of the process of clinical decision-making that prescribers go through in order to assess the appropriateness of medications prescribed by others, since the medications that service users arrive with would have been prescribed by a range of practitioners in different settings. The focus of this thesis is on judgments made about service users' current medications by prescribers in the SAS, rather than the original decisions made by prescribers elsewhere. It would have been very difficult to trace the original prescribers and this was beyond the resources of this thesis. Prescribers were therefore asked how they assess the appropriateness of prescribing at the SAS and the following themes emerged: review of medications, assessing risk, guideline adherence versus successful prescribing, history-taking, communication, lifestyle change, adherence, addiction and understanding the relationship between SUDs and mental health disorders.

### **7.3.2.1. Review of medications**

The classes of medications reviewed varied among prescribers with only three of them stating that they reviewed all of service users' medications for their appropriateness. These three prescribers were doctors (two consultants with 12 and 41 years prescribing experience and a locum doctor with 16 years of prescribing experience):

*So I'd... look at the list of drugs prescribed and see how they matched up to what I thought the person was... showing in terms of... addiction illness,... physical illness and mental illness, and then I'd look at those that... I would look to prescribe and look at the ones that other people might prescribe, [...] and link up with the other prescribers if I didn't think what was going on was appropriate, but link up with the other prescribers anyway to let them know what I've done [P3, consultant].*

*Classes such as antidepressants, antipsychotics or that sort of thing. I mean, I would think anything, any medications could be covered, so. Nothing is excluded, I would say all the medications... just because they come here for addiction doesn't mean we don't look at them as a whole. So I would say any medication. I mean you'll look at them the same way you would look at them, see, if you were the GP, you just look at... the whole presentation [P5, locum doctor].*

In addition to psychiatric medications, the third consultant psychiatrist reported reviewing a relatively narrower group of medications when compared to the other consultants:

*It would be mainly antidepressants, antipsychotics, anxiolytics, mood stabilisers. We would also be reviewing certain physical health aspects such as proton pump inhibitors, some basic review of antihypertensives, because alcohol, particularly alcohol withdrawal has an effect on your blood pressure, and alcohol consumption as well, and sometimes blood pressure completely resolves once the individual refrains from drinking... We also, of course, review the prescription of analgesia, the appropriateness of that, particularly opiate-based analgesia, and substitute prescribing [P7, consultant].*

The remaining eight prescribers reported that they reviewed only medications within their areas of expertise:

*...we tend to, well I mean at least me, tend to concentrate more on psychotropic medications, unless otherwise we are aware that their other medications for physical health problems are interfering with psychotropic medications [P8, SPR].*

*I think for... each patient that I see, usually, whether it's a new patient or... review patients then... I assess the medication and, well not medication that they are getting for their physical health but... for mental health and for substance misuse I'll do [P13, SPR].*

Nurse prescribers (NPs) also described a limited remit of prescribing and consequently focused on medications within their scope of practice during reviews:

*For... me it would just be the, the small range of, you know, detoxification and relapse prevention in relation to alcohol. Anything else it's what's prescribed by the GP, ... I don't review that or question that. If the GP's seen fit to initiate it then I don't see that it's my place to... say otherwise [P6, NP].*

*So I... don't really see, with psychiatric medication, that that would be within my... remit really. If somebody came and they were prescribed 100mgs of Methadone and they couldn't even open their eyes then, yeah, I could, you know, I would be assessing the... appropriateness of the dosage and making necessary adjustments to things like that [P10, NP].*

Nurse prescribers further described involving doctors at the SAS or service users' GP if they had particular concerns about clinical management:

*As I say, if I was particularly concerned about someone's mood... or... I have particular concerns about the medication I would... defer to a medic. You know, it's... not an area I feel strongly confident on [P6, NP].*

*Again, I think if I thought there was something that wasn't right I would be asking a medic to have a look at that patient, I wouldn't be making any changes myself [P10, NP].*

*I'd probably look at it [medications] at the...initial assessment and if there's anything that comes up or that was sort of glaringly obvious ..., I'd refer to the GP and ... ask the GP to review, if they're prescribing, because obviously they're putting their signature to the prescription and I think it's up to them to... review that [P11, NP].*

The practice of medication review therefore varied considerably among prescribers. When compared to less experienced prescribers, the most experienced doctors (consultants and the locum doctor) in this study tended to review all service users' medications presumably due to their more extensive clinical knowledge. Other doctors and nurse prescribers tended to focus on medications within their remit, with the former considering their expertise to be largely around psychiatric medications, addiction medications and sometimes opioids, and the latter describing their expertise as being limited to addiction medications. The focus of prescribers on only medications within their remit may result in fragmentation of service delivery (Detsky, Gauthier and Fuchs, 2012).

Although nurse prescribers described referring service users who they had concerns about to SAS doctors or GPs, their limited area of competence implies that inappropriate or problematic prescribing of psychiatric medications and opioids may sometimes not be picked up by them. This finding is particularly important because evidence from the medication appropriateness study (see section 5.9.6) suggests that service users assessed by nurse prescribers and doctors were not significantly different in the number of prescribed medications they were taking. Consequently, it appears nurse prescribers were assessing service users with complex medication regimen.

#### **7.3.2.2. Assessing risk**

The evaluation of risk is a theme that was highlighted by all prescribers as a means through which they assess the appropriateness of service users' medications. All the twelve

prescribers said they considered the risk posed by a medication, including drug-drug interactions and drug-disease interactions, when assessing its appropriateness. Prescribers tended to consider the issue of risk particularly carefully because the service user group they treat are people with SUDs. Some of the quotations relating to risk assessment captured this:

*Well if it's going to do ..., first of all, less harm than the actual substance, not more harm, that's a possibility in pregnant people, people with liver disease, advanced kidney disease or heart problems,... any multi, lots of organ problem, or near organ failure then, so the actual prescription can... be worse than... doing nothing ... but mostly... you're doing less harm [P5, locum doctor].*

One prescriber described a service user who she felt had an inappropriate and high risk prescription of olanzapine (an antipsychotic). The service user was an elderly man who was being prescribed olanzapine (25mg) at a dose higher than that stated in the BNF without monitoring by a psychiatrist:

*[...] I have a... patient on my caseload who has a very old diagnosis of paranoid schizophrenia dating from his late teens, and he's now in his sixties, and for this he's prescribed a very high dose of medication called olanzapine, which is an antipsychotic, which has quite a few well known side-effects, and he's prescribed over the limit in the British National Formulary... and he's not under the supervision of a specialist, which he should be. So I would label that as an inappropriate prescription because (a) he's elderly, which means that he's more prone to... cardiac disease, and the drug, because it has high metabolic complications, can cause diabetes which can lead to heart disease. It can cause arrhythmias, he's not being monitored regularly with regards to that, and he's not being monitored with regards to his clinical symptoms, which, you know, are actually, from a psychosis point of view, negligible [P12, SHO].*

The SHO described contacting the service user's GP concerning the antipsychotic medication. His GP refused to alter it due to the service user's stability on the dose for a prolonged period and lack of psychotic symptoms. There was therefore no change made to the antipsychotic.

Risks posed by interactions between prescribed drugs and substances were also highlighted by prescribers as well as the need to address such risks:

*For example, if somebody came into treatment and they were on, I'll use methadone and alcohol cos it's an easy example. So if they were prescribed methadone for opiate dependence, and there was no evidence that they were using opiates on top of that prescription but they were drinking twenty units of alcohol a day, the first thing I would want to do is, is reduce the risk to that person's health, and the... first line that I would take is, right, that person needs to stop drinking. So you would have the appropriate intervention for them to stop drinking: could be detoxification ... if X amount of time... down the line this person's drinking heavily, on top of a methadone prescription, and shows no motivation to change their alcohol use, then I would have to consider whether methadone needed to be reduced and stopped because of the risk to that person's health [P10, NP].*

*It depends on the risk involved. If we're... prescribing, if I use methadone, let's say, for an example, and somebody's using heroin on top of the prescription and maybe drinking dependently and there's lots of other risky things going on and that behaviour doesn't change, then to continue prescribing would be dangerous and we'd have to look at reducing that down and stopping that prescription... obviously the risks outweigh not doing anything [P11, NP].*

Similarly, risks posed by drug-drug interactions were highlighted by prescribers:

*... for example, you know, if somebody's taking citalopram and they are on aspirin that is ... also a concern for me and I will be looking at that and be exploring with the patient because of the ... risk associated [with] bleeding. So, you know, obviously there are certain medications very explicitly we know are not the best combinations so we will be obviously assessing their suitabilities [P8, SPR].*

The fact that risk assessment was mentioned by all prescribers is not surprising as medical practice emphasizes the need to evaluate the risk and benefit of therapeutic decisions (Pantilat, 2008). In medical ethics, the *Principle of Beneficence and Nonmaleficence* aims to produce net benefit over harm (Beauchamp and Childress, 1989; Gillon, 1994). The use of medications among service users with SUDs sometimes raises complex clinical and

ethical issues. For instance, the principles of beneficence require that all persons have equal access to effective medications (Cohen et al., 2002). This can however come into tension with the nonmaleficence principle when the presence of SUDs raises concerns about potential harmful interactions that could occur between medications and substances.

Furthermore, as seen in the case of the service user with schizophrenia described above, there is sometimes conflict between balancing effectiveness and risk (Barber, 1995). While higher-than-recommended doses of antipsychotics may be needed to effectively manage psychotic symptoms, it carries significant risks of antipsychotic-related adverse effects (Royal College of Psychiatrists, 2014b). Furthermore, this evidence also highlights how the views of different prescribers could differ concerning prescribing appropriateness. While the SAS prescriber with a more limited overview of the circumstances of antipsychotic prescribing was focused on the potential risks of high dose prescribing, the GP presumably with a deeper understanding of the circumstances of prescribing was of the opinion that the benefit of the high dose of antipsychotic exceeded the risk and therefore made no change to its dose.

Risks posed by medication-substance interactions such as interactions between medications and alcohol and illicit drugs have been implicated in many adverse events among substance users. For example, benzodiazepines and alcohol are usually involved in opioid-related overdose and fatalities (Darke, Duflou and Torok, 2011; Darke and Hall, 2003). Antidepressants in combination with CNS depressants such as alcohol, benzodiazepines and opioids have also been associated with mortality in the UK (Cheeta et al., 2004). Furthermore, substances such as alcohol could result in hepatic impairment (Osna, 2009), thereby inhibiting the ability of the liver to metabolise medications. Harm resulting from medication use may be more common in people with such impairment (Amarapurkar, 2011). Consequently, safety measures such as regular monitoring and assessment of the appropriateness of prescribed medications should be in place in order to avoid doing harm to service users.

### **7.3.2.3. Guideline adherence versus successful prescription**

Eight prescribers mentioned guidelines when assessing the appropriateness of prescribing:

*And during the comprehensive assessment you try to get more information about why they were prescribed certain medication, why they think they were prescribed, what the class of*

*that medication is, for how long they've been having it, the dose of the medication and what... the effects are now, and then all that information is collated and then taken back and... then measured against the guideline... to see whether we think... there's some inappropriateness or not, yeah [P7, consultant].*

*...or sort of somebody that's got maybe a very mild sort of low mood but not what you would say depression, and being prescribed high dose of ... antidepressants over long periods of time. Inappropriate lengths of time, longer than, for example the, the guidelines would suggest is necessary, or it's not being reviewed and you just go on and on [P5, locum].*

Five of the eight prescribers acknowledged that prescribing may not be in conformity with guidelines for a variety of reasons. One doctor described a situation where a service user is struggling:

*... we shouldn't be blindly following a set protocol and not swaying... from it, when you very clearly see the individual is... struggling [P7, Consultant].*

Other prescribers described the importance of the circumstances of prescribing:

*And I think any comment about any prescribing should only be made when you know about the circumstances in which the decision was made because I think it's... very easy to criticise another person's prescribing unless you've looked at the circumstances when they started the prescribing and whether it's been reviewed and so forth, and whether they think you should continue. For example, we prescribe very high doses of some drugs, now some people say that... you shouldn't prescribe at those levels, but they are appropriate if you know about the circumstances, you know [P1, NP].*

*... prescribing is something of an art as well as a science, so... prescribers will sometimes prescribe things that they know are not really indicated but with the aim of achieving a particular goal. For example, somebody may believe that they can't possibly stop using alcohol or other drugs without a detox, so the prescriber might prescribe a short, ...brief low dose detox even though they thought a medicated detox wasn't indicated because the person didn't experience significant withdrawal symptoms. And so, in a sense, that would be an inappropriate prescription in that it, it isn't for a standard indication, but it might be*

*a successful prescription because it achieves the goal of somebody becoming abstinent from alcohol or other drugs [P3, Consultant].*

While guidelines provide best practice recommendations for disease management, they are not applicable to all groups of patients (Tinetti, Bogardus and Agostini, 2004). It is not possible for guidelines to encompass all possible comorbidities and circumstances (Geleris and Boudoulas, 2011). Clinical trials that usually serve as the foundation of guidelines are carried out in homogeneous groups of patients (Geleris and Boudoulas, 2011). However, in real life settings patients rarely have only the characteristics of those enrolled in trials, with those seen in everyday practice representing a wide spectrum of cases ranging from the very mild to the very complex (DeMaria, 2008). Recommendations from such guidelines cannot therefore be directly extrapolated to the heterogeneous population of people with SUDs who are likely to have multiple health problems and complex situations (Hughes, 2011; Humphreys et al., 2005). Evidence from this study suggests that the appropriateness of prescribing cannot be viewed solely from the perspective of guidelines as there is need for an appreciation of the context of prescribing. Furthermore, a successful prescription among people with SUDs may well be a prescription that is pharmacologically inappropriate. The range of problems people with SUDs experience and the need to prevent relapse to substance use may make pharmacological appropriateness of lesser importance if prescribing assists in maintaining the service user's stability.

#### **7.3.2.4. History-taking**

All the eight doctors and one of the four nurse prescribers identified history-taking as a part of their assessment of the appropriateness of service users' medications. The prescribers described considering the information obtained during history-taking when assessing prescribing appropriateness:

*Looking at the history of ... their substance use, ... history of any physical health problems, mental health history, and current mental state as well ... so I'd get the full history and I think then you can kind of gauge whether something might be inappropriately prescribed [P11, NP].*

*In the... new assessment clinic, you know, having taken... a comprehensive medical and mental health history, I talk through... with the patient about why they've been prescribed something, why they think they've been prescribed something, and their perceived benefit, their knowledge... of risks, and then I have a look, ... using the history that I've taken and*

*the physical health check that the nursing assistants kindly do for us, I formulate an opinion based on those as to whether a medication is... appropriate or not [P12, SHO].*

Two nurse prescribers reported that they asked service users about their medications, however they did not go beyond this to exploring the appropriateness of prescribing:

*...I would, in as much as part of the assessment, I would ask the service user what medication, are they on any medications. If they are, what it is, what dose, what's it prescribed for and are they taking it. That would be the total sum of my assessment. I wouldn't move to beyond exploring that condition or whether that was appropriate, I don't think that's my place [P6, NP].*

Another nurse prescriber described the fact that he does not spend a lot of time on assessing the appropriateness of prescribing:

*I don't spend a lot of time assessing the appropriateness of medication, that isn't the reason for me being there... [P1, NP].*

Prescribers described some challenges with self-report when obtaining service users' histories. These include problems with the reliability of information provided by service users as some of them may withhold information:

*It could be that patients may not tell you what medications they're on, which means then the focus would be completely defeated, because if it's not mentioned, we all tend to rely on the patient [to say] what medication they are on, if they chose not to say that they're on a benzodiazepine then the purpose of screening will be defeated. So better be aware of that, where we are getting the information and, you know, are we actually collating the information from the GP, and then ... putting that information in the text, or is it that we are just depending on the service user to tell us what medication they are taking... [P8, SPR].*

*...but I think sometimes patients are not candid with the prescriber..., I can think of one woman in particular, who, when I questioned her, she hadn't revealed to the GP that she was drinking very heavily. She said she was very anxious and the GP accepted this and*

*prescribed her the Propranolol. It was pretty clear to me though that this was alcohol withdrawal that she was suffering from, and she hadn't been candid with the GP [P1, NP].*

Prescribers also described service users who do not know details of their medications such as the name and reason for medication use. Some may be cognitively impaired by substances. Consequently, prescribers may have to contact GPs concerning needed information:

*I think in the first assessment, ... you don't always have a long history from a GP, sometimes, you know, in our clinic patients have self-referred and you literally have the booklet in front of you that they have completed and the initial referral sheet, and that's it ... So in that first assessment, it's the strength of your history [that] is going to determine what you do, so, and sometimes... you get patients... who come in here and sometimes they're slightly intoxicated, they're ... cognitively impaired and you have to try and decipher the history through these difficulties... Patients don't necessarily remember drugs as well ... you know, patients remember, well I take the blue one and then the red one... I like to take... a full history, make them a follow-up appointment, use that time in between to contact GP and..., collect some collateral history and find out what medication they're on..., before I ... prescribe anything, because I think that's safer [P12, SHO].*

Prescribers therefore discussed challenges they encountered during history-taking. Such challenges raise questions about the quality of information available to prescribers for decision-making, especially, during service users' first assessment at the SAS. During periods when service users are actively misusing substances, prescribers lose access to the most fundamental tool in medicine, the patient's self-report (Action on Addiction, 2013). People with SUDs may be less than open and sometimes manipulative (Action on Addiction, 2013; McKeown, Matheson and Bond, 2003). It is therefore good practice to use other evidence to corroborate self-report.

The findings of this study showed that although some prescribers stated that they contacted service users' GPs for further information concerning medications, this was not routine practice. The practice of depending on information obtained from service users in assessing appropriateness implies that some medications which are potentially inappropriate may not be identified, as service users may not disclose information concerning them. Lack of disclosure may result from the need to obtain such medications for non-legitimate reasons (Hall et al., 2008; Martyres, Clode and Burns, 2004). Stigma

may also play a role in non-disclosure (Pound et al., 2005). For instance, people with mental health problems have reported feeling stigmatised and labelled by their medications (Smith, Francis and Rowley, 2000). People on prescribed benzodiazepines have also reported feeling ashamed of taking them (North, Davis and Powell, 1995).

There is the potential for unnecessary prescribing as prescribers may go ahead to prescribe undisclosed medications. People with SUDs have been reported to present fraudulently to multiple prescribers requesting for medications such as opioid analgesics and benzodiazepines (Bendtsen et al., 1999; White and Taverner, 1997). Consequently, in addiction medicine, the patient's self-report needs to be viewed circumspectly (Action on Addiction, 2013), and where possible collateral information should be obtained.

Cognitive impairment was identified as another challenge in relation to history-taking. Impairment in memory and attention is a recognised problem in people who use substances such as alcohol. Over half of people with AUDs are impaired due to alcohol-related brain damage (Bates et al., 2002; Sullivan and Pfefferbaum, 2005). Majority of cases go undiagnosed (Royal College of Psychiatrists, 2014a). Similarly, illicit drugs such as cannabis and ecstasy have been associated with cognitive impairment (Fletcher et al., 1996; Schilt et al., 2008). Impairment may vary from mild to severe memory deficits such as in Wernicke-Korsakoff Syndrome (Parsons, 1998). Consequently, memory deficits may lead to the inability of service users to remember information accurately or forgetfulness. This will negatively impact on the ability of prescribers to judge the appropriateness of prescribing, especially, where they rely on the information provided by service users.

Only one nurse prescriber described considering the information obtained during history-taking when assessing prescribing appropriateness. This finding may have resulted due to the more limited scope of practice of nurse prescribers when compared doctors. Nurse prescribers have a discrete area of practice and as already highlighted in section 7.3.2.1, they describe a strong focus on medications within their remit when assessing appropriateness. Previous studies have also shown that nurse prescribers only tend to take professional responsibility for their areas of competence (Bradley and Nolan, 2007; Scafton, McKinnon and Kane, 2012). The limited scope of nurse prescribers' practice implies that they may be unable to capture some medications that have been inappropriately prescribed for service users.

### 7.3.2.5. Communication

This theme was described by all prescribers. They described communicating with other SAS prescribers or prescribers outside the SAS when dealing with issues around prescribing appropriateness:

*The first thing I'm gonna do with a couple of those cases, simply discuss it with one of my medical colleagues here actually, that's my first step, because it's... the degree or level of reaction to the inappropriateness that, I think, needs checking out with the medical colleague. And then it... generally results in alerting the patient and alerting the GP, and saying to the patient, you need to go and see the GP to get reviewed, and then the GP, who's usually the prescriber, will review them hopefully [P1, NP].*

*... I might question the appropriateness of, say, an antidepressant medication or I might suggest that the patient's mental health is reviewed, if I saw somebody that was on an antipsychotic and I thought that it either wasn't treating the psychosis or there was no evidence of psychosis and they seemed heavily sedated, then I might question whether that medication was the... right medication, but I would then ask a medic to assess the appropriateness of it and consider further prescribing [P10, NP].*

Doctors at the SAS also described communicating with GPs:

*Well... mainly I would be contacting other people to take over the prescriptions [psychiatric medications], in which case they're usually delighted cos they... usually realise themselves that this isn't really a very good prescription but they're struggling in trying to get a more sensible sort of prescription, so they're usually delighted that we should take it over. Sometimes there are prescriptions that I'd be a bit doubtful about but wouldn't really be in my sort of remit to prescribe and so I'd... essentially... write to the prescribers and express my doubts and possibly ask them to review, which they do [P3, Consultant].*

*Because... if I find... something that's maybe been overlooked or prescribed wrongly, then I will let the GP know about it, and it could be anything. Doesn't have to be addiction medication or psychiatric medication, it could be anything [P5, locum doctor].*

Furthermore, communication with other prescribers sometimes depended on whether SAS prescribers felt immediate action should be taken concerning inappropriate prescribing:

*For the example I started with [patient with schizophrenia on supra-BNF dose of Olanzapine], I wrote to the... GP saying, you know, Mr So-and-So is stable and is relatively symptom free on this but I'm worried about this monitoring [Olanzapine monitoring], would you be able to instigate some monitoring and consider re-referral back to the community mental health team, and I copied it into his former psychiatrist, even though they'd discharged him. Nothing as yet has come of that and the patient's very reluctant... to reduce this medication but, so that's a wait and see scenario. But generally if I think something's really inappropriate and I'm in a position to contact the original prescriber I'll try to do that, but I'd always discuss a case with my consultant and make a decision about whether or not I need to do something imminently [P12, SHO].*

*... if I felt that, you know, it [inappropriate prescribing]... definitely needed to be addressed, I would take it to our prescribing, either prescribing governance meetings or speak to one of the consultants here and seeing if there's a way round of dealing with that [P11, NP].*

Evidence from these interviews show that good communication is essential for safe and effective care of service users (Action on Addiction, 2013). Nurse prescribers often communicated with doctors at the SAS when addressing issues around inappropriate prescribing. These doctors seemed to have been a valuable source of support to nurse prescribers when making decisions about prescribing. Similarly, the more junior doctors (non-consultants) also relied on the support of their senior colleagues in dealing with issues around prescribing. There was also evidence that SAS prescribers provided support to GPs around prescribing and also played a “safety net” function. Addiction specialist doctors such as consultant psychiatrists are skilled in working with people with the most severe and complex needs and provide expert advice to other doctors and non-medical prescribers on clinical management including prescribing (Public Health England, 2014d).

Furthermore, inappropriate prescribing appears to be on a continuum ranging from mild inappropriateness which prescribers may not necessarily seek advice from senior colleagues about, to severe inappropriateness which may require expert opinion.

### **7.3.2.6. Lifestyle change**

Six prescribers (two nurse prescribers and four doctors) described the way that lifestyle changes may sometimes preclude the need for medications for comorbid mental health problems and sleep problems:

*And again, sort of the antidepressants and looking at other people's lifestyles and... trying to improve that so they don't... necessarily need their medication [P11, NP].*

*The second example which can be thought of is prescribing antidepressants, particularly ...SSRIs [selective serotonin reuptake inhibitors] which have been commenced with... people who have... a mental health problem, but also a comorbid substance misuse or comorbid addiction like regular alcohol use, and there's lots of mounting evidence that alcohol has an impact on mental health, particularly on mood...so these... medications have been started without really suggesting any lifestyle intervention like, you know, changing the alcohol habit, which in itself could have helped the person recover from their mood symptoms [P7, Consultant].*

*I mean... mainly the ones who are successful in coming off drugs or substances and alcohol, then sometimes they would... themselves see that the problems that they used to have, like sort of sleep reversal, sleep without structure, or anxiety, low mood or... emotionality, these things can subside after they... come off the substance use and they are stabilised [P13, SPR].*

Although change of lifestyle can have a positive impact on mental disorders and sleep, lifestyle recommendations are often underutilised in mental health (Walsh, 2011). SAS prescribers appear to suggest that lifestyle interventions should be initially utilised before prescribing of psychiatric medications. The provision of lifestyle advice such as the need for alcohol abstinence could be helpful in ameliorating mental health symptoms of patients (Davidson, 1995; Frances, 1997; Schuckit, 2006) and also lead to improvement in sleep (Arnedt, Conroy and Brower, 2007; Stein and Friedmann, 2005).

### **7.3.2.7. Adherence to prescribed medications**

Adherence to prescribed medications was mentioned as a theme by four prescribers (one consultant, two NPs and the SHO). These prescribers described service users' non-adherence to their medications:

*...equally you find that they're not taking several of the medications they're prescribed, or at least they're not taking them in the way that's prescribed, they take them when they feel like it, or if they feel unwell then they take one tablet, which is... depending on the tablets of course, but commonly that isn't going to make any difference to anything, it's... the wrong way to take them [P3, consultant].*

*And ...often people..., don't comply fully with their medication anyway [P11, NP].*

Furthermore, a nurse prescriber described how service users may sometimes be on multiple medications that are not reviewed with resultant non-adherence:

*So, you know, and most have been on them, I think there's a lot of medications as well that are long-term prescriptions and they're not reviewed, you know, they're set up by GPs and put on repeats with often people not really knowing why they're taking them, and often aren't taking them [P6, NP].*

The responses of prescribers indicate that many service users do not take their medications as prescribed. This is similar to findings in the literature which indicate that non-adherence is a problem especially among people with SUDs (Azar et al., 2010; Cohn et al., 2011; Weiss, 2004). Sajatovic et al. (2006) found that active SUDs are associated with non-adherence. This is because active SUDs could lead to intoxication, with poor judgments including non-adherence resulting from the cognitive and psychoneurological effects of substances (Bates et al., 2002; Sajatovic et al., 2006). Cognitive and other psychoneurological conditions are a frequent occurrence in people with SUDs (Royal College of Psychiatrists, 2014a; Schilt et al., 2008). In addition to lack of optimal benefit from prescribed medications, non-adherence is a predictor of adverse outcomes such as treatment drop-outs and relapse among people with SUDs (Mitchell and Selmes, 2007a; Sannibale et al., 2003).

Factors contributing to non-adherence are numerous and include patient and prescriber factors. Patient factors include level of health literacy, degree of involvement in clinical decision-making as well as substance use (Brown and Bussell, 2011; Margolese et al., 2004). Prescriber factors that serve as contributors to non-adherence include complexity of the prescription regimen including polypharmacy (Duerden, Avery and Payne, 2013), communication barriers and number of prescribers (Brown and Bussell, 2011). Non-

adherence to prescribed medications lead to failure to translate potentially effective treatments into health gains for service users (National Institute for Health and Clinical Excellence, 2009). It may ultimately lead to worsening of service users' conditions and represents a waste of healthcare resources (Chapman and Horne, 2013; Horne et al., 2005).

#### **7.3.2.8. Addiction to prescribed medications**

Addiction to prescribed medications was identified as a theme by four prescribers (two consultants, one SPR and one NP). The prescribers described situations in which service users were prescribed medications (especially opiates) with dependence potential for prolonged periods without review and the subsequent development of dependence on them:

*But we also see ... people who are dependent on prescribed medication, so they're finding it difficult to wean themselves off a medication that they were prescribed for a condition. Again, a common problem out of that is people who have some sort of pain, pain management, again, commonly lower back pain, and being prescribed opiate-based analgesia or codeine, dihydrocodeine type of medication, which then is not reviewed and is prescribed for a prolonged period of time and the patient continues to use it not understanding that they've become dependent and then when they try to come off it they start experiencing withdrawal and hence they think they're not ready, but actually it's the medication causing all these symptoms and the withdrawal from these medications [P7, consultant].*

Similarly, another doctor described service users who were initially prescribed high doses of opiates in pain clinics but later became dependent to them:

*Again, a lot of people would come to us, particularly from the general hospital where they've had some clear pathology, pancreatitis for example, and the question would be what's the appropriate level of... analgesia, and that's often quite a difficult problem, ... the sort of protocol used by the pain clinics tends to be an escalating dose of opiates and so we often end up seeing people who are on a high dose of opiate, and then addicted to the high dose of opiate, and we then have to think well we can't withdraw them totally from the opiates because they've got genuine pathology, but this dose is too high. So... it's kind of finding a ... sensible sort of balance then [P3, consultant].*

One doctor also described service users who are likely dependent on benzodiazepines:

*It's not uncommon to see patients on hypnotics, such as benzodiazepines. Binge on... a benzodiazepine for a number of years for, the initial intention was for insomnia, but it's... highly likely that they have become dependent on that, so we'd definitely consider that as inappropriate [P8, SPR].*

As described in section 6.5.2.4, addiction to prescribed medications is a widespread problem (Centers for Disease Control and Prevention, 2011; Home Affairs Committee, 2013). In the UK, 1.5 million people are believed to be addicted to prescription drugs, surpassing the number of people in treatment for illicit drug addiction (Home Affairs Committee, 2013). The problem of addiction to prescribed medications, especially, opioids for pain treatment, was also highlighted by prescribers. The treatment of pain with opioids is challenging because of their dependence potential (Ballantyne and Mao, 2003). Consequently, prescribers are usually faced with the challenge of ensuring effective pain control while trying to reduce the possibility of dependence (Wiedemer et al., 2007). Ensuring effective pain control requires regular monitoring and review.

Lack of medication review may result from inadequate care co-ordination and fragmentation of care when service users are transferred between health-care sectors and providers (Department of Health, 2005b; 2006d; Hofmarcher, Oxley and Rusticelli, 2007). In pain clinics, the prevalent view that “pain is what the patient says it is” (McCaffery, 1968) often leads to the use of escalating doses of opioids (Stannard, 2013), on which patients may eventually become dependent. On the other hand, in addiction medicine, clinicians are well aware of the risk of misuse of prescribed medications and the fact that the psychopathology of addiction often means that patients may sometimes demand more medications than they need (Action on Addiction, 2013). Consequently, addiction medicine is more structured, including limit setting, monitoring, behavioural rules and seeking external corroboration of patients’ self-report (Action on Addiction, 2013). This structure is designed to reduce risk to both the patient and the public. People with SUDs and comorbid pain may well benefit from a team approach incorporating the differing views of pain medicine and addiction medicine clinicians (Action on Addiction, 2013).

#### **7.3.2.9. Understanding relationship between SUDs and mental disorders**

The need to understand the relationship between SUDs and mental disorders when assessing prescribing appropriateness was described by five prescribers who were all doctors (three consultants, one specialist registrar and the SHO). One of the doctors described the following strategies that could assist in understanding this relationship (this

substantial quotation from the doctor was included because it highlights pointers to reaching a mental health diagnosis in the presence of SUDs):

*Well it may be difficult to reach a diagnosis while somebody is currently using. The kind of pointers that you ... could use would be what ... sort of person were they before they started using substances, ... is there a strong family history of disorders that are known ..., to have a ... genetic element to them, and those would be really the most important things to look for. Of course the problem there is that, certainly with drugs such as heroin and those kinds of drugs, people often start using at a very young age so you don't really have much of a picture of what they were like before they started using anything. So in the absence of that you can look at their mental state while they are using, and that's really quite difficult I think. ...if somebody had a really severe depressive disorder... you would pick up the hopelessness in their life..., the total lack of ... any positive kind of feelings or enjoyment... but there'd be a lot of grey in the middle where you're not sure about it. And when you're not sure, the only way that you can then determine what's going on... is to go for a period of total abstinence, or if not total abstinence, at... the very least, stable moderation of drug use and... see what happens to the person's mental state ... [P3, consultant].*

This quotation describes how challenging it can be to establish the relationship between SUDs and mental disorders. As discussed in section 1.5.2.1, intoxication and withdrawal symptoms of substances are similar to those of mental disorders (Boden and Fergusson, 2011; Fergusson, Boden and Horwood, 2009; Nunes and Levin, 2004). This may lead to uncertainty when diagnosing mental disorders. Substance-induced symptoms have been found to resolve within weeks of abstinence or moderation in substance use unlike symptoms associated with independent mental disorders (Brown and Schuckit, 1988; Davidson, 1995).

In addition to understanding the relationship between SUDs and mental health disorders, one doctor highlighted the challenge of establishing diagnosis of a mental disorder during service users' first assessment and its impact on judging medication appropriateness:

*And also just meeting a patient once you can't build a big enough picture to establish a diagnosis of depression or schizophrenia, so you don't know whether or not the medication is appropriate for that cos you haven't had a big enough assessment [P9, consultant].*

The relationship between SUDs and mental disorders is complex and there is sometimes uncertainty around diagnosis when these conditions co-exist. Despite this challenge, doctors described using a variety of strategies in teasing out this complex relationship. Nurse prescribers however did not describe exploring this relationship. The widespread prescribing of psychiatric medications in people with co-occurring mental disorders and SUDs may reflect the inability of clinicians such as GPs to address this connection in their busy work environment. As a result, some of the medications for these conditions may be inappropriately prescribed. There have however been arguments for the treatment of both SUDs and mental disorders when they co-exist due to the poor prognosis of such service users as well as the risk of suicide (Burns, Teesson and O'Neill, 2005; Davis et al., 2008; Lingford-Hughes et al., 2012; Martín-Santos et al., 2006).

### **7.3.3. Factors considered before initiating medication changes**

One of the areas this study explored was the factors considered by prescribers before initiating changes to service users' medications. The A-MAI study showed that almost half of service users have at least one inappropriate medication at first SAS visit. However, none of the medications identified to be inappropriate were changed by prescribers. The factors considered before initiating medication changes were explored with SAS prescribers. The following factors were described by prescribers: communication, nature of addiction, benefit and risk of medications and prescribing expertise.

#### **7.3.3.1. Communication**

Communication was described by all prescribers. It involved discussing with service users in order to understand their views and also involving the prescriber of the medication:

*Well, firstly I discuss with the ... patient to see what ... the patient's view is, and explain ... what I think, ... which are the reasons for this inappropriateness, and also I... sort of communicate with the prescriber ..., I give them my thoughts, and then they would be able to review... things again. So basically communicating with the... service user as well as the prescriber [P13, SPR].*

Similarly, another doctor described communicating with service users when making decisions about medications but also highlighted the fact that there are usually negotiations around management plans:

*So I ask the patient what they think about their prescription, if they have any ... concerns, any worries about where things are at the moment, side effects, future, long-term risks and benefits, and the perceived benefit they're getting from it, and what they're expecting with regards to me making changes, and are they expecting me to make a change, do they think I'm going to keep it the same, do they think I'm going to add something, take something away. And then I put forward my proposed management plan and then it becomes a bit of to and fro sometimes [P12, SHO].*

However, prescribers also highlighted the fact that there is sometimes ineffective communication which ultimately affects decisions around prescribing. Service users' lack of communication and engagement with the service was described by prescribers:

*... if somebody is not engaging, if they're not attending appointments, if they're not providing urine samples for toxicology and... you're struggling to make contact with them, you know, ... the only choice I guess you've got then is to say, you know, ... these are all the avenues I've tried to get in touch with you, you know, you're not attending appointments, therefore you leave me no choice but to alter your medication. But again, you know, you... can hold somebody's prescription before it comes to that. You know, it would be very... rare that I think that... had to happen without somebody knowing first [P10, NP].*

*Then again there may be somebody who really is ... not ... engaging with us and is perhaps really using us as a free drug supply. That's unusual I think, but if it does happen, ... under those circumstances..., it's a case of, I think, very often stating, this is what is going to happen [reducing or stopping script]... but ... that's pretty rare... it's unusual that I get involved in that kind of reducing against a person's will, and that's partly because I don't prescribe for that many heroin users, you see, so I've got quite a small number [P1, NP].*

Other prescribers highlighted obstacles such as service user resistance to medication changes:

*If they... don't agree with it then they don't want to use it, and this is a common problem in addiction. Most people don't wanna come off Methadone to go onto Buprenorphine, ... they don't want to do it. They've been on it before, or they've heard stories about it and*

*they don't want to do it, in which case you don't get as far as actually making the change. So in a way it doesn't happen then because the patient just refuses. Or lowering the doses, all these sort of things [P5, locum].*

*I mean sometimes you have to be very, you know, tentative and sensitive because obviously, like I said before, people can be quite precious about their prescriptions, even though you can see that it's not, you know, appropriate or not necessary at that time... [P11, NP].*

The relationship between healthcare professionals and their patients has changed over the years from a predominantly paternalistic model to one in which patients have increasingly become active partners whose views are important, and should be incorporated into the care process (Bezreh et al., 2012; Elwyn, Edwards and Kinnersley, 1999). Therefore, it is not surprising that all prescribers described the importance of communication with service users before initiating medication changes. Effective communication assists in building a therapeutic relationship with patients. Such a positive relationship assists the prescriber in eliciting information and is useful in decision-making concerning treatment (Barnett, 2001). There is evidence that building and maintaining such therapeutic relationships can lead to positive client and treatment outcomes (Leach, 2005).

There were also downsides to communication as service users may not engage with the service or they may be resistant to medication changes. While resistance to change may lead to continued prescribing of medications considered to be inappropriate by prescribers, they sometimes described setting boundaries including stopping medications if service users are not engaging with treatment. Boundary setting in addiction medicine may result from the need to protect the service user from harm and minimise the risk of diversion of medications (Action on Addiction, 2013).

### **7.3.3.2. Nature of addiction**

Nine prescribers (three nurse prescribers and six doctors) highlighted the nature of addiction such as loss of control and the experience of withdrawal symptoms as possible hinderances to initiating medication changes. One doctor described service users' difficulties in coming off diazepam that has been prescribed over a long period of time:

*Sometimes patients... can be very difficult and can be challenging... for example, let's say if somebody's on Diazepam 30mgs for a number of years and when you try and reason*

*with them and trying to cut them down they can be very challenging because of their... perceived difficulties in coming off them [P8, SPR].*

Pressure resulting from a sense of entitlement by service users was also described by prescribers:

*...because some people are very challenging, demanding... they have a lot of previous history of treatment so they sort of know what they want, how they want it, and it might not be what you want to, necessarily to give them. So yeah, it could be... challenging straight away... So there could be lots of demands, challenges, difficulties, when patients present [P5, locum].*

*And then our... patient population is also quite complex in terms of their needs. So there will be a group of people who would be using or wanting or demanding medication to suffice their substance misuse habit. So it would be them trying to forcefully get a prescription [P7, Consultant].*

*... some of the service users are keen to secure medication [P6, NP].*

Addiction is characterised by loss of control over drug use (Action on Addiction, 2013). Loss of control refers to loss of the ability to regulate and control behaviour (Griffiths, 2013). Loss of control may underline service users' perceived need for medications, as they may want medications for other effects (such as their pleasurable or euphoric effects) rather than their therapeutic benefits. Similarly, the experience of withdrawal symptoms may lead to service users resisting medication changes even when these medications are perceived to be inappropriate by prescribers.

As discussed in section 6.5.2.4 under 'fear of losing medications', service users and prescribers may hold different views concerning the need for medications. This variation in views may occur to a higher degree among people with SUDs compared to other patient groups due to the nature of addiction. Some previous studies have shown that patients' demand for medications can sometimes lead to uncomfortable prescribing decisions (Bendtsen et al., 1999; Britten and Ukoumunne, 1997; Macfarlane et al., 1997). Moreover, prescribing could be used as a means of terminating challenging consultations (Britten, 1995). This is particularly likely to be the case among service users as they may pressure clinicians into prescribing medications.

### 7.3.3.3. Benefit and risk

Prescribing practice is centred around the benefits that patients can gain from medications (General Medical Council, 2013), with the lowest possible harm. Although prescribers have described assessing risk (section 7.3.2.2) when considering the appropriateness of prescribing decisions, it re-surfaced when prescribers discussed factors considered before initiating medication changes. All prescribers described evaluating the benefit and risk of medication changes. This may include stopping a medication before contacting the original prescriber if it poses immediate risk:

*There have been occasions ... when I felt that prescribing, you know, ... the combination of medications that the patient's on..., the risks are significantly high enough that I need to do something about it and then I've acted and let the... original doctor know and invited them to contact me if they've got any concerns or questions [P12, SHO].*

*Obviously if it's a... serious one which needs to be changed now, then obviously we'll make those changes now and let the GP know over the phone. So it depends on how acute the change should be made [P8, SPR].*

Prescribers also described situations where medications may remain unchanged if they are perceived to be low risk:

*I generally don't take any actions at all, unless I felt that this was actively harmful to somebody [P1, NP].*

*Unless there was, I thought there was a ... particular risk, ... it wouldn't be as urgent [P9, Consultant].*

*If something was just inappropriate, like Methadone, there was a situation where, you know, one person might say well why not and another might say better if it was reduced, then that's... as I say, that... would then be a... task to... motivate the person to think about changing it [P3, Consultant].*

The interest of the service user should also be considered when making medication changes:

*The other side of it as well is, you know, you've got patients that have been in mental health services for many... years as well and, you know, you could really destabilise them if... their medications are altered or changed. So you have to kind of be very flexible, I think [P10, NP].*

*Yeah, I mean people can... string you along, and... get more out of you than they actually should be, but that's normally for a short while, because it's sometimes good to calm the situation down, even if you give them a milligram or two too much of something, because always you get them back again a month later when things have calmed down. And then, yeah, so one might... feel they've given somebody a...bit, bit too lenient sometimes with medication, but it's just the... patient group, they could be in... real dire straits in their life and it might make them safer by giving them a little bit more of something that you wouldn't normally do in ... a normal population, for example the benzodiazepines, hypnotics, things like that, so [P5, locum doctor].*

The initiation of medication changes revolved around the benefit and risk posed by medications. Prescribers described taking action on those with immediate risk. This implies that where medications are inappropriate but not posing immediate risk, prescribers may take less action. Prescribers described concerns about destabilizing service users' health when considering medication changes. Similar concerns have also been expressed by providers including general practitioners about stopping medications such as benzodiazepines prescribed for elderly patients (Iliffe et al., 2004). Patients prescribed benzodiazepines have often described their reliance on it (Cook et al., 2007; Iliffe et al., 2004) and attribute characteristics beyond an ordinary medication such as affording control over daily stress and prolonging life to their use (Cook et al., 2007). Consequently, benzodiazepines were considered necessary in maintaining a normal life. Most of these patients also expressed resistance to reducing or discontinuing them and fear of being left suffering without these medications (Cook et al., 2007) .

Medications such as benzodiazepines have sometimes been prescribed for reasons that extend beyond their recognised indications. For instance, they have been found to be prescribed out of sympathy for those with complex circumstances such as dysfunctional relationships and domestic violence (Rogers et al., 2007). Evidence from this study suggests that before SAS prescribers initiate medication changes they consider the impact such changes will have on the service user's life as a whole. If therefore stopping an

inappropriate medication will lead to disintegration of the service user's life, a decision may be made to continue such medications for the service user's benefit.

#### **7.3.3.4. Prescribing expertise**

Prescribing expertise was another factor highlighted by prescribers as a consideration before initiating medication changes. All prescribers expressed reluctance at altering medications that are outside their remit of practice:

*If the patient has been discharged from the mental health services but is on an antidepressant and I see, or... has got a diagnosis of mental disorder, and I see them in SAS clinic and I think their... dose of the medication needs to be tweaked, rather than referring them to another specialist community mental health unit, I could do that. But with regards to their physical health medication, I wouldn't necessarily change anything, I think that could be dealt with by their GP. I would normally ask the GP to look into it. Obviously they are more expert in that ... field [P14, SPR].*

*... because the... nurse prescribers at LAU, our... remit of ...medications that we can prescribe is very, very small. So myself, I would only prescribe addiction medication, I wouldn't prescribe an antidepressant or an antipsychotic or, or change the doses even, of those medications, that isn't within my sort of specialist knowledge [P10, NP].*

In addition to expressing reluctance to changing medications outside his area of expertise, one doctor also highlighted that even where the prescribed medications are within his area of expertise, he would contact the original prescriber to alter medications if he has any concerns:

*[...] if it's ... been prescribed by others, ... how can I make change? You know, I sometimes say that if... its medications, which are in my area of ... expertise, like psychotropic medication, I would say that it's better that this person is not on this medication, or reduced. And usually, ... when it's psychotropic medication like antidepressants or, or antipsychotics then GPs would... actually sort of act on what is recommended [P13, SPR].*

The reluctance of doctors to make changes to service users' medications might have resulted because they have limited knowledge of the reasons why the medications were prescribed and the circumstances surrounding prescribing in the first place. Moreover,

prescribers may also want to avoid taking responsibility for medications they did not initiate. It has also been recognised elsewhere that physicians may not stop inappropriate medications due to a sense of discomfort in stopping medications initiated by other physicians (Kroenke and Pinholt, 1990; Tamblyn et al., 2003).

Specialists may tend to focus on their areas of expertise and may not take a holistic approach to treatment, resulting in suboptimal patient care or even adverse outcomes (Lipscombe, Hux and Booth, 2005). Specialisation in medical practice has been criticised as it often leads to fragmentation of patient care (Detsky et al., 2012). As has been discussed, nurse prescribers may not have adequate knowledge and experience in areas outside their scope of practice. The nursing and midwifery council has further recommended that nurse prescribers should only practice within their area of competence (Nursing and Midwifery Council., 2006).

#### **7.3.4. Negotiation of medication changes with service users**

One of the questions explored in the interview with prescribers is how potential changes to service users' medications are negotiated with them. Shared decision-making was identified as the means through which such changes are negotiated.

##### **7.3.4.1. Shared decision-making**

All prescribers described negotiating medication changes with service users through shared decision-making. Shared decision-making involves both service user participation in decision-making as well as a further step of agreement being reached between the service user and the healthcare professional concerning treatment (Charles, Gafni and Whelan, 1997). With the exception of circumstances where prescribers had to withdraw medications due to lack of engagement (section 7.3.3.1), all prescribers described working in collaboration with service users to achieve goals jointly set with them:

*I... think it's collaborative. I think that the best way to achieve change is to do it in collaboration with the service user. I've got a lady, for example, who was on multiple prescriptions, and drinking, and is hugely... at risk of overdose. Very ... unwilling to change. She's been on these medications for twenty years, and one of the ways we've negotiated change is... to line the prescriptions out and ask her to identify which the least important one is in her life, and that's the one that we're reducing... hopefully she sees the positives of doing that, she feels better for doing it, she feels more in control of her life,*

*less medicated, and hopefully that might open the door for further reductions elsewhere [P10, NP].*

*I think the easier way to... sort of stop this inappropriate prescribing is when you've got the patient on board with you. So if... the patient has been explained fully, in... a sort of collaborative way, then if they agree with what you're saying or what you are trying to do then it would be much easier to... implement those sort of changes that you want to do [P13, SPR].*

*... either by talking to the patient and explaining, you know, I usually tell the patient ... what I'm going to be doing, cos I ...like to work ...collaboratively with my patients [P12, SHO].*

Similarly, another nurse prescriber described working collaboratively with service users to facilitate the realisation of set goals:

*And I think, for the most part, for me, very much it would be about (sighs) I see my role is about facilitating change but it's ultimately about what the service user wants to achieve their goal and I think it's about giving them as much choice about what and how they do. So for me it's not about imposing a change on, it's about working with them to support them setting realistic goals [P6, NP].*

Shared decision-making gives patients a voice in their own management (Hamann, Leucht and Kissling, 2003). It is a two-way communication in which the patient and the prescriber share information, deliberate about treatment options, weigh risks and benefits together and then agree on treatment decisions to be implemented (Charles et al., 1997). This assists in ensuring that patient-specific goals are not just elicited but that patients take responsibility by being actively involved in the line of action that is agreed with the prescriber for their management. Some patients may however be resistant to change. Patient resistance has been discussed in section 7.3.3.1. Patients' resistance has been identified as a reason needed changes are sometimes not made to medications (Kroenke and Pinholt, 1990; Tamblyn et al., 2003). The negotiation of medication change may thus be a continuous process where healthcare professionals elicit patients' beliefs and attitudes and try to address them appropriately (Bezreh et al., 2012; Marinker and Shaw, 2003). It is

important to involve service users in treatment decisions in order to obtain optimal outcomes (Barry et al., 2000).

### **7.3.5. Impact of the A-MAI on prescribers' practices**

The A-MAI was used by SAS prescribers to assess the appropriateness of service users' medications during their first visit and three-month follow-up appointment. Prescribers were asked for their views on how the use of the A-MAI impacted on their clinical practice. Nine prescribers (two nurses and seven doctors) stated that the A-MAI prompted them to reflect on prescribing decisions. One nurse prescriber described the fact that it made her consider prescribing in more depth including reviewing service users' medications:

*[...] I think since you've been doing this and we've had a look at this, it's... definitely made me think a bit more about people's prescriptions and sort of, not just at the initial assessment but asking them afterwards as well. Yeah, so it's... kind of made me think a bit more about reviewing people, yeah [P11, NP].*

Similarly, one doctor described the A-MAI as having increased her awareness of different aspects of prescribing while also providing a structure for assessing prescribing appropriateness:

*I think just being... more aware of the different aspects of prescribing, like thinking about indication, contraindication, interactions, and that kind of thing, adverse reactions, you know, perhaps I... think about things a... bit more, in a bit more of a structured way, ... as a result of reading and filling out MAIs [P12, SHO].*

In addition, another doctor described the A-MAI as highlighting the important domains in assessing prescribing appropriateness:

*We have been using the scale that you introduced as part of your study, which has been quite helpful as well, which makes you think about particular things when thinking of inappropriateness... I think it's a good scale, it makes you think of the domains, which are pretty much essential in establishing why something should be considered inappropriate [P7, consultant].*

There were however three prescribers (two nurses and a doctor) who felt the A-MAI did not have any significant impact on their prescribing practice:

*Well as far as the study goes it's fine, yeah, otherwise it wouldn't have changed my prescribing habits, because I think this is the way doctors look at things in any case... it wouldn't have made me more aware of, or less aware of anything like that, no [P5, locum doctor].*

Prescribers were also asked how long it took them to complete the A-MAI for each medication and their responses varied from two minutes to about ten minutes. Generally, prescribers felt the completion time depended on how much relevant information they had for assessing appropriateness and also the complexity of the regimen:

*...roughly I would say approximately five minutes, three to five minutes, it depends on how complex their medication is. If it's a simple medication they're much more easier, [if] it's a complex kind of medication then probably spend more time. And all depends on how much information I've got in front of me, otherwise it'll take more time for me to ask patients... [P8, SPR].*

*Yeah,... it really varied. If you had all this information at hand, the diagnosis, duration, frequency, it was done, I would say, on an average of five minutes. For each medication I would say well two to three minutes, but if you were unsure about the drug, drug interaction then that took some more time, and if you weren't sure about the doses and... duration then that took some more time, so it was very variable. So I would say on an average between two to six minutes [P7, consultant].*

*I don't think it took me very long, but... I guess if somebody came in on multiple prescriptions I would be wanting to check the drug interactions. So that would take, obviously, longer to do. But generally it didn't take long... two to five minutes [P10, NP].*

The majority of prescribers described the A-MAI as having a positive impact on their prescribing practice. However, there were a few who felt it had no impact. Nurse prescribers' views on the impact of the A-MAI were quite varied with two of them reporting no impact. Despite the positive views expressed by most prescribers, the time taken to complete the A-MAI for each medication implies that where service users are on

complex medication regimen, there is the potential to increase clinicians' workload. This may prohibit the use of the A-MAI in clinical practice.

### **7.3.6. Medication omissions**

The result of the medication appropriateness study described in section 5.9.2 showed that there were no omissions of opioids or psychiatric medications among service users' medications. This finding was further explored in the interviews with prescribers. The following quotation expresses a consultant's views on medication omissions:

*Very unusual [medication omissions], I would think. Almost by definition, people who are coming to an addiction clinic are taking a number of drugs, or certainly one drug that they're addicted to, and they're usually adept at collecting other prescriptions along the way. So I... think omissions are probably quite unusual (P3, consultant).*

Similarly, one nurse prescriber expressed her views on medication omissions thus:

*... I can't think of anything really that springs to mind where I've felt that this person needs that. I would say ... I've seen more the other way, when people are on lots of medications and not, you know, not aware of what it's for and not taking it as prescribed. So I don't think, ... I can't recall an omission, but that might also be about my limited knowledge and skills around assessing for them (P6, NP).*

Another consultant stated that thiamine and other B vitamins may sometimes be omitted:

*Maybe B vitamins and thiamine in people that are chronic heavy drinkers. They're often malnourished with risk of thiamine deficiency and deficiency of other B vitamins. So if someone was heavily drinking and not prescribed those that might be regarded as a medication omission. Fortunately, most GPs are quite good at prescribing thiamine and B vitamins (P9, consultant).*

Medication omissions were considered by prescribers, both nurses and doctors, to be very uncommon among service users attending the SAS. However, omission of thiamine and other B vitamins may sometimes occur.

### **7.3.7. Summary of prescribers' interviews**

The evidence from this study shows that the assessment of the appropriateness of prescribed medications is a complex judgment. In particular, prescribers described assessing appropriateness by either checking or carrying out the following: reviewing of medications, assessing risk, guideline adherence versus successful prescription, history-taking, communication, lifestyle change, addiction to prescribed medications, medication adherence and understanding the relationship between SUDs and mental disorders.

Besides a few more experienced doctors, all other prescribers (doctors and nurse prescribers) tended to review medications within their competency. These prescribers described a strong focus on medications within their areas of expertise when assessing appropriateness. While doctors focused on reviewing psychiatric and addiction medications and sometimes opioids, nurse prescribers described a more limited area of expertise comprising only addiction medications. Nurse prescribers further described referring service users who they had concerns about their medications to SAS doctors or service users' GPs. SAS doctors particularly represented a valuable source of support to nurse prescribers when dealing with issues around prescribing. The more junior doctors (non-consultants) also relied on their senior colleagues, especially consultants, for expert advice on medications. There was further evidence that SAS prescribers provided support to GPs in the management of service users.

Prescribers identified problems with the quality of information provided by service users when taking their history. Although all prescribers reported taking service users' histories, doctors and nurse prescribers largely differed in how they utilised the history taken when assessing the appropriateness of medications. Doctors described considering the information obtained during history-taking when assessing appropriateness while only one nurse prescriber described utilising the history taken in the assessment of medication appropriateness. The poor quality of information by service users and the divergent approaches of nurse prescribers and doctors to history-taking and medication review may lead to prescribers missing out inappropriately prescribed medications. This may be more of a problem among nurse prescribers due to their focus on a limited area of practice.

Judgment on the appropriateness of prescribing among service users also involves assessing risk. This risk may result from potential adverse effects secondary to drug interactions or interactions between substances and medications. Where there is a high

level of potential risk, prescribers often intervened by using appropriate interventions such as detoxification or in some cases discontinuing prescribed medications. Risk appeared to be on a continuum with prescribers addressing medications that posed immediate risk.

The limited applicability of guidelines to service users was also recognised by prescribers. There was an acknowledgment that successful prescribing may not always be the pharmacologically appropriate prescribing represented by guidelines. Successful prescribing is prescribing that produces good physical, psychological and social outcomes and this may well be outside guideline recommendations. Moreover, the need to maintain service users' equilibrium with minimal risk of harm in spite of their complex problems should be paramount when evaluating the appropriateness of prescribing decisions. Judgments on the appropriateness of prescribing will need to involve consideration of the whole individual's context. Doctors further highlighted the challenge of diagnosing mental disorders among people with SUDs. This theme was not mentioned by nurse prescribers probably due to their more limited scope of practice.

The factors considered by prescribers before initiating medication changes include communication, nature of addiction, benefit and risk of medication and their prescribing expertise. Communication involves discussing with service users as well as understanding their views. Consequently, the involvement of service users in decision-making was critical in communication. While such a positive relationship is essential before initiating medication changes, it also has its drawbacks as resistance and pressure from service users as well as the psychopathology of addiction may influence decision-making.

Prescribers highlighted the trade-offs they sometimes have to make through consideration of the risks and benefits of prescribing decisions. While medications may need to be initiated for reasons beyond mere pharmacological appropriateness, concerns about destabilising a service user may prohibit medication changes. Prescribers described negotiating potential changes to service users' medications through shared decision-making. Most prescribers described the positive impact of the A-MAI on their clinical practice, although there were a few others who reported a lack of benefit.

Owing to the fact that the interviews were conducted with prescribers after they had taken part in the medication appropriateness study where they utilised the A-MAI, it is possible that participation in this study may have influenced some of their responses to the different areas explored in the interviews. Consequently, prescribers' responses might be different if

they were interviewed before taking part in the medication appropriateness study. Section 7.3.8 presents the researcher's reflections on other factors that may have influenced study findings.

### **7.3.8. Reflections on service user and prescriber interviews**

The interviews in this study contributed towards a greater understanding of the perceptions of service users concerning the appropriateness of prescribing decisions made by their prescribers while interviews with prescribers were used to understand their responses to inappropriate prescribing. These studies were limited because participants were only recruited from a single site. The findings may therefore lack generalizability to service users and prescribers in other addiction services, especially given the changes that have occurred in drug and alcohol treatment services in the UK. There has been an increase in the number of third sector organisations providing drug and alcohol services. Medical expertise has also diminished in these services.

Furthermore, data collection was by a single researcher. There is the possibility that the researcher's own perspectives may have affected interpretations that were made. However, the conduct, analysis and interpretation of data were overseen by a thesis advisory panel which strengthens the validity of findings as they are not limited to the perspective of the researcher. This is in line with recommendations for ensuring rigour in qualitative research (Barbour, 2001; Mays and Pope, 1995). The validity and transferability of study findings are considered below.

#### **7.3.8.1. Validity**

Validity can be considered to be the quality, rigor or trustworthiness of qualitative research (Davies and Dodd, 2002; Lincoln and Guba, 1985; Stenbacka, 2001). There are various techniques for ensuring that research findings are credible in qualitative research (Whittemore, Chase and Mandle, 2001). Patton (1999) has suggested that sufficient details should be provided concerning data collection and analysis so that others can assess study quality. Details of the interview and data analysis process for the interviews were therefore presented in sections 6.4.1 and 6.4.2 respectively. Previous researchers have further advocated the use of quotations because it assists in linking the data, interpreting them and drawing conclusions (Beck, 1993; Spencer et al., 2003a). The use of quotations is therefore a means of demonstrating the validity of research findings in this thesis. However, it is by no means the only indicator of quality in qualitative research. There have been suggestions that the quality of qualitative inquiry could be enhanced by reporting competing themes

and explanations (Mays and Pope, 2000; Patton, 1990). Consequently, competing themes were presented in order to provide alternative explanations for study findings.

Respondents' validation has also been recommended as a validity check in qualitative research (Lincoln and Guba, 1985). However, there are limitations to its use as a validity test. For instance, the findings reported by a researcher are usually for a wider audience, provide an overview of the research outcomes and are different from the perspectives of respondents who have their own individual concerns (Mays and Pope, 1996; 2000). Consequently, respondent validation was not carried out as a validity test for the interviews. Other issues that may impact on study quality including the researcher's influence on the research process have been presented in section 3.5 under reflexivity.

#### **7.3.8.2. Transferability**

Qualitative research usually seeks depth and attempts to understand phenomena in context-specific settings (Ambert et al., 1995; Patton, 1999). This is achieved by studying a small number of participants in-depth without the aim of generating statistically representative findings (Malterud, 2001). The qualitative studies therefore involved a small number of participants (12 prescribers and 14 service users). In qualitative inquiry, the aim with respect to external validity is to ascertain the extent to which study results can be applied (transferred) to other settings, and this is usually achieved through a description of context such as demographics of participants and study setting (Malterud, 2001; Onwuegbuzie and Leech, 2007; Patton, 1999).

In this study, participants and clinic setting have been described previously (sections 3.2 for SAS setting, 6.5.1 for service user characteristics and 7.3.1 for prescriber characteristics), thus enabling the reader to judge the transferability of findings to their own setting. As described in section 6.5.1, twenty of the 23 eligible service users were invited for interview because the remaining could not be contacted before their three-month follow-up visit. With the exception of two service users who declined interview, all 14 service users who turned up for their follow-up appointment were interviewed. Interviews were therefore carried out with a convenience sample of service users on prescribed opioids and/or psychiatric medications.

Convenience sampling involves selection of the most accessible participants for research (Marshall, 1996). It has however been criticised because it may result in poor quality data (Marshall, 1996). It is possible that this study may well have benefited from a purposive

sampling design where service users are actively selected based on a framework of variables that might influence their perspectives on prescribing appropriateness such as gender, age, referral substance and type of illness. There is however very limited knowledge in this area and it is possible that these variables do not have any influence on the views of service users.

Convenience sampling was necessary because people with SUDs are particularly difficult to recruit for research (Blanco et al., 2008). For instance, some of the service users who were invited for interviews did not attend their follow-up appointment. Furthermore, the effective implementation of a sampling framework would have been difficult because variables highlighted above were not evenly distributed among service users. For example, none of the service users invited for interviews was less than 25 years. There were also small numbers of female subjects and those on other substances besides alcohol. There were only three females among interviewed service users. None of the service users were on other referral substances besides alcohol and heroin. Consequently, the views of these groups of service users (females and those with referral substances other than alcohol and heroin) were under-represented in the interviews and are therefore areas to explore in future studies.

During the interview phase of this study, two service users refused to be interviewed while four others who initially agreed did not attend the interviews. When the characteristics of these service users were examined, they did not differ from those of the service users who were interviewed (see appendix 6.3). However, without exploring the perspectives of these service users concerning their prescribed medications, it is not possible to determine if they may differ in their perspectives. For example, it is possible that those service users who declined interview may have less concern about the appropriateness of their prescribed medications.

Twelve of the 14 SAS prescribers who took part in the medication appropriateness study were interviewed because one prescriber (an SPR) left the SAS before the interviews began while the other prescriber (an SPR) was not interviewed due to the time limitations of this thesis. The prescribers interviewed differed in their professions (nurses and doctors), grades, years of experience, age and gender. There were more female nurse prescribers but more male doctors among interviewed prescribers. Although data obtained from under-represented prescriber groups (male nurse prescribers and female doctors)

support the findings of this research, there may be some benefit in exploring their perspectives in future studies for any sources of variation. Recent research has suggested that gender may indirectly influence doctors' prescribing habits (The Medical Bag, 2014).

## Chapter 8: Discussion and conclusion

This chapter will provide an integrated discussion of the results obtained from the secondary data analysis, medication appropriateness study, interviews with service users and SAS prescribers as well as its implications for research and practice. The aims of this thesis and research questions have been previously described in section 3.1, while a description of the methodology is given in section 3.4. Briefly, the aims of this thesis were to assess the level and nature of appropriateness of current prescribed medications for service users while also exploring SAS prescribers' responses to inappropriate prescribing. These aims were achieved using a mixed methods design.

The mixed methods design adopted in this thesis facilitated the use of quantitative and qualitative methods in addressing the research questions. It allowed the strength of each method to be harnessed (Creswell et al., 2011). For instance, quantitative approaches alone were inadequate for the exploration of the complex and multi-dimensional concept of appropriateness. While quantitative methods provided a description of the pattern of prescribing for service users and estimates of the levels of inappropriate prescribing, interviews with prescribers provided a means for an understanding of their responses to inappropriate prescribing and the process of clinical decision-making when assessing prescribing appropriateness. Interviews with service users further aided an understanding of their perspectives on the appropriateness of their medications.

Integration of the results of the four research studies is first presented. This is followed by an evaluation of the methodology of this thesis. Thereafter the overall strengths and weaknesses of the studies are considered, and implications for practice and recommendations for future research are given.

### **8.1. Integration of findings from studies**

Integration of the results were carried out under five themes namely: prescribing pattern, functional outcomes, medicines optimisation, history-taking and effect of A-MAI. These themes serve as a means of summarising and integrating the different studies. Some themes resonate more strongly across different studies as shown in table 8.1.

Table 8.1: Themes from research studies

Themes	Secondary data analysis	Medication appropriateness study	Service user interviews	Prescriber interviews
Prescribing pattern	Nearly half of service users were prescribed antidepressants.  Over a quarter of service users were prescribed four or more medications.	Two-thirds of service users were prescribed antidepressants.  Almost half of service users had one or more inappropriate medications at their first SAS visit.		
Medicines optimisation <sup>a</sup>		Most service users take their medications regularly. Some of these medications were prescribed outside guideline recommendations. There were no omissions of psychiatric medications and/or opioids.	There were varied viewpoints regarding review of medications with lack of review and addiction to prescribed medications sometimes described. Ineffective communication about medications sometimes occurred between service users and prescribers. Most people who benefit from their medications appear to be adherent to them.	Medication review varied among prescribers with the most experienced doctors tending to review all of service users' medications. Other doctors and nurse prescribers focused on medications within their expertise. SAS prescribers further described communicating with service users, other SAS prescribers <sup>37</sup> and GPs when dealing with problems around prescribed medications. Non-adherence to prescribed medications was reported to be common among service users while medication omissions are rare.
Functional outcomes			Benefits from medications were reported by service users including those prescribed outside guideline standards. Conflicts sometimes existed between guideline standards and service users' views and also between service users' preferences and prescriber-assessed needs.	Prescribers described evaluating the benefits and risks of medications when assessing prescribing appropriateness. There seemed to be a greater focus on the outcome of prescribing rather than its pharmacological appropriateness.
History-taking				Doctors and nurse prescribers differed in how they utilised information collected during history-taking when assessing appropriateness. Challenges encountered during history-taking were centred around problems associated with self-report among service users.
A-MAI		The 'cost' dimension had the highest number of 'don't knows'.		Most prescribers considered the A-MAI to be useful to their prescribing practice.

<sup>a</sup>Medicines optimisation comprises medication monitoring and review, omissions, adherence and collaboration among stakeholders.

<sup>37</sup>SAS doctors were a valuable support to nurse prescribers and GPs in addressing issues around prescribed medications. The more junior doctors relied on their consultant psychiatrists in dealing with prescribing problems.

Some themes such as medicines optimisation and effect of A-MAI cut across both quantitative and qualitative studies. Other themes such as prescribing pattern, functional outcomes and history-taking were unique to either the quantitative or qualitative studies.

### **8.1.1. Prescribing pattern**

Evidence concerning the types and quantities of prescribed medications taken by service users were obtained from the secondary data analysis and the medication appropriateness study. Both studies found high levels of prescribing of antidepressants. Antidepressants were the most prevalent group of medications in these studies, followed by analgesics comprising substitute opioids, non-substitute opioids and non-opioid analgesics. Evidence from the medication appropriateness study showed that these antidepressants were mostly prescribed for depression or anxiety disorders. As already described in chapter 1 (section 1.5.2.1), this is not surprising given that co-occurrence of SUDs with mental disorders (in particular, mood and anxiety disorders) is well documented in the literature.

The medication appropriateness study found that almost a third of antidepressants had inappropriate A-MAI dimensions. The A-MAI dimension with the highest number of inappropriateness was 'indication'. NICE (2009) recommends that antidepressants should only be prescribed for depression of a certain level of severity. However, service users coming into treatment with mild depression such as low mood were on antidepressants. This research was limited because SAS prescribers were not present when antidepressants were prescribed. They therefore lacked contextual information on their prescribing. While it is possible that the antidepressants had led to an improvement in mood over time, they might have been initially prescribed for mild depression. There was also evidence of antidepressant prescribing in response to stressful life situations such as marital distress in the service user interviews.

While there may be greater need for prescribing of antidepressants to assist service users in coping with their diverse life and health problems, such prescribing has also raised concerns about the medicalisation of life's challenges (Baldwin et al., 2014; Horwitz and Wakefield, 2007). There seems to be a growing trend in using antidepressants to treat instances of emotional unhappiness (Manninen, 2006). This evidence coupled with the possibility that SUDs may negate the pharmacological effect of antidepressants (Ramsey, Engler and Stein, 2005) as well as the potential for dangerous drug interactions (Gillman, 2005; Morgan et al., 2004) and side effects (Pagura et al., 2011) brings to the fore the need

to consider other alternatives such as non-pharmacological therapies in the management of depression and anxiety disorders. Furthermore, pharmacotherapy for depression in people with SUDs appears to have mixed evidence with some reviews showing a beneficial effect (Iovieno et al., 2011; Nunes and Levin, 2004) while others question their efficacy (Lingford-Hughes et al., 2012; Pedrelli et al., 2011; Torrens et al., 2005). Non-pharmacological therapies such as psychotherapies may therefore represent a viable alternative for this client group.

Psychotherapies have been reported to be comparable with antidepressants when used in the treatment of depression and anxiety disorders in non-substance using populations (Roshanaei-Moghaddam et al., 2011; Spielmans, Berman and Usitalo, 2011). The psychotherapies evaluated against antidepressants by Spielmans, Berman and Usitalo, (2011) were cognitive and/or behavioural, psychodynamic, interpersonal or supportive in nature while Roshanaei-Moghaddam et al. (2011) compared cognitive behavioural therapy (hereafter CBT) with antidepressants or anxiolytics for the treatment of depression and anxiety. CBT has also been found to have modest effect in the management of life's challenges including marital distress (Butler et al., 2006).

Behavioural therapies such as contingency management and psychotherapies such as twelve-step facilitation, CBT (Kay-Lambkin, Baker and Lewin, 2004), motivational interviewing (hereafter MI) (Kay-Lambkin, Baker and Lewin, 2004) or a combination of these (Kelly, Daley and Douaihy, 2012; Riper et al., 2014) have shown promise in the management of comorbid SUDs and mental disorders. Psychotherapies could be useful in any of the following ways:

- They could alleviate the symptoms of depression or anxiety;
- They could assist service users in understanding their comorbidity thereby improving coping with cravings. They may thereby reduce substance use;
- They could improve both symptoms of depression and anxiety and SUDs (Hesse, 2009).

Moreover, MI has shown additional benefit in promoting treatment engagement (Kay-Lambkin et al., 2004; Martino et al., 2000). Twelve-step facilitation groups may be useful in comorbidity management for enhancing coping skills (Lopez Gaston et al., 2010; Humphreys, Moos and Cohen, 1997), promoting recognition of stress and problems

(Moos, 2008), increasing self-efficacy (Morgenstern et al., 1997) and providing social support (Bond, Kaskutas and Weisner, 2003). These non-pharmacological treatments may well have a place in the management of instances of emotional distress and less severe forms of depression and anxiety disorders among people with SUDs. Where the severity of depression and anxiety disorders leads to poor engagement with psychotherapies (Knowles et al., 2015), antidepressants may be prescribed before psychotherapy is initiated.

Antidepressants and psychotherapy may also be combined for more effective management of comorbidity (Kelly, Daley and Douaihy, 2012). For example, there is evidence suggesting that the best outcomes in terms of reduction in drinking levels and improvement in mood among people with major depression and AUDs may occur when antidepressants are combined with psychotherapy (Kelly, Daley and Douaihy, 2012; Moak et al., 2003).

When compared to the high prevalence of chronic pain reported among people with SUDs (Caldeiro et al., 2008; Dunn et al., 2014; Peles et al., 2005; Rosenblum et al., 2003), the fact that only 10% of service users were taking non-substitute opioids in the database study may be due to a number of reasons: under-reporting of prescribed opioid use, focus of thesis on prescribed opioids and not on those obtained from illicit sources or over-the-counter, use of other medications in pain management or undertreatment of pain.

Under-reporting of prescribed opioid use may result from fear of losing access to this medication among service users (Action on Addiction, 2013). The focus of this thesis on prescribed opioids rather than those obtained through other means may also have contributed to the low prevalence of opioids. The use of prescribed medications often occurs in the context of drugs accessed through other means among service users. While access to illicit opioids cannot be ruled out in the SAS population, it is also pertinent to state that the study population were predominantly those misusing alcohol. Issues around illicit opioid use may therefore be less salient when compared to a predominantly opioid-using population. There was evidence in the medication appropriateness study of the treatment of pain with other classes of medications such as anticonvulsants. Some anticonvulsants such as pregabalin and gabapentin are licensed for the treatment of some forms of chronic pain in the UK (Moore et al., 2009). It is also possible that there may be a tendency to undertreat pain among service users. Service users are at increased risk of pain under-treatment due to the potential for dependence on opioids, the possibility of

dangerous drug interactions with illicit substances as well as other prescribed medications (Prince, 2001).

The SAS routine clinical data showed that over one-quarter of service users were on four or more medications (polypharmacy). This finding appears to reflect the fact that service users also had other co-existing conditions. The tendency for people with SUDs to have comorbid conditions have been recognised elsewhere (Delgadillo et al., 2012; Dickey et al., 2002; Regier et al., 1990).

Furthermore, the medication appropriateness study found that almost half of service users had at least one inappropriate medication at their baseline assessment in the SAS and over one-quarter of opioids and/or psychiatric medications had inappropriate A-MAI dimensions. Inappropriate A-MAI dimensions include indication, effectiveness, dose, duration, duplication, directions, drug-disease interactions, drug-drug interactions and cost. These inappropriate dimensions varied across the psychiatric medications and opioids assessed in this small-scale study. The result of this study cannot be compared to previous studies because it is the first of its kind. The level of inappropriate prescribing is indicative of suboptimal prescribing of opioids and psychiatric medications among service users referred to the SAS. Further studies are required to investigate prescribing appropriateness among service users referred to other addiction services.

### **8.1.2. Functional outcomes**

This theme was expressed in the service user and prescriber interviews. As described in section 6.5.2.1, it refers to physical, social and psychological functioning. The service user interviews showed that most service users described benefit from their medications, including improvement in their physical, psychological and social functioning. Among these were those prescribed outside guideline recommendations. There was therefore sometimes conflict between service users' perspectives and the recommendations in guidelines.

As discussed in section 1.4.2, recommendations including dosing and duration are usually established in clinical trials which inform clinical guidelines (Tucker and Roth, 2006). Sometimes, due to lack of robust evidence, recommendations may be based on the opinions of experts (Geleris and Boudoulas, 2011). In clinical trials that inform guidelines for the management of people with co-occurring SUDs and psychiatric disorders or chronic pain, SUDs are often an exclusionary criterion (Furlan et al., 2006; Ostacher, 2011; Samet

and Walley, 2008). Consequently, these guidelines cannot be extrapolated to this population.

While guidelines represent an important source of information, they have often been criticised due to their disease-specific focus and limited applicability to the varying needs of individual patients (Farquhar, Kofa and Slutsky, 2002). Consequently, the frame of reference in these guidelines for assessing appropriateness cannot be used for people with comorbidity since “one size does not fit all”.

Evidence from this thesis suggests that the wider physical, psychological and social outcomes of people with SUDs may be particularly important when assessing the appropriateness of this client group’s medications. Although prescribing outside guideline recommendations carries its own risks including the potential for greater severity of unwanted side effects (Ali and Ajmal, 2012), there needs to be a weighing of such risks against more pragmatic outcomes that may be of great importance to the service user. Such prescribing is particularly important among service users because of their often complex circumstances encompassing health, social and economic problems (Humphreys et al., 2005; Lloyd, 1998) as well as the paucity of the evidence-base for their management. There may well be a greater need to elicit the views of service users when assessing their outcomes and also to determine the level of risk they are willing to tolerate (Tinetti, Bogardus and Agostini, 2004). Furthermore, in the UK, the NHS constitution states that the service it provides must reflect the needs and preferences of patients (Department of Health, 2013c). There is therefore a need for appreciation of service users’ perspectives (Elwyn, Edwards and Britten, 2003).

Medications may play a pivotal role in assisting service users maintain equilibrium in their wider life. Prescribers described concerns about destabilising service users’ well-being and, by extension, their lives when making prescribing decisions. In essence, although a medication may be considered inappropriate from a medical perspective, it may be appropriate in another sense if it prevents destabilisation of the service user’s health and wider life. For instance, this study found that a GP who continued prescribing a supra-BNF dose of an antipsychotic for a person with schizophrenia refused to reduce the dose when contacted by a SAS prescriber who considered the high dose inappropriate. The GP justified the high dose as the person was mentally stable on such a dose. The views of these two clinicians therefore varied on prescribing appropriateness. The findings of this thesis

suggest that evaluations of appropriateness may inevitably be a matter of debate among prescribers, and also between prescribers and service users in some circumstances.

Moving beyond the medical perspective by considering context and service users' preferences, introduces subjectivity into decision-making concerning appropriateness. For instance, two service users with the same health conditions may have different preferences and situations which may lead to different prescribing decisions for both of them. Barber et al. (2005) have argued that the introduction of subjectivity is appropriate when making a value judgment such as this. Considering all these perspectives further improves the quality of prescribing (Barber et al., 2005).

In addiction medicine, incorporating service user's preferences or choices in decision-making is sometimes a difficult issue. People with SUDs tend to have a particularly strong sense of entitlement to being prescribed medications and they may seek to influence prescribing decisions. Both prescriber and service user interviews showed that there is sometimes conflict between physician-assessed needs and service users' preferences. Service users' preferences may be due to the pleasurable effects of medications or they may want medications for the purpose of suspending reality (Cribb and Barber, 1997) or for diversion to the illicit drug market. Preferences for certain medications such as opioids may also be driven by craving or the need to avoid withdrawal symptoms (Action on Addiction, 2013).

Opioid prescribing in people with SUDs is particularly challenging due to their dependence potential (Action on Addiction, 2013; Rosenblum et al., 2008). Evidence from service user and prescriber interviews showed that opioid prescribing may be problematic. A service user described developing addiction to his opioid medication (dihydrocodeine). Prescribers also described situations where service users prescribed high opioid doses for prolonged periods subsequently became dependent.

Pain specialists and addiction specialists often have different philosophies and operate separately from each other (Action on Addiction, 2013). In the specialty of pain medicine, the prevalent view is that pain is what the patient says it is and it is therefore more oriented towards support (affirmation and acceptance of the patient's experience). On the other hand, addiction specialists understand that addiction is characterised by loss of control and there is therefore an orientation towards structure (limit setting, behavioural rules,

monitoring and seeking collateral information in addition to patients' self-report). There is a need for collaborative work between pain and addiction specialists in order to ensure safe and effective management of pain among people with SUDs (Action on Addiction, 2013). There is limited evidence of the effectiveness of opioids over the long duration of treatment typical of chronic pain (Noble et al., 2010). Total relief of chronic pain may not always be possible (Department of Health (England) and the devolved administrations, 2007; Prince, 2001). Additional measures such as psychological and behavioural therapies that could assist in minimising the discomfort from chronic pain may need to be considered. These therapies include interventions aimed at increasing self-management, cognitive change and behavioural change (Roditi and Robinson, 2011). Current approaches to the management of chronic pain recognise the benefits of these therapies in addition to pharmacological treatment (Roditi and Robinson, 2011). This sort of multimodal treatment approach have been reported to result in improvement in pain and restoration of daily functioning (McCracken and Turk, 2002), and may well have a place in the management of comorbid chronic pain and SUDs.

Taken together, prescribing appropriateness entails much more than the narrow pharmacological appropriateness presented in guidelines. It is sometimes an area of conflict with divergent views among stakeholders. Conflicts may exist between service users and prescribers' views, and also among different prescribers. Assessment of the appropriateness of prescribing among service users needs to incorporate their physical, psychological and social functioning as well as their preferences and the risks posed by medications. The potential risk posed by medications may necessitate some sort of structure for prescribing to be safe. This broad view of appropriateness raises the need for a collaborative effort between service users and the different prescribers managing their pain and psychiatric comorbidities in order to improve understanding of appropriateness and for optimal prescribing decisions to be reached.

### **8.1.3. History-taking**

For decision-making concerning prescribing to be safe and effective, there is first the need to gather relevant patient's information such as medical history, medication history including medication adherence, and undertaking of physical investigations (Lum, Mitchell and Coombes, 2013). Prescribers' interviews showed that there were differences between doctors and nurse prescribers in history-taking. Only one nurse prescriber described

considering information obtained during history-taking when assessing the appropriateness of medications.

The difference between nurse prescribers and doctors appears to have resulted due to nurse prescribers' narrower scope of practice. Unlike doctors, nurse prescribers have a discrete area of practice which they are expected to adhere to (Nursing and Midwifery Council., 2006). There is however the possibility that the safety of prescribed medications may be affected by comorbidities and co-prescribed medications. Without giving adequate consideration to them when assessing appropriateness, the risk posed by prescribed medications may go unnoticed.

A national evaluation of nurse independent prescribing in England in 2007 reported that there is scope for improved history-taking among this group (Latter et al., 2007). The findings from this study suggest that there may be training needs in this area to equip nurse prescribers in applying the history they have taken to the assessment of appropriateness. Furthermore, there may well be need for nurse prescribers to develop competence in the assessment of service users' comorbid mental health conditions and pain for optimal decision-making about prescribing (see section 8.4.4 for more details).

Prescribers' interviews further highlighted problems with the information provided by service users ranging from problems resulting from cognitive impairment to deliberate non-disclosure of information. When service users are actively misusing substances, prescribers lose access to the most fundamental tool in medicine, the patient's self-report (Action on Addiction, 2013). Use of other forms of evidence to corroborate service users' self-report is therefore necessary. While some prescribers described contacting service users' GPs for further information concerning medications, this was not done by all prescribers. Depending on information obtained from only service users in assessing appropriateness implies that medications which are potentially inappropriate may not be identified if service users fail to mention them. There is the possibility that prescribers may go ahead to prescribe such undisclosed medications. In addiction medicine, there should be careful consideration of self-report and collateral information should be sought where possible (Action on Addiction, 2013). This is however challenging in practice. There is therefore the need for ready availability of information about service users when they attend substance misuse services. Means through which this could be achieved are discussed in section 8.4.2.

#### **8.1.4. Medicines optimisation**

Medicines optimisation ‘requires evidence-informed decision-making about medicines, involving effective patient engagement and professional collaboration to provide an individualised, person-centred approach to medicines use, within the available resources’ (National Institute for Health and Care Excellence, 2013). It is a patient-centred approach that aims to produce the best outcomes from the use of medicines (Royal Pharmaceutical Society, 2013). Healthcare professionals need to work together to individualise care, monitor outcomes more carefully, review medicines more frequently and support patients when needed (Royal Pharmaceutical Society, 2013). The aspects of medicines optimisation that will be discussed in this section include monitoring and review, adherence, medication omissions and collaboration among stakeholders.

##### **Monitoring and review**

Both prescriber and service user interviews explored medication assessment and review. Some service users described regular review of their medications while others suggested there were problems with medication review, including review of repeat prescriptions. There was support for this finding in the medication appropriateness study as some medications such as benzodiazepines and non-benzodiazepine hypnotics had been prescribed for longer than recommended by the BNF (Joint Formulary Committee, 2010) and UK guidelines (Baldwin et al., 2013) without review. Prescribers further described situations in which service users became dependent on benzodiazepines and opioids due to prolonged use and lack of medication review. This thesis suggests that one possible explanation for overly long duration of treatment besides benefits reported by service users is lack of medication review.

Lack of medication review may be a particular problem among people with SUDs because they are often challenging to manage (Deehan et al., 1997; McKeown, Matheson and Bond, 2003) with multiple health problems, polypharmacy and high rates of non-attendance of appointments (Milward, Lynskey and Strang, 2014; Mitchell and Selmes, 2007b). The database study showed that over one-quarter of service users were taking four or more prescribed medications. GPs have often described these patients as time-consuming (Deehan et al., 1997; McKeown, Matheson and Bond, 2003) as the presence of

comorbidities, polypharmacy (Duerden, Avery and Payne, 2013) and service users' complex circumstances (Lloyd, 1998) increases clinical workload.

There is limited time available in general practice to deal with this often complex group of people. General practice consultations often do not last longer than 10 minutes (Bashir, King and Ashworth, 1994), and it is not possible to address all of service users' problems within this short time frame. Evidence from the interviews with service users further suggests that they were sometimes not listened to with one service user describing the very short time interval in which he was prescribed an antidepressant. These service users were consequently dissatisfied with treatment decisions. In addition to the complex situations of service users described above, GPs may not listen to service users due to suspicions concerning requests for prescribed drugs, and/or wider stigmatisation of people with SUDs (Matheson et al., 2003; McKeown, Matheson and Bond, 2003). Healthcare professionals fear being manipulated and dislike dealing with service users who they may not trust (Action on Addiction, 2013). Ironically, the need for regular review and effective communication ought to be greater in this population due to the higher potential for dangerous drug interactions, dependence and fatalities resulting from overdose (Prince, 2001) and also because they may sometimes need to be prescribed outside guideline recommendations. Strategies that could ensure adequate monitoring and review of service users in practice are highlighted in section 8.4.3.

### **Adherence**

The medication appropriateness study, service users' interviews and prescribers' interviews all addressed the issue of medication adherence. The medication appropriateness study found that most service users reported taking their medications regularly while prescriber interviews suggested that non-adherence is a significant problem among people with SUDs. Interviews with service users showed that those who perceived benefit from their medications were more likely to take them regularly. The Perceptions and Practicalities Approach (Horne et al., 2005) that has been used in describing factors contributing to non-adherence in mental health populations suggests that non-adherence may be due to perceptual factors such as patients' beliefs about their illness and treatment as well as practical factors that include patients' capability and resources. Two key beliefs have been identified within this approach: beliefs about the need for medicines and concerns about the adverse effects of medicines (Chapman and Horne, 2013).

Evidence from previous studies have shown that patients' beliefs such as their perceived benefit from medications is a major reason for adherence (Byrne et al., 2006; Janz and Becker, 1984; Loffler et al., 2003). Loffler et al. (2003) found perceived benefit to be the main reason reported by patients with schizophrenia for adherence to neuroleptics. When compared to those without SUDs, previous studies (Owen et al., 1996; Sajatovic et al., 2006; Weiss, 2004) among people with mental disorders have found higher levels of non-adherence among those with SUDs. SUDs represent a significant risk factor for non-adherence among people with mental disorders (Jonsdottir et al., 2013; Montes et al., 2013) probably due to intoxication (Owen et al., 1996) and the negative effect of substances on cognitive function including memory, attention and learning (Berry et al., 1993; Horner, 1997; Royal College of Psychiatrists, 2014a; Schilt et al., 2008; Sullivan and Pfefferbaum, 2005). The findings of this thesis suggest that lack of benefit from psychiatric medications may be an additional reason for the high levels of non-adherence reported among people with SUDs.

The differences obtained between the results of the medication appropriateness study and those of the prescriber interviews may have resulted because majority of the service users in this study perceived their medications to be beneficial. Most service users appeared to have consciously made decisions about adherence according to their beliefs about the efficacy of their medications. Their indication of interest to participate in a research study may also imply that they have a high level of innate motivation when compared to other service users and this may have been reflected in their high levels of adherence.

The high levels of adherence reported in the medication appropriateness study may also reflect overestimation of adherence by service users or problems with recalling information (Chesney, 2000; Schechter and Walker, 2002). Patients may report a high level of adherence to avoid embarrassment or being judged (Schechter and Walker, 2002; Tiv et al., 2012). However, the possibility of this was mitigated in this study as service users were informed that information about their adherence will not be disclosed to healthcare professionals. Adherence was assessed on a separate questionnaire that was not attached to the A-MAI that was rated by prescribers. Despite this limitation, results from this thesis indicate that there is a need for prescribers to enquire about the effects of medications from service users. Addressing instances where medications are reported to be ineffective or suboptimally effective may be helpful in promoting adherence, with the potential for realising full benefit from medications and avoiding waste (Chapman and Horne, 2013).

Previous research suggests that addressing such concerns may assist in supporting adherence (Clatworthy et al., 2009; Nunes et al., 2009).

### **Medication omissions**

Medication omissions were explored in the medication appropriateness study and interviews with prescribers. Both studies showed that omissions were generally uncommon in service users' medications though omission of thiamine and other B vitamins may sometimes occur. This finding is corroborated in the literature.

Ferguson, Soryal and Pentland (2000) found that slightly over half of known alcoholics and only one-quarter of heavy drinkers received thiamine as in-patients. Omission of thiamine among people with AUDs may lead to severe consequences such as the development of Wernicke-Korsakoff syndrome (Cook and Thomson, 1997; Thomson, Guerrini and Marshall, 2009). The occasional omission of medications such as thiamine and other B vitamins implies that there may still be need to sensitize GPs and other prescribers about the importance of prescribing these medications to those with AUDs.

### **Collaboration among stakeholders**

The findings of the prescriber interviews suggest that SAS doctors were a valuable source of support for nurse prescribers when dealing with prescribing issues. Consultant psychiatrists were likewise an important support for other doctors. SAS prescribers also supported GPs in prescribing-related issues.

Nurse prescribers described a strong focus on medications within their scope of practice during assessment though they described communicating with SAS doctors when they had concerns about service users' medications. Apart from consultant psychiatrists, most of the other doctors also tended to address medications within their remit during assessment. This narrow focus was further described by both nurse prescribers and doctors when considering medication changes, as they described reluctance in changing medications outside their remit of practice. There was however evidence that where medications pose immediate risk, necessary action would be taken including stopping such medications and contacting service users' GPs. It appears SAS prescribers played a role in preventing medication-related harm.

While there are no legal restrictions on the clinical conditions that may be treated by nurse prescribers, clinical areas of practice are usually defined and agreed with employers (National Prescribing Centre, 2012; Nursing and Midwifery Council., 2006). In the case of those working in addiction medicine, their area of competence is around prescribing for drug and alcohol dependence (Public Health England, 2014c). Although it is recommended that nurse prescribers adhere to their areas of competence for safe practice (Public Health England, 2014c), it could be argued that this limited focus may well compromise service users' safety where their comorbidities and co-prescribed medications that are outside this area put them at risk.

Generally, the tendency for doctors who have a much broader training to focus on medications within their remit without taking a more holistic approach to management may result in suboptimal care. A strict focus by doctors only on their areas of practice has the potential to lead to fragmentation of patient care (Detsky et al., 2012). This may explain how some service users go on to accumulate unnecessary medications in clinical practice over time since no healthcare professional really takes responsibility for the review of all their medications. This is despite the particular challenge service users pose in terms of complexity and risk issues. Service users often have complex needs including severe comorbid mental (Delgadillo et al., 2012; Marsden et al., 2000; Strathdee et al., 2002; Virgo et al., 2001; Walsh and Copello, 2014; Weaver et al., 2003;) and physical health problems (Dickey et al., 2002). In order to meet these needs, Public Health England (2014c) has recommended that addiction specialist doctors such as consultant psychiatrists work alongside non-medical prescribers and other doctors in a multidisciplinary team.

The drug and alcohol treatment system has however undergone some changes in commissioning in recent years. This has involved a move from mainly NHS service provision to a more mixed economy of service providers (Public Health England, 2014c). These changes have led to a decrease in the number of doctors including consultant addiction psychiatrists in treatment systems (Public Health England, 2014c), with nurses taking on more prescribing roles. Consequently, there is a reduction in the capacity of these new treatment systems for specialist expertise and complex case management.

There is a real risk of reduction in the quality of prescribing and decision-making as a result of these changes as nurse prescribers and GPs may not have ready access to support and specialist knowledge when required. The potential for specialists to provide clinical

supervision that will assist nurse prescribers make clinically appropriate decisions is also greatly hampered. It appears future prescribing practice in alcohol and drug treatment systems will mostly involve nurse prescribers. There is therefore the need for the training of nurse prescribers so that they can be well-equipped to manage service users, including complex clients, adequately. Similarly, there is the need to further strengthen GPs to effectively manage service users.

Taken together, the studies in this thesis clearly show that there is room for improvement in medicines optimisation. Results from these studies suggest that the practice of monitoring and reviewing medications examined in this thesis may be inadequate. It appears GPs may still need to be sensitized on the need for thiamine and other B vitamins among people with SUDs. The focus of prescribers on medications within their area of practice without a more holistic approach to treatment may result in suboptimal care. Furthermore, the recent reduction in medical expertise, including consultant psychiatrists, in alcohol and drug treatment systems poses a challenge that may negatively impact on the management of service users. The findings of this thesis suggest that there may be need for further training of nurse prescribers and GPs so that they can provide optimal care to service users including those with complex needs.

### **8.1.5. Effect of A-MAI**

Prescribers at the SAS were asked their views on how the A-MAI impacted on their clinical practice in their interviews and the majority of them described it as having a positive impact on their practice. They described the A-MAI as prompting them to reflect on their prescribing, providing a structure for assessing prescribing appropriateness, highlighting important appropriateness domains and also prompting review of service users' medications. Nurse prescribers' views on the impact of the A-MAI were quite varied, with half of them reporting no impact. This may have resulted because of the way in which the A-MAI was used in this study. Medications assessed by nurse prescribers included those outside their scope of practice and they may thereby have found the A-MAI less useful since they have very limited expertise in prescribing medications for conditions outside their remit. For instance, in order to judge whether a medication is appropriate for an indication, there is the need to know what medications might be prescribed and what might be appropriate in a particular situation. There would also be need to make a decision concerning whether service users have those indications. For the A-MAI to be perceived as beneficial, there may be a need for medical and therapeutic knowledge.

Furthermore, the time taken to complete the A-MAI varied among different prescribers. The time reported differed depending on the complexity of service users' medication regimen and the information available for assessing appropriateness. Where service users are on multiple medications, there is the potential for the use of the A-MAI to increase clinicians' workload. This may prohibit its wide usage in clinical practice. Strategies that may encourage a wide uptake of the A-MAI in clinical practice are discussed in section 8.4.3.

The cost dimension on the A-MAI was problematic for prescribers because most of them do not know the cost of medications. The cost dimension on the A-MAI accordingly had the highest proportion of 'don't know' recorded by prescribers. Inadequate knowledge of cost may have implications for the NHS as doctors may prescribe expensive medications when there are cheaper alternatives that are equally effective. There may well be need for prescribers to be supported in making cost-effective prescribing decisions.

## **8.2. Comment on thesis methodology**

The researcher utilised both quantitative and qualitative methods in this thesis. The quantitative methods include a scoping review, secondary data analysis and survey that follow a postpositivist philosophical approach. Postpositivism has been previously considered in section 3.4.1.1. Briefly, it aims to address some of the weaknesses of positivism (Guba, 1990). Unlike positivism, it acknowledges that imperfect observations and errors are possible (Creswell, 2009). A postpositivist perspective resonates both in these quantitative methods and the interpretation of findings.

A postpositivist stance was evident in the scoping review as this review allowed for the questioning of methods and assessment of the quality of included studies. The secondary data analysis and survey were also influenced by postpositivism because they involved the use of quantification to assess relationships (Guba and Lincoln, 1994). The secondary data analysis, in particular, allowed for a description of the different types of medications prescribed for service users attending this SAS. It specifically addressed four research questions. However, one of them relating to variables associated with psychiatric polypharmacy could not be addressed because of the large number of independent variables compared to the dependent variable (see section 4.3.4.6). Despite this limitation, this study provided valuable information on the medications prescribed for service users

and informed aspects of the questionnaire survey as the medications assessed in the survey were selected from it.

The questionnaire survey addressed some of the gaps identified in the scoping review. It involved the use of questionnaires by SAS prescribers to assess the appropriateness of opioids and/or psychiatric medications prescribed for service users. The MOQ was used to assess for the presence of omissions of opioids and/or psychiatric medications at service users' first SAS appointment while the A-MAI was used to assess multiple dimensions of appropriateness of prescribed opioids and/or psychiatric medications during service users' first SAS visit and three-month follow-up appointment. The MOQ and A-MAI questionnaires were designed to collect both quantitative and qualitative data. The qualitative data allowed for an understanding of the reasons particular ratings were made on the questionnaires by prescribers. Although postpositivism is often associated with quantitative inquiry, it has been argued that it also sees research as broad and complex, and allows for the use of qualitative methods in addition to quantitative ones (Clark, 1998; Guba and Lincoln, 1994; Racher and Robinson, 2003).

Despite the advantages of the survey design in allowing quantification of the level of inappropriate prescribing in this thesis, it only partially addressed the research questions. This is due to the reasons already described in section 5.9.11. Briefly, the reasons include absence of medication omissions and use of 'don't know' ratings by prescribers. The former meant that medication omissions could not be explored further while the latter prevented the summation of A-MAI scores for service users. This prevented assessment of change in appropriateness between baseline and three-month follow-up appointment as well as the factors associated with this. If this had been possible, this study could have assessed whether prescribing appropriateness improved or declined using the summated score. Factors predicting prescribing appropriateness could not be adequately explored in the logistic regression analysis due to small numbers.

Qualitative methods used include semi-structured interviews with service users and prescribers following the underlying principle of phenomenology. Phenomenology has already been described in section 3.4.1.2. It aims to explore complexity of views thereby highlighting similarities and differences rather than condensing them into a small number of categories as in quantitative inquiry (Creswell, 2009). The questionnaire survey informed aspects of the service user interviews as those interviewed were service users

found to be on prescribed opioids, psychiatric medications or both in the survey. The interviews with service users explored their perceptions concerning the appropriateness of their prescribed medications while prescriber interviews explored how they responded to inappropriate prescribing. The purpose was to engage indirectly through participants' experiences with their views on appropriateness. For instance, while some service users described benefit from their medications, others did not. A phenomenological approach therefore enabled these different views to be represented. Limitations of the interviews have been described in section 7.3.8.

Qualitative and quantitative methods were combined in this thesis. Although both methods are usually seen as opposites, some authors (Casebeer and Verhoef, 1997; Popay and Williams, 1998) have counselled that they are not. For instance, Popay and Williams (1998) suggest that the concept of measurement is not absent in qualitative inquiry as is often assumed. Qualitative research in fact does include measurement and quantification through the use of words such as 'many', 'most' and 'all' and themes are sometimes described as more or less prominent. These measurement approaches were used in the semi-structured interviews carried out in this thesis.

Furthermore, the result of the questionnaire survey showed that there is sometimes variability of views among prescribers concerning the appropriateness of prescribing decisions. Potential reasons for variable views are discussed in section 5.9.10. One reason highlighted is that assessment of appropriateness may be affected by prescribers' judgments on the risk posed by medications. It has been argued that risk cannot be measured as an absolute value (Slomka et al., 2008). It is socially constructed and subject to value judgments and power relationships (Slovic, 1999). These pieces of evidence suggest that information obtained from research is not always exclusively qualitative or quantitative in nature.

Similarities that have been acknowledged between qualitative and quantitative research include the need to formulate a research aim and develop research objectives, clarity of questions, justifying a sampling strategy and a detailed analysis plan as well as a commitment of both types of studies to understanding of the world, commitment to rigour and critique in the research process (Casebeer and Verhoef, 1997; Reichardt and Rallis, 1994). The use of both qualitative and quantitative methods allowed for the utilisation of the strength of each method (Creswell et al., 2011), leading to a greater insight than could

have been provided by one method. For instance, while the questionnaire survey found that almost half of service users were prescribed one or more inappropriate medications, the interviews with service users showed that most of them reported benefits from their medications, including those prescribed outside guideline recommendations. There were therefore varied views about appropriateness.

The use of both qualitative and quantitative inquiry was facilitated by pragmatism, a worldview that is pluralistic in nature (Creswell, 2009; Creswell and Plano Clark, 2011) and employs “what works” (Creswell et al., 2011; Morgan, 2007). Pragmatism is typically associated with mixed methods research (Feilzer, 2010; Morgan, 2007; Tashakkori and Teddlie, 2003). The researcher used a mixed methods design to address different aspects pertaining to the appropriateness of prescribing for service users in a SAS and to gain a more complete understanding by combining methods as well as showing areas for future research.

### **8.3. Strengths and limitations of this research**

Due to the multiple methods employed in this thesis, there was an increased awareness of the factors that may influence the validity of its findings. Qualitative and quantitative methods generate different types of knowledge (Whittemore et al., 2001). Furthermore, quantitative methods such as surveys may be limited by the type of questions asked or the perception of study participants whereas knowledge generated from qualitative methods such as interviews may depend on the researcher’s judgments and interpretation. A critique of the studies in this thesis has been carried out in sections 4.5, 5.9.11 and 7.3.8. This section therefore provides a brief overview of the strengths and weaknesses of these studies and of this thesis as a whole.

The use of a combination of qualitative and quantitative methods is a key strength of this thesis as they provided both breadth and depth of understanding. Quantitative methods were employed as a starting point, firstly with analysis of SAS routine clinical data to provide an overview of the different classes of medications taken by service users during their first episode of treatment at the SAS. There were however quality issues relating to inaccurate data and the self-report method used by service users. It is therefore a possibility that this study underestimated the number of prescribed medications and consequently polypharmacy. Despite its limitations, this study was necessary because it represents the first attempt to examine all prescribed medications taken by people with SUDs. A particular strength of this study is that it included all relevant service users during the

period examined. It was therefore comprehensive in its description of service users' prescribed medications. Use of routinely collected data also represented a relatively fast and inexpensive method of research. The strengths and weaknesses of this study have been considered in detail in section 4.5.

The analysis of routine clinical data was followed by a scoping review that ascertained the appropriateness of opioids for relief of chronic pain and psychiatric medications prescribed for people with SUDs. Limitations of the studies included in this review have been presented in chapter 2 (section 2.7). Briefly, screening and extraction of data from included studies were carried out by a single researcher with the implication that some potential studies might have been missed. The focus on only studies published in English may also have resulted in potential studies being missed. Furthermore, none of the studies was carried out in a substance misuse setting. The studies in this review were of mixed quality with over half of them assessing guideline adherence. However, use of guidelines may be restrictive because they usually focus on particular health conditions or medications (Hughes, 2011) while ignoring patients' comorbidities, co-prescribed medications, life circumstances and their choices (Tinetti, Bogardus and Agostini, 2004). This review highlighted the need for studies assessing multiple areas of appropriateness of opioids and psychiatric medications among people with SUDs in a substance misuse setting. This scoping review represented the first review in this under-researched area and highlighted areas for future research.

Following the findings of the scoping review, a survey was carried out that involved the use of questionnaires by SAS prescribers to assess appropriateness: the MOQ was used to assess for omissions of opioids and/or psychiatric medications while the A-MAI was used to assess multiple dimensions of appropriateness of opioids and/or psychiatric medications for service users in a SAS. The study limitations have been previously described in section 5.9.11. The limitations include the fact that diagnosis and associated medication management were based on service users' self-report. In addition, the questionnaires used in assessing adherence and omissions have not been previously validated as they were developed for the purpose of this study. Although face validity was assessed during the pilot stage, there is a need for more extensive testing of the psychometric properties of these questionnaires. There is also a need for testing of the psychometric properties of the A-MAI as it was adapted from the original MAI for this study. Factors predicting prescribing appropriateness could not be adequately explored in the logistic regression

analysis due to small numbers. Lack of medication omissions also meant that this area could not be explored further using statistical analysis.

Despite these limitations, the use of the adapted-MAI was a strength of this study as it allowed for clinical judgment when assessing prescribing appropriateness. Judgments on the appropriateness of service users' medications were also service user-focused and incorporated their preferences or subjective views when compared to previous studies. Service users who could not speak English or who were too intoxicated to be assessed by prescribers were excluded from this study. Service users assessed by non-prescribers were also excluded. The findings of this study are therefore not generalizable to the groups of excluded service users. In defence of these limitations, this small scale study was necessary due to lack of prior research assessing all the dimensions covered in this study. This is also the first study to assess the appropriateness of medications in a substance misuse setting. Detailed information on the strengths and limitations of this study are presented in section 5.9.11.

The qualitative study carried out with service users assisted in exploring their perspectives on the appropriateness of their prescribed medications. Prescribers' interviews explored how they responded to inappropriate prescribing. The limitations of these qualitative interview studies have been considered in detail in section 7.3.8 and include the recruitment of participants from a single site and data collection by a single researcher. In particular, service users of white background were over-represented in the interviews with service users. This is a reflection of the population of people attending the SAS where this research was carried out. Over 90% of those in the A-MAI study were of white ethnicity (see section 5.9.3). In addition, a number of service users did not take part in the interview based on the pre-specified exclusion criteria. The views and experiences of groups excluded are therefore under-represented in the service user interviews. Prescribers' responses in the interviews might have been biased due to participation in the medication appropriateness study before they were interviewed. There is also the possibility that they provided socially desirable responses. A reflexive account that considered the possible influences of the researcher on the research process is presented in section 3.5.

In relation to this thesis as a whole, a key limitation is that all the studies were carried out in a single SAS in England (as described in section 3.2). The use of a single SAS implies that the findings may lack generalizability to other addiction services especially with the

recent changes in UK drug and alcohol treatment systems. Medical expertise in UK drug and alcohol treatment systems is being decimated, with a proliferation of nurse prescribing. Furthermore, the SAS where this research was carried out no longer exists in its original form and specialist NHS addiction clinics are now a rarity. Further research involving the new drug and alcohol service providers is warranted to establish if these findings are applicable. The main strength associated with using a single site for the studies in this thesis is the opportunity to build a picture of the appropriateness of prescribing in this setting. The use of a single site further allowed the results of the initial studies to inform subsequent studies. For instance, the findings of the study analysing routine clinical data informed the selection of medications assessed in the medication appropriateness study.

#### **8.4. Implications for practice**

In the UK, the quality of healthcare has been identified as a priority by the UK Government (Department of Health, 2013a). The knowledge generated from this thesis may assist clinicians in the NHS in assessing the quality and safety of prescribing for people with SUDs especially those with comorbid mental disorders and chronic pain, and make improvements where necessary. Indeed, this thesis explored the quality of prescribing for people with SUDs as it sought to assess the appropriateness of their medications while also exploring prescribers' responses to inappropriate prescribing decisions. The suggestions offered here are tentative as the findings of this thesis may not be applicable in other addiction services.

Evidence from the studies in this thesis suggests that the appropriateness of prescribing is a complex concept which cannot be viewed solely from the narrow pharmacological model represented in guidelines. There is a need for consideration of the physical, psychological and social functioning of service users and their preferences when judging the appropriateness of prescribing decisions. This research suggests that a holistic view of appropriateness may result in it being a value judgment which may sometimes vary depending on who is assessing appropriateness. What is appropriate is sometimes a matter of debate among clinicians, and between clinicians and service users (MacDonald and Murray, 2007). A holistic assessment of appropriateness therefore entails trying to achieve a balance between pharmacological appropriateness, service users' choices or preferences, and the risks and benefits of prescribing. The correct balance will depend on the context of prescribing.

For optimal assessment of prescribing appropriateness, there is the need for collaborative work between service users and healthcare professionals. This would often require negotiation between clinicians and service users. Consequently, clinicians need to be both knowledgeable and skilful when dealing with this client group. There is also the particular need for clinicians to be vigilant when prescribing for service users. Sections 8.4.1 addresses knowledge and skill requirements of clinicians while section 8.4.2 deals with how vigilance can be effectively implemented. Sections 8.4.3 and 8.4.4 further describe the implications of this research for primary care and addiction services, respectively, while section 8.4.5 considers the utility of non-pharmacological therapies among service users.

### **8.4.1. Knowledge and skills**

In dealing with service users with comorbid SUDs and mental disorders or chronic pain, all prescribers, irrespective of the setting in which they work, need adequate knowledge of the pathophysiology of these disorders as well as the pharmacology of medications for their management. Knowledge of pharmacology is essential in order to determine whether the medication is the right one to be prescribed and how it should be prescribed for optimal benefit. This is particularly apposite given the evidence that service users may need to be prescribed outside guideline recommendations.

Furthermore, there is a need to build therapeutic relationships with service users as treatment plans are only likely to be successful if service users have a positive relationship with the clinician and are willing to cooperate with them (Dordevic and Jankovic, 2006). Effective communication skills are essential in building this relationship. There was evidence in the service user interviews of ineffective communication and consequent dissatisfaction with prescribing decisions. Skills in communication entail listening skills, showing empathy and concern (Action on Addiction, 2013) and discussion of treatment benefits and risks. Listening skills are important in ensuring that the clinician understands the service user (Cushing and Metcalfe, 2007). Furthermore, asking for service users' views and helping them think through the problem is likely to be effective in addressing prescribing problems. There is also a need to discuss the benefits and risks of treatment with service users especially as there is often need for a trade-off between them. The treatment goals should be discussed and agreed at the onset of therapy. For instance, in the management of chronic pain among service users, it is helpful for them to understand that complete absence of pain may be an unrealistic goal (Prince, 2001). A decrease in pain with improved functioning may be more feasible. Effective communication could also

assist in addressing service users' perceived barriers to medication change. There may well be need for follow-up appointments to come to a mutual decision and to review those that have been made (Cushing and Metcalfe, 2007).

#### **8.4.2. Vigilance**

This section describes how clinicians could be effective in monitoring service users' prescribed medications. The implications highlighted here are relevant to primary care, addiction services and mental health services.

As discussed in sections *1.5.1* and *1.5.2*, chronic pain and mental disorders commonly co-exist with SUDs and their presence will be the norm among this population. Additional measures that may be needed when prescribing medications with dependence potential among those used in the management of these disorders (for example, opioids and benzodiazepines) include limiting the quantities dispensed to service users at a time (Passik, 2009), pill count, urine drug testing to detect illicit substances, assessing whether medications are being taken (Fishbain et al., 2008) as well as the use of medication contracts (Chelminski et al., 2005). Medication contracts may be helpful in service users who are about initiating these medications to reach an agreement on the conditions under which they would be discontinued (Chelminski et al., 2005). These support measures may be useful in ensuring that prescribing of these medications is adequately structured and safe (Action on Addiction, 2013).

Access to specialist consultations when dealing with service users, especially complex people, could greatly improve decision-making concerning therapy. Clinicians prescribing opioids for chronic pain need a basic competence in identifying and managing SUDs and access to addiction clinic consultation. Likewise, those prescribing psychiatric medications need a basic knowledge of addiction medicine and access to addiction specialists when needed. Addiction clinicians need to be knowledgeable about chronic pain management and mental health problems and also have access to pain clinic and mental health consultations.

Where different service providers are involved in the care of service users, there is a need for them to collaborate as they deliver services or coordinate their care with one another. It may be possible to have one person such as the GP as the care co-ordinator or one provider as the primary provider. This provider could assist in managing care among other providers. Good communication among these different providers would be essential to reducing the potential for multiple prescribing, drug interactions and conflicting treatment plans (Action on Addiction, 2013). The trend for service users to move around different prescribers expressing choice may be counterproductive in the context of addictions.

There is a need for effective communication and linkage of electronic patients' records among all providers involved in caring for service users for safety reasons, especially as the quality of information obtained from service users may be poor. Good communication is required because active dependence compromises service users' self-report (Bailey, Hurley and Gold, 2010). Other sources of information such as medical records and interviews with family may be needed for corroboration (Action on Addiction, 2013).

In addition, information should be shared among the different service providers on service users' progress, barriers to progress, treatment aims and management (Marsh, Dale and Willis, 2007). This information should be readily available to clinicians involved in the care of service users so that discrepancies and inconsistencies can be easily verified. This could be facilitated through telephone discussions concerning the care of service users, joint videoconferencing involving the service user and the service providers, and use of electronic or paper letters. Providers of IT services to these service providers may need to be instructed on the agreed structure of the communication method to ensure ready access to information. There may well be need for the structure to be agreed upon nationally to facilitate interoperability and ready transfer of information (Royal Pharmaceutical Society, 2012).

### **8.4.3. Implications for primary care**

This section focuses on the implications of this research for primary care. It is divided into two areas: strategies for addressing inappropriate GP prescribing and strategies for addressing inappropriate prescribing among service users.

#### **8.4.3.1. Strategies for addressing inappropriate GP prescribing**

The following strategies for addressing inappropriate GP prescribing are considered in this section: medication review, training, audit and feedback and the use of technology.

## Medication review

The medication appropriateness study and service user interviews suggested that review of medications including repeat prescriptions of psychiatric medications and opioids is sometimes a problem in primary care settings. Effective monitoring of repeat prescribing and dispensing for people with SUDs by general practice and pharmacy staff, respectively, is essential because they may be at increased risk from the adverse effects of medications. Monitoring could be through regular audit of repeat prescribing and dispensing systems (Duerden et al., 2011), to flag up when reviews are needed and identify prescriptions that are no longer necessary. Audits of repeat prescribing systems are necessary with the introduction of the Electronic Prescription Service (Duerden, Avery and Payne, 2013) which allows for electronic transfer of prescriptions between general practices and community pharmacies across England. Without appropriate monitoring, this system may compound the problem of inappropriate prescribing and wastage in the NHS as there may be continued prescribing of medications that are no longer needed.

Furthermore, when complex patients such as those on multiple medications visit their GPs, the consultation may focus on limited conditions with insufficient time for medication review (Blenkinsopp, Bond and Raynor, 2012). Alternative options that may assist in improving medication review include the involvement of other healthcare professionals in medication review. In the UK, healthcare professionals such as practice-based pharmacists and practice-based nurses may carry out medication reviews, and such reviews do not always have to be face-to-face with service users as it could be done through review of service users' records or through the telephone (British Medical Association and the NHS Confederation, 2003). These healthcare professionals may be designated to take up the responsibility of carrying out regular reviews of service users' medications. For instance, regular review of records by nurses or pharmacists could assist in flagging up medications such as benzodiazepines that have exceeded the time specified in guidelines. This can be communicated to the GP for further action.

At present, the General Medical Services (GMS) contractual requirements (British Medical Association and the NHS Confederation, 2003) include a clinical medication review which should be undertaken every 15 months for all patients prescribed repeat medications. Clinical Medication Review (also called type 3 review) involves a face-to-face review of medications and condition with the patient (Clyne, Blenkinsopp and Seal, 2008). In people with SUDs co-existing with chronic pain or mental disorders, medication review may need

to be carried out during routine follow-up appointments in order to ensure medications are still appropriate, assess drug interactions and also prevent the development of dependence on medications. The other healthcare professionals suggested here could take up this role for optimal management of service users.

Assessment tools such as the MAI may have a place in medication review. Duerden, Avery and Payne (2013) have suggested that tools for medication review should be developed. The present study explored prescribers' perspectives on the impact of an adapted version of the MAI on their prescribing practice and the majority of prescribers described it as having a positive impact. There was however an awareness of the potential for the A-MAI to increase clinical workload where a service user's medication regimen is complex. Where service users are on few prescribed medications, the A-MAI could be used in its present form for medication review. However, for the A-MAI questionnaire to be widely used in clinical practice, there may well be a need to reduce the number of items on it. Such a modified questionnaire may assist in standardising the process of medication review while also ensuring that important areas concerning medication appropriateness are covered. It may also be useful as a prompt to the need for a review of repeat prescriptions or as a checklist for GPs to consider before prescribing medications.

Evidence from this thesis suggested that SAS prescribers reviewed the medications of service users when they attend the service. SAS prescribers contacted GPs if there were serious problems with service users' medications. SAS prescribers were therefore a sort of "safety net" against potential medication-related risks. Support from specialist addiction services has been recognised by GPs to be crucial in providing better care for service users especially those who are considered to be complex (McKeown, Matheson and Bond, 2003). With the ongoing changes in commissioning in UK drug and alcohol treatment services, specialist addiction services with experienced senior prescribers are increasingly rare. There is now a dearth of services that can provide this "safety net" function.

#### Training needs of GPs

There is a need for further training of GPs to adequately manage people with SUDs. GPs have sometimes reported lack of adequate knowledge and skill in the management of people with SUDs (McKeown, Matheson and Bond, 2003), who often have complex comorbidities such as mental disorders and chronic pain. It appears there is a need for continuing professional development in the management of service users' mental health

problems and chronic pain. This may include improving prescribing knowledge, reflection on practice and identifying service users' needs in these areas. GPs who usually have the primary responsibility of ensuring care continuity (Freeman and Hughes, 2010) as well as initiation of prescribing decisions in the community, should be competent in mental health, pain and addiction medicine.

Barriers to safe and effective management, such as stigma, also need to be addressed among clinicians. This could be achieved by providing training to address negative assumptions and beliefs about addiction (Action on Addiction, 2013). This training could be provided by addiction specialist doctors such as consultant psychiatrists, GPs with expertise in managing SUDs or pharmacists with expertise in these areas. Additional skills needed by all prescribers (including GPs) working with service users have been highlighted in section 8.4.1.

#### Audit and feedback

GP prescribing of medications used in the management of comorbid mental disorders and chronic pain could be audited periodically with detailed feedback provided to them. Feedback will need to include specific recommendations for changes in prescribing (Lexchin, 1998). Practice-based pharmacists could carry out such audits and provide feedback. A study found that personalised feedback letters and targeted educational bulletins were effective in improving antibiotic prescribing behaviour in primary care (Hux, Melady and DeBoer, 1999). A review of the effectiveness of educational interventions in improving prescribing in primary care concluded that the more personalised the intervention, the more effective it is (Figueiras, Sastre and Gestal-Otero, 2001). Consequently, personalised feedback letters may be effective in changing prescribing behaviour of GPs.

For audit and feedback to be successful in changing prescribing behaviour, the prescriber should recognise that there is a need for improvement on current practice. This recognition could be facilitated by having periodic discussions among groups of prescribers (peer group) (von Ferber et al., 1992), to review the audit results and discuss means of improving performance. Some studies have reported improvements in physician prescribing behaviour due to participation in such groups (Reilly and Patten, 1978; von Ferber, 1993).

#### Use of technology to aid decision-making

The safety and quality of prescribing can be improved through electronic prescribing (Creswell et al., 2013). Electronic prescribing is usually part of an electronic health record system or could be a stand-alone system (Sweidan et al., 2010). Electronic prescribing involves

The utilisation of electronic systems to facilitate and enhance the communication of a prescription or medicine order, aiding the choice, administration and supply of a medicine through knowledge and decision support and providing a robust audit trail for the entire medicines use process (NHS Connecting for Health, 2007, p.18).

Electronic prescribing can assist in preventing inappropriate prescribing by reducing the risk of prescribing contra-indicated medications, preventing duplication, reducing inappropriate dosing, promoting adherence to best practice recommendations and cost-effective prescribing (Black et al., 2011; Kaushal, Shojania and Bates, 2003). Evidence from this thesis shows that prescribers do not have adequate knowledge of the cost of medications. Electronic prescribing systems provide a means to ensure that cost-effective medications are prescribed when considering two or more medications of equal efficacy. In addition, it was reported that there may sometimes be omission of thiamine and other B vitamins by GPs. Electronic prescribing systems may be programmed to remind clinicians about the need to prescribe these medications for service users with AUDs. Due to the fact that inappropriate prescribing is a complex, multidimensional problem (Lexchin, 1998), changing prescribing behaviour will likely need to involve a combination of the strategies highlighted above.

#### **8.4.3.2. Strategies for addressing inappropriate prescribing among service users.**

Regular medication reviews mentioned above may lead to the identification of inappropriate medications. This section therefore considers how to work effectively with service users in order to facilitate change of such medications. Furthermore, the findings of this research suggest that service users may be resistant to medication changes. Evidence-based interventions that have been found to be effective in reducing or discontinuing chronic use of medications may be used. Such evidence-based interventions that have been effective in reducing chronic use of benzodiazepines among patients include brief advice by GPs supplemented by self-help books (Bashir, King and Ashworth, 1994), letters from GPs (Cormack et al., 1994; Heather et al., 2004) and clinical pharmacist's recommendations (Hanlon et al., 1996).

Cormack et al. (1994) found that both a letter from a GP to patients advising benzodiazepine reduction and a letter supplemented by information sheets significantly reduced benzodiazepine intake compared to a control group among long-term benzodiazepine users in south-west England. Bashir, King and Ashworth (1994) assessed the effect of a short GP consultation supplemented by self-help books among long-term benzodiazepine users and reported similar findings. Heather et al. (2004) found that both a GP letter to patients advising reduction of benzodiazepine use and a short consultation with the patient's GP or practice nurse or pharmacist reduced benzodiazepine consumption. All three studies excluded people with SUDs. They found no evidence of deterioration in mental or general health as a result of these interventions. Hanlon et al. (1996) further reported that recommendations by a clinical pharmacist to elderly patients and their doctors in an outpatient setting reduced inappropriate prescribing. These interventions may well be useful in reducing or stopping inappropriate medications among service users.

#### **8.4.4. Implications for addiction services**

Evidence from the interviews with prescribers suggest that besides the more experienced doctors such as consultant psychiatrists, the other doctors and the nurse prescribers tended to focus on medications within their remit when reviewing service users' medications. Nurse prescribers further described the valuable support they obtained from SAS doctors when dealing with problems around prescribing while the more junior doctors (that is, non-consultants) relied on the support of their consultants for prescribing issues they could not address. Recent changes have however led to a reduction in the medical expertise (including consultant psychiatrists) of drug and alcohol treatment systems (Public Health England, 2014c), with a potential risk of reduction in the quality of prescribing and decision-making. With the decline in medical expertise, it appears the onus for prescribing and management of service users, including complex clients, will now primarily rest with nurse prescribers. This raises serious concerns about the future review practices of psychiatric medications in addiction services if nurse prescribers are not further strengthened to work with service users, including complex clients.

There is the need to equip nurse prescribers to work with service users, especially complex cases. There is a further need for training in diagnostic and therapeutic skills to enable nurse prescribers manage complex service users especially those with comorbid mental disorders and chronic pain. Practice should include regular supervision of nurse prescribers

by an experienced doctor or nurse prescriber to ensure that they are making optimal clinical decisions. The differences between nurse prescribers and doctors in this study in how they utilised the history they obtained when assessing prescribing appropriateness imply that another area for further training may be in carrying out clinical assessments including history-taking. Other skills required for optimal management of service users are described in section 8.4.1.

#### **8.4.5. Consideration of non-pharmacological therapies**

The choice of therapy for the management of comorbid SUDs and mental disorders or chronic pain may be medications or non-pharmacological therapies or a combination of both. Medications are often very accessible but they may not be the optimal solution. There is the need for consideration of the use of non-pharmacological treatment options for the management of mental disorders and chronic pain in people with SUDs. Psychotherapies such as CBT, MI and 12-step approaches may be particularly helpful in the management of less severe forms of depressive and anxiety disorders especially as there is limited evidence to support the use of medications in these situations (Fournier et al., 2010; Kirsch et al., 2008).

Similarly, management of chronic pain and its psychological complications could benefit from these psychotherapies as well as behavioural therapies targeted at enhancing self-efficacy, cognitive and behavioural change (Roditi and Robinson, 2011). These alternative options should be considered because evidence of the long-term effectiveness of opioids in chronic pain is weak (Noble et al., 2010; Passik, 2009) and there is the risk of opioid dependence with long-term use (Deyo and Weinstein, 2001). These psychotherapies and behavioural therapies may also be combined with pharmacological treatments for effective management of comorbid chronic pain (Passik, 2009) and mental disorders (Kelly, Daley and Douaihy, 2012; Moak et al., 2003).

### **8.5. Recommendations for future research**

In this thesis, the focus has been on assessing the appropriateness of prescribing of opioids and psychiatric medications for people with SUDs while also exploring addiction service prescribers' response to inappropriate prescribing decisions. A key focus for future studies is the need to assess the appropriateness of prescribing for people with SUDs from the original prescriber's perspective. There is a need to focus on prescribing by general

practitioners since they usually initiate or continue the prescribing of most medications (Freeman and Hughes, 2010). Quantitative studies are needed to assess the scale of prescribing for service users in primary care settings as well as the appropriateness of prescribed medications. Such studies should shed light on the different types of medications service users are being prescribed and the proportion of people on them. The appropriateness of prescribed medications could be assessed using the medication appropriateness index or a variant of it.

Qualitative interviews proved to be particularly useful in this thesis and could be carried out in future research to explore GPs' views on the appropriateness of prescribing within their practice around SUDs and comorbidities. This study could further entail exploring how GPs manage service users with complex needs, including referral to other services, their practice around review of medications and their training/support needs. Such a qualitative study should also elicit the views of service users, given the contested nature of 'appropriateness'. Some non-participant observation of GP and service user interactions might also be possible.

This research was carried out in a single SAS that no longer exists in its original form and some of the findings therefore may not be generalizable to present-day alcohol and drug treatment systems. Further research should involve multiple sites (including services run by NHS and third sector organisations), especially given the recent changes that have led to an increasingly mixed economy of service providers in addictions, to establish if the findings of this thesis are applicable. Given the reducing levels of medical expertise among SAS staff, an important area to explore will be the role and scope of nurse prescribers: including their views on the changing drug treatment landscape, management of service users (especially those with complex needs), the support available to nurse prescribers and their training needs. Service users offered NHS services may also be compared with those being managed by third sector organisations on the following outcomes: prescribing appropriateness, polypharmacy, adverse events such as overdose, patient satisfaction and recovery. The views of service users on the quality of care they receive should also be compared. Evidence obtained from these studies may well inform future practice and policy in this area.

Studies are also needed to assess the psychometric properties of the questionnaires used in this thesis such as the A-MAI, adherence questionnaire and medication omissions questionnaire. In addition, qualitative studies are needed to assess the usefulness of the A-

MAI to healthcare professionals as a checklist to consider before prescribing as well as an aid in the medication review process. Interviews could be undertaken with healthcare professionals working in addiction services and primary care to determine how the A-MAI could be further adapted for use in clinical practice in these settings. This interview may consider which A-MAI dimensions are more relevant for service users with SUDs. A-MAI dimensions that are considered to be relevant could be used to develop a more compact version of the A-MAI that would take less time to complete. This may be used routinely in clinical practice for the review of service users' medications in primary care and addiction services.

## **8.6. Conclusion**

This thesis addressed the following aims:

- To investigate the level and nature of appropriateness of current medications of service users in a SAS;
- To explore prescribers' responses to inappropriate prescribing in a SAS.

These aims were addressed through a mixed methods design involving a secondary analysis of routinely collected data, questionnaire surveys in the medication appropriateness study, and interviews with service users and SAS prescribers. This research demonstrated the presence of inappropriate prescribing of psychiatric medications and opioids among service users attending a SAS. Assessment of the appropriateness of prescribing appears to be a value judgment that may differ between prescribers, and also between service users and prescribers. This thesis found that the appropriateness of prescribing for people with SUDs is sometimes an area of conflict.

Appropriateness can be understood in terms of the reductive pharmacological model. However, the evidence base for this model does not often include people with SUDs. An alternative model is the outcome-focused way of prescribing. In this model, appropriate prescribing is conceptualised as that which produces good outcomes for service users irrespective of whether it is outside guideline endorsement. People with SUDs often have a myriad of problems and prescribing that is inappropriate by guideline standards could be considered to be appropriate in another sense if it assists them in maintaining their stability and prevents relapse to substance use. Optimal assessment of prescribing appropriateness should therefore involve a balance between pharmacological appropriateness, risks and

benefits of prescribing including service users' outcomes, service users' preferences and context.

Prescribers' responses further showed that responding to inappropriate prescribing is a complex process that involved considering the benefits and risks of medications, their expertise, the nature of addiction as well as communication with service users and prescribers. Nurse prescribers described relying on the expertise of SAS doctors when dealing with issues around prescribing. SAS prescribers were also a sort of "safety net" against medication-related risks as they intervened and contacted GPs if there are serious problems with service users' medications. Recent changes in the UK drug and alcohol field have led to diminishing medical expertise and an increasing reliance on non-medical prescribing. In addition, specialist NHS addiction clinics such as the Leeds Addiction Unit are now a rarity in the UK, with resultant lack of specialist addiction medicine support for GPs when needed. These changes pose a threat to the quality of decision-making around medications by non-medical prescribers and GPs. It appears there is a need to further empower non-medical prescribers and GPs to effectively manage service users with comorbidity. Further research is now required, especially with the changes that have taken place in UK drug and alcohol services, to establish if the findings of thesis are applicable.

# Appendices

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Appendix 4.5: Comparison of sociodemographic characteristics between service users with and without psychiatric polypharmacy

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Appendix 7.2: Topic guide for interviews with prescribers

## Appendix 2.1: Search strategy used in Medline (1946 to February Week 4 2012)

- 1 (alcoholi\$ or drinker\$ or drinking).tw.
- 2 exp alcohol-related disorders/ or exp amphetamine-related disorders/ or exp cocaine-related disorders/ or exp opioid-related disorders/
- 3 exp Substance-Related Disorders/  
((drug or alcohol\$ or narcotic\$ or heroin or opiate\$ or opioid\$ or opium or cocaine or crack cocaine or cannabis or marijuana or marihuana or hashish or phencyclidine or benzodiazepine\$ or barbiturate\$ or amphetamine\$ or MDMA or hallucinogen\$ or ketamine or lsd or inhalant\$ or substance\$) adj2 (abuse\$ or misuse\$ or use\$ or problem\$ or depend\$ or addict\$ or disorder\$)).ti,ab.
- 5 exp Street Drugs/
- 6 or/1-5
- 7 exp Polypharmacy/
- 8 polypharmacy.tw.
- 9 exp Medication Errors/
- 10 Medication Errors.tw.
- 11 exp Drug Interactions/
- 12 exp Guideline Adherence/
- 13 medication appropriateness index.tw.
- 14 beer\$ criteria.tw.
- 15 prescribing appropriateness index.tw.
- 16 ACOVE indicator\$.tw.
- 17 Assessing Care of Vulnerable Elderly indicator\$.tw.
- 18 START criteria.tw.
- 19 screening tool to alert to right treatment.tw.
- 20 STOPP criteria.tw.
- 21 screening tool of older persons prescription\$.tw.
- 22 (underprescrib\$ or overprescrib\$ or misprescrib\$ or overus\$ or underus\$ or misus\$).tw.
- 23 (inappropriate prescrib\$ or inappropriate prescription\$).tw.
- 24 exp Inappropriate Prescribing/
- 25 (dose\$ or dosage\$).tw.
- 26 Pharmacological Appropriateness Rating of Medicines.tw.
- 27 or/7-26
- 28 exp Prescriptions/
- 29 (Prescription\$ or prescrib\$).tw.
- 30 exp Drug Prescriptions/
- 31 (drug prescription\$ or drug prescrib\$ or medication prescrib\$ or medication prescription\$).tw.
- 32 pharmacotherap\$.tw.
- 33 or/28-32
- 34 27 and 33

35 (((selective serotonin reuptake inhibitors or serotonin) and noradrenaline reuptake inhibitors) or monoamine oxidase inhibitors or tricyclic drugs or agomelatine or amitriptyline or amoxapine or acetylcarnitine or alaproclate or amersergide or amineptine or amiflamine or bupropion or befloxatone or brofaromine or benactyzine or butriptyline or citalopram or caroxazone or cilosamine or chlorpoxiten or clorgyline or cimoxatone or clomipramine or clorimipramine or clovoxamine or desipramine or deanol or deprenyl or demexiptiline or dibenzipin or dothiepin or doxepin or diclofensine or duloxetine or dosulepin or escitalopram or etoperidone or fluoxetine or fluvoxamine or femoxetine or fluparoxan or fluotracen or flupentixol or imipramine or iproniazid or idazoxan or isocarboxazid or iprindole or lofepramine or mianserin or maprotiline or metapramine or mirtazapine or moclobemide or melitracen or minaprine or nortriptyline or nefazodone or nomifensine or nialamide or oxaflozan or paroxetine or phenelzine or pargyline or protriptylin or prosulpride or reboxetine or rolipram or setiptiline or seleginine or tianeptine or tetrindole or tranlycypromine or tomoxetine or trazodone or trimipramine or venlafaxine or viqualine).ti,ab.

36 Exp Antidepressive Agents/

37 35 or 36

38 6 and 34 and 37

39 Animals/

40 Humans/

41 39 not (39 and 40)

42 38 not 41

43 (benperidol or chlorpromazine or flupentixol or haloperidol or levomepromazine or pericyazine or perphenazine or pimozide or prochlorperazine or promazine or sulpiride or trifluoperazine or zuclopenthixol or amisulpride or aripiprazole or clozapine or olanzapine or paliperidone or quetiapine or risperidone or sertindole or zotepine or fluphenazine or pipotiazine or risperidone).ti,ab.

44 exp Antipsychotic Agents/

45 43 or 44

46 6 and 34 and 45

47 46 not 41

48 (nitrazepam or loprazolam or lormetazepam or temazepam or zaleplon or zolpidem or zopiclone or chloral hydrate or diazepam or alprazolam or chlordiazepoxide or lorazepam or oxazepam or buspirone or bromazepam or meprobamate or clonazepam).ti,ab.

49 (cyclopyrrolone\$ or z?drug\$ or benzodiazepine\$).ti,ab.

50 (anxiolytic\$ or hypnotic\$).ti,ab.

51 or/48-50

52 6 and 34 and 51

53 52 not 41

54 (buprenorphine or codeine or diamorphine or dihydrocodeine or dipipanone or fentanyl or hydromorphoneormeptazinol or methadone or morphine or oxycodone or papaveretum or pentazocine or pethidine or tramadol).ti,ab.

55 exp Analgesics, Opioid/

56 (opiate\$ or opioid\$).ti,ab.

57 or/54-56

58 6 and 34 and 57

59 58 not 41

60 (carbamazepine or eslicarbazepine or ethosuximide or gabapentin or lamotrigine or levetiracetam or oxcarbazepine or phenobarbitone or phenobarbital or primidone or phenytoin or pregabalin or rufinamide or topiramate or sodium valproate or vigabatrin or valproate or valproic acid or zonisamide).ti,ab.

61 exp Anticonvulsants/

62 60 or 61  
63 6 and 34 and 62  
64 63 not 41  
65 exp Lithium/  
66 6 and 34 and 65  
67 66 not 41

## Appendix 2.2: Search strategy used in PsycINFO (1946 to February Week 4 2012)

- 1 (alcoholi\$ or drinker\$ or drinking\$).tw.  
((drug or alcohol\$ or narcotic\$ or heroin or opiate\$ or opioid\$ or opium or cocaine or crack  
cocaine or cannabis or marijuana or marihuana or hashish or phencyclidine or
- 2 benzodiazepine\$ or barbiturate\$ or amphetamine\$ or MDMA or hallucinogen\$ or ketamine  
or lsd or inhalant\$ or substance\$) adj2 (abuse\$ or misuse\$ or use\$ or problem\$ or depend\$  
or addict\$ or disorder\$)).ti,ab.
- 3 illicit drug.tw.
- 4 street drug.tw.
- 5 or/1-4
- 6 exp Polypharmacy/  
7 polypharmacy.tw.
- 8 medication error\$.tw.
- 9 exp Drug Interactions/  
10 drug interaction\$.tw.
- 11 exp Treatment Guidelines/  
12 treatment guideline\$.tw.
- 13 guideline adherence.tw.
- 14 medication appropriateness index.tw.
- 15 beers criteria.tw.
- 16 prescribing appropriateness index.tw.
- 17 ACOVE indicator\$.tw.
- 18 Assessing Care of Vulnerable Elderly indicator\$.tw.
- 19 START criteria.tw.
- 20 screening tool to alert to right treatment.tw.
- 21 STOPP criteria.tw.
- 22 screening tool of older persons prescription\$.tw.
- 23 Pharmacological Appropriateness Rating of Medicines.tw.
- 24 (underprescrib\$ or overprescrib\$ or misprescrib\$ or overus\$ or underus\$ or misus\$).tw.
- 25 (inappropriateprescrib\$ or inappropriate prescription\$).tw.
- 26 exp Drug Dosages/  
27 (dose\$ or dosage\$).tw.
- 28 or/6-27
- 29 exp Prescription Drugs/  
30 exp "Prescribing (Drugs)"/  
31 (prescription\$ or prescrib\$ or prescription drug\$ or drug prescription\$ or drug prescrib\$ or  
medication prescription\$ or medication prescrib\$).tw.
- 32 pharmacotherap\$.tw.
- 33 or/29-32
- 34 28 and 33  
(((selective serotonin reuptake inhibitors or serotonin) and noradrenaline reuptake  
inhibitors) or monoamine oxidase inhibitors or tricyclic drugs or agomelatine or  
amitriptyline or amoxapine or acetylcarnitine or alaproclate or amersergide or amineptine or  
amiflamine or bupropion or befloxatone or brofaromine or benactyzine or butriptyline or  
citalopram or caroxazone or cilosamine or chlorpoxiten or clorgyline or cimoxatone or  
clomipramine or clorimipramine or clovoxamine or desipramine or deanol or deprenyl or  
demexiptiline or dibenzipin or dothiepin or doxepin or diclofensine or duloxetine or  
35 dosulepin or escitalopram or etoperidone or fluoxetine or fluvoxamine or femoxetine or  
fluparoxan or fluotracen or flupentixol or imipramine or iproniazid or idazoxan or  
isocarboxazid or iprindole or lofepramine or mianserin or maprotiline or metapramine or  
mirtazapine or moclobemide or melitracen or minaprine or nortriptyline or nefazodone or  
nomifensine or nialamide or oxaflozan or paroxetine or phenelzine or pargyline or  
protriptylin or prosulpride or reboxetine or rolipram or setiptiline or seleginine or tianeptine  
or tetrindole or tranlycypromine or tomoxetine or trazodone or trimipramine or venlafaxine  
or viqualine).ti,ab.
- 36 exp Antidepressant Drugs/  
37 35 or 36
- 38 5 and 34 and 37

39 animal.po.  
 40 human.po.  
 41 39 not (39 and 40)  
 42 38 not 41  
 (benperidol or chlorpromazine or flupentixol or haloperidol or levomepromazine or pericyazine or perphenazine or pimozide or prochlorperazine or promazine or sulpiride or trifluoperazine or zuclopenthixol or amisulpride or aripiprazole or clozapine or olanzapine or paliperidone or quetiapine or risperidone or sertindole or zotepine or fluphenazine or pipotiazine or risperidone).ti,ab.  
 43  
 44 exp Neuroleptic Drugs/  
 45 antipsychotic\$.ti,ab.  
 46 or/43-45  
 47 5 and 34 and 46  
 48 47 not 41  
 (nitrazepam or loprazolam or lormetazepam or temazepam or zaleplon or zolpidem or zopiclone or chloral hydrate or diazepam or alprazolam or chlordiazepoxide or lorazepam or oxazepam or buspirone or bromazepam or meprobamate or clonazepam).ti,ab.  
 49  
 50 (cyclopyrrolone\$ or z?drug\$ or benzodiazepine\$).ti,ab.  
 51 (anxiolytic\$ or hypnotic\$).ti,ab.  
 52 or/49-51  
 53 5 and 34 and 52  
 54 53 not 41  
 (buprenorphine or codeine or diamorphine or dihydrocodeine or dipipanone or fentanyl or hydromorphone or meptazinol or methadone or morphine or oxycodone or papaveretum or pentazocine or pethidine or tramadol).ti,ab.  
 55  
 56 exp Opiates/  
 57 (opiate\$ or opioid\$).ti,ab.  
 58 or/55-57  
 59 5 and 34 and 58  
 60 59 not 41  
 (carbamazepine or eslicarbazepine or ethosuximide or gabapentin or lamotrigine or levetiracetam or oxcarbazepine or phenobarbitone or phenobarbital or primidone or phenytoin or pregabalin or rufinamide or topiramate or sodium valproate or vigabatrin or valproate or valproic acid or zonisamide).ti,ab.  
 61  
 62 exp Anticonvulsive Drugs/  
 63 anticonvulsant\$.tw.  
 64 or/61-63  
 65 5 and 34 and 64  
 66 65 not 41  
 67 exp Lithium/  
 68 5 and 34 and 67  
 69 68 not 41

### Appendix 2.3: Search strategy used in Embase (1974 to 2012 March 05)

1 (alcoholi\$ or drinker\$ or drinking\$.tw.  
2 addiction/ or alcoholism/ or drug dependence/ or withdrawal syndrome/  
3 ((alcohol or drug or narcotic\$ or entactogen\$ or amphetamine\$ or psilocybin or solvent\$ or  
4 heroin or opiate\$ or opioid\$ or opium or cocaine or crack cocaine or cannabis or marijuana  
5 or marihuana or hashish or phencyclidine or benzodiazepine\$ or barbiturate\$ or MDMA or  
6 hallucinogen\$ or ketamine or lsd or inhalant\$ or substance\$) adj2 (abuse\$ or misuse\$ or  
7 use\$ or problem\$ or depend\$ or addict\$ or disorder\$)).ti,ab.  
8 exp street drug/  
9 exp illicit drug/  
10 or/1-5  
11 exp polypharmacy/  
12 polypharmacy.tw.  
13 exp medication error/  
14 medication error\$.tw.  
15 drug interaction/ or \*drug alcohol interaction/ or \*drug inhibition/ or \*drug potentiation/  
16 \*practice guideline/  
17 practice guideline\$.tw.  
18 treatment guideline\$.tw.  
19 guideline adherence.tw.  
20 medication appropriateness index.tw.  
21 beers criteria.tw.  
22 prescribing appropriateness index.tw.  
23 ACOVE indicator\$.tw.  
24 Assessing Care of Vulnerable Elderly indicator\$.tw.  
25 screening tool to alert to right treatment.tw.  
26 screening tool of older persons prescription\$.tw.  
27 STOPP criteria.tw.  
28 START criteria.tw.  
29 Pharmacological Appropriateness Rating of Medicines.tw.  
30 exp inappropriate prescribing/  
31 (inappropriate prescription\$ or inappropriate prescrib\$.tw.  
32 drug dose/ or \*dosage schedule comparison/ or \*drug dose comparison/ or \*drug dose  
33 escalation/ or \*drug dose increase/ or \*drug dose reduction/ or \*drug dose regimen/ or  
34 \*drug overdose/ or \*drug underdose/ or \*optimal drug dose/ or \*recommended drug dose/  
35 (underprescrib\$ or overprescrib\$ or misprescrib\$ or overus\$ or underus\$ or misus\$.tw.  
36 or/7-29  
37 exp prescription/  
38 (prescription\$ or prescrib\$.tw.  
39 (drug prescription\$ or drug prescrib\$ or medication prescription\$ or medication  
40 prescrib\$.tw.  
41 pharmacotherap\$.tw.  
42 or/31-34  
43 30 and 35  
44 (((selective serotonin reuptake inhibitors or serotonin) and noradrenaline reuptake  
45 inhibitors) or monoamine oxidase inhibitors or tricyclic drugs or agomelatine or  
46 amitriptyline or amoxapine or acetylcarnitine or alaproclate or amersergide or amineptine or  
47 amiflamine or bupropion or befloxatone or brofaromine or benactyzine or butriptyline or  
48 citalopram or caroxazone or cilosamine or chlorpoixiten or clorgyline or cimoxatone or  
49 clomipramine or clorimipramine or clovoxamine or desipramine or deanol or deprenyl or  
50 demexiptiline or dibenzipin or dothiepin or doxepin or diclofensine or duloxetine or  
51 dosulepin or escitalopram or etoperidone or fluoxetine or fluvoxamine or femoxetine or  
52 fluparoxan or fluotracen or flupentixol or imipramine or iproniazid or idazoxan or  
53 isocarboxazid or iprindole or lofepramine or mianserin or maprotiline or metapramine or  
54 mirtazapine or moclobemide or melitracen or minaprine or nortriptyline or nefazodone or  
55 nomifensine or nialamide or oxaflozan or paroxetine or phenelzine or pargyline or

protriptylin or prosulpride or reboxetine or rolipram or setiptiline or seleginine or tianeptine  
 or tetrindole or tranylcypromine or tomoxetine or trazodone or trimipramine or venlafaxine  
 or viqualine).ti,ab.  
 38 exp antidepressant agent/  
 39 antidepressive\$.tw.  
 40 or/37-39  
 41 6 and 36 and 40  
 42 human/  
 43 nonhuman/  
 44 exp animal/  
 45 43 or 44  
 46 45 not (42 and 45)  
 47 41 not 46  
 (benperidol or chlorpromazine or flupentixol or haloperidol or levomepromazine or  
 pericyazine or perphenazine or pimozide or prochlorperazine or promazine or sulpiride or  
 48 trifluoperazine or zuclopenthixol or amisulpride or aripiprazole or clozapine or olanzapine  
 or paliperidone or quetiapine or risperidone or sertindole or zotepine or fluphenazine or  
 pipotiazine or risperidone).ti,ab.  
 49 exp neuroleptic agent/  
 50 antipsychotic\$.ti,ab.  
 51 or/48-50  
 52 6 and 36 and 51  
 53 52 not 46  
 (nitrazepam or loprazolam or lormetazepam or temazepam or zaleplon or zolpidem or  
 54 zopiclone or chloral hydrate or diazepam or alprazolam or chlordiazepoxide or lorazepam or  
 oxazepam or buspirone or bromazepam or meprobamate or clonazepam).ti,ab.  
 55 (cyclopyrrolone\$ or z?drug\$ or benzodiazepine\$).ti,ab.  
 56 (anxiolytic\$ or hypnotic\$).ti,ab.  
 57 or/54-56  
 58 6 and 36 and 57  
 59 58 not 46  
 (buprenorphine or codeine or diamorphine or dihydrocodeine or dipipanone or fentanyl or  
 60 hydromorphone or meptazinol or methadone or morphine or oxycodone or papaveretum or  
 pentazocine or pethidine or tramadol).ti,ab.  
 61 exp opiate/  
 62 opioid\$.tw.  
 63 or/60-62  
 64 6 and 36 and 63  
 65 64 not 46  
 (carbamazepine or eslicarbazepine or ethosuximide or gabapentin or lamotrigine or  
 66 levetiracetam or oxcarbazepine or phenobarbitone or phenobarbital or primidone or  
 phenytoin or pregabalin or rufinamide or topiramate or sodium valproate or vigabatrin or  
 valproate or valproic acid or zonisamide).ti,ab.  
 67 exp anticonvulsive agent/  
 68 anticonvulsant\$.ti,ab.  
 69 or/66-68  
 70 6 and 36 and 69  
 71 70 not 46  
 72 exp lithium/  
 73 6 and 36 and 72  
 74 73 not 46

## Appendix 2.4: Adapted Quality Assessment Tool for Quantitative Studies

Study author:

Year:

### A) SELECTION BIAS

(Q1) Are the individuals selected to participate in the study likely to be representative of the target population?

1. Very likely (included all eligible patients during specified period)
2. Somewhat likely
3. Not likely
4. Can't tell

(Q2) What percentage of selected individuals agreed to participate?

1. 80-100% agreement
2. 60-79% agreement
3. Less than 60% agreement
4. Not applicable
5. Can't tell

RATE THIS SECTION: 1. Strong 2. Moderate 3. Weak

### B) STUDY DESIGN

Indicate the study design

- 1 Randomized controlled trial
- 2 Controlled clinical trial
- 3 Cohort analytic
- 4 Case-control
- 5 Interrupted time series
- 6 Other specify \_\_\_\_\_
- 7 Can't tell

Was the study described as randomized? If NO, go to Component C.

No Yes

If Yes, was the method of randomization described?

No Yes

If Yes, was the method appropriate?

No Yes

RATE THIS SECTION: 1. Strong 2. Moderate 3. Weak

### C) CONFOUNDERS

(Q1) Were there important differences between groups prior to the intervention?

- 1 Yes
- 2 No
- 3 Can't tell (the sample with SUDs were not compared to those without it). SUDs were co-morbid with depression

The following are examples of confounders:

- 1 Race
- 2 Sex
- 3 Marital status/family
- 4 Age
- 5 SES (income or class)
- 6 Education
- 7 Health status
- 8 Pre-intervention score on outcome measure

(Q2) If yes, indicate the percentage of relevant confounders that were controlled (either in the design (e.g. stratification, matching) or analysis)?

- 1 80 – 100%
- 2 60 – 79%
- 3 Less than 60%
- 4 Can't Tell

RATE THIS SECTION: 1. Strong 2. Moderate 3. Weak

**D) DATA COLLECTION METHODS**

(Q1) Were data collection tools shown to be valid?

- 1 Yes
- 2 No
- 3 Can't tell

(Q2) Were data collection tools shown to be reliable?

- 1 Yes
- 2 No
- 3 Can't tell (used already existing admin data)

RATE THIS SECTION: 1. Strong 2. Moderate 3. Weak

**E) WITHDRAWALS AND DROP-OUTS**

(Q1) Were withdrawals and drop outs reported in terms of numbers and/or reasons per group?

- 1 Yes
- 2 No
- 3 Can't tell
- 4 Not applicable

(Q2) Indicate the percentage of participants completing the study. (If the percentage differs by groups, record the lowest).

- 1 80 -100%
- 2 60 - 79%
- 3 less than 60%
- 4 Can't tell

RATE THIS SECTION: 1. Strong 2. Moderate 3. Weak

**GLOBAL RATING**

**COMPONENT RATINGS**

Please transcribe the information from the previous sections onto this page. Rate this section

- A SELECTION BIAS 1. Strong 2. Moderate 3. Weak
- B STUDY DESIGN 1. Strong 2. Moderate 3. Weak
- C CONFOUNDERS 1. Strong 2. Moderate 3. Weak
- D DATA COLLECTION METHODS 1. Strong 2. Moderate 3. Weak
- E WITHDRAWALS AND DROP-OUTS 1. Strong 2. Moderate 3. Weak 4. Not applicable

**GLOBAL RATING FOR THIS PAPER (circle one):**

- 1 STRONG (three or more STRONG ratings with no WEAK ratings)
- 2 MODERATE (less than four STRONG ratings and one WEAK rating)
- 3 WEAK (two or more WEAK ratings)

## **Appendix 2.5: List of excluded studies**

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### Appendix 3.1: Consultation process questionnaire

How often do you think these medications are inappropriately prescribed for patients with substance use disorders? Please tick the relevant box for each of the medications.

Medications	Frequently	Sometimes	Rarely	Never
Antidepressants				
Antipsychotics				
Anxiolytics and hypnotics				
Antihypertensives				
Positive inotropic drugs (digoxin, digitoxin, enoximone, milrinone)				
Nitrates				
Anti-arrhythmics (amiodarone, disopyramide, flecainide, propafenone, adenosine)				
Proton pump inhibitors (PPIs)				
Other antiulcer drugs (antacids, H <sub>2</sub> receptor antagonists, prostaglandin analogues and others)				
Opioids including substitute opioids				
Analgesics excluding opioids (NSAIDs, antimigraine drugs, paracetamol and nefopam)				
Anticonvulsants				
Drugs used in asthma and COPD management (adrenoceptor agonists, antimuscarinic bronchodilators, theophylline, compound preparations, leukotriene receptor antagonists, cromoglicates and others)				
Cholesterol-lowering agents				
Drugs used in substance dependence (disulfiram, acamprosate, bupropion, NRT, varenicline and lofexidine)				
Vitamins				
Minerals				
Antimanic agent (lithium)				
Corticosteroids				
Thyroid hormones				
Antihistamines				
Antidiabetic agents				
Antihyperuricaemics				
Anticoagulants				
Hormone replacement therapy				
Laxatives and purgatives				
Antimuscarinics				
Opioid antagonists				
Dopaminergic agents used in parkinsonism (cabergoline, pergolide, apomorphine, pramipexole, ropinirole, rotigotine, levodopa, co-beneldopa, co-careldopa, rasagiline, selegiline, entacapone, tolcapone and amantadine)				
Antifibrinolytic agents				

Lubricants				
Antiandrogens				
Mucolytics				
Skeletal muscle relaxants				
Anaesthetics				
Drugs affecting intestinal secretions (ursodeoxycholic acid, aprotinin, pancreatin)				
Aminosalicylates				
Antiobesity drugs				
hormone antagonists (anastrozole, exemestane, fulvestrant, letrozole, tamoxifen, toremifene, degarelix)				
CNS stimulants (atomoxetine, dexamphetamine, methylphenidate, modafinil)				
Systemic nasal decongestants				
Antiglaucoma agents				
Antimicrobials				
Antiplatelet agents				
Antispasmodics (alverine, mebeverine, peppermint oil)				
Drugs affecting immune system (azathioprine, cyclosporin, mercaptopurine, methotrexate)				
Drugs affecting bone metabolism (calcitonin, parathyroid hormone, bisphosphonates, strontium)				
Topical corticosteroids with antimicrobials				
Combined contraceptive pill				
Antimotility agents (co-phenotrope, loperamide)				
Antiemetics				
Supplements (ensure, fortisip, fortijuice and others)				
Topical preparations for acne				
Antihaemorrhoidals				
Drugs used for urinary incontinence				
Emollients				
Topical preparations for psoriasis				
Other drugs for rheumatic diseases (glucosamine, chondrontin)				

## Appendix 4.1: Favourable ethical opinion letter for secondary data analysis



### National Research Ethics Service

NRES Committee South West - Exeter

South West REC Centre  
Level 3  
Block B  
Lewins Mead  
Whitefriars  
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BS1 2NT

Telephone: 0117 342 1332  
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09 November 2011

Miss Obirenjeyi Kudehinbu  
Alcuin Research Resource Centre  
Second floor  
Room 209B  
University of York  
Heslington  
York  
YO10 5DD

Dear Miss Kudehinbu

**Study title:** A retrospective study of the medications of service users  
with problematic or dependent substance use  
**REC reference:** 11/SW/0296

Thank you for your e-mail of 28 October 2011 responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

#### Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

#### Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

#### Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

*Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.*

This Research Ethics Committee is an advisory committee to the South West Strategic Health Authority  
The National Research Ethics Service (NRES) represents the NRES Directorate within  
the National Patient Safety Agency and Research Ethics Committees in England

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

**It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).**

**You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Confirmation should also be provided to host organisations together with relevant documentation.**

#### Approved documents

The documents reviewed and approved by the Committee are:

Document	Version	Date
Evidence of insurance or indemnity		08 July 2011
Investigator CV	3.3	18 October 2011
Letter from Sponsor		26 October 2011
Letter from Statistician		19 October 2011
Other: CV - Charlie Lloyd	3.3	18 October 2011
Protocol	3.3	18 October 2011
REC application	3.3	18 October 2011
Referees or other scientific critique report		27 October 2011
Response to Request for Further Information		

#### Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

#### After ethical review

##### Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports

- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

11/SW/0296	Please quote this number on all correspondence
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With the Committee's best wishes for the success of this project

Yours sincerely

*Kristin Peck*

pp Dr Lee Burton  
Vice Chair  
NRES Committee South West - Exeter

Enclosures: "After ethical review – guidance for researchers" [SL-AR2]  
Copy to: Mrs Sue Final (sue.final@york.ac.uk)  
Mr Allison Thompson, Leeds Partnerships Foundation Trust (athompson11@nhs.net)

**Appendix 4.2: Prescribed medications taken by service users at their first SAS treatment episode**

<b>Medications</b>	<b>No. of service users on medications (1783)</b>
Antidepressants	868 (48.7%)
Antipsychotics	266 (14.9%)
Anxiolytics/hypnotics	295 (16.5%)
Antihypertensives	282 (15.8%)
Proton Pump Inhibitors (PPIs)	264 (14.8%)
Antacids	24 (1.3%)
Analgesics (including opioids, NSAIDs and others)	519 (29.1%)
Anticonvulsants	116 (6.5%)
Drugs used in asthma and COPD management	118 (6.6%)
Cholesterol-lowering agents	95 (5.3%)
Drugs used in treating substance dependence (disulfiram, acamprosate, bupropion, NRT, varenicline and lofexidine)	52 (2.9%)
Vitamins and minerals	498 (28.1%)
Antimanic agent (lithium)	32 (1.8%)
Antibiotics	39 (2.2%)
Corticosteroids <sup>a</sup>	46 (2.6%)
Thyroid hormones	32 (1.8%)
Antihistamines	45 (2.5%)
Antidiabetic agents	37 (2.1%)
Antihyperuricaemics	21 (1.2%)
Anticoagulants	22 (1.2%)
Hormone replacement therapy	22 (1.2%)
Laxatives and purgatives	22 (1.2%)
Antimuscarinics	32 (1.8%)
Antispasmodics <sup>b</sup>	22 (1.2%)
Immunosuppressants <sup>c</sup>	5 (0.3%)
Drugs affecting bone metabolism	3 (0.2%)
Emollients and barrier preparations	6 (0.3%)
Positive inotropic drugs	3 (0.2%)
Antiplatelet agents <sup>d</sup>	3 (0.2%)
Others <sup>e</sup>	10 (0.6%)

Note: All medications were classified into only one group (for example, aspirin was grouped only under NSAIDs and not antiplatelet agents). <sup>a</sup> Includes corticosteroids with antimicrobials, <sup>b</sup> includes drugs that are believed to be direct relaxants of intestinal smooth muscle such as alverine, mebeverine and peppermint oil, <sup>c</sup> does not include corticosteroids, <sup>d</sup> excludes aspirin, <sup>e</sup> others include secretin, hydrogen sulphate, tiopronin, glucosamine, chondroitin, compound haemorrhoidal preparations, compound preparations for psoriasis.

**Appendix 4.3: Comparison of sociodemographic characteristics between service users with and without polypharmacy (n and % presented for all characteristics except age)**

Sociodemographic characteristics	Service users without polypharmacy	Service users with polypharmacy	P-values
Age <sup>a</sup> Total	38.4 ± 10.4 1285	46.2 ± 11.1 476	P < 0.0005 <sup>#</sup>
Gender Male Female Total	730 (56.8%) 555 (43.2%) 1285	295 (62%) 181 (38%) 476	0.05 <sup>+</sup>
Ethnicity <sup>b</sup> White Other Not stated Total	1108 (86.2%) 60 (4.7%) 117 (9.1%) 1285	411 (86.3%) 28 (5.9%) 37 (7.8%) 476	0.42 <sup>+</sup>
Housing status <sup>c</sup> Rented Home owner Homeless Other Total	735 (60.5%) 232 (19.1%) 174 (14.3%) 74 (6.1%) 1215	260 (57.3%) 113 (24.9%) 51 (11.2%) 30 (6.6%) 454	0.04 <sup>+</sup>
Referral source <sup>d</sup> Self GH/A&E GP Psychiatrist Drug services Other Total	415 (32.3%) 124 (9.6%) 270 (21%) 93 (7.2%) 196 (15.3%) 187 (14.6%) 1285	138 (29%) 78 (16.4%) 110 (23.1%) 48 (10.1%) 44 (9.2%) 58 (12.2%) 476	P < 0.0005 <sup>+</sup>
Referral substance <sup>e</sup> Alcohol Opioids Other Total	948 (73.8%) 238 (18.5%) 99 (7.7%) 1285	427 (89.7%) 25 (5.3%) 24 (5%) 476	P < 0.0005 <sup>+</sup>
Employment status <sup>f</sup> Employed Unemployed Other Total	266 (21.9%) 670 (55.2%) 277 (22.8%) 1213	63 (14%) 215 (47.8%) 172 (38.2%) 450	P < 0.0005 <sup>+</sup>

Note: The level of significance was set at 0.4% after taking the total number of variables (12) into consideration due to Bonferroni adjustment for multiple testing. <sup>a</sup>Mean and standard deviation presented for age, <sup>b</sup>other ethnicity includes Asian or Asian British, Black or Black British, Mixed and other ethnic groups, <sup>c</sup>other housing status includes supported housing and traveller, <sup>d</sup>other referral sources includes social services, criminal justice and others, <sup>e</sup>other referral substances includes sedatives, cannabis, stimulants, hallucinogens, polyuse and solvents, <sup>f</sup>other employment status includes inactive, not stated and others, <sup>#</sup>calculated using independent sample t-test, <sup>+</sup>calculated using chi-squared test.

**Appendix 4.4: Comparison of key measures of addiction between service users with and without polypharmacy**

Addiction measures	Service users without polypharmacy	Service users with polypharmacy	P-values
LDQ <sup>a</sup> Total	17 (9, 24) 1259	18.5 (10, 25) 464	0.026 <sup>*</sup>
CORE-10 Total	21.4 ± 9.3 1261	23.1 ± 8.5 467	P < 0.0005 <sup>#</sup>
SSQ Total	13.9 ± 5.6 1233	13.7 ± 5.5 454	0.45 <sup>#</sup>
EQ5D <sup>a</sup> Total	0.7 (0.3, 0.9) 1256	0.3 (0.08, 0.7) 470	P < 0.0005 <sup>*</sup>
Number of previous SAS episode <sup>a</sup> Total	1 (1, 2) 1285	1 (1, 2) 476	0.04 <sup>*</sup>

Note: The level of significance was set at 0.4% after taking the number of variables (12) into consideration due to Bonferroni adjustment for multiple testing. <sup>a</sup>Median and interquartile range presented because data not normally distributed, <sup>\*</sup> calculated using Wilcoxon rank sum test, <sup>#</sup> calculated using independent samples t-test.

**Appendix 4.5: Comparison of sociodemographic characteristics between service users with and without psychiatric polypharmacy (n and % presented for all characteristics except age)**

Sociodemographic characteristics	Service users without psychiatric polypharmacy	Service users with psychiatric polypharmacy	P-value
Age <sup>a</sup> Total	40.5 ± 11.2 1731	42.9 ± 10.2 30	0.23 <sup>#</sup>
Gender Male Female Total	1009 (58.3%) 722 (41.7%) 1731	16 (53.3%) 14 (46.7%) 30	0.59 <sup>+</sup>
Ethnicity <sup>b</sup> White Other Not stated Total	1491 (86.1%) 86 (5%) 154 (8.9%) 1731	28 (93.3%) 2 (6.7%) 0 30	0.15 <sup>*</sup>
Housing status <sup>c</sup> Rented Home owner Homeless Other Total	976 (59.5%) 340 (20.7%) 222 (13.5%) 102 (6.2%) 1640	19 (65.5%) 5 (17.2%) 3 (10.3%) 2 (6.9%) 29	0.91 <sup>*</sup>
Referral source <sup>d</sup> Self GH/A&E GP Psychiatrist Drug services Other Total	546 (31.5%) 200 (11.6%) 379 (21.9%) 130 (7.5%) 237 (13.7%) 239 (13.8%) 1731	7 (23.3%) 2 (6.7%) 1 (3.3%) 11 (36.7%) 3 (10%) 6 (20%) 30	P < 0.0005 <sup>*</sup>
Referral substance <sup>e</sup> Alcohol Opioids Other Total	1355 (78.3%) 260 (15%) 116 (6.7%) 1731	20 (66.7%) 3 (10%) 7 (23.3%) 30	0.008 <sup>*</sup>
Employment status <sup>f</sup> Employed Unemployed Other Total	329 (20.1%) 868 (53.1%) 437 (26.7%) 1634	0 17 (58.6%) 12 (41.4%) 29	0.02 <sup>+</sup>

Note: The level of significance was set at 0.4% after taking the number of variables (12) into consideration due to Bonferroni adjustment for multiple testing. <sup>a</sup>Mean and standard deviation presented for age, <sup>b</sup>other ethnicity includes Asian or Asian British, Black or Black British, Mixed and other ethnic groups, <sup>c</sup>other housing status includes supported housing and traveller, <sup>d</sup>other referral sources includes social services, probation and others, <sup>e</sup>other referral substances includes sedatives, cannabis, stimulants, hallucinogens, polyuse and solvents, <sup>f</sup>other employment status includes inactive, not stated and others, \*calculated using Fisher's exact test, +calculated using chi-squared test, #calculated using independent sample t-test.

**Appendix 4.6: Comparison of key measures of addiction between service users with and without psychiatric polypharmacy**

<b>Measures of addiction</b>	<b>Service users without psychiatric polypharmacy</b>	<b>Service users with psychiatric polypharmacy</b>	<b>P-values</b>
LDQ	17 (9, 24) 1693	16.5 (11.8, 22) 30	0.98 <sup>a</sup>
CORE-10	21.8 ± 9.1 1698	25.3 ± 7.5 30	0.04 <sup>b</sup>
SSQ	13.8 ± 5.6 1659	14.9 ± 5.3 28	0.32 <sup>b</sup>
EQ5D	0.6 (0.2, 0.8) 1697	0.3 (0.2, 0.6) 29	0.007 <sup>a</sup>
Number of previous SAS episodes	1 (1, 2) 1731	1 (1, 2) 30	0.36 <sup>a</sup>

<sup>a</sup>Analysed using Wilcoxon rank sum test, <sup>b</sup>analysed using independent samples t-test

## Appendix 4.7: A study of the psychotropic prescriptions of people attending an addiction service in England

# A study of the psychotropic prescriptions of people attending an addiction service in England

Adejoke Obirenjeyi Oluyase, Duncan Raistrick, Yasir Abbasi, Veronica Dale and Charlie Lloyd

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### Abstract

**Purpose** – The purpose of this paper is to examine the prescribed psychotropic medications taken by newly referred people with a range of substance use disorders (SUD) who attend a specialist community addiction service.

**Design/methodology/approach** – Anonymised data on newly referred people ( $n = 1,537$ ) with SUD attending a specialist community addiction service for their first episode of treatment between August 2007 and July 2010 were obtained from the database of the service. Data were cleaned and the percentage of people taking prescribed psychotropic medications at their first episode of treatment was calculated.

**Findings** – More than half (56.1 percent) of people attending the service were taking prescribed antidepressants and anxiolytics at their first episode of treatment whilst 15.2 percent of people were taking prescribed antipsychotics. Alcohol and opioids were the primary referral substances for 77.4 percent and 15.2 percent of people respectively. People referred for "other" substances (cannabis, stimulants, sedatives, hallucinogens, solvents and polydrug use) made up the remaining 7.5 percent and had the highest percentage of prescribed psychotropics (antipsychotics = 47 percent, antidepressants and anxiolytics = 64.3 percent) compared to those referred for alcohol and opioids ( $p < 0.0005$ ).

**Originality/value** – To the best of the authors' knowledge, this is the first study of psychotropic prescribing among people with a range of SUD in the UK. The high prevalence of psychotropic prescribing raises questions about the appropriateness of these prescriptions and calls for scrutiny of prescribing practice in this group of people.

**Keywords** Substance misuse, Drug addiction, England, Community health services, Substance use disorders, Mental disorders, Psychotropic medications, Antidepressants, Anxiolytics, Antipsychotics

**Paper type** Research paper

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### Introduction

The prescribing of psychotropic medications in England is increasing. Between 1998 and 2010, antipsychotics and antidepressants increased annually by 5.1 and 10 per cent, respectively (Ilyas and Moncrieff, 2012). Similar trends have been reported in other countries such as Australia and the USA (Stephenson *et al.*, 2012; Pincus *et al.*, 1998). This increase in psychotropic prescribing has its cost implications to the National Health Service (NHS) of England. For instance, in 2010, psychiatric medications accounted for 10 per cent of the cost of medications in England with psychotropics such as antidepressants, antipsychotics, mood stabilisers, hypnotics and anxiolytics making up about 70 per cent of this cost (Ilyas and Moncrieff, 2012).

Mental disorders such as mood and anxiety disorders frequently co-occur with substance use disorders (SUD). A nationally representative survey of the non-institutionalised population of

the USA found the prevalence of mood and anxiety disorders to be 20.1 and 17.7 per cent, respectively, among respondents with SUD in the preceding 12 months (Grant *et al.*, 2004). Furthermore, 20 and 15 per cent of respondents with any 12-month mood and anxiety disorders, respectively, had at least one SUD. Earlier studies in the USA have also found this frequent co-occurrence (Kessler *et al.*, 1996; Regier *et al.*, 1990). In clinical populations, the reported prevalence of mood and anxiety disorders among people with SUD is much higher with UK studies showing frequencies of 70 per cent and above (Delgado *et al.*, 2012; Weaver *et al.*, 2003). However, the high prevalence of these mental disorders among people with SUD has been a subject of debate due to problems inherent in distinguishing independent mental disorders from substance-induced mental disorders and the resulting implications on treatment strategies (Schuckit, 2006; O'Brien and Charney, 2004). Intoxication and withdrawal symptoms of substances often resemble those of mood and anxiety disorders and they could sometimes be severe (Grant *et al.*, 2004; Raimo and Schuckit, 1998).

Despite this co-occurrence, people with SUD are one of the groups most vulnerable to the adverse consequences of psychotropic medications such as dependence, side effects and drug interactions resulting in overdose and mortality. People with SUD are more likely to become dependent when treated with psychotropic medications such as benzodiazepines (Manthey *et al.*, 2012). SUD have also been found to increase the risk of extrapyramidal symptoms (EPS) such as akathisia, parkinsonism, dyskinesia and dystonic reactions among people with schizophrenia (Potvin *et al.*, 2009). Furthermore, the interactions occurring between psychotropic medications and substances such as alcohol and illicit drugs have been implicated in many adverse events among substance users. Benzodiazepines and alcohol have often been found to be used in combination with opioids such as heroin and oxycodone in opioid-related overdose and fatalities (Darke *et al.*, 2011; Darke and Hall, 2003). Antidepressants have also been found to be used in combination with central nervous system (CNS) depressants such as alcohol, benzodiazepines and opioids in antidepressant-related mortality in the UK (Cheeta *et al.*, 2004). Deaths resulting from combining antidepressants and other drugs are more likely in people with SUD compared to those without SUD. There is therefore a need to be cautious when prescribing psychotropic medications to people with SUD. Knowledge of psychotropic medications prescribed to people with SUD is important for their safety and could possibly highlight problematic areas in prescribing.

Previous studies that explored the prevalence of psychotropic prescribing in the UK have focused on primary care patients and specific patient groups such as the elderly and children (Guthrie *et al.*, 2010; Hsia and MacLennan, 2009; Chan *et al.*, 2006; Wong *et al.*, 2003). A study of psychotropic prescribing using computer data from 12 general practices in England found that 10.1 per cent of patients were prescribed an antidepressant, anxiolytic or hypnotic whilst 0.8 per cent of patients were on antipsychotics within a year period (Chan *et al.*, 2006). Another study comparing psychotropic prescribing among elderly people (aged 65 years and above) with and without dementia using data obtained from 315 general practice databases in Scotland found the prevalence of antidepressants to be 10.8 per cent in those without dementia and 28.7 per cent in those with dementia whereas 16.3 per cent with dementia and 7.5 per cent without dementia had an anxiolytic or hypnotic prescribed within a year period (Guthrie *et al.*, 2010). Other studies have focused on single classes of psychotropics such as antipsychotics and antidepressants (Harris *et al.*, 2012; Lockhart and Guthrie, 2011; Kaye *et al.*, 2003). There is no literature related to psychotropic medication prescribing in people who use substances. Consequently, this study aimed to examine the prescribed psychotropic medications taken by newly referred people with a range of SUD who attend a specialist community addiction service (Leeds Addiction Unit (LAU)) in Leeds, UK.

## Methods

### Setting

The LAU is a statutory NHS tier 3 addiction service that provides specialist addiction treatment to adults (18 years and above). Tier 3 addiction services such as the LAU provide assessment, community treatment (detoxification, maintenance and psychosocial interventions) and

aftercare (National Treatment Agency for Substance Misuse, 2006). People may self-refer or they could be referred from other sources such as general practitioners (GP), psychiatrists, hospital, social services, probation, drug services as well as drug treatment and testing order. People classified as newly referred clients include those previously discharged from LAU but attending due to a new treatment episode. The data therefore represents new treatment episodes and some individuals will appear more than once over this period.

#### *Study population and data sources*

Anonymised data on new treatment episodes between August 2007 and July 2010 were obtained from the LAU electronic database. This study focused specifically on the first new treatment episode people attending the LAU had between August 2007 and July 2010 in order to avoid representation of multiple episodes of the same person in this analysis. The prescribed psychotropic medications people were taking at their first episode of treatment during the study period was explored. The total number of newly referred people during this period was 1,537. People attending for their first new treatment episode had a mean of 1.7 (SD = 1.0) episodes in the past. The maximum number of treatment episodes during the study period was four. A total of 212 (13.8 per cent) people had two new treatment episodes whilst 21 (1.4 per cent) had three new treatment episodes and two (0.1 per cent) had four new treatment episodes.

The LAU electronic database contains information on newly referred people and their prescriptions. It has been developed over the last 20 years. Information entered into the electronic database is obtained through a self-completion assessment booklet that is sent out to people before their first appointment at the LAU. The completed booklets are collected from people at their appointment and entered into the database by secretaries of the different clinical teams, who have been trained in the use of the database. This booklet contains demographic information as well as information on substances used, prescribed medications, quality of life, social satisfaction, level of dependence and psychological well-being. Quality of life and social satisfaction are assessed using the EuroQol (EQ 5D) and Social Satisfaction Questionnaire, respectively (Raistrick *et al.*, 2007; Brooks *et al.*, 2003). The Leeds Dependence Questionnaire and the Clinical Outcomes in Routine Evaluation ten item measure (CORE-10) are used in assessing level of dependence and psychological well-being, respectively (Connell and Barkham, 2007; Raistrick *et al.*, 1994). The CORE-10 is a short version of the 34 item CORE – Outcome Measure (Evans *et al.*, 2002; Barkham *et al.*, 2001). Approval for this study with Research Ethics Committee (REC) reference 11/SW/0296 was granted by the South West Exeter REC on the 9 November 2011 and subsequently by the Research and Development department of the Leeds Partnership NHS Foundation Trust.

#### *Classification of psychotropic medications*

Psychotropic medications have been defined as medications that can affect mental processes (Chan *et al.*, 2006). They are usually prescribed for the treatment of mental disorders. The main classes of psychotropic medications considered in this study were those classified as antipsychotics, antidepressants, hypnotics and anxiolytics in the CNS chapter of the British National Formulary (BNF) No. 59 (Joint Formulary Committee, 2010). Hypnotics and anxiolytics will be referred to as "anxiolytics" in the remaining sections for simplicity. All medications were assigned only to one class of psychotropics. For example, some antipsychotics such as prochlorperazine are also used as anxiolytics and antiemetics (Joint Formulary Committee, 2010). However, they were classified as antipsychotics in this study. This was because the indications for the prescriptions were not consistently recorded on the database.

#### *Statistical analysis*

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS v 18). Descriptive statistics for continuous variables are expressed as mean (SD) and those for categorical variables as frequency and proportion. Between group comparisons on categorical variables are presented using  $\chi^2$ -tests. Statistical significance was at the 5 per cent level and all reported *p*-values are two-sided.

## Results

### Characteristics of the study sample

Table 1 shows the characteristics of people attending the LAU for their first episode of treatment between August 2007 and July 2010. The majority of the study population were males (58.2 per cent) with a mean age of 40.3 (SD = 11.0). They were mostly white (84.9 per cent). The distribution of ethnicity is similar to that of Leeds and also that of England and Wales. Alcohol was the primary referral substance for 77.4 per cent of people whilst 15.2 and 7.5 per cent had opioids and "other" substances as their primary substances, respectively. Among the different sources of referral, self-referral accounted for the highest proportion of referrals (30.8 per cent). Almost six out of every ten people lived in rented accommodation, with 13.5 per cent being homeless. Due to the fact that almost eight out of every ten people had alcohol as their primary referral substance, the demographics of the study population was compared to that of people in contact with structured treatment for alcohol in England and they were found to be similar (National Treatment Agency for Substance Misuse, 2011). The only exception was housing status which was not comparable due to differences between the categories of housing used by the LAU and that used by the National Treatment Agency for Substance Misuse.

### Medications

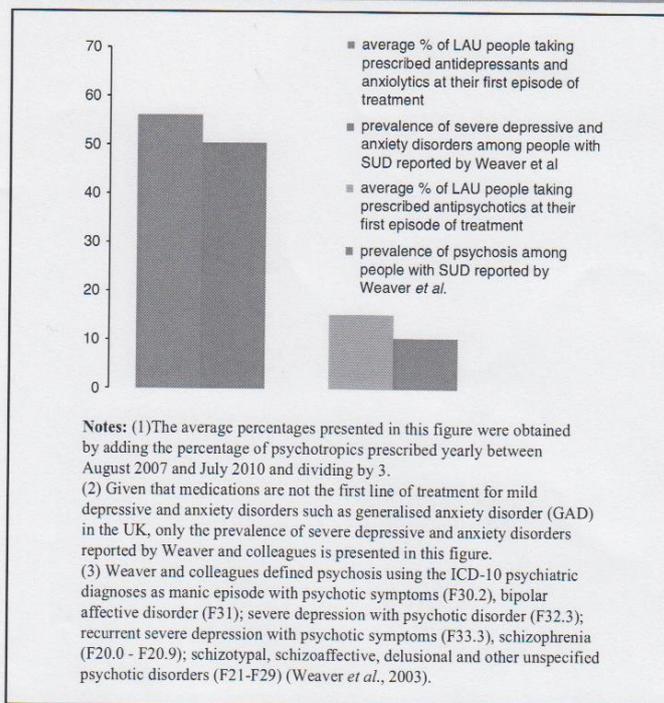
Figure 1 provides a description of the average percentage of LAU people taking prescribed psychotropic medications at their first episode of treatment between August 2007 and July 2010 compared with the prevalence of mental illnesses reported by Weaver and colleagues in a

**Table 1** A table showing the characteristics of people ( $n = 1,537$ ) attending the LAU for their first episode treatment between August 2007 and July 2010

	<i>n</i>	%
<i>Gender</i>		
Males	894	58.2
Females	643	41.8
<i>Ethnicity<sup>a</sup></i>		
White	1,305	84.9
Mixed	48	3.1
Asian or Asian British	17	1.1
Black or Black British	5	0.3
Other ethnic groups	6	0.4
<i>Housing status<sup>b</sup></i>		
Homeless	208	13.5
Supported	92	6.0
Rented	863	56.1
Traveller	3	0.2
Home owner	281	18.3
<i>Referral substance</i>		
Alcohol	1,189	77.4
Opioids	233	15.2
Other <sup>c</sup>	115	7.5
<i>Sources of referral</i>		
Hospital	167	10.9
General practitioner (GP)	337	21.9
Psychiatrist	120	7.8
Drug services non-statutory	92	6.0
Drug services statutory	117	7.6
Self	473	30.8
Social services	33	2.1
Other <sup>d</sup>	198	12.9

Notes: <sup>a</sup>There were no missing values for ethnicity. However, 156 (10.1 per cent) people ticked that they "prefer not to say" their ethnicity. <sup>b</sup>Housing status for 90 people were missing and therefore does not add up to 100 per cent. <sup>c</sup>Comprises those referred for cannabis (35 per cent), stimulants (37 per cent), sedatives (12 per cent), hallucinogens (4 per cent), solvents (1 per cent) and polydrug use (10 per cent). <sup>d</sup>Comprises those referred from probation, drug treatment and testing order (DTTO) and other sources of referral

**Figure 1** A comparison of the average percentage of LAU people taking prescribed psychotropic medications at their first episode of treatment between August 2007 and July 2010 with the prevalence of mental illnesses in a substance misusing population in the UK

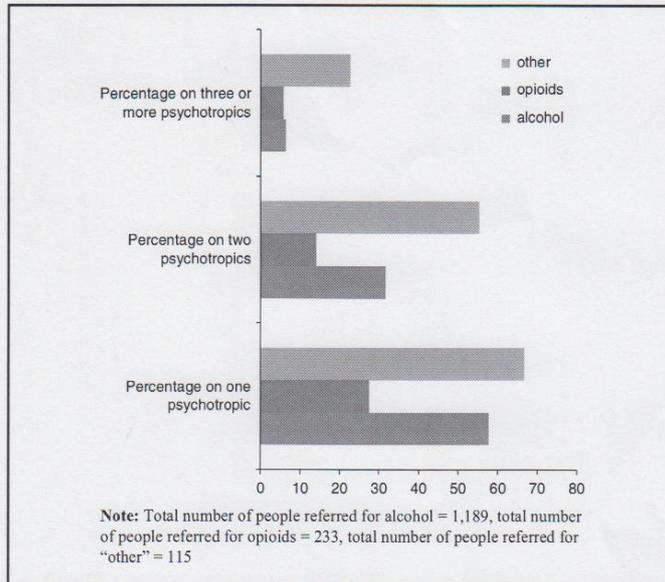


substance misusing population in the UK (Weaver *et al.*, 2003). The study by Weaver and colleagues measured the prevalence of comorbidity of substance misuse and mental illness in substance misuse and community mental health services between January 2001 and February 2002. Given that medications are not the first line of treatment for mild depressive and anxiety disorders such as generalised anxiety disorder in the UK (National Institute for Health and Clinical Excellence (NICE), 2010, 2011), only the prevalence of severe depressive and anxiety disorders reported by Weaver and colleagues were compared with the prevalence of prescribed antidepressants and anxiolytics. The proportion of antidepressants and anxiolytics prescribed to the LAU population exceeded the reported prevalence of severe depressive and anxiety disorders in a substance misusing population. Similarly, the proportion of antipsychotics exceeded the reported prevalence of psychotic disorders in a substance misusing population.

#### *Primary referral substance and number of psychotropic prescriptions*

The prescription of psychotropic medications was common among all the people referred for different substances at the LAU. Figure 2 shows the percentage of people with different primary referral substances prescribed psychotropic medications. Among people referred for "other" substances, 82 per cent were being prescribed at least one psychotropic medication whilst 67 and 39 per cent of those referred for alcohol and opioids were on at least one psychotropic

**Figure 2** A comparison of the number of prescribed psychotropic medications among people with different primary referral substances



medication, respectively ( $p < 0.0005$ ). Similarly, those referred for "other" substances had the highest proportion of people on one, two and three or more psychotropics.

#### Primary referral substance and class of psychotropic prescriptions

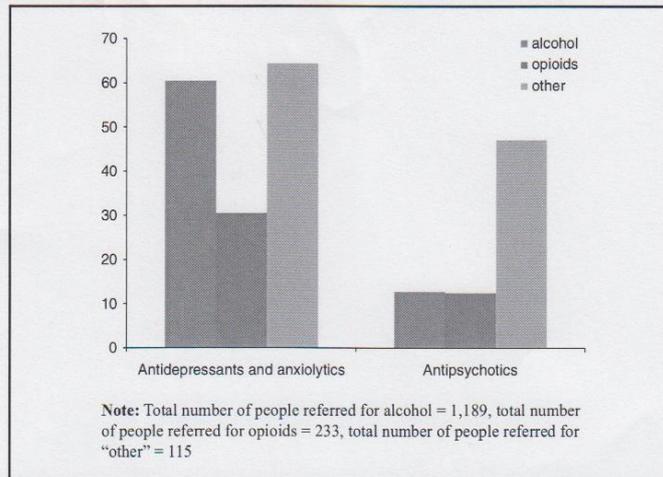
Figure 3 shows the proportion of different classes of psychotropic medications prescribed to people with different referral substances. People referred for "other" substances had the highest number of prescriptions (64.3 per cent) of antidepressants and anxiolytics compared to the remaining two groups ( $p < 0.0005$ ). Similarly, those referred for "other" substances had the highest number of antipsychotic prescriptions ( $p < 0.0005$ ). People referred for alcohol and "other" substances were approximately two times more likely to be on antidepressants and anxiolytics compared to those referred for their opioid use. In addition, those referred for "other" substances were almost four times more likely to be on antipsychotics compared to the other two groups and almost half (47 per cent) of the "other" group were on antipsychotics.

#### Discussion

##### Prescribing of antidepressants and anxiolytics

In our study, almost six out of every ten people (56.1 per cent) newly referred to the LAU for their first episode of treatment between August 2007 and July 2010 were taking prescribed antidepressants and anxiolytics. This is higher than the estimated prevalence of severe depressive and anxiety disorders among treatment populations of people with SUD found by Weaver and colleagues and greatly exceeds the prevalence of these disorders in the UK general population (Weaver *et al.*, 2003; McManus *et al.*, 2009). The adult psychiatric morbidity survey (APMS) carried out in 2007 found that 7.5 per cent of the UK population had symptoms of depressive and anxiety disorders that may require treatment (McManus *et al.*, 2009). Furthermore, the prevalence of antidepressants and anxiolytics in this study exceeds that found

**Figure 3** A comparison of the percentage of different classes of psychotropic medications prescribed to LAU people based on their primary referral substance



in primary care settings in the UK. A study of 12 general practices in England found that 10.1 per cent of patients were prescribed an antidepressant or anxiolytic within a year period (Chan *et al.*, 2006). Another study that examined time trends in GP antidepressant prescribing for the population of Tayside in Scotland found that the prevalence of antidepressants increased from 8.0 per cent in 1995/1996 to 13.4 per cent in 2006/2007. However, this study did not include prescriptions of anxiolytics (Lockhart and Guthrie, 2011).

The observed difference in prescribing of antidepressants and anxiolytics between LAU people and the prevalence reported by Weaver and colleagues could have resulted because LAU people had a higher prevalence of co-morbid severe depressive and anxiety disorders. It is also probable that these medications were prescribed for other indications not examined in our study or that they were prescribed for symptoms mimicking mental disorders when, in fact, the symptoms were substance related. Intoxication and withdrawal symptoms of alcohol and other substances often resemble those of anxiety and depressive disorders and they can sometimes be severe, although resolving within two to four weeks of abstinence (Grant *et al.*, 2004; Raimo and Schuckit, 1998). The adverse consequences of substance misuse are likely to make people unhappy and this may mistakenly be diagnosed as a depressive disorder (Horwitz and Wakefield, 2007). Consequently, such depressive disorders may be unnecessarily treated with medications. Furthermore, antidepressants have only a modest benefit in people with co-morbid depressive and SUD (Nunes and Levin, 2004). There is therefore the possibility that prescribers, including GPs, have inappropriately prescribed antidepressants and anxiolytics to the people in this study. The extent to which this was the case could not be determined in the current study as we had no information on the original prescriber's clinical decision-making processes. However, the extent of this prescribing argues for more research on this issue and further consideration of prescribing practice in this group of people.

The time interval for a GP consultation (ten minutes) (NHS Employers, 2009) may be inadequate for an in-depth review of the clinical history of complex patients especially people with SUD and might potentially result in situations where GPs reach for the "quick" fix with medications. A recent study carried out in the USA found that antidepressants are increasingly being prescribed without evidence of psychiatric diagnoses with the proportion of such prescribing by non-psychiatrist physicians rising from 59.5 to 72.7 per cent between 1996 and 2007 (Mojtabai and Olfson, 2011).

### Prescribing of antipsychotics

Among the newly referred people attending the LAU, 15.2 per cent were prescribed antipsychotics. The percentage of LAU people prescribed antipsychotics is higher than the prevalence of psychosis reported by Weaver and colleagues and greatly exceeds the prevalence of psychotic disorders in the UK general population (Weaver *et al.*, 2003; McManus *et al.*, 2009). The APMS carried out in 2007 found the prevalence of psychotic disorders to be 0.4 per cent in the UK general population (McManus *et al.*, 2009). However, the definition of psychosis used in the APMS is different from that used in Weaver's study. Only the prevalence of schizophrenia, bipolar disorder and manic depression were assessed in the APMS. The prevalence of antipsychotics in this study exceeds that found in most UK primary care settings with the exception of specific patient groups such as elderly patients with dementia. Chan and colleagues found the prevalence of antipsychotic prescribing to be 0.8 per cent in 12 UK general practices within a year period whilst another study assessing psychotropic prescribing in elderly people (aged 65 years and older) with and without dementia in Scottish general practices found the prevalence of antipsychotic prescribing to be 17.7 and 1 per cent in those with and without dementia, respectively (Guthrie *et al.*, 2010; Chan *et al.*, 2006).

The observed difference in prescribing of antipsychotics and the prevalence of psychotic disorders reported by Weaver and colleagues may have resulted because people at the LAU had a higher prevalence of psychotic disorders. On the other hand, some antipsychotics are now licensed for some non-psychotic disorders such as refractory depression and anxiety disorders. NICE guidance recommends the addition of some atypical antipsychotics such as olanzapine, quetiapine and risperidone to antidepressants for the treatment of refractory depression (NICE, 2010). Furthermore, antipsychotics such as prochlorperazine are also licensed as antiemetics and adjuncts for short-term use in the management of severe anxiety disorders (Joint Formulary Committee, 2010).

Due to the limited documentation of diagnoses on the LAU database, it was not possible to determine the indications for the antipsychotic prescriptions. Excessive prescribing of antipsychotics could potentially expose people to serious adverse effects and sudden death (Straus *et al.*, 2004; Ucock and Gaebel, 2008). A recent meta-analysis found that SUD increase the risk of EPS among patients with schizophrenia (Potvin *et al.*, 2009).

People referred for "other" substances had the highest prevalence of antipsychotic prescribing. The "other" group included those mostly referred for cannabis (35 per cent) and stimulants (37 per cent). Previous studies have shown that increased cannabis and stimulant use are associated with psychotic symptoms (Fiorentini *et al.*, 2011; Van Os *et al.*, 2002). In spite of this, there is ongoing debate about the potential causal relationship between cannabis and schizophrenia due to issues arising from the presence of confounding factors such as the presence of psychosis before cannabis use (self-medication with cannabis), genotype, personality and genetic susceptibility to psychosis (Fergusson *et al.*, 2006; Macleod *et al.*, 2004).

### Study limitations

The limitations of this study include the fact that it was a retrospective study of routinely collected data and therefore there were quality issues relating to missing or inaccurate data. This study may consequently have underestimated the prescribing of psychotropic medications. Furthermore, we did not have adequate information required to understand the reasons behind prescribing. For instance, the reasons for prescribing were not documented for most of the prescriptions. Therefore, we could only describe the prescriptions of people without being able to state their corresponding indications. A recent study carried out by Ilyas and colleagues in the UK has emphasised the need for more research on the reasons and duration for prescribing of psychotropic medications (Ilyas and Moncrieff, 2012). Unfortunately, this study was unable to shed light on these aspects of prescribing. Our ongoing research in this field is designed to explore these issues further by exploring the appropriateness of prescriptions of psychotropic medications taken by people referred to the LAU.

This study showed that a large percentage of people with SUD are on psychotropic medications with consequent cost implications to the NHS. However, no economic analysis was carried out because it was not the focus of this study. Information needed for economic analysis such as whether the medication is generic or branded, dose and duration of prescription were not available on the LAU electronic database. The price the NHS pays for prescriptions often differs from those quoted in the BNF due to discounts offered by wholesalers and manufacturers as well as container and dispensing fees (NHS Business Services Authority, 2013). Besides the cost of medicines, there is the need for the inclusion of the cost of prescribing and dispensing in an economic analysis. However, this will require a different methodology which was not the focus of this study.

The prescriptions of people involved in this study were compared based on their primary referral substance in order to examine the patterns of prescribing. However, this represents a simplification of the use of substances. In reality, a substantial percentage of alcohol users also use other illicit drugs and vice versa (Grant *et al.*, 2004; Regier *et al.*, 1990).

The data for this study were self-reported and thus subject to response and recall bias. This study examined the prescriptions of newly referred people in a single addiction service and may not be representative of the prescriptions of newly referred people in other outpatient addiction services. To our knowledge, this is the first study that provides a description of psychotropic prescriptions taken by people with a range of SUD attending a specialist addiction service.

### Conclusion

This study found that significant proportions of newly referred people to the LAU were on prescribed psychotropic medications. The observed prevalence of prescribed psychotropic medications exceeds the reported prevalence of mental illnesses in people with SUD as well as the prevalence of psychotropic medications in most primary care populations. There is the possibility that some of the psychotropic medications were inappropriately prescribed. Inappropriate prescribing has cost implications which are not limited to the cost of medicines but includes the cost of prescribing, dispensing and rationalising prescription regimens. People with SUD are more likely to experience adverse consequences such as dependence, side effects and drug interactions resulting in overdose and mortality from psychotropic medications. The high prevalence of psychotropic prescribing argues for investigation of the appropriateness of these prescriptions and further consideration of prescribing practice in this group of people.

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# THE UNIVERSITY *of* York

## The Department of Health Sciences

### A study of the appropriateness of service users' prescriptions

#### INFORMATION SHEET FOR SERVICE USERS

We would like to invite you to take part in our research study on the prescriptions you are taking. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. We'd suggest this should take about 10 minutes.

#### **What is the purpose of the study?**

The purpose of this study is to assess whether your prescriptions are right for you. Prescribing for people who use alcohol and other drugs may sometimes not be right for them because they may receive too little or too much medications compared to other people. We will therefore be asking you what you think about your prescriptions and how you take them. We will also be asking prescribers what they think about your prescriptions.

#### **Why have I been invited to participate?**

You have been invited to participate in this study because you have been newly referred to the Leeds Addiction Unit (LAU) and are being assessed by a prescriber today. All newly referred service users being assessed by a prescriber will be invited to participate in this study.

#### **Do I have to take part?**

No, it is up to you to decide whether or not to join the study. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

#### **What will happen to me if I take part?**

If you decide to take part in this study, you will be given a questionnaire where you will be asked to write down all the prescriptions you are taking. With your consent, information concerning you and your health conditions will be extracted from your medical records in order for us to understand your situation better. If you indicate on the consent form that you are interested in being interviewed, we may want to interview you in three months' time for 30 to 60 mins during one of your LAU appointments in order to explore your feelings concerning your prescriptions and how this affects your sense of well-being. If this date is not suitable for you, we will try to find a more convenient date. In these circumstances, as it would not be your usual appointment date, we will be happy to reimburse your transport expenses.

#### **What are the risks of taking part?**

Participation in this study is highly unlikely to result in any physical risk to you. However, if you feel anxious or distressed talking about your prescriptions during the interview with the researcher,

the interview will be stopped and you would be asked if you would like to speak to one of the therapists at the LAU.

**Will my taking part in the study be kept confidential?**

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. All information which is collected about you during the course of the research will be kept strictly confidential. No one will be able to identify you from the study and we will not share the information you provide with anyone who is not a member of the research team. However, during the interview you may mention something which suggests you or others have been or is at risk of harm. If so, we would suggest sources of support, but may also have to inform the appropriate staff at the LAU after discussing this with you.

**What will happen if I don't want to carry on with this study?**

If you withdraw from the study, we will use the data collected up to your withdrawal.

**What if there is a problem?**

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions on 01132 952775 or oak501@york.ac.uk. If you remain unhappy and wish to complain formally, you can do this by contacting the NHS complaints procedure (0345 015 4033).

**What will happen to the results of the research study?**

The results will be written up in a thesis and published in journals and conferences. You will be sent a summary of the results of this study.

**Who is organising and funding the research?**

This study is being funded by the Collaboration for Leadership in Applied Health Research and Care (CLAHRC) and supported by the University of York. It is also being undertaken as a piece of student research towards the award of a Doctorate at the University of York.

**What will happen to the information I provide if I lose authority to consent?**

If you lose authority to consent, you will be withdrawn from the study but any data you gave prior to then will be used in this study.

**Where can I get further information concerning this study?**

You can get more information about this study by contacting the study's chief investigator (Obirenjeyi Kudehinbu-Oluyase). You can also contact the chief investigator if you decide to withdraw from the study through the following means:

Telephone: 01132 952775 (Monday, Tuesday and Thursday between 11am and 4.00pm)

Email: oak501@york.ac.uk. Thank you for taking the time to read this information sheet and considering whether to take part in this study.

# THE UNIVERSITY *of York*

The Department of Health Sciences

A study of the appropriateness of service users' prescriptions

## CONSENT FORM FOR SERVICE USERS

Name of Researcher: Obirenjeyi Kudehinbu-Oluyase

Please  
each  
initial  
box

1. I confirm that I have read and understand the information sheet dated 8<sup>th</sup> June 2012 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.
3. I understand that relevant sections of my medical records and data collected during the study, may be looked at by the research team, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.
4. I agree to be contacted by telephone and email for interview in this study.
5. I agree to my interview being audio-recorded.
6. I agree to direct quotes from me being used in the reports of this study.
7. I agree to being contacted in the future about the possibility of taking part in further research.
8. I agree to the data I provide for this study being used even if I lose capacity to consent in the future.
9. I agree to the Leeds Addiction Unit holding my consent form.
10. I agree to take part in the above study.

\_\_\_\_\_  
Name of patient

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Name of person taking consent

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

If you have any questions, please contact the chief investigator Obirenjeyi Kudehinbu-Oluyase on 01132 952775 or [oak501@york.ac.uk](mailto:oak501@york.ac.uk).

**Appendix 5.3: Medical/medication history form**

1. Date \_\_\_\_\_ 2. Patient ID# \_\_\_\_\_ 3. Evaluator ID# \_\_\_\_\_

4. Prescribed drugs taken

Medication	Dose	Frequency	Length of use	Reason for use	Who made diagnosis?	When?



# THE UNIVERSITY *of York*

## The Department of Health Sciences

### A study of the appropriateness of service users' prescriptions

#### INFORMATION SHEET FOR PRESCRIBERS

We would like to invite you to take part in our research study on the appropriateness of prescriptions for service users. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. We'd suggest this should take about 10 minutes.

#### **What is the purpose of the study?**

The purpose of this study is to assess the use and appropriateness of prescriptions of psychotropic medications such as antidepressants, antipsychotics, anxiolytics/hypnotics, antimanic agents, anticonvulsants, opioids (including substitute opioids) and medications used in treating substance dependence (disulfiram, acamprosate, lofexidine, bupropion and baclofen) for service users who are newly referred to the Leeds Addiction Unit (LAU). Prescribing for service users with substance use disorders (SUD) is a relatively unexplored area and the few studies available mostly examine prescribing appropriateness by assessing adherence to treatment guidelines relating to the adequacy of the duration of medication therapy and dosage. However, other important aspects of medication appropriateness such as the presence of drug interactions, unnecessary prescriptions and medication omissions (underutilisation), which are equally important, have been rarely considered despite their contribution to morbidity, adverse events and increased health care costs. Furthermore, the reasons for prescribing decisions among service users with SUD have not been well researched.

We would therefore wish to find out how you rate the appropriateness of the prescriptions of interest using the Medication Appropriateness Index (MAI) and the Assessment of Underutilisation of Medication (AOU) Index respectively. We would be interested in changes you make to service users prescriptions from their first assessment to their three month follow-up review and would be interviewing you to explore how you assess the appropriateness of service users' prescriptions towards the end of this study.

#### **Why have I been invited to participate?**

You have been invited to participate in this study because you are a medical prescriber at the Leeds Addiction Unit (LAU). All medical prescribers at the LAU will be invited to participate in this study.

#### **Do I have to take part?**

No, it is up to you to decide to join the study. If you agree to take part, we will then ask you to sign two consent forms, out of which one will be given to you to keep. You are free to withdraw at any time, without giving a reason.

#### **What will happen if I decide to take part?**

If you decide to take part in this study you will be administered a demographics questionnaire where you will fill in your demographic information. You will be given the AOU to assess omission (underutilisation) of the prescriptions of interest during service users' first assessment whilst you will be given the MAI to assess the appropriateness of the prescriptions of interest during service users' first assessment and three month follow-up review. This study will last for six months. You will be interviewed for 30 to 60mins towards the end of the study (at six months) to explore how you assess prescribing appropriateness.

#### **Will my taking part in the study be kept confidential?**

Yes. We will follow ethical and legal practice and all information we obtain from you will be handled in confidence. All information which is obtained from you during the course of the research will be kept strictly confidential. No one will be able to identify you from the study and we will not share the information you provide with anyone who is not a member of the research team.

**What will happen if I don't want to carry on with this study?**

If you withdraw from the study, we will use the data collected up to your withdrawal.

**What will happen to the results of the research study?**

The results of this study will be written as a PhD thesis, published in journals and presented in conferences. We would also feedback the results to you. The results of this study should be published by 2013.

**Who is organising and funding the research?**

This study is being funded by the Collaboration for Leadership in Applied Health Research and Care (CLAHRC) and supported by the University of York. It is also being undertaken as a piece of student research towards the award of a Doctorate in the Department of Health Sciences at the University of York.

**What will happen to the information I provide if I lose authority to consent?**

If you lose authority to consent, you will be withdrawn from the study but any data you gave prior to then will be used in this study.

**Where can I get further information concerning this study?**

You can get more information about this study by contacting the study's chief investigator (Obirenjeyi Kudehinbu-Oluyase). You can also contact the chief investigator if you decide to withdraw from the study through the following means:

Telephone: 01132 952775 (Monday, Tuesday and Thursday between 11am and 4.00pm)

Email: [oak501@york.ac.uk](mailto:oak501@york.ac.uk)

Thank you for taking the time to read this information sheet and considering whether to take part in this study.

# THE UNIVERSITY *of York*

**The Department of Health Sciences**

**A study of the appropriateness of service users' prescriptions**

## CONSENT FORM FOR PRESCRIBERS

Name of Researcher: Obirenjeyi Kudehinbu-Oluyase

Please  
initial  
each  
box

- |   |   |
|---|---|
| 1. I confirm that I have read and understand the information sheet dated 8 <sup>th</sup> June 2012 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.                                 | <input style="width: 40px; height: 20px;" type="checkbox"/> |
| 2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my legal rights being affected.  | <input style="width: 40px; height: 20px;" type="checkbox"/> |
| 3. I understand that relevant sections of data collected from me during the study, may be looked at by individuals from the research team, where it is relevant to my taking part in this research. I give permission for these individuals to have access to these data. | <input style="width: 40px; height: 20px;" type="checkbox"/> |
| 4. I agree to my interview being audio-recorded.  | <input style="width: 40px; height: 20px;" type="checkbox"/> |
| 5. I agree to direct quotes from me being used in the reports of this study.  | <input style="width: 40px; height: 20px;" type="checkbox"/> |
| 6. I agree to the data I provide for this study being used even if I lose capacity to consent in the future.  | <input style="width: 40px; height: 20px;" type="checkbox"/> |
| 7. I agree to the Leeds Addiction Unit holding my consent form.   | <input style="width: 40px; height: 20px;" type="checkbox"/> |
| 8. I agree to take part in the above study.   | <input style="width: 40px; height: 20px;" type="checkbox"/> |

Name of patient	Date	Signature
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Name of person taking consent	Date	Signature
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If you have any questions, please contact the chief investigator Obirenjeyi Kudehinbu-Oluyase on 01132 952775 or oak501@york.ac.uk.

### Appendix 5.7: Demographic information questionnaire for prescribers

1. Name: \_\_\_\_\_
2. Age (years): \_\_\_\_\_
3. What is your sex? (Please tick one box)    Male        Female
4. How do you describe your ethnicity? (Please check the one that applies to you)

<input type="checkbox"/> White British	<input type="checkbox"/> Other	<input type="checkbox"/> African
<input type="checkbox"/> White Irish	<input type="checkbox"/> Indian	<input type="checkbox"/> Other Black
<input type="checkbox"/> Other white	<input type="checkbox"/> Pakistani	<input type="checkbox"/> Chinese
<input type="checkbox"/> White and Black Caribbean	<input type="checkbox"/> Bangladeshi	<input type="checkbox"/> Other
<input type="checkbox"/> White and Black African	<input type="checkbox"/> Other Asian	<input type="checkbox"/> Prefer not to say
<input type="checkbox"/> White and Asian	<input type="checkbox"/> Caribbean	
5. What is your current position? (Please check the one that applies to you)

<input type="checkbox"/> Nurse prescriber
<input type="checkbox"/> Senior House Officer
<input type="checkbox"/> Registrar
<input type="checkbox"/> Consultant
6. What year did you qualify as a prescriber? \_\_\_\_\_
7. How many years have you practiced for? \_\_\_\_\_

Thank you for taking the time to complete this questionnaire

## Appendix 5.8: The Medication Appropriateness Index

Patient ID# \_\_\_\_\_ Evaluator \_\_\_\_\_ Date \_\_\_\_\_

Drug Code \_\_\_\_\_ Drug \_\_\_\_\_

To assess the appropriateness of the drug, please answer the following questions and circle the applicable rating:

- |   |                            |         |                           |         |
|---|----------------------------|---------|---------------------------|---------|
| 1. Is there an indication for the drug?   | A _____<br>Indicated       | B _____ | C _____<br>Not Indicated  | Z<br>DK |
| Comments:   |                            |         |                           |         |
| 2. Is the medication effective for the condition?                                     | A _____                    | B _____ | C _____                   | Z<br>DK |
| Comments:   |                            |         |                           |         |
| 3. Is the dosage correct?   | A _____<br>Correct         | B _____ | C+ or C-<br>Incorrect     | Z<br>DK |
| Comments:   |                            |         |                           |         |
| 4. Are the directions correct?  | A _____<br>Correct         | B _____ | C _____<br>Incorrect      | Z<br>DK |
| Comments:   |                            |         |                           |         |
| 5. Are the directions practical?  | A _____<br>Practical       | B _____ | C _____<br>Impractical    | Z<br>DK |
| Comments:   |                            |         |                           |         |
| 6. Are there clinically significant drug-drug interactions?                           | A _____<br>Insignificant   | B _____ | C _____<br>Significant    | Z<br>DK |
| Comments:   |                            |         |                           |         |
| 7. Are there clinically significant drug-disease/condition interactions?              | A _____<br>Insignificant   | B _____ | C _____<br>Significant    | Z<br>DK |
| Comments:   |                            |         |                           |         |
| 8. Is there unnecessary duplication with other drug(s)?                               | A _____<br>Necessary       | B _____ | C _____<br>Unnecessary    | Z<br>DK |
| Comments:   |                            |         |                           |         |
| 9. Is the duration of therapy acceptable?   | A _____<br>Acceptable      | B _____ | C _____<br>Not acceptable | Z<br>DK |
| Comments:   |                            |         |                           |         |
| 10. Is this drug the least expensive alternative compared to others of equal utility? | A _____<br>Least expensive | B _____ | C _____<br>Most expensive | Z<br>DK |
| Comments:   |                            |         |                           |         |

### USE OF THE MEDICATION APPROPRIATENESS INDEX (MAI)

For further information/articles using the MAI address inquiries to Joseph T. Hanlon, PharmD, MS, Department of Medicine (Geriatrics), Pharmacy and Therapeutics, and Epidemiology, University of Pittsburgh and Health Scientist, Center for Health Equity Research and Promotion (CHERP) and Geriatric Research Education and Clinical Center (GRECC) VA Pittsburgh Healthcare System, Kaufmann Medical Building-Suite 514, 3471 5<sup>th</sup> Ave, Pittsburgh, PA 15213, Tel#- 412-692-2360, Fax#- 412-692-2370, Email: jth14@pitt.edu

- A. General Instructions (See Hanlon JT, Schmader KE, et al. J Clin Epidemiol 1992;45:1045, and Fitzgerald LS, Hanlon JT, et al. Ann Pharmacother 1997;31:543-8).

This instrument is intended for the evaluation of the appropriateness of medications prescribed by a health care provider. It may also be used to evaluate self-medication practices by patients. It requires, at a minimum, that a medical history problem list and medication list is available for review. Medication history information obtained from patients can be helpful in applying the MAI. Before evaluation, review the case information available and medication profile for each patient. It is important that clinical judgment must be applied in regards to patient's preference, and life expectancy. Complete the scale for each regularly scheduled active medication. The MAI can be used to assess the use of "prn" or as needed medication used frequently. Each question in the scale pertains to the individual patient and drug in question. Read each question carefully and circle the score (A, B, C or Z) that represents your assessment. If you do not understand the question, consult the specific instructions below for clarification. If you do not know the answer to the question, consult a standard medication text or software such as the AHFS Drug Information, Drug Facts and Comparisons, Micromedex, Clinical Pharmacology (an electronic drug reference and teaching guide), or UpToDate®, unless the specific instructions for the question indicates an alternative source. At times, you may require additional information from the patient's chart to answer a question. In that case, circle Z and specify the necessary information in the comments section. Some regimens contain combination drugs. If the individual components are available and used as single entities, then complete the scale for each individual drug. Finally, please note your reasons for any rating of B or C in the comments section.

B. Scoring A summated MAI score per drug can be calculated by the application of weights. (see Samsa G, Hanlon JT, Schmader KE, et al. A summated score for the Medication Appropriateness Index: development and assessment of clinimetric properties including content validity. *J Clin Epidemiol* 1994;47:891-6). For items coded as inappropriate ("C"), apply the following weights for individual criterion as follows:

<u>Criterion</u>	<u>Relative Weight Applied to Inappropriate Ratings</u>
Is there an indication for the drug?	3
Is the medication effective for the condition?	3
Is the dosage correct?	2
Are the directions correct?	2
Are there clinically significant drug-drug interactions?	2
Are there clinically significant drug-disease interactions?	2
Are the directions practical?	1
Is this drug the least expensive alternative compared to others of equal utility?	1
Is there unnecessary duplication with other drugs?	1
Is the duration of therapy acceptable?	1

To calculate a weighted MAI score per patient, sum MAI scores for each drug in patients' regimens [see Schmader K, Hanlon JT, et al. *J Am Geriatr Soc* 1994;42:1241 and Hanlon JT, Weinberger M., et al. *Am J Med* 1996;100:428-37.; Schmader KE, Hanlon JT, Pieper CF, Sloane R, Ruby CM, Twersky J, Dove-Francis S, Branch LG, Lindblad CI, Artz M, Weinberger M, Feussner JR, Cohen HJ. Effectiveness of geriatric evaluation and management on adverse drug reactions and suboptimal prescribing in the frail elderly. *Am J Med* 2004].

### C. Other measures that can be used to assess suboptimal prescribing

(see Dimitrow MS, Airaksinen MS, Kivelä SL, Lyles A, Leikola SN Comparison of prescribing criteria to evaluate the appropriateness of drug treatment in individuals aged 65 and older: a systematic review. *J Am Geriatr Soc* 2011;59:1521-30.)

To assess unnecessary use of medications (i.e., polypharmacy), one may use combined MAI ratings from questions 1, 2, and 8 (see Hajjar ER, Hanlon JT, Sloane RJ, Lindblad CI, Pieper CF; Ruby CM, Branch LC, Schmader KE. Unnecessary drug use in the frail elderly at hospital discharge. *J Am Geriatr Soc* 2005;53:S178.)

To assess the underuse of medication consider the use of implicit measure (Assessment of Underutilization (AOU) of Medication (Wright RM, Sloane RJ, Pieper CF, Ruby-Scelsi CM, Twersky J, Schmader KE, Hanlon JT. Underuse of indicated medications among physically frail older US veterans at the time of hospital discharge. *Am J Geriatr Pharmacother* 2009;7:271-280) or alternatively the use of explicit criteria (e.g., Barry PJ, Gallagher P, Ryan C, et al. START (screening tool to alert doctors to the right treatment)—an evidence-based screening tool to detect prescribing omissions in elderly patients. *Age and Ageing* 2007;36:632-638).

D. Specific Instructions For Rating

**Question 1:** Is there an indication for the drug?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
indicated marginally indicated not indicated do not know

*Definition:* Indication is defined as the sign, symptom, disease, or condition for which the medication is prescribed. The question assesses whether there is sufficient reason for the use of the drug. Sufficient reason includes not only curative and palliative therapy but also preventive therapy for a disease, condition or drug effect.

*Instructions:* A drug is not indicated if no condition exists for its use. Answer the question with the conditions found in the problem list. If score = C, then questions 9 and 10 are scored C.

*Examples:* Hydrochlorothiazide (HCTZ) is prescribed and hypertension is recorded on the problem list = A (indicated). Olanzapine is prescribed and psychosis, schizophrenia, etc. is not documented = C (not indicated). KCl for prevention of hypokalemia in the setting of digoxin and diuretic use = A. Isoniazid and positive PPD plus immunosuppressive condition = A. KCl and diuretics alone, no hypokalemia = C.

**Question 2:** Is the medication effective for the condition?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
effective marginally effective ineffective do not know

*Definition:* Effective is defined as producing a beneficial result. The question assesses whether the drug prescribed is capable of being effective for the indication in a population of patients.

*Instructions:* Indication and effectiveness are tightly but not perfectly linked items. Physicians may prescribe a drug for a given condition because of theoretical and standard practice reasons (indication) but investigators may demonstrate in clinical trials that the drug is ineffective (hydergine and memory enhancement). Conversely, an indication may not be documented for a drug yet the drug may work well for the intended effect (KCl and diuretics). In those cases, the reviewer must note the assumed indication in the comments. In addition, any drug considered by the FDA to be “less than effective” and appears on the DESI list (<http://www.cms.hhs.gov/medicaid/drugs/drug11.asp>) should be rated as ineffective (“C”). Also drugs in which the potential risks outweigh the potential benefits, and thus are incapable of being effective in actual practice should be rated as ineffective (“C”). For example, those classified by as high risk drugs by AGS 2012 Bers Criteria should be rated as ineffective (“C”). The exception would be the use of drugs from this list that are essential medications for use in palliative care (see De Lima L. International Association for Hospice and Palliative Care list of essential medicines for palliative care. *Ann Oncol.* 2007;18:395-9). Also in patients with limited life expectancy and medication takes a longer period of time to reap the benefits then should be rated as ineffective (“C”).

*Examples:* HCTZ for hypertension = A. H2 antagonist prophylaxis in a person with a history of NSAID induced gastric ulcer = C, Meperidine (Demerol<sup>®</sup>) for pain = C. Statin newly prescribed for LDL >130mg/dl in patient with expected life expectancy (Life expectancy can be estimated using the National Vital Statistics Reports United States Life Tables 2007;56(9) ([http://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56\\_09.pdf](http://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56_09.pdf)) is less than 1 year= C (takes 1- 2 years for statin to be effective).

**Question 3:** Is the dosage correct?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
correct marginally correct incorrect do not know

*Definition:* Dosage is defined as the total amount of medication taken per 24-hour period for regularly scheduled medications.

*Instructions:* Amounts within the dosage range for initial and maintenance therapy noted in the specified texts are correct. Other sources may specify newer, more appropriate therapeutic class specific ranges (e.g., ACCP consensus conference on antithrombotic therapy) or specific geriatric dosage ranges (e.g., APhA Geriatric Drug Dosage Handbook). These ranges should supersede the standard texts as long as the reference is given. Hence, one should take into account known age-related changes in drug pharmacokinetics and pharmacodynamics. Some patients may have drug labs/levels/Vs. If dosage is too low then circling “C-” else if too high then circle “C+”. In summary, a dosage is incorrect if it is outside the accepted geriatrics dose range; if there is no accepted geriatrics dose range, then to be incorrect it must be outside the standard range. A dosage may also be incorrect if not adjusted for renal insufficiency, drug levels and laboratory or vital signs outcomes. For drugs being tapered to be discontinued, (e.g., anticonvulsants) low dosage and/or low levels will be considered correct.

*Examples:* Glyburide in patient with estimated creatine clearncs=42ml/min - incorrect due to decreased renal clearance of drug in the elderly. Captopril for CHF given in dosage range of 6.25mg bid to 37.5 mg bid = A. Furosemide 20-40 mg a day for hypertension = B. Full dose Ranitidine 150mg bid for PUD greater than 8 weeks = C+ since maintenance therapy dose is 150 qhs. Lovastatin at highest end of usual dosage range with still elevated cholesterol = B since necessary and will need to add additional therapy. Patient with chronic cancer pain and only on 4 gms of acetaminophen in divided doses and still rates pain as moderate to severe = B since necessary and will need to add additional therapy. Warfarin 1mg/day for mechanical valve and INR to =1.2= C- ; Warfarin 5mg/7.5 mg alternating every other day for atrial fibrillation with INR = 2.8 = A. Although lab value above “normal range”, since in therapeutic range of 2.0-3.0 for this anticoagulation indication, dosage is correct.

**Question 4:** Are the directions correct?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
 correct marginally correct incorrect do not know

*Definition:* Directions are defined as the instructions in the use of a medication by a patient. The question assesses the route of administration, relationship to food and liquid, the schedule and time of the day.

*Instructions:* The directions are incorrect when they specify the wrong route of administration, give wrong or no instructions regarding food and liquid (when specific directions regarding relationship to food or liquid exist), specify the wrong schedule or the wrong time of day (when specific directions regarding relationship to schedule and time of day exist). See appendix IV listing of medications with food and fluid requirements, schedule/time of day requirements and those medications that should not be taken with grapefruit juice (Mertens-Talcott SU, et al. grapefruit-drug interactions: can interactions with drugs be avoided?. J Clin Pharmacol 2006; 46(12):1390-416). For new drugs consult the latest edition of the Drugs, Supplements, and Herbal Information at <http://www.nlm.nih.gov/medlineplus/druginformation.html>. For information regarding meds that can't be crushed and given via enteral tube, see <http://www.ismp.org/tools/donotcrush.pdf> update. When possible, examine nurses medication administration records and/or administration time schedules to determine time of administration in relationship to meals. When MAI is used to evaluate patients that are in institutional care settings, route, food liquid, schedule and time of day requirements do not apply. If patient goes from institutional to ambulatory care settings, for consistency purposes application may be limited to only medications requiring a specific schedule/ time of day.

*Examples:* Captopril 25mg tid =C (incorrect) - should be taken on an empty stomach; glipizide 10mg one qd = C (incorrect) - should specify before breakfast; Ibuprofen 400mg one tid with meals and hs with snack = A (correct). Nifedipine XL 60 mg qd is (A). Quinine one qd is incorrect (C), should specify take at bedtime. Furosemide one q day = C (should specify q AM). K-Dur and no directions regarding food/liquid = C. Nitropaste 1" qid = C (must specify nitrate-free interval). Patient taking Nifedipine XL 60 mg qd with 8oz of grapefruit at breakfast=C

**Question 5:** Are the directions practical?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
 practical marginally practical impractical do not know

*Definition:* Practical is defined as capable of being used or being put into practice. This question assesses whether the directions for use are practical for the patient to take or nurse to administer and take into consideration the potential for patient compliance without sacrificing efficacy. When applicable, consideration of what drugs are available on formulary should be made.

*Instructions:* A drug schedule is considered impractical if the drug can be administered less frequently and still maintain efficacy. Irregular day-to-day schedules that have more regular alternatives are also impractical. In addition, medications specified to be given around the clock on a fixed qxhours when a more flexible schedule is sufficient is impractical.

*Examples:* Coumadin 5mg qd except Tuesday and Sunday 10mg qd - impractical (C) when 6mg qd is easier; Glipizide 5mg bid is impractical (C) when 10mg qam is equally effective - Trazodone 75mg qhs - practical (A) since once daily and can cue into bedtime routine. Nifedipine 10mg tid is impractical (C) since equally effective alternative, Nifedipine XL 30mg qd, is simpler to administer. Albuterol MDI 2 puffs q6h-impractical(C) since qid is sufficient.

**Question 6:** Are there clinically significant drug-drug interactions?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
 insignificant marginally insignificant significant do not know

*Definition:* A drug-drug interaction is defined as the effect that the administration of one medication has on another drug. Clinical significance connotes a harmful interaction. This question assesses whether the drug in question interacts with another drug in the patient's regimen by affecting its pharmacokinetics (i.e., absorption, distribution, metabolism and excretion) or pharmacodynamics (i.e., the effect that it has on the body).

*Instructions:* A drug interactions text, such as Hansten's Drug Interactions and Updates, or software program (e.g. Micromedex, UpToDate® etc.) or specific articles (Malone DC, Abarca J, Hansten PD, Grizzle AJ, Armstrong EP, van Bergen RC, Duncan-Edgar BS, Solomon SL, Lipton RB. Identification of serious drug drug interactions: results of the partnership to prevent drug-drug Interactions. J Am Pharm Assoc 2004;44: 142-151 or specific CMS guidelines for nursing homes) will serve as the reference for significant interactions. If no interaction exists, then an A rating is automatic. A "B" rating will be given when the reference/program indicates an interaction but no clinical evidence exists for toxicity or adverse effect. If the reference/program indicates an interaction and sufficient clinical information is available and evidence of toxicity or adverse effect (including lack of effect) does exist, then the interaction is significant ("C"). If the reference/program indicates an interaction and clinical information is not available, then the interaction may also be considered significant ("C"). The drug that causes the change in pharmacokinetics or pharmacodynamics examples is the one that merits the C rating.

*Examples:* Significant pharmacokinetic interaction - Cimetidine added to warfarin in a patient with a prolonged PT or signs of bleeding="C". Significant pharmacodynamic interaction a tricyclic antidepressant or an opioid added to a benzodiazepine, two CNS drugs can result in a patient having increased falls or confusion=C. In the absence of sufficient clinical information, patient is taking digoxin and is now started on verapamil and no reduction in digoxin dose="C for quinidine ". NSAID (e.g., naproxen) for osteoarthritis started on a patient taking warfarin chronically for atrial fibrillation=C (since increases risk of bleeding).

**Question 7:** Are there clinically significant drug-disease/condition interactions?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
insignificant marginally insignificant significant do not know

*Definition:* Drug-disease interaction is defined as the effect that the drug has on a pre-existing disease or condition. Clinical significance connotes a harmful interaction. This question assesses whether the drug in question may be worsening the patient's disease or condition. A previous history of an idiosyncratic allergic reaction to a drug (e.g., penicillin, sulfa drugs, etc) is considered a preexisting condition. Specific disease states and specific drugs or drug classes constitute drug-disease interactions determined to be clinically significant by consensus of a clinical panels

*Instructions:* Information about drug-disease interactions is listed in the precautions or contraindications sections of the above specified texts/software. If no interaction exists according to the references, then an "A" rating is automatic. If the drug is contraindicated or highly risky ("extreme caution") for a patient condition, then the drug-disease is significant (C). Appendix IV lists drug-disease interactions to avoid based on a consensus survey of a panel of health care professionals. If a drug-disease combination is listed then the drug receives a C, otherwise the drug receives an A. If the drug needs routine caution ("warning, precaution") in the setting of a patient condition and the patient shows clinical evidence of disease worsening following the prescription of the drug, then the drug-disease interaction is also significant (C). If the references indicate an interaction ("warning, precaution") and the patient shows no evidence of disease worsening, then the rating is marginal (B).

*Examples:* Non-aspirin, non-COX2 NSAIDs in a patient with recent history of PUD and no PPI=(C) significant; High anticholinergic Tricyclic antidepressants (i.e., doxepin, amitriptyline, imipramine) started in patient with LUTs=C; Dicloxacillin prescribed for someone with a previous history of rash with penicillin=C (clinically significant). Codeine prescribed for someone with a previous history of gastrointestinal distress=B.

**Question 8:** Is there unnecessary duplication with other drug(s)?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
necessary marginally necessary unnecessary do not know

*Definition:* Unnecessary duplication is defined as nonbeneficial or risky copying of drug(s). Unnecessary duplication exists when two drugs from the same chemical or pharmacological class are prescribed simultaneously.

Instructions: The VA Medication Classification System will be utilized on VA PBM website. The evaluator will look up the generic names of all regularly scheduled medications in the index to determine the class of each individual drug. Then the evaluator will refer to Appendix V to see if modifications need to be considered in the evaluation. In general, 2 drugs from the same subclass of the major therapeutic classifications will be considered unnecessary duplication. In some instances, all subclasses (sedative/hypnotics) will be considered as one class. In some cases, the subclasses are broken down into more discrete categories (i.e., antihypertensives, other). If two (or more) drugs from the same class are prescribed simultaneously and the order in which prescribed cannot be determined then they are unnecessarily duplicated. If the order of prescribing is known, then the last drug added receives a C and the other drug receives a B. If the order of prescribing is not known, then randomly pick one drug to receive a C and the other to receive a B.

*Examples:* Same pharmacologic class - ranitidine added to a regimen with cimetidine then ranitidine receives a C. Flurazepam 15mg qhs and Diazepam 5mg tid then flurazepam randomly picked and receives a C. Cimetidine and sucralfate prescribed simultaneously for peptic ulcer disease, randomly assign one drug to receive a C and the other to receive a B.

**Question 9:** Is the duration of therapy acceptable?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
 acceptable marginally acceptable unacceptable do not know

*Definition:* Duration is defined as the length of therapy. This question assesses whether the length of time that the patient has received the drug is acceptable.

*Instructions:* If the duration of therapy is outside the information source specified range, then the length is unacceptable. If it is within the range or no data exists to make a clear decision, then the length is marginally or fully acceptable. Other sources, which may include the medical record, may specify newer, more acceptable durations of therapy, especially in geriatric conditions. Those sources supersede the specified texts if the reference is available. In general, for a chronic condition, a prolonged duration of therapy will be acceptable.

*Examples:* Haloperidol in a patient with dementia for 1 year and no psychotic features = C. Digoxin in a patient with remote history of CHF and in NSR - marginally acceptable (B); INH prophylaxis for 12 months in recent skin test converter – acceptable (A). 10 to 14 day course of ampicillin for urinary tract infection - acceptable (A); 12 months of nitrofurantoin in patient with indwelling urinary catheter - unacceptable (C). If drug is not indicated (question 1), then duration = C.

**Question 10:** Is this drug the least expensive alternative compared to others of equal utility?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
 less expensive equally expensive more expensive do not know

*Definition:* This question assesses how the cost of the drug compares to other agents of equal efficacy and safety.

*Instructions:* A drug is more expensive if it costs more (at least 10%) than the average cost/charge of alternatives of equal utility. Alternatives should be considered as medications within the same therapeutic class (see question 8 for definition). To operationalize, evaluator can use the local institutional setting prices (e.g., cost per month or per day supply or cost per dose) as their standard. If site-specific cost data is not available for assessment, evaluators are encouraged to utilize the Redbook AWP prices or cost index in Drug Facts and Comparisons as their standard.

*Examples:* Ciprofloxacin for an *E. coli* UTI that was sensitive to Ampicillin - more expensive = C; Lactulose for constipation before trying psyllium - more expensive =C; Morphine SR in hospice patient is rated A, although may be more expensive than IR form it is more convenient and preferred by patient and therefore demonstrates greater utility. If drug is not indicated (question 1), then expense = C.

### Appendix 5.9: UK-Medication Appropriateness Index

1. Is the drug indicated?	<b>A</b> Indicated	<b>B</b> Possible indication	<b>C</b> Not Indicated
2. Is it (the drug) effective for the condition?	<b>A</b> Effective	<b>B</b> Marginally effective	<b>C</b> Ineffective
3. Is the dosage correct?	<b>A</b> Correct (dosage)	<b>B</b> Adequate but not ideal	<b>C</b> Incorrect (dosage)
4. Are the directions correct?	<b>A</b> Correct (direction)	<b>B</b> Adequate but not ideal	<b>C</b> Incorrect (direction)
5. Are the directions practical, clear and unambiguous for this patient?	<b>A</b> Practical	<b>B</b> Scope for improvement	<b>C</b> Impractical
6. Are there clinically significant drug-drug interactions?	<b>A</b> No significant (drug to drug interaction)	<b>B</b> Marginally significant	<b>C</b> Significant (drug to drug interaction)
7. Are there any clinically significant drug-disease/condition interactions?	<b>A</b> No significant (drug disease interaction)	<b>B</b> Marginally significant	<b>C</b> Significant (drug disease interaction)
8. Is there unnecessary duplication with other drug(s)?	<b>A</b> No duplication	<b>B</b> Duplication with possible justification	<b>C</b> Unnecessary duplication
9. Is the duration of therapy acceptable?	<b>A</b> Acceptable duration	<b>B</b> Questionable duration	<b>C</b> Unacceptable duration
10. Is the drug you are assessing less expensive than alternative drugs of equal efficacy? - using the BNF	<b>A</b> Less expensive	<b>B</b> Equally Expensive	<b>C</b> More Expensive

#### USE OF THE UK-MEDICATION APPROPRIATENESS INDEX

This instrument is intended for the evaluation of medications prescribed normally in a primary care setting. It requires, at a minimum, that *a medical history problem list and medication list is available for review*. Before evaluation, review the case information available and medication profile for each patient and

complete the scale for *each regularly scheduled active medication*. Each question relates to the individual patient and drug in question. For each item please follow the specific instructions below. Read each question carefully and circle the score (A, B or C) that represents your assessment. ONLY CIRCLE ONE SCORE. If you do not know the answer to a question then the following are recommended texts:

- BNF
- Stockley's Drug Interactions (Pharmaceutical press ISBN 0853695040 October 2002, Edition 6)

Some regimens contain combination drugs. These are scored as single items, considering the properties of all constituents in turn. Finally, *please note your reasons for any rating of B or C in the comment section of each case study.*

### Specific Instructions For Rating:

#### Question 1:

A \_\_\_\_\_ B \_\_\_\_\_ C  
 Indicated                      Possible indication                      Not indicated

#### *Definition:*

This is defined as there being an adequate indication for the use of this drug in one of the problems present at the time when it was prescribed. Indication is defined as the sign, symptom, disease, or condition for which the medication is prescribed. The question assesses whether there is sufficient reason for the use of the drug. Sufficient reason can also include preventative therapy as well as curative or palliative.

#### *Instructions:*

Answer this question based purely upon the information presented. If there is a clear indication presented in either the problem list, clinical history or information from hospital letters then = (A).

If the drug is only possibly indicated by the information presented then = (B). Do not base your judgement on the list of drugs prescribed, this alone is not evidence of an indication. Other evidence must be presented to support an indication either in the problem list, clinical history, information from hospital letters or test results.

If there is no information to support an indication other than the fact that the drug has been prescribed then = (C).

#### Example:

Bendrofluazide 2.5mg is prescribed and hypertension is documented = (A).

The patient is prescribed bendrofluazide 2.5mg with no history or a diagnosis of hypertension, but there is repeated blood pressure reading such as 170/90, 160/92 = (B).

Haloperidol is prescribed but there is no evidence of psychosis, schizophrenia, movement disorder, etc., and no further information to suggest a relevant condition then = (C).

#### Question 2:

A \_\_\_\_\_ B \_\_\_\_\_ C  
 Effective                      Marginally effective                      Ineffective

#### *Definition:*

Effective refers to evidence of efficacy in this population. It is defined as producing a beneficial result. The question assesses whether the drug prescribed is capable of being effective for a given indication which is listed in the patient's problem list, clinical history, information from hospital letters or test results

#### *Instructions:*

Indication and effectiveness are tightly but not perfectly linked items. Assessors should evaluate each drug for clinical effectiveness based on the actual or assumed indication\*. Effectiveness may also be based on a risk to benefit assessment of each drug.

*\*Note:* If there is no indication for the drug in question the assessor may be forced to infer / assume an indication from the list of drugs. However, if you are forced to make any inferences or assumptions in order to answer this item then you must record these in the comments section, together with reasons to support these inferences / assumptions. For example, a patient may have been prescribed insulin but no indication is

listed. In this case you may be forced to assume that the patient has diabetes mellitus in order to say whether the drug is effective for that condition.

*Example:*

A drug should generally be scored as (A) 'Effective' when there are guidelines for its use in relation to the actual or assumed indication and where it is prescribed within the boundaries of these guidelines. Evidence should also exist to support a beneficial treatment effect. Example: Guidelines and evidence exist to support the use and clinical efficacy of Diazepam for the treatment of short term anxiety, an indication which is documented in the patients records. Therefore Diazepam scored (A) Effective.

A drug should be scored as (B) 'Marginally effective' when there are guidelines for its use in relation to to the actual or assumed indication although evidence suggests a suboptimal treatment effect, or guidelines state it is not the drug of first choice. This perhaps could be drugs which are marked in the BNF as .

A drug should be scored as (C) 'Ineffective' if there are no guidelines for its use in relation to the actual or assumed indication, if it is prescribed beyond the boundaries of any guidelines which do exist or if evidence suggests that no beneficial treatment effect is likely to be obtained. Example: Guidelines support the use of Diazepam for the treatment of anxiety over a short period. However long term use is cautioned against. The patients' records presented indicate a prolonged history of anxiety. Therefore Diazepam scored as either (B) Marginally Effective or (C) Ineffective. Another example of this is co-danthramer in an elderly patient who perhaps has constipation due to a cardiovascular accident( CVA) only. Co-danthramer in this case would be prescribed out of the current guidelines and score (C).

**Question 3:**

A \_\_\_\_\_ B \_\_\_\_\_ C  
Correct (dosage) Adequate but not ideal Incorrect (dosage)

*Definition:*

Dosage is defined as the total amount of medication taken per 24-hour period (or longer, if appropriate) for regularly scheduled medication.

*\*Note:* If there is no indication for the drug in question the assessor may be forced to infer / assume an indication from the list of drugs. However, if you are forced to make any inferences or assumptions in order to answer this item then you must record these in the comments section, providing in addition the question number and reasons to support these inferences / assumptions. For example, a patient may have been prescribed Lustral® but no indication is listed. In this case you may be forced to assume that the patient has clinical depression in order to say whether the dosage is effective for that condition.

*Instructions:*

BNF (current edition) dose ranges for the elderly should be used. Hence, one should take into account known age-related changes in drug pharmacokinetics and pharmacodynamics. Some patients may have laboratory tests or investigations, these should be viewed with respect to the dose and therefore the dose may be incorrect and hence label (C). If you consider blood test results to be important, and they are not recorded, you should score (C).

Also, consider other objective data such as vital signs, calculated creatinine clearance and lab values (e.g., blood chemistries, cholesterol, PT/INR). In summary, a dosage is incorrect if it is outside the accepted geriatrics dose range; if there is no accepted geriatrics dose range, then to be incorrect it must be outside the standard range. A dosage may also be incorrect if not adjusted for renal failure or drug levels if tested for, e.g. digoxin. For drugs being tapered to be discontinued, (e.g., oral steroids) low dosage will be considered correct.

*Examples:*

Paracetamol 2g/dose BD incorrect, 24 hour dose correct so it should be scored (A); however, single dose incorrect ie direction is incorrect (see Question 4 for direction).

An example of (B) "adequate but not ideal" could be diclofenac 50mg 1 daily.

Flixotide® 250mcg inhaler BD. The dose is not stated as 250mcg is the strength. The dose should be "one, two or even three puffs BD", so in this situation the dose is (C).

**Question 4:**

A \_\_\_\_\_ B \_\_\_\_\_ C  
 Correct (directions)      Adequate but not ideal      Incorrect (directions)

*Definition:*

Directions are defined as the instructions for the use of a medication by a patient. These instructions are those which are given on a prescription and will therefore subsequently be dispensed to the patient by the pharmacist.

*Instructions:*

The directions are incorrect or insufficient if given with no specific instruction (with notable exceptions such as warfarin, insulins etc) or specify the wrong schedule or the wrong time of day (when specific directions regarding relationship to schedule and time of day exist).

*Examples:*

An example of the correct direction (A) could be digoxin 125mcg 1 OM.

An example of (B) direction 'adequate but not ideal' could be Paracetamol 500mg 1 tablet when required.

Statins in the morning, Isosorbide Mononitrate 10am and 10pm, Quinine in the morning (when indicated for leg cramp), QDS for inhaled corticosteroids instead of BD cf also with practical implications. Atenolol "as directed" are all (C).

"Statutory labels" (additional directions such as "warning may cause drowsiness" or "with or after food" which you should be able to find in the current BNF Appendix 9) can be assumed to be included on the directions; these will be placed on the label by the pharmacist.

**Question 5:**

A \_\_\_\_\_ B \_\_\_\_\_ C  
 Practical      Scope for improvement      Impractical

*Definition:*

"Practical" is defined as capable of being used or being put into practice. This question assesses whether the directions for use are practical for the patient to take, and also takes into account whether the patient may be able to follow the instructions. This question should assess whether the directions appear to be clear and unambiguous.

*Instructions:*

A drug schedule is considered impractical if the drug could be administered less frequently and still maintain efficacy. Irregular day-to-day schedules that have more regular alternatives are also impractical. In addition, medications to be given at a specific time when a more flexible schedule is sufficient is impractical.

*Examples:*

A practical direction (A) could be Lisinopril 10mg 1 BD.

Any drug which can be given less frequently because, for instance the availability of long acting (modified release) preparations could be rated as (B) scope for improvement.

Warfarin doses which are complicated, such as varying alternative day dosing, which could be made easier by having the same dose each day - impractical (C). Adizem MR® 90mg 1 BD is impractical (C) since equally evidence-based alternative, Adizem XL® 180mg 1 OD, is simpler to administer. Atenolol 25mg 1 BD incorrect (C) when atenolol 50mg 1 OD is just as clinically justified. Fosmax® may be impractical (C) for a completely bed bound patient and other forms of calcium replacement may be better to prescribe.

**Question 6:**

A \_\_\_\_\_ B \_\_\_\_\_ C  
 No significant (Drug-drug interaction)      Marginally significant      Significant (Drug-drug interaction)

*Definition:*

A drug-drug interaction is defined as the effect that the administration of one medication has on another drug. This question assesses whether the drug in question interacts with another drug in the patient's regimen by affecting its pharmacokinetics (i.e., absorption, distribution, metabolism and excretion) or pharmacodynamics (i.e., the effect that it has on the body). These types of interactions should be assessed on a risk to benefit ratio, indeed some drugs are prescribed specifically for their interaction properties e.g. to increase the therapeutic level by reducing metabolism. This could include potential drug-drug interactions.

*Instructions:*

In a drug interactions textbook, such as the BNF, clinically significant interactions are denoted by the symbol •. Another recommend text to use is “Stockley’s Drug Interactions”, referenced above.

*Examples:*

An (A) rating would be given in the situation where none of the drugs interacted.

A marginally significant drug-drug interaction (B) could be the prescribing of a low dose cardiac glycoside, such as digoxin 62.5mcg and a low dose diuretic such as frusemide 20mg 1 OM. Significant pharmacokinetic interaction (C) - Cimetidine added to a stable Theophylline patient which could result in Theophylline toxicity. Significant pharmacodynamic interaction (C) - a tricyclic antidepressant or another benzodiazepine added to an existing benzodiazepine, which results in a patient having increased falls or confusion. NSAID (e.g., naproxen) for osteoarthritis started on a patient taking warfarin long term for atrial fibrillation= (C) (since increases risk of bleeding).

**Question 7:**

A	B	C
No significant (drug-disease interactions)	Marginally significant	Significant (drug-disease interactions)

*Definition:* Drug-disease interaction is defined as the effect that the drug has on a pre-existing disease or condition, or simple effects of ageing i.e.changes in renal and hepatic function. This question assesses whether there is a significant risk that the drug in question may worsen the patient's disease or condition. One must also consider allergies, for example a previous history of allergic reaction to a specific drug may be considered a pre-existing condition. This could also include potential drug-disease interactions.

\*Note: If you are forced to make any inferences or assumptions regarding the existence of any pre-existing disease or condition based purely upon the drug list then you must record these in the comments section, providing the question number and reasons to support these inferences / assumptions.

*Instructions:*

If no interaction exists according to the information presented, then an (A) rating should be given.

If the risk is present of a drug-disease interaction, but at a very low level, then the rating is marginal (B).

If the drug is contraindicated or highly risky ("extreme caution") for a patient’s condition, then the drug-disease interaction is significant (C). If the drug needs routine caution in the setting of a patient’s condition and the patient shows clinical evidence of disease worsening following the prescription of the drug, then the drug-disease interaction is also significant (C).

*Examples:*

An (A) rating would be given in the situation where no drug-disease interaction was present.

A diabetic patient prescribed a thiazide diuretic, the hypoglycaemic effect is antagonised, however, this is thought not to be clinically significant and could therefore be classed as (B) marginally significant. NSAID in a patient with recent history of peptic ulcer disease (PUD) - (C) significant; Tricyclic amitriptyline worsens preexisting constipation = (C). If a patient is allergic to penicillin and amoxicillin is given then the drug – disease interaction is significant. = (C).

Non selective beta blockers in a patient with asthma/ chronic obstructive pulmonary disease (COPD)-(C) significant. Oral corticosteroids for asthma/COPD in a patient with diabetes or osteoporosis (C). Chlorpramide is a ( C ) when prescribed in the elderly because safer short-acting alternatives exist. (Chlorpramide is long acting and the patients age can affect this known side effect). Parkinson disease can be exacerbated or worsened by the prescribing of any piperzine or phenothiazines drug, this may be considered as significant (C).

**Question 8:**

A	B	C
No duplication	Duplication with possible justification	Unnecessary duplication

*Definition:*

Unnecessary duplication is defined as nonbeneficial or risky co-prescribing of drug(s). Unnecessary duplication can exist when two drugs from the same chemical or pharmacological class are prescribed simultaneously, or when a single drug could have been prescribed for more than one condition instead of using multiple drug therapy.

*Instructions:*

Look at each drug prescribed for each condition. Could one drug be used for more than one condition? Caution must be exercised when two drugs in the same class may be used together synergistically. Look for generic and brand name duplication i.e. Tenormin® and atenolol, Zocor® and simvastatin. Look for ways in which rational drug prescribing could help reduce polypharmacy.

*Examples:*

Bendrofluzide 2.5mg 1 OD and atenolol 50mg 1 OD may be considered (A) a combination used to hypertension.

Ramipril 1.25mg 1 OD, atenolol 25mg 1 OD and Adalat® LA 20mg 1 OD recently prescribed for hypertension may be considered (B) when the two previous treatments were not prescribed at therapeutic doses, for example the ramipril was not titrated to a therapeutic dose (2.5- 5mg) even in the elderly.

Same pharmacological class - ranitidine added to a regimen with cimetidine = (C) (ranitidine). Ranitidine added to the prescription of Lansoprazole, unnecessary will not work, = (C) (ranitidine). SSRI plus a tricyclic antidepressant, while not always inappropriate, but in this age-group likely to be unnecessary, so therefore rate as (C).

**Question 9:**

A	B	C
Acceptable duration	Questionable duration	Unacceptable duration

*Definition:*

Duration is defined as the length of therapy. This question assesses whether the length of time that the patient has received the drug is acceptable.

*\*Note:* If there is no indication for the drug in question the assessor may be forced to infer / assume an indication from the list of drugs. However, if you are forced to make any inferences or assumptions in order to answer this item then you must record these in the comments section, together with reasons to support these inferences / assumptions.

*Instructions:*

If the duration of therapy is outside what would normally be expected then it should be classed as unacceptable (C). If the duration of treatment is correct using existing guidelines or knowledge then this should be marked as acceptable therapy (A). In general, for a chronic condition there will naturally be long term medication which is acceptable, although there should be evidence of review and laboratory tests. There are some medications which should never be prescribed long term and therefore should always be assessed as unacceptable. A (B) rating ‘questionable’ could be given to drugs that are prescribed for a condition but there is little evidence of review or monitoring if this is what is recommended.

*Examples:*

An example of a drug prescribed for a long period of time which is acceptable (A) may be salbutamol in an asthmatic patient.

A “questionable duration” rating (B) could perhaps be given to amiodarone when prescribed for paroxysmal supraventricular without any evidence of blood tests in the last 6 months. Clinical guidelines recommend that when amiodarone is prescribed long term laboratory tests (T3/T4) should be performed every 6 months.

Warfarin for resistant atrial fibrillation long term could be considered acceptable so long as the patient was having regular INR checked. However, warfarin therapy for a one off deep vein thrombosis (DVT) given long term may be considered unacceptable (C) especially in a geriatric age range. Benzodiazepines given long term could be considered unacceptable (C). Long term oral corticosteroids given without a justified therapeutic reason may be considered inappropriate (C).

**Question 10:**

A \_\_\_\_\_ B \_\_\_\_\_ C  
Less expensive                      Equally expensive                      More expensive

*Definition:*

This question examines the cost of the drug which has been rated in the other nine criteria. It also assesses whether the prescribing of this drug is justified (cost wise) in relation to other commercially available alternatives of equal efficacy, therapeutic class and safety and whether there is a cheaper generic alternative. "Less expensive" means that the drug being assessed is less expensive i.e. the alternative(s) is/are more expensive (if there were any). "More expensive" means that the drug being assessed is more expensive than any of its alternatives, if there were any.

*Instructions:*

For each branded drug is there a generic alternative available? If so then a (C) should be given. Also if there is an alternative medication within the same therapeutic class which is more cost effective, i.e. cheaper than (C). If the drug is listed as not indicated or ineffective for the condition then it is not cost-effective and therefore is assessed as (C). Also drugs which are given as BD when a larger dose could safely be given OD are not cost-effective and therefore a (C) response should be given. A (B) rating may apply when the alternative drug from the one prescribed is approximately the same cost.

*Examples:*

Ranitidine prescribed in a patient taking warfarin is rated (A), although it may be more expensive than cimetidine, it is less likely to cause a clinically significant interaction.

An example of a (B) rating could perhaps be ramipril and lisinopril at equivalent doses to treat post myocardial infarction

Lactulose for constipation before trying Fybogel® - would be classed as (C) more expensive, likewise with the prescribing of Zyloric® instead of allopurinol (C). Atenolol 50mg 1 OD is more cost effective than 25mg 1 BD, so if atenolol 25mg 1 BD was prescribed then this would be rated as (C).

**Appendix 5.10: Adapted-Medication Appropriateness Index (A-MAI)**

Drug \_\_\_\_\_ Dose \_\_\_\_\_ Frequency \_\_\_\_ Duration \_\_\_\_\_ Diagnosis \_\_\_\_\_

Medication Appropriateness Index. Please state your reasons for rating B, C or DK in the spaces provided

1. Is the drug indicated?	A Indicated	B Possible indication	C Not Indicated	Z DK
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If you rated B, C or DK, please explain why:_____	_____	_____	_____	_____
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2. Is it effective for the condition?	A Effective	B Marginally effective	C Ineffective	Z DK
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If you rated B, C or DK, please explain why:_____	_____	_____	_____	_____
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3. Is the dosage correct?	A Correct	B Adequate but not ideal	C Incorrect	Z DK
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If you rated B, C or DK, please explain why:_____	_____	_____	_____	_____
---	-------	-------	-------	-------

4. Are the directions correct?	A Correct	B Adequate but not ideal	C Incorrect	Z DK
--------------------------------	--------------	-----------------------------	----------------	---------

If you rated B, C or DK, please explain why:_____	_____	_____	_____	_____
---	-------	-------	-------	-------

5. Are the directions practical?	A Practical	B Scope for improvement	C Impractical	Z DK
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If you rated B, C or DK, please explain why:_____	_____	_____	_____	_____
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6. Are there clinically significant drug-drug interactions?	A Insignificant	B Marginally significant	C Significant	Z DK
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If you rated B, C or DK, please explain why:_____	_____	_____	_____	_____
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7. Are there clinically significant drug-disease/condition interactions?	A Insignificant	B Marginally significant	C Significant	Z DK
--	--------------------	-----------------------------	------------------	---------

If you rated B, C or DK, please explain why:_____	_____	_____	_____	_____
---	-------	-------	-------	-------

8. Is there unnecessary duplication with other drug(s)?	A No duplication	B Duplication with possible justification	C Unnecessary	Z DK
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If you rated B, C or DK, please explain why:_____	_____	_____	_____	_____
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9. Is the duration of therapy acceptable?	A	B	C	Z
	Acceptable	Questionable	Not acceptable	DK
If you rated B, C or DK, please explain why:_____				
10. Is this drug the least expensive alternative compared to others of equal utility?	A	B	C	Z
	Least expensive	Equally expensive	More expensive	DK
If you rated B, C or DK, please explain why:_____				

**A. General Instructions**

This instrument is intended for the evaluation of the appropriateness of medications prescribed by a health care provider. It requires, at a minimum, that a medical history problem list and medication list is available for review. Medication history information obtained from patients can be helpful in applying the MAI. Before evaluation, review the case information available and medication profile for each patient. It is important that clinical judgment must be applied in regards to patient's preference. Complete the scale for each regularly scheduled active medication. The MAI can be used to assess the use of "prn" or as needed medication used frequently. Each question in the scale pertains to the individual patient and drug in question. Read each question carefully and circle the score (A, B, C or Z) that represents your assessment. If you do not understand the question, consult the specific instructions below for clarification. If you do not know the answer to the question, consult a standard medication text such as the British National Formulary (BNF), the Maudsley Prescribing Guidelines in Psychiatry or the Summary of Product Characteristic (SPC) of the medication. At times, you may require additional information from the patient's chart to answer a question. In that case, circle Z and specify the necessary information in the comments section. Some regimens contain combination drugs. If the individual components are available and used as single entities, then complete the scale for each individual drug. Finally, please note your reasons for any rating of B, C or Z in the comments section.

**OPERATIONAL DEFINITIONS FOR RATING THE MAI**

**Question 1:** Is there an indication for the drug?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
indicated possible indication not indicated do not know

*Definition:* Indication is defined as the sign, symptom, disease, or condition for which the medication is prescribed. The question assesses whether there is sufficient reason for the use of the drug. Sufficient reason includes not only curative and palliative therapy but also preventive therapy for a disease, condition or drug effect.

*Instructions:* A drug is not indicated if no condition exists for its use. Answer the question with the conditions reported by the patients. If you disagree with the indication, please state the reason in the comments section and rate 'C' (not indicated).

*Examples:* Risperidone is prescribed and psychosis/schizophrenia is reported = A (indicated). Olanzapine prescribed for treatment resistant depression = B since indicated but would have to be added to an antidepressant. Olanzapine is prescribed and psychosis/schizophrenia is not reported = C (not indicated). Continued use of sertraline and other SSRIs during manic phase of bipolar illness = C.

**Question 2:** Is the medication effective for the condition?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
effective marginally effective ineffective do not know

*Definition:* Effective refers to evidence of efficacy in this population. It is defined as producing a beneficial result. The question assesses whether the drug prescribed is capable of being effective for a given indication which is reported by the patient.

*Instructions:*

Indication and effectiveness are tightly but not perfectly linked items. Assessors should evaluate each drug for clinical effectiveness based on the reported indication\*. This should also involve consideration of patients' views on effectiveness. Effectiveness may also be based on a risk to benefit assessment of each drug.

*\*Note:* If there is no indication for the drug in question the assessor may be forced to infer / assume an indication such as that reported by the patient. However, if you are forced to make any inferences or assumptions in order to answer this item then you must record these in the comments section, together with reasons to support these inferences / assumptions. For example, a patient may have been prescribed sertraline but signs/symptoms of depression are not present. In this case you may be forced to assume that the patient has depression in order to say whether the drug is effective for that condition. Furthermore, an indication may not be documented for a drug yet the drug may work well for the intended effect (for example, use of a medication for an unlicensed indication). Depending on the circumstance, this may be considered effective. Drugs in which the potential risks outweigh the potential benefits, and thus are incapable of being effective in actual practice should be rated as ineffective ("C").

*Examples:*

A drug should generally be scored as (A) 'Effective' when there are guidelines for its use in relation to the reported indication and where it is prescribed within the boundaries of these guidelines. Evidence should also exist to support a beneficial treatment effect. Example: Guidelines and evidence exist to support the use and clinical efficacy of olanzapine for the treatment of schizophrenia and patient also reports benefit. Therefore olanzapine scored (A) Effective. If patient reports no benefit, then a score of 'Marginally effective' (B) or 'Ineffective' (C) may be given depending on the circumstance.

A drug should be scored as (B) 'Marginally effective' when there are guidelines for its use in relation to the reported indication although evidence suggests a suboptimal treatment effect, or guidelines state it is not the drug of first choice. This perhaps could be drugs which are marked in the BNF as .

A drug should be scored as (C) 'Ineffective' if there are no guidelines for its use in relation to the indication, if it is prescribed beyond the boundaries of any guidelines which do exist or if evidence suggests that no beneficial treatment effect is likely to be obtained. Example: Guidelines support the use of Diazepam for the treatment of anxiety over a short period. However, long term use is cautioned against. The patient's records presented indicate a prolonged history of anxiety. Therefore Diazepam scored as either (B) Marginally Effective or (C) Ineffective. Continued use of sodium valproate in a pregnant woman with bipolar illness = C.

**Question 3:** Is the dosage correct?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z \_\_\_\_\_  
correct                      adequate but not ideal                      incorrect      do not know

**Definition:**

Dosage is defined as the total amount of medication taken per 24-hour period (or longer, if appropriate) for regularly scheduled medication.

*\*Note:* If there is no indication for the drug in question the assessor may be forced to infer / assume an indication such as that reported by the patient. However, if you are forced to make any inferences or assumptions in order to answer this item then you must record these in the comments section. For example, a patient may have been prescribed sertraline but there are no signs/symptoms of depression. In this case you may be forced to assume that the patient has clinical depression in order to say whether the dosage is effective for that condition.

*Instructions:*

BNF (current edition) dose ranges should be used. Hence, one should take into account known age-related changes in drug pharmacokinetics and pharmacodynamics. Some patients may have laboratory tests or investigations, these should be viewed with respect to the dose and therefore the dose may be incorrect and hence label (C). Also, consider other objective data such as vital signs and lab values (e.g., blood chemistries, cholesterol, PT/INR). In summary, a dosage is incorrect if it is outside the standard dose range. A dosage may also be incorrect if not adjusted for renal failure or drug levels if tested. For drugs being tapered to be discontinued, (e.g., anticonvulsants, antipsychotics) low dosage will be considered correct.

*Examples:* 50mg of sertraline prescribed for depression = A. 2.5mg of olanzapine prescribed for schizophrenia = C.

**Question 4:** Are the directions correct?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
correct                      adequate but not ideal                      incorrect                      do not know

*Definition:*

Directions are defined as the instructions for the use of a medication by a patient.

*Instructions:*

The directions are incorrect or insufficient if given with no specific instruction or specify the wrong schedule or the wrong time of day (when specific directions regarding relationship to schedule and time of day exist).

*Examples:* An example of the correct direction (A) could be zolpidem 10mg nocte. An example of (B) direction ‘adequate but not ideal’ could be diazepam 2mg prn since it does not state the maximum dose that should not be exceeded.

**Question 5:** Are the directions practical?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
practical                      scope for improvement                      impractical                      do not know

*Definition:* Practical is defined as capable of being used or being put into practice. This question assesses whether the directions for use are practical for the patient to take, and also takes into account whether the patient may be able to follow the instructions. This question should assess whether the directions appear to be clear and unambiguous.

*Instructions:*

A drug schedule is considered impractical if the drug could be administered less frequently and still maintain efficacy. Irregular day-to-day schedules that have more regular alternatives are also impractical. In addition, medications to be given at a specific time when a more flexible schedule is sufficient is impractical.

*Examples:*

Trazodone 75mg qhs - practical (A) since once daily and can cue into bedtime routine. Olanzapine 5mg bd – impractical (C) since 10mg can be prescribed once daily. Any drug which can be given less frequently because of the availability of long acting (modified release) preparations could be rated as (B) scope for improvement.

**Question 6:** Are there clinically significant drug-drug interactions?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
insignificant                      marginally significant                      significant                      do not know

*Definition:* A drug-drug interaction is defined as the effect that the administration of one medication has on another drug. Clinical significance connotes a harmful interaction. This question assesses whether the drug in question interacts with another drug in the patient's regimen by affecting its pharmacokinetics (i.e., absorption, distribution, metabolism and excretion) or pharmacodynamics (i.e., the effect that it has on the body).

*Instructions:* A drug interactions text, such as the British National Formulary (BNF), the Maudsley Prescribing Guidelines in Psychiatry and the Summary of Product Characteristics of the medication can be used in assessing drug-drug interactions. Where other sources are used, they should be stated. For instance, interactions where there is a black dot in the British National Formulary (BNF) under the drug interactions section signifies a clinically significant interaction. If no interaction exists, then an A rating is automatic. A “B” rating will be given when the reference indicates an interaction but no clinical evidence exists for toxicity or adverse effect. If the reference/program indicates an interaction and sufficient clinical information is available and evidence of toxicity or adverse effect (including lack of effect) does exist, then the interaction is significant (“C”). If the reference/program indicates an interaction and clinical information is not available, then the interaction may also be considered significant (“C”). The drug that causes the change in pharmacokinetics or pharmacodynamics is the one that merits the C rating.

*Examples:* Methadone (especially greater than 100mg) given with antipsychotics that prolong the QT interval = C due to increased risk of ventricular arrhythmias. Prescription of phenelzine to a patient who is dependent on cocaine = C due to risk of hypertensive crisis.

**Question 7:** Are there clinically significant drug-disease/condition interactions?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
insignificant marginally significant significant do not know

*Definition:* Drug-disease interaction is defined as the effect that the drug has on a pre-existing disease or condition (including substance use disorders), or simple effects of ageing i.e. changes in renal and hepatic function. This question assesses whether there is a significant risk that the drug in question may worsen the patient's disease or condition. One must also consider allergies, for example a previous history of allergic reaction to a specific drug may be considered a pre-existing condition. This could also include potential drug-disease interactions.

*\*Note:* If you are forced to make any inferences or assumptions regarding the existence of any pre-existing disease or condition then you must record these in the comments section, providing the reasons to support these inferences / assumptions.

*Instructions:*

If no interaction exists according to the information presented, then an (A) rating should be given.

If the risk is present of a drug-disease interaction, but at a very low level, then the rating is marginal (B).

If the drug is contraindicated or highly risky ("extreme caution") for a patient's condition, then the drug-disease interaction is significant (C). If the drug needs routine caution in the setting of a patient's condition and the patient shows clinical evidence of disease worsening following the prescription of the drug, then the drug-disease interaction is also significant (C).

*Examples:* High anticholinergic Tricyclic antidepressants (i.e., doxepin, amitriptyline, imipramine) started in patient with Lower Urinary Tract Symptoms = C. Codeine prescribed for someone with a previous history of gastrointestinal distress with no evidence of worsening =B.

**Question 8:** Is there unnecessary duplication with other drug(s)?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
necessary marginally necessary unnecessary do not know

*Definition:* Unnecessary duplication is defined as nonbeneficial or risky co-prescribing of drug(s). Unnecessary duplication exists when two drugs from the same chemical or pharmacological class are prescribed simultaneously, or when a single drug could have been prescribed for more than one condition instead of using multiple drug therapy.

*Instructions:*

Look at each drug prescribed for each condition. Could one drug be used for more than one condition? Caution must be exercised when two drugs in the same class may be used together synergistically. Look for generic and brand name duplication i.e. lustral® and sertraline. Look for ways in which rational drug prescribing could help reduce polypharmacy. If two (or more) drugs from the same class are prescribed simultaneously and the order in which prescribed cannot be determined then they are unnecessarily duplicated. If the order of prescribing is known, then the last drug added receives a C and the other drug receives a B. If the order of prescribing is not known, then randomly pick one drug to receive a C and the other to receive a B.

*Examples:* Flurazepam 15mg qhs and Diazepam 5mg tid then flurazepam randomly picked and receives a C.

**Question 9:** Is the duration of therapy acceptable?

A \_\_\_\_\_ B \_\_\_\_\_ C \_\_\_\_\_ Z  
acceptable marginally acceptable unacceptable do not know

*Definition:*

Duration is defined as the length of therapy. This question assesses whether the length of time that the patient has received the drug is acceptable.

\*Note: If there is no indication for the drug in question the assessor may be forced to infer / assume an indication such as that reported by the patient. However, if you are forced to make any inferences or assumptions in order to answer this item then you must record these in the comments section.

*Instructions:*

If the duration of therapy is outside what would normally be expected then it should be classed as unacceptable (C). If the duration of treatment is correct using existing guidelines or knowledge then this should be marked as acceptable therapy (A). In general, for a chronic condition there will naturally be long term medication which is acceptable, although there should be evidence of review and laboratory tests. There are some medications which should never be prescribed long term and therefore should always be assessed as unacceptable. A (B) rating 'questionable' could be given to drugs that are prescribed for a condition but there is little evidence of review or monitoring if this is what is recommended.

*Examples:*

An example of a drug prescribed for a long period of time which is acceptable (A) may be olanzapine in a patient with psychosis/schizophrenia. Diazepam or other benzodiazepines prescribed for greater than 4 weeks = C due to the risk of dependence.

**Question 10:** Is this drug the least expensive alternative compared to others of equal utility?

A _____	B _____	C _____	Z
less expensive	equally expensive	more expensive	do not know

*Definition:*

This question examines the cost of the drug which has been rated in the other nine criteria. It also assesses whether the prescribing of this drug is justified (cost wise) in relation to other commercially available alternatives of equal efficacy, therapeutic class and safety and whether there is a cheaper generic alternative. "Less expensive" means that the drug being assessed is less expensive i.e. the alternative(s) is/are more expensive (if there were any). "More expensive" means that the drug being assessed is more expensive than any of its alternatives, if there were any.

*Instructions:*

A drug is more expensive if it costs more (at least 10%) than the average cost/charge of alternatives of equal utility. Alternatives should be considered as medications within the same therapeutic class. To operationalize, evaluator can use the BNF prices (e.g., cost per month or per day supply or cost per dose) as their standard. For each branded drug is there a generic alternative available? If so then a (C) should be given. Also if there is an alternative medication within the same therapeutic class which is more cost effective, i.e. cheaper than (C). A (B) rating may apply when the alternative drug from the one prescribed is approximately the same cost.

*Examples:*

Escitalopram prescribed for depression when citalopram or other cheaper SSRIs have not been tried = C.

**Appendix 5.11: Case study of W. T.**

W.T is a 37 year old woman who has experienced a lot of difficulties in the last few years. She has been through a very difficult divorce and lost custody of her two children to her ex-husband 3 years ago. She reports feeling depressed about her situation. She says at that time she started to drink alcohol on a daily basis to cope with her feelings about the loss of her children. She describes a current pattern of drinking of 4 cans of 5% lager per day (8.8 units). She reports that she finds it very difficult to control her alcohol intake and has been increasingly concerned about it, so she decided to self-refer to the LAU for assistance with her drinking. She has also been having sleep problems for the past 3 weeks.

W.T has no family history of depression.

**Past medical history**

She was diagnosed with depression 2.5 years ago by her GP.  
She was also diagnosed with insomnia 2 weeks ago.

**Present medications**

Sertraline 50mg tab o.d prescribed 2 years ago by her GP.  
Zopiclone 7.5mg tab nocte prescribed 2 weeks ago by her GP.

Please could you kindly use the medication appropriateness index (MAI) to rate the appropriateness of these medications? We would be discussing about your ratings during the prescribing governance meeting on Friday. I have attached a copy of the medication appropriateness index (MAI) to this mail.

**Appendix 5.12: Medication Omission Questionnaire**

1. Are any of the medications of interest not being prescribed for an active condition without reason?

Yes  No

If yes, please state the medications not being prescribed and any action you will take below:

Medications not being prescribed	Action to be taken concerning medications not being prescribed

**Appendix 5.13: Reasons for marginally appropriate A-MAI ratings at first SAS visit**

<b>Reasons for ratings of marginally appropriate on the A-MAI</b>	<b>Number of service users with marginally appropriate ratings</b>
<b>Indication rated as ‘marginally appropriate’</b>	
No obvious signs of depression but could be because antidepressant is effective	1
Possibility of alcohol-related depression	4
Depressive symptoms are present but there is insufficient history for assessment	1
Long-term use of antidepressant despite improvement in depressive symptoms	1
Unlicensed prescribing of antipsychotic for paranoia	1
Prochlorperazine is not first line in the management of anxiety disorder	1
Possible dependence on z-drug due to chronic use	1
Z-drug indicated only for short-term use for sleep problems	2
Benzodiazepine indicated for short-term use for sleep problems	1
Long term use of opioids for pain	2
Beta-blocker is not first-line agent as an anxiolytic	1
<b>Effectiveness rated as ‘marginally effective’</b>	
Lack of optimal benefit from antidepressants due to alcohol misuse	5
Depressive symptoms still present in service user despite use of antidepressants. Depressive symptoms are unlikely to be secondary to alcohol misuse	2
Antidepressant (trazodone) not first line in the management of sleep problems	1
Presence of anxiety and depressive symptoms in service user. Service user feels medication is only slightly effective	1
Service user still experiencing depressive symptoms	1
Service user still experiencing paranoia	1
Prochlorperazine is not first line in the management of anxiety disorder. Alcohol misuse may be worsening service user’s anxiety problems	1
Lack of optimal benefit from benzodiazepines	1
Lack of optimal benefit from z-drug	3
Z-drug only has short-term benefit and should be used for limited time	1
Service user reports lack of optimal benefit from beta-blocker for anxiety disorder	1
<b>Dosage rated as ‘adequate but not ideal’</b>	
Probable need for higher dose of antidepressant	3
Dose of antidepressant is above BNF maximum dose in recent guidelines. Dose was within limit of past BNF recommendation	1
Tapering of benzodiazepine dose due to lack of indication	1
Need to aim for lower doses of opioids as service user has been on present dose for a long time	1
Development of bradycardia with current dose of beta-blocker	1
<b>Directions rated as ‘adequate but not ideal’ for correctness</b>	
Direction should rather be qds for benzodiazepine (chlordiazepoxide bd) prescribed for alcohol detoxification	1
<b>Directions rated as ‘adequate but not ideal’ for practicality</b>	
Service user unclear about the length of treatment for chlordiazepoxide prescribed for alcohol detoxification	1
<b>Drug-drug interactions rated as ‘marginal’</b>	
Combination of two antidepressants with serotonergic activity	1
Possible potentiation of CNS depressant effect of morphine by alcohol and amitriptyline	2
Possible reduction of serum concentration of quetiapine by depakote (divalproex sodium)	1
<b>Drug-disease/condition interactions rated as ‘marginal’</b>	
Alcohol (20 – 60 units of alcohol per week) may affect the effectiveness of antidepressant	1

Possibility of interaction between alcohol and z-drug	2
<b>Medication duplication with possible justification</b>	
Co-prescribing of two antidepressants	2
Co-prescribing of fluoxetine, prochlorperazine and propranolol for anxiety problems	1
<b>Marginally acceptable duration of therapy</b>	
Use of antidepressants without regular review	4
Commenced a reducing regimen of methadone with a view to discontinuing	1
Use of opioid (morphine) without regular review	1
Co-codamol prescribed for symptomatic relief. Service user also needs to abstain from alcohol for pain relief	1
Duration of co-codamol needs to be limited due to dependence risk	1
Duration of acamprosate needs to be reviewed due to length of treatment	1
<b>Comparability of medication cost to those of equal utility</b>	
Fluoxetine is comparable to other SSRIs in its cost	1

## Appendix 5.14: Favourable ethical opinion letter for Medication Appropriateness Study



### Health Research Authority

#### NRES Committee Yorkshire & The Humber - Humber Bridge

Yorkshire and the Humber Research Ethics Office  
First Floor  
Millside  
Mill Pond Lane  
Leeds  
LS6 4RA

Telephone: 0113 3050127  
Facsimile: 0113 8556191

09 July 2012

Mrs Obirenjeyi Adejoke Kudehinbu-Oluyase  
Alcuin Research and Resource Centre, Second floor, Room 209B  
University of York  
Heslington  
YO10 5DD

Dear Mrs Kudehinbu-Oluyase

**Study title:** A study of the use and appropriateness of prescriptions of psychotropic medications and medications used in the management of substance use disorders among service users in an addiction service

**REC reference:** 12/YH/0325

The Research Ethics Committee reviewed the above application at the meeting held on 27 June 2012. Thank you for attending to discuss the study.

#### Ethical opinion

The Committee explained that twenty minutes is not a sufficient amount of time for participants to consider taking part in the study. You explained that you will ensure that all clients fully understand the study before consent is taken. You also stated that you will ensure that participants understand that they can withdraw from the study at any time.

Members asked you to explain the recruitment procedure for service users. You explained that service users will be given information about the study by the receptionist when they attend for their appointment. If an individual is interested in taking part, the receptionist will inform you of this. You informed members that the service user will have their health check before seeing you in a private room at the unit. You explained that at this point if the client is happy to proceed, consent will be taken and you will carry out the assessment. You stated that you will re-contact participants regarding taking part in the interviews at 3 months. Members asked you if the interviews will require the participant to attend an additional appointment. You stated that the interviews will be carried out at the routine 3 month follow up appointment. Members asked you to include this information about the interview in the participant information sheet and consent form.

The Committee asked you if it would be possible to send the study information out with Leeds Addiction Unit appointment letter. Mr Lloyd explained that when a service user attends the LAU they can be assigned either to a prescriber or a therapist. Mr Lloyd stated that as the research only involves those assigned to a prescriber; it would be a waste of

A Research Ethics Committee established by the Health Research Authority

resources to send the study information out to all service users. Mr Lloyd also explained that by providing the study information at LAU will allow service users to have the opportunity to discuss the study with you and ask questions in a controlled environment.

Members highlighted that the participant information sheets suggests that all participants will take part in the interview stage, but that the application form suggests that only a sample of the those recruited will go on to the interview stage. You stated that a sample of those recruited will be invited to take part in the interview. The Committee asked you to make this clear in the information sheet for participants.

The Committee asked you to explain what will happen to the interview recordings. You stated that audio recordings will be stored on the LAU computer and destroyed after 3 years according to LAU policy.

Members asked if the nurse prescribers will be asked about specific prescriptions or general prescribing practice. You explained that the prescribers will be asked general questions regarding prescribing and will not be asked to share any personal information relating to service users.

The Committee highlighted to the researchers that there is a potential for disclosure during the study, both by service users and prescribers. You stated that you will act upon disclosure if the participant or others are at risk and that this has been explained in the service user information sheet.

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

#### **Ethical review of research sites**

##### **NHS Sites**

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

##### **Conditions of the favourable opinion**

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

*Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.*

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>

*Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.*

*For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.*

*Sponsors are not required to notify the Committee of approvals from host organisations*

1. Both consent forms should include a clause allowing participants to consent to their interview being audio-recorded.
2. Statement 7 on the service user consent form should be more specific about when and why participants may be contacted in the future.
3. The service user participant information sheet should explain that not all participants will be invited to take part in the interview stage of the study.

**It is responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).**

**You must notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.**

#### **Approved documents**

The documents reviewed and approved at the meeting were:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Evidence of insurance or indemnity		08 June 2012
Investigator CV		08 June 2012
Letter from Sponsor		08 June 2012
Letter from Statistician		08 June 2012
Other: CV- C Lloyd (Academic Supervisor)		08 June 2012
Other: Topic Guide for interview with service users	3.1	08 June 2012
Other: Topic Guide for interview with prescribers	3.1	08 June 2012
Participant Consent Form: Consent form for service users	3.1	08 June 2012
Participant Consent Form: Consent form for prescribers	3.1	08 June 2012
Participant Information Sheet: Information sheet for service users	3.1	08 June 2012
Participant Information Sheet: Information sheet for nurse prescribers	3.1	08 June 2012
Participant Information Sheet: Information sheet for medical prescribers	3.1	08 June 2012
Protocol	3.1	08 June 2012
Questionnaire: Medication appropriateness index (Validated)		
Questionnaire: Assessment of underutilisation of medication index (Validated)		
Questionnaire: Nurses Questionnaire (Non-validated)	3.1	08 June 2012
Questionnaire: Medications questionnaire for service users (Non-validated)	3.1	08 June 2012
Questionnaire: Questionnaire for documenting medication changes by Chief Investigator (Non-validated)	3.1	08 June 2012
Questionnaire: Demographic information questionnaire for prescribers (Non-Validated)	3.1	08 June 2012
REC application	3.1	08 June 2012

A Research Ethics Committee established by the Health Research Authority

Referees or other scientific critique report		
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#### **Membership of the Committee**

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

#### **Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

#### **After ethical review**

##### Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

##### Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

<b>12/YH/0325</b>	<b>Please quote this number on all correspondence</b>
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With the Committee's best wishes for the success of this project

Yours sincerely



pp  
**Dr Lynn Cawkwell**  
**Chair**

Email: nicola.mallender-ward@nhs.net

*Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments*

## Appendix 5.15: Minor amendment acknowledgement letter



### Health Research Authority

#### NRES Committee Yorkshire & The Humber - Humber Bridge

Yorkshire and the Humber Research Ethics Office  
First Floor  
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30 August 2012

Mrs Obirenjeyi Adejoke Kudehinbu-Oluyase  
Alcuin Research and Resource Centre, Second floor, Room 209B  
University of York  
Heslington  
YO10 5DD

Dear Mrs Kudehinbu-Oluyase

**Study title:** A study of the use and appropriateness of prescriptions of psychotropic medications and medications used in the management of substance use disorders among service users in an addiction service

**REC reference:** 12/YH/0325

**Amendment number:** AM01

**Amendment date:** 28 August 2012

Thank you for your letter of 28 August 2012, notifying the Committee of the above amendment.

You have submitted minor changes to the format of the questionnaires listed below.

The Committee does not consider this to be a "substantial amendment" as defined in the Standard Operating Procedures for Research Ethics Committees. The amendment does not therefore require an ethical opinion from the Committee and may be implemented immediately, provided that it does not affect the approval for the research given by the R&D office for the relevant NHS care organisation.

#### Documents received

The documents received were as follows:

Document	Version	Date
Questionnaire: Questionnaire for documenting medication changes by Chief Investigator	3.1	28 August 2012
Questionnaire: Combined questionnaire	3.1	28 August 2012

**Appendix 5.16: Indications for prescribed medications at first SAS visit**

<b>Indications reported by service users</b>	<b>No of service users with diagnoses (n = 60)</b>
Depression	18 (30%)
Depression and anxiety	3 (5%)
Anxiety	5 (8.3%)
Sleep problem	10 (16.7%)
Liver cirrhosis	1 (1.7%)
Type 2 diabetes mellitus	1 (1.7%)
Osteoporosis	1 (1.7%)
Peptic ulcer	3 (5%)
Abdominal abscess	1 (1.7%)
Migraine	1 (1.7%)
Asthma	3 (5%)
Paranoia	1 (1.7%)
Sinus problem	1 (1.7%)
Arthritis	2 (3.3%)
Oesophageal erosion	2 (3.3%)
Heart problem	1 (1.7%)
Pain	10 (16.7%)
Alcohol misuse	5 (8.3%)
Chronic Obstructive Pulmonary Disease (COPD)	2 (3.3%)
Opiate dependence (dihydrocodeine and heroin)	3 (5%)
Hypercholesterolaemia	3 (5%)
Hypertension	6 (10%)
Scalp problem	1 (1.7%)
Schizophrenia	1 (1.7%)
Fluid retention	2 (3.3%)
Psychosis	1 (1.7%)
Cyclothymia	1 (1.7%)
Breathlessness	1 (1.7%)
Indigestion	3 (5%)
Tobacco dependence	1 (1.7%)
Stomach problem	3 (5%)
Hypothyroidism	1 (1.7%)
Nausea	1 (1.7%)
Hay fever	2 (3.3%)
Eczema	1 (1.7%)
Bipolar disorder	1 (1.7%)
Oral contraception	1 (1.7%)
Vitamin supplement	17 (28.3%)

# THE UNIVERSITY *of York*

The Department of Health Sciences

A study of the appropriateness of service users' prescriptions

## TOPIC GUIDE FOR INTERVIEW WITH SERVICE USERS

- The purpose of this interview is to explore your views on your prescriptions. It is hard to predict how long the interview will take but it is likely to be between 30 to 60 mins. However, you can stop at any point if you do not want to continue.
- There are no right or wrong answers as I am interested in what you think about your prescriptions. I am interested in your views.
- If you are happy with this, I would like to record this interview. It will then be transcribed verbatim i.e. it will be typed up, recording everything that was said.
- I may use direct quotations from your interview in writing up my thesis but these would be anonymous i.e. your name will not be used.
- Everything you tell me will be kept in confidence unless you tell me something which suggests that you or others are at risk of harm. In this situation, I may also have to inform the appropriate staff at the LAU after discussing this with you.
- Do you have any questions before we start this interview?
- Are you happy to sign the consent form and continue?

### 1. Introduction

#### Medications

- What prescribed medicines are you taking? Who prescribed them, when, dosage, frequency, length of use and medications used in the past for the same condition.
- How and why they were prescribed these drugs. Was there a careful assessment first? Were they needed in the service user's view, are they still needed now?
- Are medications reviewed and how often?

#### Substance use

- Do you use alcohol at present: quantity used, type of alcohol product and strength. Amount used on a typical day, days used in the last 28 days.
- Before first visit to LAU, description of pattern of alcohol use. Has service user made any changes to alcohol use since coming to the LAU. What changes?
- Has your alcohol affected any of your health conditions in the past and now: how and which health condition?
- Do you use illicit drugs at present: quantity used, type of drug. Amount used on atypical day, days used in the last 28 days.
- Before first visit to LAU, description of pattern of drug use. Has service user made any changes to drug use since coming to the LAU. What changes?
- Has your drug use affected any of your health conditions in the past and now: how and which health condition?
- When did health conditions and substance use start?

2. Service users' feelings about the effectiveness of their prescribed medicines. Compare the effectiveness of medicines when using substances and when not (or when substances reduced).

3. Adherence: Do you often take your medications as prescribed, why? How do you take your medications? Can you describe how you use your medications and substances on a typical day? Any adverse effects: what effects and what medications and substances are involved?

4. Medications service users are not receiving but feel they should be prescribed and why? Actions taken concerning such medications e.g. consultation with a health care professional (HCP), what did the HCP say? Have medicines been obtained from other sources; which sources?
5. What service users consider important in assessing if their prescribed medicines are right for them and why?
6. Were any prescribed medicines changed on coming to the LAU? If so, which and in what way?
7. Involvement in the process of change of medications of interest at the LAU
  - Service users' feelings concerning these changes. Why do you think these changes were made? Were there improvements?
  - Service user involvement in these decisions
  - Level of satisfaction with involvement
  - Ways in which service users can be more involved
8. Influence of medications on patient outcomes
  - Impact of medications on service users' quality of life
  - Degree to which medications are helping users recover from their substance use.

Is there anything else we have missed or should have talked about?

Thank you for your time.



Appendix 6.2b: A part of the coding framework for service user interviews

Initial code list	Renaming codes	Amendment of codes	Final codes
Medication review Reminders about review appointments Attendance of medication review appointments	Medication review	Assessment and review	Assessment and review
Assessment	Assessment		
Medication monitoring	Medication monitoring		
Alleviation of symptoms Improved functioning Need for medicines	Benefit from medications	Benefit from medications	Functional outcomes
Benefits and risks of medicines	Benefits and risks	Trade-off of risks and benefits	
Effect of alcohol on antidepressants	Impact of alcohol on antidepressants	Interference of alcohol with antidepressants	
Antidepressants as a crutch Antidepressants as a support in decision-making	Antidepressants as a crutch	Antidepressants as a medical crutch	
Control/freedom of choice Tell them what you want Craving Right to medication	Right to medications	Entitlement to medications	Entitlement to medications

Appendix 6.2c: A part the coding framework for prescriber interviews

Initial code list	Renaming codes	Amendment of codes	Final codes
Guideline adherence Use of prescribing protocols Measuring prescribing against guidelines	Guideline adherence	Guideline adherence versus successful prescribing	Guideline adherence versus successful prescribing
Prescribing outside guidelines Patient-focused prescribing Successful prescribing Prescribing as an art and science	Successful prescribing		
Risk of drug-drug interactions Risk of drug-disease interactions Harmful effects of medicines Overdosing	Assessing risk	Assessing risk	Assessing risk
Discussion with other SAS prescribers Discussion with service users Taking over prescriptions Communication with prescribers outside the SAS Writing to prescribers outside the SAS	Communication	Communication	Communication

**Appendix 6.3: Comparison of interviewed service users with those who were not interviewed**

Characteristics of service users	Interviewed service users (n = 14)	Service users not interviewed (n = 6)	P-values
Age (mean, SD)	48.2 ± 9.8	46 ± 6.8	0.62 <sup>a</sup>
Gender (n, %)			
Males	11 (78.6%)	2 (33.3%)	0.12 <sup>b</sup>
Females	3 (21.4%)	4 (66.7%)	
Housing status (n, %)			
Rented	7 (50%)	3 (50%)	1.00 <sup>b</sup>
Home owner	3 (21.4%)	2 (33.3%)	
Other	4 (28.6%)	1 (16.7%)	
Referral substance (n, %)			
Alcohol	12 (85.7%)	5 (83.3%)	0.36 <sup>b</sup>
Opioids	2 (14.3%)	0	
Cocaine	0	1 (16.7%)	
Referral source (n, %)			
Self	8 (57.1%)	3 (50%)	0.36 <sup>b</sup>
GP	5 (35.7%)	1 (16.7%)	
Other	1 (7.1%)	2 (33.3%)	
LDQ (median, IQR)	18.5 (9.3, 23.8)	23 (10, 28)	0.55 <sup>c</sup>
CORE-10	25.5 ± 10.4	23.6 ± 10.2	0.72 <sup>a</sup>
SSQ	9.9 ± 6.8	16.4 ± 6.6	0.09 <sup>a</sup>
EQ 5D (median, IQR)	0.7 (0.4, 0.9)	0.8 (0.06, 0.9)	0.96 <sup>c</sup>
Number of previous SAS episodes (median, IQR)	1 (0, 2)	0.5 (0, 1.3)	0.66 <sup>c</sup>
Number of substances used in the past 12 months (median, IQR)	2 (1.8, 4.3)	2 (1, 2.3)	0.40 <sup>c</sup>
Number of prescribed medicines (median, IQR)	2.5 (1, 5.3)	3.5 (1.8, 9)	0.48 <sup>c</sup>

Note: The significance level was 0.4% (that is 0.004) due to Bonferroni adjustment for multiple testing. <sup>a</sup>Assessed using the independent samples t-test, <sup>b</sup>assessed using Fisher's exact test, <sup>c</sup>assessed using the Wilcoxon rank sum test.

# THE UNIVERSITY *of York*

## The Department of Health Sciences

### A study of the appropriateness of service users' prescriptions

#### INFORMATION SHEET FOR PRESCRIBERS

We would like to invite you to take part in our research study on the appropriateness of prescriptions for service users. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. We'd suggest this should take about 10 minutes.

#### **What is the purpose of the study?**

The purpose of this study is to assess the use and appropriateness of prescriptions of psychotropic medications such as antidepressants, antipsychotics, anxiolytics/hypnotics, antimanic agents, anticonvulsants, opioids (including substitute opioids) and medications used in treating substance dependence (disulfiram, acamprosate, lofexidine, bupropion and baclofen) for service users who are newly referred to the Leeds Addiction Unit (LAU). Prescribing for service users with substance use disorders (SUD) is a relatively unexplored area and the few studies available mostly examine prescribing appropriateness by assessing adherence to treatment guidelines relating to the adequacy of the duration of medication therapy and dosage. However, other important aspects of medication appropriateness such as the presence of drug interactions, unnecessary prescriptions and medication omissions (underutilisation), which are equally important, have been rarely considered despite their contribution to morbidity, adverse events and increased health care costs. Furthermore, the reasons for prescribing decisions among service users with SUD have not been well researched.

We would therefore wish to find out how you rate the appropriateness of the prescriptions of interest using the Medication Appropriateness Index (MAI) and the Assessment of Underutilisation of Medication (AOU) Index respectively. We would be interested in changes you make to service users prescriptions from their first assessment to their three month follow-up review and would be interviewing you to explore how you assess the appropriateness of service users' prescriptions towards the end of this study.

#### **Why have I been invited to participate?**

You have been invited to participate in this study because you are a medical prescriber at the Leeds Addiction Unit (LAU). All medical prescribers at the LAU will be invited to participate in this study.

#### **Do I have to take part?**

No, it is up to you to decide to join the study. If you agree to take part, we will then ask you to sign two consent forms, out of which one will be given to you to keep. You are free to withdraw at any time, without giving a reason.

#### **What will happen if I decide to take part?**

If you decide to take part in this study you will be administered a demographics questionnaire where you will fill in your demographic information. You will be given the AOU to assess omission (underutilisation) of the prescriptions of interest during service users' first assessment whilst you will be given the MAI to assess the appropriateness of the prescriptions of interest during service users' first assessment and three month follow-up review. This study will last for six months. You will be interviewed for 30 to 60mins towards the end of the study (at six months) to explore how you assess prescribing appropriateness.

**Will my taking part in the study be kept confidential?**

Yes. We will follow ethical and legal practice and all information we obtain from you will be handled in confidence. All information which is obtained from you during the course of the research will be kept strictly confidential. No one will be able to identify you from the study and we will not share the information you provide with anyone who is not a member of the research team.

**What will happen if I don't want to carry on with this study?**

If you withdraw from the study, we will use the data collected up to your withdrawal.

**What will happen to the results of the research study?**

The results of this study will be written as a PhD thesis, published in journals and presented in conferences. We would also feedback the results to you. The results of this study should be published by 2013.

**Who is organising and funding the research?**

This study is being funded by the Collaboration for Leadership in Applied Health Research and Care (CLAHRC) and supported by the University of York. It is also being undertaken as a piece of student research towards the award of a Doctorate in the Department of Health Sciences at the University of York.

**What will happen to the information I provide if I lose authority to consent?**

If you lose authority to consent, you will be withdrawn from the study but any data you gave prior to then will be used in this study.

**Where can I get further information concerning this study?**

You can get more information about this study by contacting the study's chief investigator (Obirenjeyi Kudehinbu-Oluyase). You can also contact the chief investigator if you decide to withdraw from the study through the following means:

Telephone: 01132 952775 (Monday, Tuesday and Thursday between 11am and 4.00pm)

Email: [oak501@york.ac.uk](mailto:oak501@york.ac.uk)

Thank you for taking the time to read this information sheet and considering whether to take part in this study.

## Appendix 7.2: Topic guide for interviews with prescribers

# THE UNIVERSITY *of York*

The Department of Health Sciences  
A study of the appropriateness of service users' prescriptions

### TOPIC GUIDE FOR INTERVIEW WITH PRESCRIBERS

- The purpose of this interview is to explore your views on the appropriateness of prescribing for people with addiction problems. This interview should take between 30 and 60 mins. However, you can stop at any point if you do not want to continue.
- With your permission, the interview will be audio recorded and transcribed verbatim.
- Direct quotes may be used while writing up this thesis but these would be anonymous.
- Do you have any questions before we start this interview?

#### Topics to be explored

1. How would you define inappropriate prescribing: probe for situations where the health condition is no longer present (or never present). Probe for omissions. Use of guidance/policies when assessing prescribing and any guidance/advice designed for LAU.
2. What classes of medications do you assess their appropriateness; why? How do you assess the appropriateness of service users' medications at the LAU, how often is prescription appropriateness assessed?
3. Do you think inappropriate prescribing is a particular problem, and if so why?
4. What types of inappropriate prescribing do you encounter? Please describe them and the reasons why they are inappropriate (who prescribed these medications, what is inappropriate about them, potential reasons for such prescribing etc).
5. What factors do you consider before assessing medications as appropriate in the presence of substance use and vice versa? Give examples
6. Challenges encountered in assessing prescribing appropriateness at service users' first assessment. Compare with assessment during service users' subsequent visits.
7. Actions taken concerning inappropriate prescriptions/omissions and when it is taken (GP responses concerning them when contacted). Which prescriptions are or are not changed at the LAU and why, factors considered before making changes to prescriptions of interest.
8. Negotiation of changes to prescriptions with service users: service user involvement in the process, service user satisfaction with changes.
9. Impact of prescription change on service users' well being
10. How would you describe your experience of using the MAI in assessing prescribing appropriateness? Why?
11. Has the MAI had any impact on how you assess the appropriateness of prescribing, how?
12. How do you find the structured format of the MAI as a means of exploring prescribing appropriateness? Time taken to complete it.
13. Is there anything you find helpful about the MAI, what and why?
14. Is there anything you find unhelpful about the MAI, what and why?
15. Suggestions on how the MAI can be improved.
16. Do you think the MAI could be used in clinical practice for assessing appropriateness?
17. Suggestions on improving practice with regard to inappropriate prescribing/omissions.

Is there anything else we have missed or should have talked about?

Thank you for your time.

# List of Abbreviations

A-MAI	Adapted Medication Appropriateness Index
APA	American Psychiatric Association
AQ	Adherence Questionnaire
ATHF	Antidepressant Treatment History Form
AUD	Alcohol Use Disorder
BAP	British Association of Psychopharmacology
BNF	British National Formulary
BPS	British Pain Society
CBT	Cognitive Behavioural Therapy
CNCP	Chronic Non-cancer Pain
DSM	Diagnostic and Statistical Manual of Mental Disorders
DUD	Drug Use Disorder
GP	General Practitioner
HSRGC	Health Sciences Research Governance Committee
ICD	International Classification of Diseases
IDU	Intravenous Drug User
MAI	Medication Appropriateness Index
MAS	Medication Appropriateness Study
MI	Motivational Interview
MOQ	Medication Omissions Questionnaire
MMR	Mixed Methods Research
MMTP	Methadone Maintenance Treatment Programme
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NP	Nurse Prescriber
ODU	Opioid Use Disorder
QATQS	Quality Assessment Tool for Quantitative Studies
RCT	Randomised Controlled Trial
SAS	Specialist Addiction Service
SCB	Self-Completion Booklet
SHO	Senior House Officer
SPR	Specialist Registrar
SUD	Substance Use Disorder

TCA	Tricyclic Antidepressant
UK	United Kingdom
USA	United States of America

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