

Outcome Measurements in Economic Evaluations of Drug Misuse Interventions

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To my grandfather

Abstract

This thesis critically evaluates the measurement of outcomes in economic evaluations of drug misuse interventions. Three different aspects of measuring outcomes are examined: one focusing on non-monetary outcomes at the individual patient level; one focusing on monetary outcomes within studies using individual patient level data; and one focusing on long-term outcomes, both monetary and non-monetary. The many limitations of measuring these outcomes in existing economic evaluations of drug misuse interventions are exposed and the problems with conducting such studies are identified. The importance of this thesis is thus in providing an overview and methodological critique of the extant economic evaluations of drug misuse interventions. In addition a decision analytic model for a drug testing in schools programme is developed to illustrate how the limitations highlighted in the methodological critique might be addressed by future research.

The findings of the thesis reveal the problems with using EQ-5D as a generic outcome measure for economic evaluations of drug misuse interventions, as is recommended by NICE in the UK. The nature of drug misuse problems requires that a wide range of different measures, including drug misuse specific measures, must be taken into account when evaluating drug misuse interventions. Similarly, the limitations with existing studies that attempt to estimate the monetary outcome of drug misuse interventions are exposed, as many studies fail to take into account all of the costs that will determine the monetary impact of an intervention for society. The thesis stresses the complexity of drug misuse and the need to measure the long-term outcomes of interventions, which may be best achieved by developing drug misuse modelling studies. However, these models are then revealed to be themselves limited, in part due to the lack of real-world data available to set their parameters.

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Author's declaration

I declare that all the work presented in this thesis has been carried out by the author, unless otherwise acknowledged. The views expressed are those of the author alone and the author takes full responsibility for the research presented in the thesis.

Chapter 1 Introduction

1.1 Outcomes of drug misuse interventions

Over the last few centuries, drug misuse has affected both individuals and society. For instance, problems related to opium addiction have been recorded in Europe, Africa, and Asia since the sixteenth century (Brownstein, 1993). Heroin smoking began in Shanghai in the 1920s and gradually spread through Asia and Europe in the 1960s and 1970s (Strang et al, 1997).

In many countries drug misuse is criminalised, such as in America where it has been considered as a criminal offence since the Harrison Act of 1914 (King, 1953). However, more recent developments in the drug misuse policies of some countries, like Portugal, have resulted in drug misuse being considered as a chronic health condition and therefore, instead of being met with criminal proceedings, drug users are referred to related treatments (van het Loo, van Beusekom and Kahan, 2002).

Regardless of whether or not drug misuse is illegal, it involves a complex of problems which are related to the patients, their family and friends, as well as other people in society. Drug misuse is more complex than other chronic diseases and the evaluation of drug misuse interventions usually includes multi-dimensional outcomes.

In the review by Rehm and colleagues (2000), the effectiveness of drug misuse treatment is categorised in 3 major dimensions: the continuation of drug misuse; improvement of medical condition; and social integration. Similarly, the review by Connock and colleagues (2007) also includes a wide range of outcomes among the opioid dependent patients: drug use, health of drug user, social effects and crime. The drug use outcome covers areas like changes in illicit drug use, concordance and retention in treatment, while the health of drug user outcome covers drug related mortality and morbidity, health related quality of life, use of health care systems and the major adverse effects of treatment. The social effects outcome covers problems related to employment and the family, and the crime outcome covers crime rates and recidivism (Connock et al, 2007). Another review of the treatment among the

opioid addicts includes categories like retention in treatment, use of primary substance, follow-up completion rate, compliance, craving, psychiatric symptoms, quality of life and severity of dependence (Amato et al, 2008).

In many countries economic evaluations are central to the decision making process for policy makers. The study by Ross (1995) shows that decision makers in Australia are highly aware of economic evaluations and some have taken these into consideration during the decision making process. Similarly, one study shows that economic evaluations have increasing potential use for decision makers in the UK (Drummond, Cooke, and Walley, 1997; Drummond, Jonsson and Rutten, 1997). Furthermore, in the UK, the guideline of NICE (National Institute for Clinical Excellence) requires that technology assessments include analysis of the cost-effectiveness of the health interventions (NICE, 2008; Claxton, Sculpher and Drummond, 2002).

In an economic evaluation there are a number of different methods that may be used to evaluate the interventions. The outcomes of the intervention may be measured in the form of a natural unit like reduction of blood pressure in a cost-effectiveness analysis, or a measure of health related utility, such as quality-adjusted life years (QALYs) in a cost-utility analysis. The outcomes can also be measured in the monetary unit of a cost-benefit analysis, such as willingness-to-pay (Drummond, M.F. et al, 2005), and there are more general outcomes measured in monetary terms that apply to all types of economic evaluations such as the savings in social resources following the intervention.

When carrying out economic evaluations certain choices have to be made about which outcomes are measured and this depends on the perspective from which the research is carried out. The decision regarding which outcomes to include usually depends on the interests of those undertaking the research, or the funding body, or the policy makers. For policy makers, the decision regarding which outcomes to include in an economic evaluation depends on their perspective. Claxton and colleagues (2010) have shown that policy makers in different countries have adopted different perspectives when making health policy. In the UK, health policies are based on the NHS perspective and are mainly determined by the effects on individuals' health after receiving treatment (Claxton et al, 2010). The new

guidelines of NICE require that QALYs should be the main health outcome measured in economic evaluations and EQ-5D is their preferred quality-of life questionnaire (NICE, 2008).

Following the guidelines set out by NICE, the policy makers for drug misuse interventions within the NHS in the UK would focus on the economic evaluation of the health related outcome when making decisions. However, reviews of outcomes of drug misuse interventions show that drug misuse is a problem related to multi-dimensional outcomes (Rehm, Guggenbuhl and Uchtenhagen, 2000; Connock et al, 2007; Amato et al, 2008). By only using EQ-5D to estimate the outcomes of drug misuse interventions, as NICE suggests, policy makers could misjudge the effectiveness of the interventions. There is very little literature and research that examines the relationship between EQ-5D and other non-monetary outcomes in drug misuse interventions, and analyses whether or not there are problems with only using EQ-5D as the single measure in economic evaluations of drug misuse interventions. The first part of this thesis will therefore analyse the relationship between EQ-5D and other non-monetary outcomes in economic evaluations of drug misuse interventions.

The non-monetary outcome is only one aspect of the economic evaluation of drug misuse interventions. It is also important to consider the monetary outcome and to know which dimensions of this outcome should be measured. In a report to the NHS Health Development Agency, Kelly and colleagues (2005) suggest that the monetary outcome can be presented as the difference of the resources used or of the resources saved. The difference of the resources used shows the cost of the resources that the patient have used as a result of the intervention, whereas the difference of resources saved estimates the savings to society from the patient having received the intervention.

It is especially important to estimate the societal cost of drug misuse interventions given that drug misuse is usually regarded as being closely related to the social resource use, particularly with respect to the criminal justice system and the health burden of hepatitis and HIV (Cartwright, 1998; Cartwright, 2008; Garfein et al, 1996; Godfrey, 2006; Hser and Anglin, 1991; Joseph, 1988; Mark et al, 2001; Masson et al, 2002; Neale et al, 2006;

Sweeney et al, 2009; Wiessing et al, 2004). Although different outcome categories have been developed (Godfrey, 2006; Simoens et al, 2006; McCollister and French, 2003), there are only a few common methods for estimating the monetary benefit within these categories.

Another issue related to the monetary outcome is that it is usually presented as the sum of the different resources used. However, it may be that certain types of patients have higher costs with respect to one resource (such as health cost) and less with respect to another (such as the cost of crime committed). By only presenting the sum of the resource used this information is lost, yet identifying the specific relationship between the types of drug users and the resources they use may help policy makers to make decisions about the allocation of resources. However, very few studies have analysed these relationships. The second part of the thesis therefore reviews the dimensions of the monetary outcome considered in existing drug misuse intervention studies and explores the relationship between specific drug user characteristics and the different dimensions of the monetary outcome.

One of the problems with clinical trials is that they usually only last for a limited period of time and the follow-up period of the intervention is rarely longer than 2 years. When comparing the different interventions, NICE has recommended that the appropriate time horizon should reflect the period when the participants are expected to experience the main differences arising from the intervention. Accordingly, if the intervention has long-term effects, it may be necessary to consider the different outcomes over the course of the patients' lifetimes (NICE, 2008). However, the time and resources required to do this are usually unavailable for clinical trials.

An alternative approach for considering the long-term outcomes of drug misuse interventions is by using decision analytic models, which are developed to synthesize the costs and the outcomes of the interventions (Buxton et al, 1997). However, only a few economic evaluation studies have developed modelling methods to estimate the simulation of lifetime costs and outcomes for drug misuse patients (French and Drummond, 2005; Zarkin et al, 2005). The third part of this thesis will therefore compare the current modelling methods for drug misuse and develop a new model for evaluating a drug misuse intervention.

1.2 Purpose and objectives of the research

The aim of this thesis is to explore the problems with measuring outcomes in economic evaluations of drug misuse interventions and the implications for policy makers. In doing so the thesis provides an overview of current economic evaluations in drug misuse research and an agenda for related studies in the future. There are 3 primary objectives of the research. The first is to explore the relationship between EQ-5D (a measure of QALYs) and other non-monetary outcome measures. This involves examining whether or not the outcome of EQ-5D reflects the trends of the outcomes in other drug misuse specific measures, and considering whether EQ-5D covers the same content as the other measures.

The second objective is to evaluate the dimensions of the monetary outcome that have been considered in existing drug misuse intervention studies. This involves examining whether or not previous economic evaluations have measured all of the relevant dimensions of the monetary outcome and whether specific relationships can be identified between patient characteristics and associated dimensions of the monetary outcome. While the first two objectives examine the individual patient level outcomes, the third objective is to explore the use of modelling studies for the economic evaluation of drug misuse interventions. This involves reviewing the existing models to reveal their limitations and building a new model that attempts to overcome many of the problems with existing studies identified throughout the thesis.

This thesis will demonstrate that the complexity of drug misuse problems demands that a wide range of both monetary and non-monetary outcomes should be considered to provide a comprehensive evaluation of drug misuse interventions from the societal perspective. Furthermore, it will be maintained that these outcomes need to be measured over long time periods to estimate the overall societal impact of drug misuse interventions. By exposing the limitations with existing economic evaluation studies, the problems that policy makers need to be aware of and that future researchers need to address will be elucidated.

1.3 Structure of thesis

1.3.1 Non-monetary outcome measures

To meet these 3 objectives, the thesis consists of 6 interrelated chapters, with 2 chapters dedicated to each objective. As NICE (2008) in the UK recommends using EQ-5D as a generic outcome measure for economic evaluations of health interventions, the first 2 chapters analyse the adequacy of this measure for drug misuse interventions through a systematic review and then a secondary data analysis of existing studies. Chapter 2 first identifies the existing drug misuse intervention studies that have considered both EQ-5D and another non-monetary outcome and then evaluates whether or not the outcome of EQ-5D reflects the trends of the outcomes of the other measures. If EQ-5D adequately reflects the trends of other measures then it may be appropriate to use it as a generic measure in economic evaluations, without considering drug misuse specific measures. This would be advantageous for policy makers as drug misuse interventions could then be evaluated using the same measure that is recommended more generally for all economic evaluations of health interventions. However, if EQ-5D does not have the same trends as other measures, then using it as the only measure may lead to policy makers misjudging the effects of a given drug misuse intervention.

It is not only the trends of the outcomes between EQ-5D and other measures that needs to be considered, however, as it is also important to know whether EQ-5D and other non-monetary outcome measures cover the same concepts. That is, whether or not the questionnaires used in other outcome measures cover similar content to that of EQ-5D. Chapter 3 thus conducts a content comparison of the drug intervention studies that consider both EQ-5D and other outcome measures. If they cover similar concepts then it may be appropriate to use EQ-5D as a single outcome measure for drug misuse intervention studies, however, if this is not the case then a wider range of measures should be taken into account.

1.3.2 Dimensions of the monetary outcome

Chapters 4 and 5 evaluate the dimensions of the monetary outcome measured in existing drug misuse intervention studies, again through a systematic review and then an empirical analysis. Chapter 4 reviews existing drug misuse intervention studies that have measured dimensions

of the monetary outcome. The chapter follows Godfrey (2006) in categorising the dimensions that it is important to consider into 2 domains and then examining whether the studies that claim to provide a societal perspective actually consider all the relevant dimensions of these domains. Given that drug misuse is associated with a range of social problems it is important to know whether existing economic evaluations actually consider all the monetary dimensions that would influence the societal impact of an intervention.

Chapter 5 proceeds to examine whether or not a profile can be developed of different types of drug misuse patient. If relationships could be identified between patient characteristics and the monetary dimensions that specific patients use then policy makers could take this into consideration and direct different interventions at different groups of drug misuse patients. To attempt to develop this profile the chapter uses an existing data sample, RESULT (Raistrick et al, 2007). The data is clustered into groups, which are then analysed to try to identify relationships between patient characteristics and different dimensions of the monetary outcome, or even just between different monetary dimensions.

1.3.3 Modelling studies

Chapters 6 and 7 focus on modelling studies in the economic evaluation of drug misuse interventions, which can potentially provide long-term estimates of the costs and outcomes of interventions. A modelling study is an analytical approach which provides a structural framework for decision making under conditions of uncertainty. It provides the full structure of the possible prognoses of the individual, brings together the relevant evidence from different resources, and translates this evidence into estimates of cost and effectiveness to predict outcomes in the long-term. Chapter 6 reviews the limited number of economic evaluation models that have previously been developed for drug misuse interventions. Using the checklist of good practice developed by Phillips and colleagues (2004), the quality of these models is examined to assess their limitations.

Chapter 7 attempts to develop a new decision analytic model to evaluate the introduction of a drug testing in schools programme. The aim of developing this model is to try to overcome the limitations that have been identified in existing economic evaluations of drug misuse

interventions. In particular, the model attempts to take into consideration a range of both monetary and non-monetary outcomes in the long-term to provide a comprehensive evaluation of the intervention from the societal perspective. Chapter 7 thus explores the possibilities and limitations of trying to address the problems highlighted throughout the thesis within a single study. The extent to which the model is able to address previously identified problems is examined and the implications for policy makers and future researchers are elucidated.

Chapter 2 Using EQ-5D as an outcome measure in the economic evaluation of drug misuse interventions: a systematic review

2.1 Background

When calculating the cost-utility or cost-effectiveness ratios in economic evaluations only one outcome measure can be considered. For policy makers it is useful if generic outcomes are measured as this allows them to compare interventions across different fields and provides standard criteria to inform their decisions about whether or not to adopt a given intervention. In a recent review by Claxton and colleagues (2010) quality-adjusted life years (QALYs) were identified as the preferred generic outcome measure for health policy makers in countries such as Australia, Canada and the UK. Indeed in the UK the NICE guideline (2008) formally requires that QALYs are used to measure health outcomes. QALYs are a measure of an individual's life years that are adjusted to take into account health-related quality of life (Drummond, M.F. et al, 2005).

There are a number of different instruments that may be used to estimate QALYs and the NICE guideline (2008) recommends the use of the EQ-5D instrument with UK population values for this purpose. The use of EQ-5D and its sensitivity to change has been established for a range of conditions including chronic conditions and mental health illnesses (Almond et al, 2004; Brazier et al, 2004; Byford et al, 2003; Haro et al, 2003; Jerant, Chapman and Franks, 2008; Lamers et al, 2006; Myers and Wilks, 1998; Sobocki et al, 2007). In economic evaluations of drug misuse, however, a large range of naturalistic outcome measures have been used and EQ-5D has not been widely tested.

It is important for policy makers to know whether or not using the EQ-5D measure leads to similar results as those estimated by other outcome measures, including measures that are specifically designed for drug misuse. The problem is further complicated as there is no "gold standard" outcome measure for drug misuse, therefore to determine whether or not EQ-5D is an adequate measure it needs to be compared with a range of drug misuse specific outcome measures. If there are similar trends between EQ-5D and other drug misuse specific outcome measures then EQ-5D may prove to be an adequate generic outcome measure in this

field. However, if there are no such similar trends, it would suggest that policy makers cannot rely on EQ-5D alone to estimate the outcomes of drug misuse interventions.

2.2 Objectives

The aim of this chapter is to review drug misuse studies that have evaluated EQ-5D and other outcome measures to determine whether or not EQ-5D is an adequate outcome measure for drug misuse interventions. The first objective is descriptive and involves identifying how many studies of drug misuse interventions have included EQ-5D as an outcome measure and which other outcomes measures they include along with it. The second objective is to examine the trends between EQ-5D and other outcome measures. In order to do this the outcomes scores identified in the studies reviewed are first standardised so that the outcome measures can be compared with one another.

2.3 Methods

2.3.1 Inclusion Criteria for this review

Type of studies: Economic evaluation studies that measure EQ-5D along with clinical outcomes for drug misuse interventions will be included. Only studies collecting individual patient level data will be included. Studies only measuring intervention costs or only measuring clinical effectiveness will not be included.

Type of intervention: Studies of interventions primarily aimed at reducing drug misuse problems will be included. All types of intervention delivered to the individual drug user or potential drug users will be considered. Studies of interventions delivered solely to the drug users' family/ partner will not be included as the focus here is only on the outcome of the individual drug users.

Type of participants: People who misuse substances, including any type of illegal substance. Studies of people with alcohol addictions or smoking problems only will be excluded.

Comparison: Studies considering at least one intervention will be included. Studies that measured outcomes either at one point of time, at different points of time, or the changes between points of time will be included.

2.3.2 Data sources and search strategy

Both electronic and manual searches are undertaken to identify studies.

Search strategy:

The search was performed in July 2010. Studies which meet the inclusion criteria are identified from the following sources. The beginning of the search is 1990, when EQ-5D was developed and discussed in the published literature. There is no language restriction.

Econlit

EMBASE

MEDLINE

PsycINFO

CRD (Centre for Reviews and Dissemination) databases

The Cochrane Library

The Cochrane Central Register of Controlled Trials (CENTRAL)

Current Controlled Trials Register

Example of searching strategy: MEDLINE; 1990 – to July 2010:

(drug misuse or drug dependen* or substance misuse or substance abuse or substance dependen* or addict* or illegal drug* or illicit drug* or inject* drug* or methadone or heroin or opiat* or opium or cocaine or crack cocaine or ecstasy or LSD or magic mushroom* or amphetamine or cannabis or marijuana or ketamine) and (EQ-5D or EuroQoL or QALY*)

2.3.3 Analysis of the extracted data

The extracted data from the identified studies must first be standardised before the results can be compared and trends can be identified. There are sophisticated statistical techniques to standardise data that would be applicable if the individual patient scores were available, such

as the Z score, which considers the variance of the individual scores within the sample. However, as the individual patient scores were not available, more simplified techniques based on the mean score of the outcome measure for the study sample are used to standardise the data, as detailed below. In addition, for 3 of the studies, the HEPC trial (Abou-Saleh et al, 2003; Abou-Saleh et al, 2008), the study by Carpentier and colleagues (2009) and the UKCBTMM trial (Drummond et al, 2004; Drummond, C. et al, 2005), the standard deviation of the mean score for each measure can be extracted from the reports to indicate the variance of the mean score.

Standard mean score

Different measures use different scales to estimate the outcomes. For example, in EQ-5D the self-reported health state scores range from -0.594 to 1 when applying the UK population value, where 1 represents the best health state (Dolan, 1997; Dolan et al, 1995; EuroQol group, 1990; Kind, Hardman and Macran, 1999). By contrast, the scores of another outcome measure, SF-12, are usually presented as 2 composite scores: MCS (mental component summary) and PCS (physical component summary). In each case the scores range from 0 to 100, where 100 represents the best state of either the individual's mental or physical health (Ware, Kosinski and Keller, 1995 and 1996). In order to compare the relative changes from the different outcome measures, standard mean scores are established, using the following formula which provides a standardised score ranging from 0 to 100:

$$\text{Standard mean score} = \text{mean score} / \text{score range} * 100$$

For instance, at the baseline of the UKCBTMM trial (Drummond et al, 2004; Drummond, C. et al, 2005), the actual mean score of EQ-5D is 0.6875 and the SF-12 physical health score (PCS) is 38.89 within the whole trial sample. Both of the scores are converted into the standard mean score as follows:

$$\text{EQ-5D standard score} = 0.6875 / 1.594 * 100 = 43.13$$

$$\text{SF-12 PCS standard score} = 38.89 / 100 * 100 = 38.89$$

Reversed score

Another problem with comparing outcome measures is that in some measures the highest score represents the worst outcome. For example, the score range of SDS (Severity of Dependence Scale) is between 0 and 15, where 15 represents the worst outcome as it indicates the greatest dependence severity (Gossop et al, 1995). There is, therefore, an initial difficulty when comparing the results of SDS with the results other outcome measures such as EQ-5D because the highest score of SDS represents the worst outcome whereas the highest score of EQ-5D represents the best outcome. However, when the scores are reversed for SDS 0 represents the worst outcome and 15 represents the best outcome, so it can easily be compared with EQ-5D. The following formula is thus used to calculate the reversed mean score when the highest score originally represents the worst outcome:

Reversed mean score = Highest score – actual mean score

Using SDS in the UKCBTMM trial (Drummond et al, 2004; Drummond, C. et al, 2005) as an example, the actual SDS mean score is 9.78 in a range from 0 to 15. The reversed mean score is therefore calculated as 5.22 (=15-9.78), which can then be converted into the standard mean score of 34.8 (=5.22/15*100). The reversed standard mean score still represents individuals' dependence severity, however, the higher score now represents a lower dependence severity and may therefore be compared with other outcome measures like EQ-5D.

Percentage of score change

Having standardised the scores, the percentage of score change is calculated using the following formula:

Percentage of score change = (follow-up standard mean score – baseline standard mean score) / baseline standard mean score*100%

The percentage of score change shows the score change in the outcome measured taken as a percentage of the standardised baseline score. If the outcome change is above 0, this reflects an improvement in the outcome measured at the follow up period, whereas if it is below 0, this reflects deterioration in the outcome measured. The degree of change in the different outcome measures may be related to the sensitivity of the measures when evaluating the outcomes among drug misuse patients.

2.4 Results

2.4.1 Description of included studies and outcome measures included

The first objective of the review was to identify studies that measured EQ-5D and at least one other outcome measure. The review identified 81 studies in total, of which only 8 were drug misuse intervention studies. Most of the excluded studies were related to opiate use for cancer patients. Within the 8 included studies, 5 studies were controlled trials, 2 were cross-sectional studies, and 1 was an on-going randomised controlled trial. This ongoing trial is not scheduled to be completed until September 2010 and published results will not be available for this thesis.

The interventions used in the included studies ranged from counselling sessions to prescribed heroin or methadone treatment. These included 2 types of HIV prevention counselling, prescribed buprenorphine, methadone maintenance treatment, prescribed heroin, and cognitive behaviour therapy.

The duration of the trials ranged from 3 months to 12 months. The follow-up periods were between 2 and 14 months. The participants were all adult drug users and the number of participants ranged from between 21 to 2,414. All of the included studies were conducted in Europe, including 3 UK studies, 2 Dutch studies, 1 Spanish study, 1 German study and 1 Danish study. Details of each included study are listed in Table 2.4.1.

The review identified 31 other outcome measures that were considered along with EQ-5D in the relevant studies, which are also listed in Table 2.4.1. Of these 31 measures, only 16 were

directly related to drug misuse. Rehm and colleagues (2000) recommend that different outcome measures can be categorised into 3 dimensions: continuation of illegal substance use and abuse; improvement of medical conditions (somatic and mental); and social integration (criminal behaviour, work, housing, personal relations). The 16 relevant outcome measures are categorised in these 3 dimensions in Table 2.4.2, and each measure can be categorised in more than one dimension depending on the problems with which it is concerned. For example, the Severity of Dependence Scale (SDS) is only concerned with problems relating to individuals' dependence severity and is therefore only categorised in the first dimension, illegal substance use and abuse. By contrast, the European Addiction Severity Index (EuropASI) is concerned with problems related to individuals' drug misuse, medical and psychological health, work satisfaction and family and other relationships, and is therefore included in all 3 dimensions. The full details of each outcome measure are listed in Appendix 1. All of the 8 studies have considered outcome measures in each of the 3 dimensions, which indicates that all the studies consider that it is important to take into account all of the dimensions to provide a comprehensive evaluation of drug misuse interventions.

Table 2.4.1 Description of included studies

Study	Population	Intervention	Follow-up period	Clinical outcome measure
Abou-Saleh et al, 2003; Abou-Saleh et al, 2008 (HEPC), UK	33 injecting drug users, recruited from drug treatment centres	Trial enhanced HIV prevention counselling intervention: Stay Safe Therapy (SST; 4 sessions) versus Simple Educational Counselling (SEC; 1 session)	6 months	-Alcohol Use Disorders Identification Test; AUDIT -Drug Injecting Confidence Questionnaire; DICQ, adopted from DTCQ - European addiction severity index; EuropASI -Hepatitis-C Knowledge Questionnaire; HCV-K -HIV Risk-Taking Behaviour Scale; RTBS -Injecting Risk Questionnaire; IRQ -Readiness to Change Questionnaire; RCQ
Carpentier et al, 2009, Netherlands	193 opiate addicts, recruited from existing methadone maintenance programme	Methadone maintenance programme	N/A	-EuropASI - WHO's Composite International Diagnostic Interview; CIDI(illegal substance section only) -Social Conformism Scale; SCS
Castillo, 2008, Spain	100 opiate addicts, recruited from existing methadone maintenance programme	Methadone maintenance programme	N/A	-IDUQoL(score not presented) -SF-36(score not presented)
Dijkgraaf et al, 2005; van den Brink et al, 2003, Netherlands	430 heroin addicts, the sub- sample from 549 heroin addicts recruited from existing methadone maintenance programmes	methadone versus heroin prescribed over 12 months	EQ-5D data: 2, 6, 10, 12 months (treatment continues through follow-up periods) Clinical outcome: 12 and 14 month	- EuropASI -CIDI -Maudsley Addiction Profile (MAP-HSS; health symptoms section only) (not presented in analysis of sub-sample) -Symptom Checklist-90; SCL-

				90 (not presented in analysis of sub-sample)
Drummond et al, 2004; Drummond, C. et al, 2005 (UKCBTMM), UK	60 opiate addicts, recruited from 10 community based clinics	Cognitive behaviour therapy (CBT) plus methadone maintenance treatment (MMT) versus MMT alone	6 and 12 months	-Brief symptom inventory; BSI -Coping responses inventory; CRI -Drug taking confidence questionnaire; DTCQ-8 - EuropASI -Severity of dependence scale; SDS -SF-12 -Stage of change readiness and treatment eagerness scale; SOCRATES -Timeline follow back; TLFB for heroin, methadone and alcohol
Hjorthoj et al, 2008 (CapOpus), ongoing trial lasts from March 2007 to September 2010, Denmark	Aim to recruit between 120 and 140 young patients (Aged 18-35) with cannabis abuse and psychosis	Specialized addiction treatment (CapOpus) plus treatment as usual versus treatment as usual over 6 months	6, 10 months	-Brief Assessment of Cognition in Schizophrenia; BACS -Client Satisfaction Questionnaire; CSQ -Continuous Performance Test, Identical Pairs version; CPT-IP -Danish Adult Reading Test; DART -Hopkins Verbal Learning Test; HVLT -Manchester Short Assessment of Quality of Life; MANSA -Neuropsychological Assessment Battery; NAB -Positive and Negative Syndrome Scale for psychosis

				<p>symptom; PANSS</p> <ul style="list-style-type: none"> - TLFB for cannabis - 12 item interviewer administrated version of WHO's Disability Assessment Schedules; WHODAS-II
<p>Lintzeris et al, 2006; Strang et al, 2010, (RIOTT), UK</p>	<p>127 heroin dependents recruited from supervised injecting clinics</p>	<p>Injected methadone treatment versus injected heroin treatment versus optimized oral methadone treatment over 6 months</p>	<p>13 and 26 weeks (treatment continues through follow-up periods)</p>	<ul style="list-style-type: none"> -Hospital Anxiety and Depression Scale; HADS -Injecting Risk Questionnaire -Maudsley Addiction Profile (crime Section only) -Opiate Treatment Index; OTI (drug use, crime and psychological health sections only) -SF-36 -Treatment Perception Questionnaire; TPQ
<p>Schafer et al, 2009 (COBRA), Germany</p>	<p>2,414 opiate addicts, recruited from 233 opiate substitution doctors/centres</p>	<p>Antiviral interferon (IFN) treatment on opiate addicts with and without hepatitis C virus (HCV) infection</p>	<p>12 months</p>	<ul style="list-style-type: none"> -BSI - EuropASI -CIDI

Table 2.4.2 List of outcome measure categories in the included studies, using dimensions suggested by Rehm and colleagues (2000)

	Continuation of illegal substance use and misuse	Improvement of medical condition	Social integration
Abou-Saleh et al, 2003; Abou-Saleh et al, 2008 (HEPC) ^a	EuropASI, IRQ, RTBS	EuropASI	EuropASI
Carpentier et al, 2009	EuropASI, CIDI	EuropASI	EuropASI
Castillo, 2008	IDUQoL	IDUQoL, SF-36	IDUQoL
Dijkgraaf et al, 2005; van den Brink et al, 2003	EuropASI	MAP-HSS, SCL-90	EuropASI
Drummond et al, 2004; Drummond, C. et al, 2005 (UKCBTMM) ^b	EuropASI, SDS, TLFB	BSI, EuropASI, SF-12	EuropASI
Hjorthoj et al, 2008 (CapOpus) ^c	TLFB	MANSA, WHODAS II	MANSA
Lintzeris et al, 2006; Strang et al, 2010, (RIOTT) ^d	IRQ, OTI	HADS, OTI, SF-36	MAP-crime, OTI
Schafer et al, 2009 (COBRA)	EuropASI, CIDI	BSI, EuropASI	EuropASI, CIDI

a: AUDIT from HEPC is excluded in the analysis because it measures consumption of alcohol, not illegal substances. HCV-K, DICQ and RCQ from HEPC are also excluded because they are the process measures for drug misuse problems.

b: The TLFB section related to alcohol problems from UKCBTMM is excluded in the analysis because it is not a measure of illegal substance use. CRI, DTCQ-8, and SOCRATES from UKCBTMM are also excluded because they are the process measures for drug misuse problems.

c: BACS, CPI-IP, DART, HVLT, NAB, and PANSS from CapOpus are excluded in the analysis, because they are specific assessment for psychosis patients. CSQ is also excluded because it is an assessment of patients' satisfaction and is not directly related to the effectiveness of the intervention.

d: TPQ from RIOTT is excluded in the analysis because it assesses patients' satisfaction and is not related to the effectiveness of the intervention.

2.4.2 Outcome comparison of the included studies

The second objective of the review is to compare the trends between EQ-5D and other outcome measures. Although there are 8 drug misuse intervention studies that have considered EQ-5D and at least one other outcome measure, only 5 of these reported the scores for both EQ-5D and the other measures. To compare the trends between EQ-5D and other outcome measures these scores are required, therefore only 5 studies are examined: the HEPC trial (Abou-Saleh et al, 2003; Abou-Saleh et al, 2008), the study by Carpentier and colleagues (2009), the Dutch prescribed heroin trial (Dijkgraaf et al, 2005; van den Brink et al, 2003), the UKCBTMM trial (Drummond et al, 2004; Drummond, C. et al, 2005) and the COBRA trial (Schafer et al, 2009). The outcome measures from these trials can be compared with EQ-5D, in each case by each of the 3 dimension in turn. In some cases the outcome measures are broken down into subscales, such as EuropASI, so more measure are examined in the results than the original 16 outcome measures identified in the review.

HEPC trial

The HEPC trial (Abou-Saleh et al, 2003; Abou-Saleh et al, 2008) recorded scores at baseline and 6 month follow-up periods, and the change between these two time points. Table 2.4.3 presents the original scores extracted from the study, the standardised mean scores and percentage score change for all of the outcome measures or the subscales of outcome measures in the HEPC trial.

In the first dimension, continuation of illegal substance use and abuse, the standardised mean scores at baseline and the follow-up period reveal that EQ-5D only has relatively similar scores to 1 of the 3 other measures (EuropASI Drug): at baseline the EQ-5D score was 51.6 and the EuropASI Drug score was 60.1 and at the follow-up period the EQ-5D score was 57.9 and the EuropASI Drug score was 65.2. The 2 measures also have similar percentage score changes: 8.49% for EuropASI Drug and 12.5% for EQ-5D. 1 of the other measures (RTBS) also records a similar percentage of score change of 10.46%, however the scores in RTBS are consistently higher than in EQ-5D. EQ-5D does not reflect the trends of the other measure (IRQ) at all, which records a percentage score change of 100%. These results show

that within the first dimension, EQ-5D only describes patients' outcomes similarly to 1 of the 3 measures at different points of time, but records similar proportional changes to 2 of the 3 measures over the period of time.

In the second dimension, improvement of medical condition, neither of the 2 measures record similar results to EQ-5D. Both measures have scores of consistently more than 30 units of the standard mean score higher than EQ-5D at both baseline and the follow-up period. However, both measures do show that, like EQ-5D, the patients' scores have improved over the follow-up period, recording percentage score changes of 4.74% (EuropASI Medical) and 6.35% (EuropASI Psychiatric), even though this is lower than the 12.5% score change of EQ-5D. In the third dimension, social integration, EQ-5D has considerably lower scores at baseline and the follow-up period than all of the 5 measures with the exception of EuropASI Economic, which EQ-5D has considerably higher scores than. However, EQ-5D does record very similar percentage score changes to 2 of the other measures: EuropASI Other relationship, which has 10.22% change, and EuropASI Work satisfaction, which has 13.54% change. EQ-5D also has quite similar percentage score changes to 2 of the other measures but not to EuropASI Economic, which is the only measure in the HEPC trial where the patient score decreased over the follow-up period, recording a -29.65% score change.

Taking all of the dimensions together, as illustrated in Figure 2.4.1, EQ-5D only describes patients' outcomes at different points of time similarly to EuropASI Drug, and generally records lower scores than most other measures, which indicates that the patients' health related quality of life outcome is generally lower than other outcomes. All of the measures except one recorded improved scores over the 6 month follow-up period, and EQ-5D reflected very similar trends of change to 4 other measures and quite similar trends to another 4 of the measures, as is illustrated by Figure 2.4.2.

Table 2.4.3 Result of included studies: HEPC

n=33	Baseline		6 month follow-up		Change at 6 month
Outcome measure	Standard mean score; A (S.D.)	Original mean score; A' (S.D.)	Standard mean score; B (S.D.)	Original mean score; B' (S.D.)	% of score change; (B-A)/A
EQ-5D ^a	51.6 (12.4)	0.823 (0.198)	57.9 (13.9)	0.923 (0.221)	12.2
Continuation of illegal substance use and abuse					
EuropASI Drug ^b	60.1 (15.3)	0.399 (0.153)	65.2 (19.6)	0.348 (0.196)	8.5
IRQ ^c	39.4	60.6	78.8	21.2	100.0
RTBS ^d	79.5 (15.1)	11.3 (8.3)	87.8 (11.3)	6.7 (6.2)	10.5
Improvement of medical condition					
EuropASI Medical ^b	88.6 (27.1)	0.114 (0.271)	92.8 (19.5)	0.072 (0.195)	4.7
EuropASI Psychiatric ^b	83.5 (22.1)	0.165 (0.221)	88.8 (18.3)	0.112 (0.183)	6.3
Social integration					
EuropASI Economics ^b	31.7 (42.8)	0.683 (0.428)	22.3 (39.4)	0.777 (0.394)	-29.7
EuropASI Family relationship ^b	87.2 (18.8)	0.128 (0.188)	92.4 (13.8)	0.076 (0.138)	6.0
EuropASI Legal ^b	87.8 (18.2)	0.122 (0.182)	92.2 (13.3)	0.078 (0.133)	5.0
EuropASI Other relationship ^b	87.1 (17.3)	0.129 (0.173)	96.0 (9.8)	0.040 (0.098)	10.2
EuropASI Work satisfaction ^b	68.7 (29.6)	0.313 (0.296)	78.0 (29.5)	0.220 (0.295)	13.5

a: The original score range of EQ-5D is between -0.594 and 1 using the UK social tariff, where 1 means that individuals have the best health state (Dolan, 1997; Dolan et al, 1995; EuroQol group, 1990; Kind, Hardman and Macran, 1999).

b: The score range of each subscale of EuropASI (European Addiction Severity Index) is between 0 and 1, where 1 means that individuals have the most problems or greatest severity in each subscale (Koeter and Hartgers, 1997; Kokkevi and Hartgers, 1995). The extracted scores are reversed in all subscales of EuropASI.

c: The IRQ (Injecting Risk Questionnaire) results from the HEPC trial is presented as percentage of individuals who shared any IV equipment in last month. The extracted IRQ results are reversed. The standard deviation of IRQ is not reported in the HEPC trial report.

d: The score range of RTBS (HIV Risk-Taking Behaviour Scale) is between 0 and 55, where 55 means that the individual has a higher incidence of HIV-related risk behaviour (Darke et al,1991a). The extracted RTBS score is reversed.

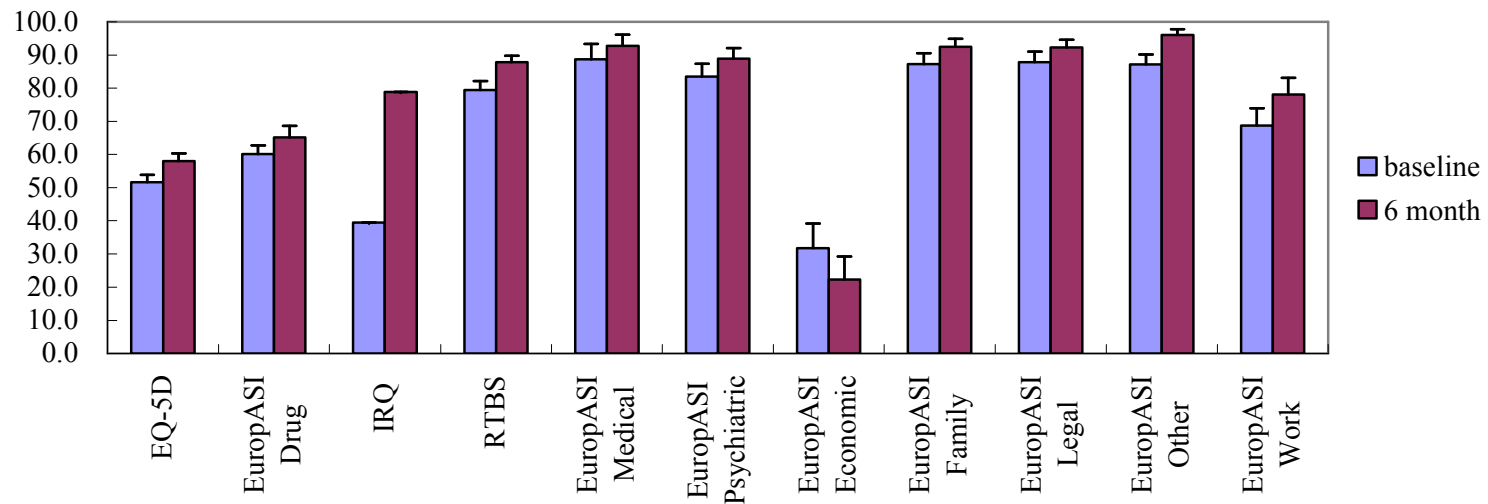


Figure 2.4.1 Standard mean scores and SEM (Standard Error of mean= SD/\sqrt{n}) bar of outcome measures at baseline and 6 month follow-up period in the HEPC trial

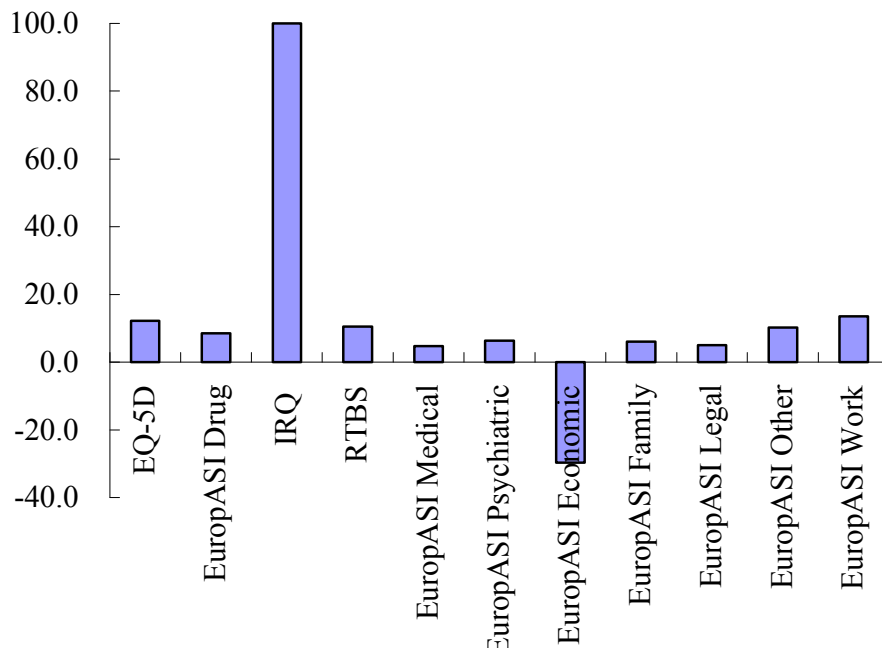


Figure 2.4.2 Percentage of score change of outcome measures between baseline and 6 month follow-up period in the HEPC trial

Carpentier et al, 2009

The study by Carpentier and colleagues (2009) is a cross-sectional study that only recorded scores at one point in time. Table 2.4.4 presents both the original scores extracted from the study and the standardised mean scores for all of the outcome measures or the subscales of outcome measures in the study. The study only considered EQ-5D, subscales of EuropASI, and CIDI, however, the CIDI scores were not reported.

The only measure in the first dimension was EuropASI Drug, which had a standardised mean score of 42.2 compared with the EQ-5D score of 41.4. There were 2 EuropASI subscales in the second dimension, with scores of 53.3 and 70.0. In the third dimension there were 3 EuropASI subscales with scores ranging between 50 and 59. As shown in Figure 2.4.3, it is only EuropASI Drug that EQ-5D has a very similar score to, which supports the findings from the HEPC trial, where this was the only other measure that had similar scores to EQ-5D at different points in time.

Table 2.4.4 Result of included studies: Carpentier et al 2009

n=193	Standard mean score; A (S.D.)	Original mean score; A' (S.D.)
EQ-5D ^a	41.4 (19.4)	0.66 (0.31)
Continuation of illegal substance use and abuse		
EuropASI Drug ^b	42.2 (16.7)	5.2 (1.5)
Improvement of medical condition		
EuropASI Medical ^b	70.0 (24.4)	2.7 (2.2)
EuropASI Psychiatric ^b	53.3 (24.4)	4.2 (2.2)
Social integration		
EuropASI Family/other relationship ^b	58.9 (20.0)	3.7 (1.8)
EuropASI Legal ^b	57.8 (25.6)	3.8 (2.3)
EuropASI Employment/support ^b	50.0 (20.0)	4.5 (1.8)

a: This study uses the UK social tariff for EQ-5D scores, hence, the original score range of EQ-5D is between -0.594 and 1, where 1 means that individuals have the best health state (Dolan, 1997; Dolan et al, 1995; EuroQol group, 1990; Kind, Hardman and Macran, 1999).

b: The score range of each subscale of EuropASI (European Addiction Severity Index) is between 0 and 9, where 9 means that individuals have the most problems or greatest severity in each subscale (Koeter and Hartgers, 1997; Kokkevi and Hartgers, 1995). The extracted scores are reversed in all subscales of EuropASI.

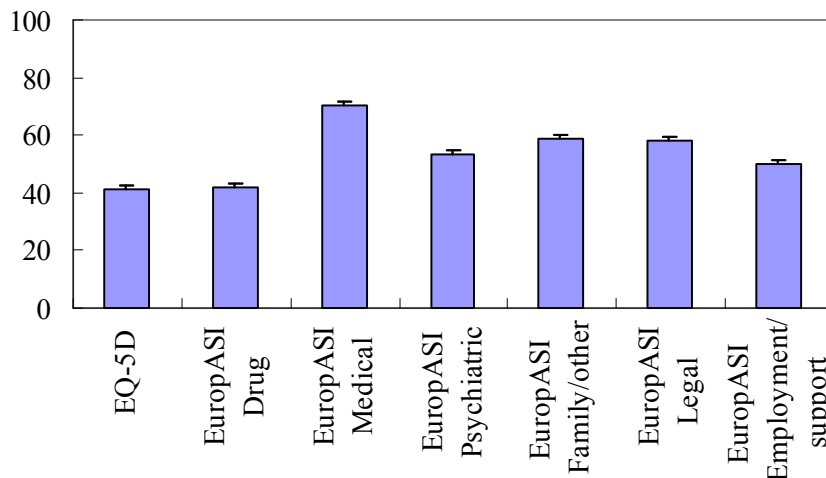


Figure 2.4.3 Standard mean scores and SEM bars of outcome measures in the study by Carpentier and colleagues (2009)

Dutch prescribed heroin trial

The Dutch prescribed heroin trial (Dijkgraaf et al, 2005; van den Brink et al, 2003) recorded scores at baseline, the 12 month follow-up period and the change between these time points. Table 2.4.5 presents the original scores, the standardised mean scores and the percentage score change for the measures in the trial. Although the trial has a sample of 433 heroin addicts at baseline, the report only presented scores for the subgroup of 193 patients who received methadone and prescribed heroin. Although the trial considered 3 different outcome measures (EuropASI, MAP-HSS and SCL-90) across the 3 dimensions, scores were only reported for 2 measures, both of which were in the second dimension, improvement of medical condition.

At baseline EQ-5D had a standardised mean score of 46.4, which is considerably lower than both the other measures, which scored 71.5 (MAP-HSS) and 80.0 (SCL-90). At the follow-up period the EQ-5D score was 51.0 which was very similar to MAP-HSS (59.3), but not to SCL-90 (72.8), as illustrated in Figure 2.4.4. However, more significantly, both of the other measures recorded negative percentage score changes over the follow-up period: -17.1% for MAP-HSS and -9.0% for SCL-90. By contrast, as shown in Figure 2.4.5, EQ-5D was the only measure to record improved scores with a 9.9% score change. EQ-5D does not therefore adequately reflect the trends of either of the other 2 measures in the trial.

Table 2.4.5 Result of included studies: Dutch prescribed heroin trial (sub-sample of patients received methadone maintenance treatment plus prescribed heroin)

n=193	Baseline		12 month follow-up		Change at 12 month
Outcome measure	standard mean score; A	mean score; A'	Standard mean score; B	mean score; B'	% of score change; (B-A)/A
EQ-5D ^a	46.4	0.740	51.0	0.813	9.9
Improvement of medical condition					
MAP-HSS ^b	71.5	11.4	59.3	16.3	-17.1
SCL-90 ^b	80.0	71.9	72.8	97.8	-9.0

a: The social tariff of EQ-5D is not stated in the trial. In a related study by van der Zanden and colleagues (2006), they have stated that they use the UK social tariff for EQ-5D scores. Assuming they also used the UK social tariff for this trial, the original score range of EQ-5D is between -0.594 and 1, where 1 means that individuals have the best health state (Dolan, 1997; Dolan et al, 1995; EuroQol group, 1990; Kind, Hardman and Macran, 1999).

b: The score range of MAP-HSS (health symptoms scale of Maudsley Addiction Profile) is between 0 and 40, where 40 means that individuals have the worst health state (Marsden et al 1998). The extracted MAP-HSS score is reversed.

c: The score range of SCL-90 (Symptom Checklist-90) is between 0 and 360, where 360 means that individuals have the worst psychological health state (Derogatis and Cleary, 1977). The extracted SCL-90 score is reversed.

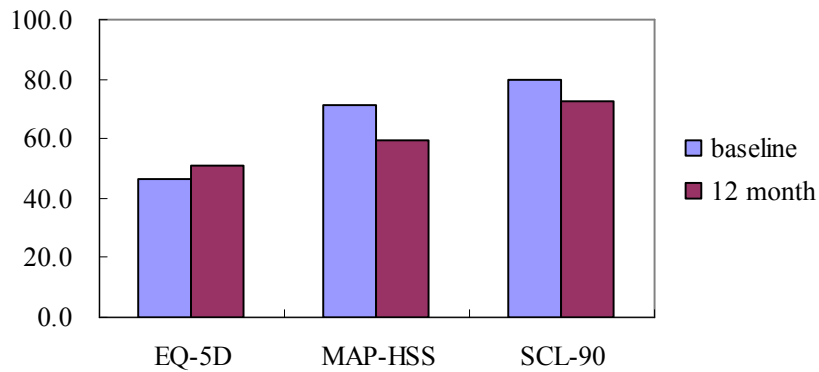


Figure 2.4.4 Standard mean scores of outcome measures at baseline and 12 month follow-up period in the Dutch prescribed heroin trial

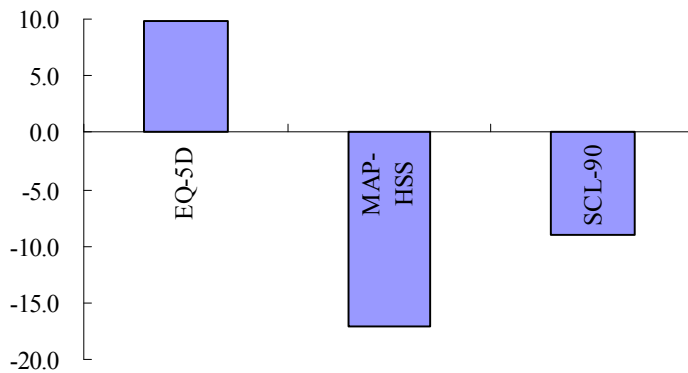


Figure 2.4.5 Percentage of score change of outcome measures between baseline and 12 month follow-up period in the Dutch prescribed heroin trial

UKCBTMM trial

The UKCBTMM trial (Drummond et al, 2004; Drummond, C. et al, 2005) recorded scores at baseline, 6 month and 12 follow-up periods, and the change between these 3 time points. Table 2.4.6 presents the original scores, standardised mean scores and the percentage score change for all of the measures in the trial.

In the first dimension, although EQ-5D has similar scores at different points in time to 3 of the other 4 measures, as illustrated in Figure 2.4.6, this is not consistent. EQ-5D also has very different percentage score change trends to all of the other measures at both 6 month and 12 month follow-up periods, as illustrated by Figure 2.4.7 and Figure 2.4.8. One of these 4 measures is EuropASI Drug, which it is worth noting since these results contrast with the findings of both the HEPC trial (Abou-Saleh et al, 2003; Abou-Saleh et al, 2008) and the study by Carpentier and colleagues (2009), where EQ-5D and EuropASI Drug had similar trends.

In the second dimension EQ-5D has similar scores at different points in time to 2 of the 5 measures, which are both subscales of SF-12 and measure health-related quality of life like EQ-5D. Of the 2 subscales, SF-12 MCS is the most similar to EQ-5D, with scores of 39.3 at baseline, 41.3 at the 6 month follow-up and 43.7 at the 12 month follow-up, compared with scores of 43.1, 47.3 and 47.0 respectively at these points in time for EQ-5D. SF-12 MCS also has a similar percentage score changes over the period, recording an 11.2% change over the 12 month follow-up period compared to 9.2% for EQ-5D. BSI also had a similar trend of proportional change to EQ-5D, with a 10.2% score change over the 6 month follow-up period and an 11.3% change over the 12 month follow-up period, compared with 9.8% and 9.2% respectively for EQ-5D. However, as illustrated in Figure 2.4.6, the BSI scores were consistently much higher than those of EQ-5D. The third dimension only includes subscales of EuropASI. Figure 2.4.6 shows that the scores of all 5 measures were much higher than EQ-5D at each point of time. Only 1 measure (EuropASI Work satisfaction) had a similar percentage score change at both 6 and 12 month follow-up periods, as shown in Figure 2.4.7 and Figure 2.4.8, with scores of 6.5% and 13.7% respectively.

As shown in Figure 2.4.7 and Figure 2.4.8, EQ-5D only consistently reflects the trends for 3 of the 15 measures (BSI, SF-12, and EuropASI Work satisfaction) over both the 6 and 12 month follow-up periods. However, it is worth stressing that there is a large diversity of scores and trends in the different measures examined in the UKCBTMM trial and it would therefore be impossible for any single outcome measure, such as EQ-5D, to reflect all of these divergent trends.

Table 2.4.6 Result of included studies: UKCBTMM

n=60	Baseline		6 month follow-up		Change at 6 month	12 month follow-up		Change at 12 month
Outcome measure	Standard mean score; A (S.D.)	Original mean score; A' (S.D.)	Standard mean score; B (S.D.)	Original mean score; B' (S.D.)	% of score change; (B-A)/A	Standard mean score; C (S.D.)	Original mean score; C' (S.D.)	% of score change; (C-A)/A
EQ-5D ^a	43.1 (21.7)	0.687 (0.346)	47.3 (17.8)	0.754 (0.283)	9.8	47.1 (19.5)	0.750 (0.311)	9.2
Continuation of illegal substance use and abuse								
EuropASI Drug ^b	70.4 (13.6)	0.296 (0.136)	69.9 (12.6)	0.301 (0.126)	-0.7	72.8 (14.4)	0.272 (0.144)	3.4
SDS ^c	34.8 (25.3)	9.78 (3.80)	50.8 (27.9)	7.38 (4.19)	46.0	55.5 (32.3)	6.67 (4.84)	59.6
TLFB of heroin PDA ^d	46.3 (34.3)	46.28 (34.31)	59.2 (37.0)	59.21 (37.01)	27.9	69.3 (38.4)	69.31 (38.39)	49.8
TLFB of methadone PDA ^d	32.3 (27.8)	32.26 (27.76)	25.2 (36.3)	25.23 (36.25)	-21.8	36.7 (44.8)	36.65 (44.79)	13.6
Improvement of medical condition								
BSI ^e	68.5 (22.3)	1.26 (0.89)	75.5 (19.8)	0.98 (0.79)	10.2	76.3 (22.5)	0.95 (0.90)	11.3
EuropASI Medical ^b	75.3 (34.1)	0.247 (0.341)	80.4 (30.0)	0.196 (0.300)	6.8	77.1 (30.1)	0.229 (0.301)	2.4
EuropASI Psychiatric ^b	78.5 (21.2)	0.215 (0.212)	74.6 (26.6)	0.254 (0.266)	-5.0	77.6 (24.5)	0.224 (0.245)	-1.1
SF-12 MCS ^f	39.3 (11.3)	39.32 (11.29)	41.3 (13.0)	41.25 (12.99)	4.9	43.7 (11.7)	43.74 (11.68)	11.2
SF-12 PCS ^f	38.9 (6.3)	38.90 (6.28)	39.9 (5.7)	39.90 (5.68)	2.6	39.3 (5.5)	39.34 (5.46)	1.1
Social integration								
EuropASI Economics ^b	16.5 (35.7)	0.835 (0.357)	30.0 (42.1)	0.700 (0.421)	81.8	29.7 (42.2)	0.703 (0.422)	80.0
EuropASI Family relationship ^b	82.8 (23.8)	0.172 (0.238)	82.5 (22.5)	0.175 (0.225)	-0.4	86.3 (20.1)	0.137 (0.201)	4.2
EuropASI Legal	87.3 (20.1)	0.127 (0.201)	82.2 (26.1)	0.178 (0.261)	-5.8	91.0 (17.0)	0.090 (0.170)	4.2

^b								
EuropASI Other relationship ^b	83.6 (20.7)	0.164 (0.207)	88.9 (16.6)	0.111 (0.166)	6.3	86.7 (18.6)	0.133 (0.186)	3.7
EuropASI Work satisfaction ^b	70.6 (36.3)	0.294 (0.363)	76.6 (30.8)	0.234 (0.308)	8.5	80.3 (26.7)	0.197 (0.267)	13.7

a: The original score range of EQ-5D is between -0.594 and 1 using the UK social tariff, where 1 means that individuals have the best health state (Dolan, 1997; Dolan et al, 1995; EuroQol group, 1990; Kind, Hardman and Macran, 1999).

b: The score range of each subscale of EuropASI (European Addiction Severity Index) is between 0 and 1, where 1 means that individuals have the most problems or greatest severity in each subscale (Koeter and Hartgers, 1997; Kokkevi and Hartgers, 1995). The extracted scores are reversed in all subscales of EuropASI.

c: The score range of SDS (Severity of Dependence Scale) is between 0 and 15, where 15 means that individual has the highest level of dependence severity (Gossop et al, 1995). The extracted SDS score is reversed.

d: The score TLFB (Timeline follow back) is presented as PDA (percentage of days abstinent) and ranges from 0 to 100, where 100 means that individual has not used the specific substance for the entire recorded period (Sobell and Sobell 1996; Sobell et al 1996).

e: The score range of BSI (Brief Symptom Inventory) is between 0 and 4, where 4 means that individual has the worst psychological health state (Derogatis and Melisaratos, 1983). The extracted BSI score is reversed.

f: The score of SF-12 is presented as two composite scores: MCS (mental component summary) and PCS (physical component summary). Both PCS and MCS ranges between 0 and 100, where 100 means individual has the best health state (Ware, Kosinski and Keller, 1995 and 1996).

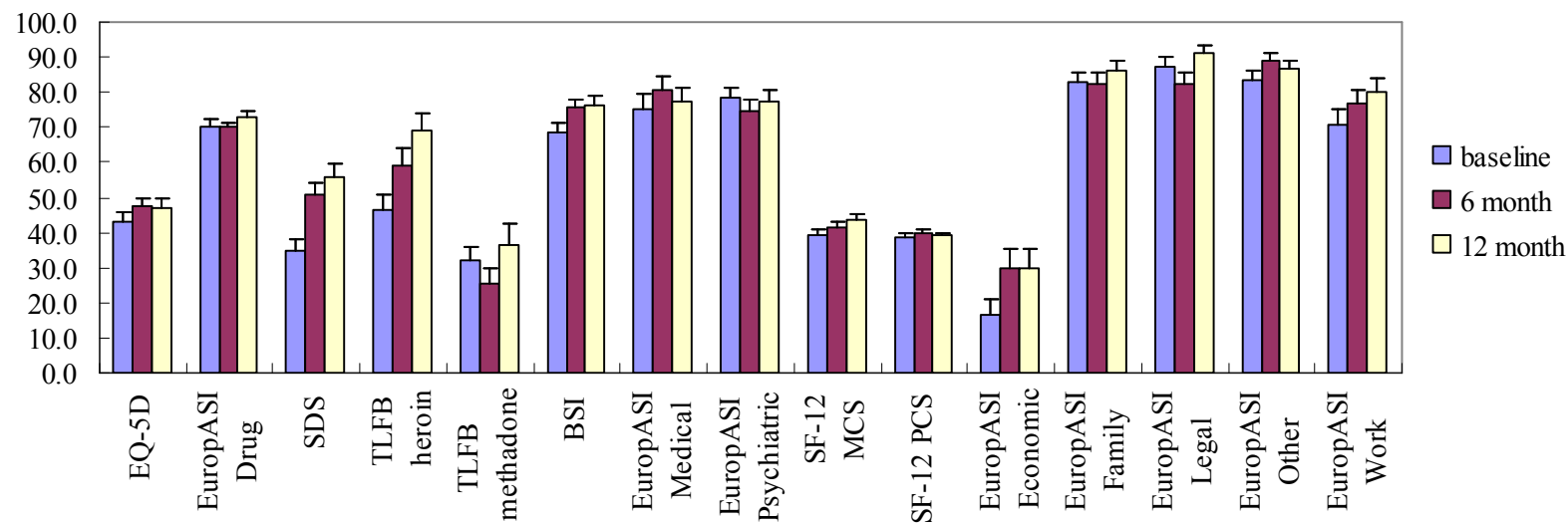


Figure 2.4.6 Standard mean scores of outcome measures and SEM bars at baseline, 6 and 12 month follow-up in the UKCBTMM trial

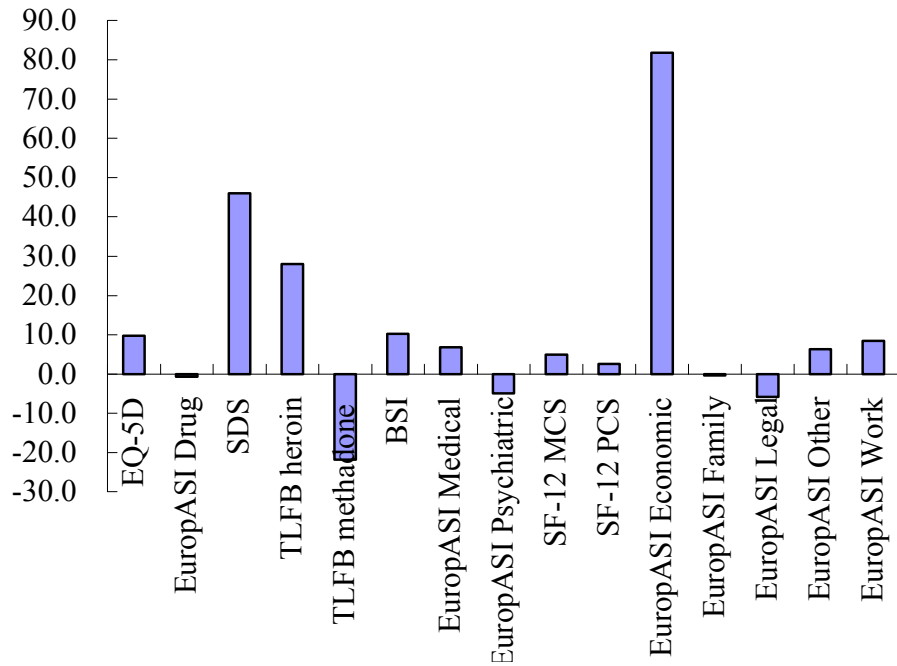


Figure 2.4.7 Percentage of score change of outcome measures between baseline and 6 month follow-up period for the UKCBTMM trial

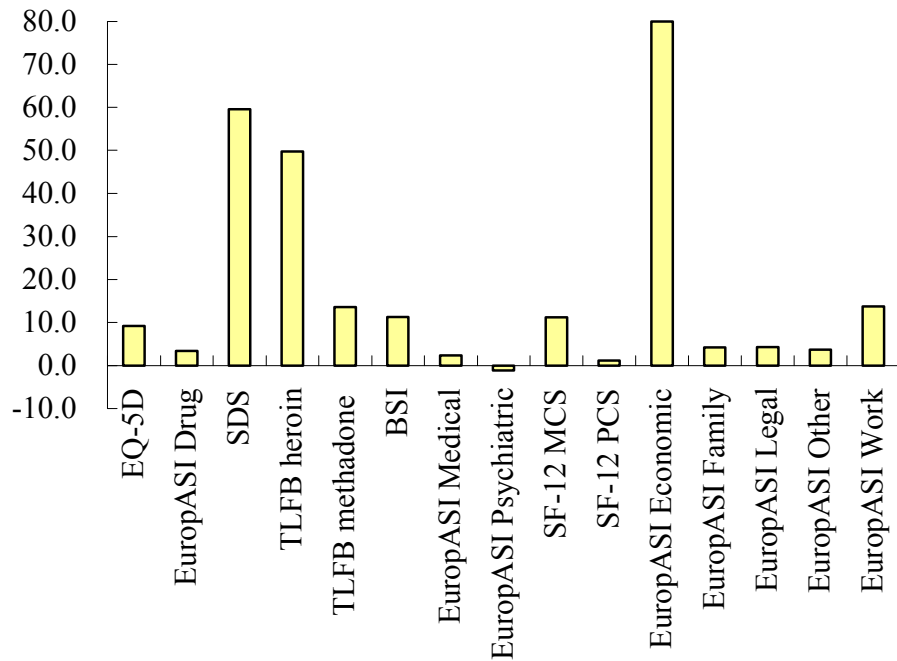


Figure 2.4.8 Percentage of score change of outcome measures between baseline and 12 month follow-up period for the UKCBTMM trial

COBRA trial

The COBRA trial (Schafer et al, 2009) recorded scores at baseline, the 12 month follow-up period and the change between these 2 time points. Table 2.4.7 presents the original scores extracted from the study, the standardised mean scores and the percentage score change for all of the measures in the trial. Although the COBRA trial examined subscales of EuropASI, CIDI and BSI, it only presented scores for BSI.

BSI is only a measure of the second dimension, improvement of medical condition. At baseline the BSI standardised mean score was 83.6, compared with 59.7 for EQ-5D. At the 12 month follow-up period the BSI score was 84.5, compared with 59.9 for EQ-5D, and the percentage score change was 1% for BSI compared with 0.4% for EQ-5D. These results show that although BSI is consistently higher, EQ-5D reflects similar trends of percentage score change, which supports the relationship between EQ-5D and BSI identified in the UKCBTMM trial. The similar trends are illustrated in Figure 2.4.9.

Table 2.4.7 Result of included studies: COBRA

n=2,414	Baseline		12 month follow-up		Change at 12 month
	standard mean score; A	mean score; A'	standard mean score; B	mean score; B'	% of score change; (B-A)/A
EQ-5D ^a	59.7	0.720	59.9	0.723	0.4
Improvement of medical condition					
BSI ^b	83.6	0.655	84.5	0.622	1.0

a: The social tariff of EQ-5D is not stated. As this trial was conducted in Germany, it is assumed that the social tariff of Germany was adopted. Therefore, the original score range of EQ-5D is between -0.207 and 1 using the social tariff of Germany, where 1 means that individuals have the best health state (EuroQol group, 1990; Szende, Oppe and Devlin ed., 2007).

b: The score range of BSI (Brief Symptom Inventory) is between 0 and 4, where 4 means that the individual has the worst psychological health state (Derogatis and Melisaratos, 1983). The extracted BSI score is reversed.

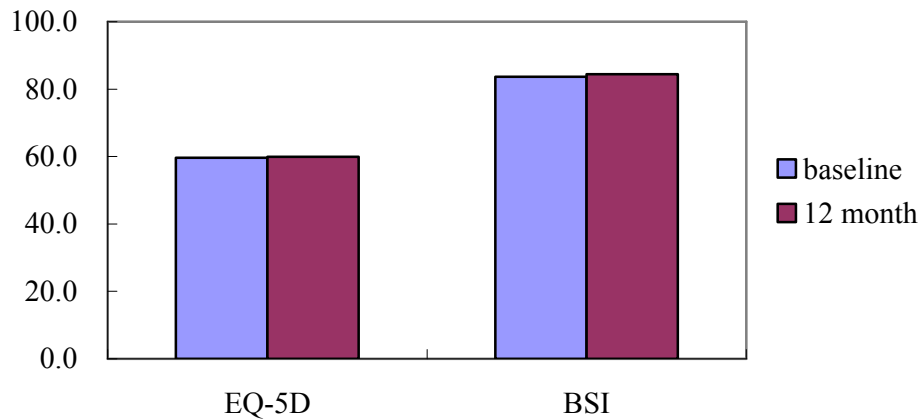


Figure 2.4.9 Standard mean scores of outcome measures at baseline and 12 month follow-up period in the COBRA trial

2.5 Conclusions and Discussion

The first objective of this chapter was simply to identify the drug intervention studies that have evaluated EQ-5D and other outcome measures. Although only 8 studies were identified, between them they covered 16 outcome measures in addition to EQ-5D. These measures have been categorised into 3 dimensions as recommended by Rehm and colleagues (2000): continuation of illegal substance use and abuse, improvement of medical conditions, and social integration. All of the 8 studies considered outcome measures in each of the 3 dimensions. This reveals that current researchers consider it important to take into account a wide range of outcome measures when evaluating drug misuse interventions and that for a comprehensive analysis measures from all 3 dimensions should be considered. This suggests that if only a single outcome measure is considered in economic evaluations, such as EQ-5D, other important measures may be neglected.

The second and most important objective of the chapter was to determine whether or not EQ-5D is an adequate generic outcome measure for evaluating drug misuse interventions. Of the 5 studies that were reviewed, EQ-5D only reflected the trends of percentage score change of the majority of measures in the HEPC trial, where it has very or quite similar trends to 8 of the 10 other measures. Across the other studies, however, EQ-5D only adequately reflected the trends of a few other measures. Both the UKCBTMM trial and the COBRA trial indicated that EQ-5D has similar trends to BSI. The UKCBTMM trial

also revealed that EQ-5D has similar trends to both the subscales of the SF-12 measure, which is probably due to it also being a health related quality of life measure, like EQ-5D. In general EQ-5D did not have similar standardised mean scores to most of the other measures, with one exception. Both the HEPC trial and the study by Carpentier and colleagues (2009) revealed EQ-5D to have similar scores to the EuropASI Drug subscale, although the UKCBTMM trial provided contrasting results.

Although EQ-5D has similar trends to a few different individual measures across the different dimensions, more generally the results indicate that EQ-5D does not adequately reflect the majority of measures in any of the 3 dimensions. One of the problems of using EQ-5D as a generic outcome measure is that there was a wide divergence of trends among the different measures considered in the studies. Where these trends differ from one another it would be impossible for any single measure, such as EQ-5D, to reflect this divergence. These results indicate not only that it is important to consider measures from all 3 of the dimensions in drug misuse intervention studies, but that it may also be important to consider a range of measures from each dimension to reflect the diversity of the scores and trends.

These results reveal the problems with using any single outcome measure to provide a comprehensive evaluation of drug misuse interventions. Policy makers need to be aware that any single outcome measure will be unable to reflect all the diverse trends of the outcome measures across all 3 of the dimensions reviewed in this chapter. This is not a problem specifically related to EQ-5D, but rather with using one outcome measure to reflect the complexity of drug misuse.

It is important to stress that these conclusions are only tentative, as there are some limitations with using the scores extracted from the studies reviewed in this chapter. The most significant of these is that the studies all presented mean average scores but individual patient scores were not available, which would be required to calculate the variance at the individual patient level. To know whether the results are statistically significant it would be necessary to take into account the variance by using more sophisticated statistical analyses, such as the Z score. From the scores extracted from the studies, it is impossible to know whether they are statistically significant, which is a major limitation when comparing EQ-5D with other outcome measures. This limitation may account for some of the divergent results between the studies highlighted above.

The problem of knowing whether the scores are statistically significant is especially important given that some of the sample sizes in the studies are quite small, only considering between 30 and 60 patients. Given this any outlying scores are more likely to distort the mean score and it would be useful to know the variance within these studies. To this extent the studies by Carpentier and colleagues (2009), the COBRA trial (Schafer et al, 2009) and the Dutch prescribed heroin trial (Dijkgraaf et al, 2005; van den Brink et al, 2003) may be more reliable as the sample sizes were all over 290, with the COBRA trial having a sample of over 2000 participants.

This chapter has only considered the results of the different measures. However, it is not only the results but also the content of the measures that can be compared to evaluate whether or not EQ-5D adequately reflects the other outcome measures. To complete the evaluation of EQ-5D as an outcome measure for drug misuse intervention studies it is therefore necessary to compare the content of the measures identified in this chapter, which provides the focus for the next chapter.

Chapter 3 Content comparison of EQ-5D and other outcome measures

3.1 Background

In the UK the NICE guideline (2008) requires that QALYs are used to measure health outcomes and to do so it recommends using the EQ-5D instrument with UK population values. The previous chapter has discussed the importance of establishing whether or not EQ-5D is an adequate generic outcome measure for drug misuse interventions and explored the trends between EQ-5D and other drug misuse specific measures. However, although some trends were identified the conclusions drawn from the results were tentative at best. In large part this was due to the limitations of the scores extracted from the studies reviewed, which provided no indication of statistical significance.

This chapter explores the same problem as the previous chapter but adopts a different approach. Where the previous chapter examined the trends between the results of EQ-5D and other outcome measures, this chapter focuses on a content comparison of the different measures. These measures rely on questionnaires to evaluate drug misuse interventions. However, there are a wide range of questionnaires used in the studies identified in the previous chapter. It is important to know how similar these questionnaires are to one another, as if a content comparison reveals that they are very similar then it may not be necessary to use so many questionnaires. Indeed if EQ-5D addresses the same questions as the other outcome measures then policy makers may be justified in using it as the only outcome measure for economic evaluations of drug misuse interventions, as recommended by NICE.

A content comparison shows whether or not questionnaires cover similar concepts to each other. The concept is the general concern that a given question aims to address, for example, a question asking whether or not the patient has experienced problems with washing or dressing themselves covers the concept of self-care. This chapter uses the WHO's content comparison technique, which was developed to provide a clear and comprehensive framework for examining individuals' well-being. The WHO's ICF (International Classification of Functioning, Disability and Health) is not an instrument, but a common reference framework for functioning in outcome research (Cieza et al, 2005).

ICF has been used as the content comparison technique in a wide range of studies, such as outcome measures for patients suffering with pain (Borchers et al, 2005; Prodingler et al, 2008), stroke patients (Geyh et al, 2007), head and neck cancer patients (Tschiesner et al, 2008), and patients who received occupational and physical therapies (Stamm et al, 2004; Stamm et al, 2006). In the study by Cieza and Stucki (2005) the ICF content comparison technique has been used to compare health related quality of life measures such as EQ-5D and SF-36. However, the ICF content comparison technique has not yet been used in drug misuse studies. The advantages of using ICF in drug misuse studies have been discussed by Broekman and colleagues (2004). For example ICF can point out the areas that are ignored or poorly developed in addiction outcome measures and can facilitate the communication in universally understandable terms between drug misuse research and other health care fields (Broekman et al, 2004). In general, using ICF allows policy makers to evaluate how EQ-5D and other outcome measures fit into the WHO's framework.

3.2 Objectives

The aim of this chapter is to use the ICF content comparison technique to evaluate the relationship between EQ-5D and other outcome measures used in drug misuse studies. As ICF has not previously been used for drug misuse studies, the first objective is to use ICF to map the concepts of EQ-5D and the other outcome measures identified in the previous chapters. The mapping is used to examine the extent to which EQ-5D adequately covers the same concepts as other measures and the amount of agreement at different levels of the ICF code between EQ-5D and other measures.

Although it is important to know whether EQ-5D covers the same concepts as other outcome measures, a further consideration is whether or not patients respond to questions covering the same concept in the same way across different measures. The second objective is therefore to examine whether or not patients respond to questions covering one concept in the same way as they respond to other questions covering that same concept, by examining one study where the individual patient responses are available. If patients respond differently to questions covering the same concept then it would suggest that it is insufficient to only consider whether or not the same concepts are covered in different measures, as there may be other factors determining how patients respond to any

given question. This information is therefore important for evaluating the relationship between EQ-5D and other outcome measures used in drug misuse studies.

3.3 Methods

3.3.1 Content comparison using ICF concepts

To meet the first objective, this chapter uses the outcome measures identified in the previous chapter as the basis for the content comparison in order to examine the extent to which EQ-5D covers the same concepts as other outcome measures used in drug misuse studies. In addition to EQ-5D, there are 16 other outcome measures that are mapped using the ICF framework. The first stage of content comparison is to identify the keyword for each question in each outcome measure. This is then mapped on to the ICF framework using linking rules detailed below. ICF is a classification system for outcomes related to individuals' well-being, which provides letter codes for different concepts. Each keyword is mapped onto the most appropriate ICF concept (where possible) and by doing this for each question within an outcome measure, a profile of the concepts covered in that measure is developed.

The ICF framework covers 4 major components: body functions (b), body structure (s), activities and participation (d), and environmental factors (e) (WHO, 2001). The linking rules of ICF have been developed (Cieza et al, 2002; Cieza et al, 2005). The component letter code is followed by a numeric code. The first digit of the numeric code is the chapter number in each component, the following 2 digits represent the second level of the description of each functioning, and the next 2 digits represent the third and fourth levels of functioning detail (WHO, 2001; Cieza et al, 2002). Taking ICF code b28010 as an example: the letter b represents the body functions component, and 2 indicates that this code is from chapter 2, sensory functions and pain. In chapter 2, the codes from b280 to b289 are all related to pain and b280 is the specific code for the sensation of pain. The code b2801 represents pain in one body part and the final digit represents the body part where the pain occurs, so b28010 means a specific pain in the head and neck. There is a detailed description for each ICF code (WHO, 2001).

Each question may be linked to an ICF code, however, in some cases it is not only the question but also the different responses that need to be linked to the ICF code. If the

question or the response options cover more than one concept then they need to be linked to more than one code (Cieza et al, 2002; Cieza et al, 2005). For example, the second question in EQ-5D is about self-care, which is linked to the ICF code, d5 (self-care). There are 3 response options for this specific EQ-5D question: (1) I have no problems with self care, (2) I have some problems washing or dressing myself, and (3) I am unable to wash or dress myself. The concepts of washing myself is linked to the ICF code d510 (washing oneself) and the concept of dressing myself is linked to d540 (dressing), so option 2 is linked to both d510 and d540. ICF does not differentiate between the degrees of the functioning, so there is no difference between the codes for options 2 and 3.

Based on the updated linking rules (Cieza et al 2005), if the concepts cannot be linked to a specific ICF code then 4 options are available: nd (not definable), nc (not covered by ICF), hc (health condition, such as a diagnosis), or pf (personal factors, such as gender). As recommended in the linking rules (Cieza et al 2002; Cieza et al 2005), the ICF linkage is carried out independently by 2 health professionals with ICF training (one is a drug misuse researcher and the other is a social worker in mental health). When there is disagreement regarding specific linkage results, a third person is consulted to resolve the disagreement. Using SPSS software, Kappa statistics are then used to assess the inter-observer agreement between the 2 people who carry out the linking process.

3.3.2 Correlation between questions covered by the same concepts

The second objective of the chapter is to examine whether or not patients respond to questions covering one concept in the same way as they respond to other questions covering that same concept. To examine this it is necessary to have the individual patient responses to the question in each measure. However, none of the drug misuse intervention studies reviewed in the previous chapter provided the individual patient responses.

As individual patient responses are not usually published, to examine the relationship between them it is necessary to use a study where they are available. For this reason the data from RESULT (Raistrick et al, 2008) are used in this chapter, which provides a sample of 401 patients at baseline and 268 patients at the 6 month follow-up period. RESULT is an economic evaluation study of treatment-as-usual drug misuse policies in the UK, which covers both EQ-5D and 4 other outcome measures: LDQ (Leeds Dependence Questionnaire), SSQ (Social Satisfaction Questionnaire), CORE (Clinical

Outcome in Routine Evaluation), and SCL (Symptom Checklist). The RESULT study can therefore be used to examine the relationship between different questions and concepts even though it is not a drug misuse intervention study.

The concepts from the RESULT questionnaires are first mapped into ICF code, using the method outlined above, and the overlapping concepts between EQ-5D and the other outcome measures are identified. The specific questions in the overlapping concepts are then examined to identify whether or not patients respond to different questions in the same concept in the same way. Spearman's correlation is designed to test the correlation for ordinal data and as this is how the responses to the questions are presented in the outcome measures, this correlation technique is used to calculate the correlation coefficient and identify the extent of the correlation between the questions in EQ-5D and other measures.

3.4 Results

3.4.1 Content comparison results

The ICF mapping for EQ-5D and the other outcome measures was conducted independently by 2 health professionals with ICF training and the Kappa coefficient was calculated to show the inter-observer agreement. The Kappa coefficient ranges between 1 and -1 and is based on the difference between the actual agreement and the expected agreement between health professionals (Viera and Garrett, 2005; Cohen, 1960). If Kappa equals 1 there is perfect agreement. If Kappa ranges from 0.61 to 0.80 there is considered to be substantial agreement and from 0.41 to 0.60 is considered to be moderate agreement. If Kappa is under 0.20 there is considered to be poor agreement (Viera and Garrett, 2005; Altman, 1991).

The ICF updated linking rules (Cieza et al, 2005) recommend that the Kappa coefficient should be given for the mapping results. The Kappa coefficient was calculated for each outcome measure in the studies at the different levels of the ICF code and the full details are in Appendix 2.1, however, the overall Kappa coefficient for each level is presented in Table 3.4.1. The table shows that at every level of ICF code there was substantial agreement overall, even though there was not substantial agreement for every individual measure at every ICF level. This reveals that the 2 health professionals who conducted the

ICF mapping shared similar interpretations of how the individual questions should be mapped onto the ICF concepts. It should be noted that this is the first time that ICF mapping for most of the outcome measures (all except EQ-5D and SF-36) has been conducted and therefore there are no other results to check the mapping against.

The high level of agreement between the 2 health professionals indicates that the mapping results are potentially reliable, and where there was disagreement a third professional confirmed which code should be used. These mapping results provide the basis for comparing the content of EQ-5D and the other outcome measures.

Table 3.4.1 Kappa coefficient of inter-observer agreement

ICF	Kappa coefficient overall
component	0.75**
Chapter 1st level	0.89**
2nd level	0.91**
3rd level	0.97**
4th level	1.00**

*: $p < 0.05$; **: $p < 0.001$

The mapping was conducted for the 8 drug misuse intervention studies identified by the review in the previous chapter. In total the studies included 24 different outcome measures or subscales of outcome measures in addition to EQ-5D. These measures covered 196 concepts in total: 51 in ICF component b, 92 in ICF component d, 21 in ICF component e and 32 that could not be mapped onto ICF concepts. The measures covered no concepts in ICF component s. EQ-5D only covered 2 concepts in ICF component b, 12 in component d and did not cover any other concepts. Of the 196 concepts covered in total there were 182 that were covered by other outcome measures and not by EQ-5D, and only 14 covered by both EQ-5D and other measures. Full details of the concepts covered by each measure are in Appendix 3, however, Table 3.4.2 shows the frequency of overlapping concepts between EQ-5D and the other measures. In addition, it shows the frequency of agreement between different measures at both the component and the first level of the ICF chapter. This thus reveals the extent to which EQ-5D covered similar concepts as other outcome measures, even when it did not cover exactly the same concept, which further indicates the extent of the similarity between the content of EQ-5D and the other measures in components b and d.

Table 3.4.2 shows that of the measures that covered concepts in component b (body functions), there was a large extent of agreement between EQ-5D and the other measures at the first level of the ICF chapter. At the first level most of these measures were in complete agreement with EQ-5D; the measure that had the least agreement, MAP-HSS, still had 6 of 10 concepts in component b in agreement at the first level. The first level for component b represents the chapter that the concepts are in, such as the mental functions or sensory functions and pain. Where there is agreement at the first level of the ICF chapter it thus reveals that the questions were concerned with the same general content.

Table 3.4.2 reveals that it was only at the second level of the ICF chapter that EQ-5D did not generally map the same concepts as other measures. In some cases there was a considerable amount of overlapping concepts, for example of the 14 concepts that SF-36 covered in component b, 9 were overlapped, and of the 5 concepts that EuropASI Family/Other covered 3 were overlapped. 4 of the measures had just under half of the concepts in component b overlapped with EQ-5D (BSI, MAP-HSS, SCL-90, and SDS), however the other 10 measures that covered concepts in component b had few or no overlapping concepts at the second level of the ICF chapter. The second level of the ICF chapter categorises the concepts in a greater level of detail. For example within mental functions (b1), options include emotional functions (b152), perceptual functions (b156) or thought functions (b160). This indicates that within component b, EQ-5D does not cover exactly the same concepts as other measures when they are considered in detail, however, EQ-5D does cover similar concepts as shown by the high level of agreement between the measures at the first level of the ICF chapter.

Turning to component d (activities and participation), Table 3.4.2 shows that there was a large extent of agreement between EQ-5D and the other measures at the first level of the ICF chapter. Most of the measures were in complete agreement with EQ-5D and even BSI, the measure that had the least agreement, had 8 of 10 concepts in component d in agreement at the first level. The chapters for component d include mobility (d4) and self-care (d5), and the high level of agreement between EQ-5D and the other measures indicates that they were concerned with the same general content and covered similar concepts.

Again, it was only at the second level of the ICF chapter that EQ-5D did not map the same concepts as other measures in component d. Table 3.4.2. shows that the only

measures that had considerable overlapping concepts with EQ-5D at the second level were SF-12, which had 9 of 13 concepts overlapped, and SF-36, which had 21 of 31 concepts overlapped. The other 20 measures that included concepts in component d all had under half of the concepts at the second level of the ICF chapter overlapped with EQ-5D. This means that EQ-5D does not generally cover exactly the same concepts as the other measures, such as lifting and carrying objects (d430) or using transportation (d470), but that there is general agreement between the measures regarding the content that should be considered.

The first objective of this chapter has been to compare the content of EQ-5D and the other outcome measures. The general agreement between EQ-5D and the other measures at the first level of the ICF chapter for components b and d, reveals that even though there are a lot of specific concepts that EQ-5D does not cover that are covered in the other measures, this does not simply indicate that the measures have no common content. Indeed they are largely in agreement about the general content and cover similar concepts if not exactly the same concepts. However, it is worth stressing that this is only the case within components b and d. It is also important to recognise how many concepts EQ-5D does not cover that are additionally covered by other measures. This is revealed by examining the 'Other concepts not in EQ-5D' column in Table 3.4.2. This takes into account all of the concepts from component e (environmental factor), under the chapters of products and technology (e1), support and relationships (e3), and services, systems and policies (e5), as well as all the concepts that could not be mapped onto the ICF code, such as suicide.

Table 3.4.2 Content comparison results

ICF category	Component b				Component d			Other concepts not in EQ-5D
	Total number of concept	Agreement at component	Agreement at chapter 1 st level	Overlapping concepts at chapter 2 nd level	Agreement at component	Agreement at chapter 1 st level	Overlapping concepts at chapter 2 nd level	
EQ-5D*	15	2	-	-	13	-	-	-
BSI	57	44	40	19	10	8	0	3
CIDI	128	16	16	3	29	24	15	83
EuropASI	262	34	34	9	79	79	24	149
EuropASI Drug	64	5	5	1	4	4	0	55
EuropASI Employment	36	2	2	0	27	27	8	7
EuropASI Family/Other	73	5	5	3	39	39	16	29
EuropASI Legal	30	2	2	0	7	7	0	21
EuropASI Medical	24	2	2	0	0	0	0	22
EuropASI Psychiatric	37	18	18	5	2	2	0	15
HADS	18	15	14	5	2	2	1	1
IDUQoL	31	1	1	0	21	20	7	9
IRQ	21	0	0	0	18	18	0	3
MANSA	26	0	0	0	15	15	6	11
MAP-crime	11	0	0	0	1	1	0	10
MAP-HSS	10	10	6	4	0	0	0	0
OTI	107	19	18	5	9	8	1	79
OTI-crime	9	0	0	0	3	3	0	6
OTI-drug	66	0	0	0	0	0	0	66
OTI-	32	19	18	5	6	5	1	7

psychological health								
RTBS	14	0	0	0	14	14	0	0
SCL-90	108	78	66	32	25	23	1	5
SDS	8	5	5	2	0	0	0	3
SF-12	22	6	6	5	13	12	9	3
SF-36	56	14	14	9	31	31	21	11
TLFB-cannabis	4	0	0	0	1	1	0	3
TLFB-heroin, methadone	9	0	0	0	2	2	0	7
WHODASII	35	6	6	2	23	22	12	6

* EQ-5D is mapped onto the following concepts: b152 (emotional functions), b280 (sensation of pain), d230 (carrying out daily routine), d4 (mobility), d450 (walking), d498 (mobility, other specified-confined to bed), d5 (self-care), d510 (washing oneself), d540 (dressing), d640 (doing housework), d760 (family relationship), d839 (education, other specified-study), d850 (remunerative employment), and d920 (recreation and leisure).

3.4.2 Results of correlation between questions in overlapping concepts

In addition to knowing whether or not EQ-5D covers the same concepts as other measures, it is also important to know whether or not patients respond to different questions covering one concept in the same way as they respond to other questions covering that same concept across the different measures. The RESULT study (Raistrick et al, 2008) was used to examine the correlation between the questions. The Kappa coefficient was calculated for each outcome measure and the overall results are shown in Table 3.4.3, with the full details in Appendix 2.2. Overall there was substantial agreement between the 2 health professionals who conducted the ICF mapping.

Table 3.4.4 shows the overlapping concepts between the outcome measures and EQ-5D in the RESULT study. In this section it is only necessary to consider the overlapping concepts; unlike in the previous section the concepts that EQ-5D did not cover do not need to be examined. Of the 4 other outcome measures in the RESULT study, 2 had overlapping concepts with EQ-5D in ICF component b (CORE and SCL) and 2 in component d (LDQ and SSQ). The overlapping concepts in component b are covered by 2 separate EQ-5D questions, whereas the overlapping concepts in component d are all covered by a single EQ-5D question. The results for the correlation are considered in turn by each EQ-5D question and are given at both the baseline and the 6 month follow-up period.

Table 3.4.3 Kappa coefficient of inter-observer agreement in RESULT

ICF component	Kappa coefficient overall
Chapter 1st level	0.61**
2nd level	0.90**
3rd level	0.81**
4th level	0.80**
	1.00*

*: $p < 0.05$; **: $p < 0.001$

Table 3.4.4 Overlapping concepts covered by the outcome measures in RESULT

ICF category	Overlapped with EQ-5D in component b	Overlapped with EQ-5D in component d
LDQ	0	2
SSQ	0	7
CORE	12	0
SCL	4	0

The responses from EQ-5D and the other 4 outcome measures all use different response ranges. EQ-5D responses range from 1 to 3, where 1 means 'no problem'. CORE and SCL responses range from 0 to 4, where 0 means 'not at all' or 'never'. LDQ responses range from 0 to 3 where 0 means 'never'. SSQ responses also range from 0 to 3 where 0 means 'very dissatisfied'. The correlation coefficient was calculated using Spearman's correlation, which ranges from -1 to 1, where -1 represents strong negative correlation and 1 represents strong positive correlation. If the coefficient is between 0.10 and 0.29 there is a weak correlation, between 0.30 and 0.49 there is medium correlation, and above 0.50 there is strong correlation (Field, 2005).

Table 3.4.5 shows the correlation between EQ-5D and all of the other questions covering ICF concept b152 (emotional functions) at both baseline and the follow-up period. Most of the results have either medium or strong correlation, although 2 questions have weak correlation (Q12 and Q33 at baseline). 7 of the 11 questions have strong correlation at the follow-up period, however only one of these (Q2) also has strong correlation at baseline. Q2 is the only question that has a coefficient of over 0.6, which reflects that this question (I have felt tense, anxious or nervous), was closest to EQ-5D Q5 (anxiety/ depression). If the different questions within the same concept were very similar to one another then strong correlation would be expected. However, the results suggest that even though there is some strong correlation, in most cases this is not consistent between the 2 time points considered.

Table 3.4.6 shows the correlation between EQ-5D and the other questions covering ICF concept b280 (sensation of pain) at baseline and the follow-up period. None of the questions have strong correlation, and the highest is CORE Q8, which has coefficients of 0.47 at baseline and 0.45 at the follow-up period. The other coefficients are all lower, which is probably because EQ-5D Q4 is a general question about pain/ discomfort, whereas the other SCL questions all ask about pain in a specific body part.

Table 3.4.7 shows the correlation between EQ-5D and the other questions covering ICF concepts d230 (carrying out daily routine), d760 (family relationships), d850 (remunerative employment) and d920 (recreation and leisure) at both baseline and the follow-up period. There are only a limited number of statistically significant correlation coefficients, all of which have weak correlation. The reason for this is that EQ-5D Q3 is a general question regarding the patients' usual activities, whereas the LDQ and SSQ

questions all refer to very specific activities or relationships. For example SSQ Q5 asks how satisfied patients are with the amount of time they are able to go out, and there is only small correlation with EQ5D Q3 at the follow-up period.

Having examined the correlation between EQ-5D and the other measures that ask questions that cover the same concepts, it is clear that in most cases the patients do not necessarily respond to different questions covering the same concept in the same way. If they did, strong correlation would be expected between the questions, however there was only any strong correlation with 1 of the 3 EQ-5D questions for which there were overlapping concepts, and even for that question (EQ-5D Q5) the strong correlation was inconsistent. The results therefore indicate that it cannot be expected that patients will respond to different questions covering the same concepts in the same way. It should be noted that this is a tentative conclusion as the correlation has only been calculated for the limited number of overlapping concepts within the one study where individual patient responses were available. To indicate whether these results apply more widely, it would be necessary to have more individual patient responses across a range of outcome measures, especially from drug misuse intervention studies.

Table 3.4.5 Correlation between EQ-5D and CORE questions which cover the same concept (ICF b152 Emotional functions) at baseline and follow-up

n=401 at baseline, n=268 at 6 month follow-up	EQ-5D Q5 Anxiety/Depression (range 1-3; 1 is 'no problem') at baseline	EQ-5D Q5 Anxiety/Depression 6 month
CORE Q1 I have felt terribly alone and isolated (range 0-4; 0 is 'not at all')	0.48**	0.47**
CORE Q2 I have felt tense, anxious or nervous	0.63**	0.62**
CORE Q9 I have thought of hurting myself	0.36**	0.41**
CORE Q11 Tension and anxiety have prevented me doing important things	0.47**	0.50**
CORE Q12 I have been happy with the things I have done	0.21**	0.26**
CORE Q14 I have felt like crying	0.44**	0.56**
CORE Q15 I have felt panic or terror	0.48**	0.56**
CORE Q17 I have felt overwhelmed by my problems	0.45**	0.56**
CORE Q27 I have felt unhappy	0.49**	0.55**
CORE Q28 Unwanted images or memories have been distressing me	0.41**	0.49**
CORE Q33 I have felt humiliated or shamed by other people	0.29**	0.37**

** : p < 0.001

Table 3.4.6 Correlation between EQ-5D, CORE and SCL questions which cover the same concept (ICF b280 Sensation of pain) at baseline and follow-up

	EQ-5D Q4 Pain/Discomfort at baseline	EQ-5D Q4 Pain/Discomfort at 6 month
CORE Q8 I have been troubled by aches, pains or other physical problems (range 0-4; 0 is 'not at all')	0.47**	0.45**
SCL Q4 Stomach pains (range 0-4; 0 is 'never')	0.23**	0.32**
SCL Q6 Chest pains	0.26**	0.30**
SCL Q7 Joint/bone pains	0.41**	0.29**
SCL Q8 Muscle pain	0.38**	0.33**

** : p < 0.001

Table 3.4.7 Correlation between EQ-5D, LDQ and SSQ questions which cover the same concepts (ICF d230 Carrying out daily routine, d760 Family relationships, d850 Remunerative employment, d920 Recreation and leisure) at baseline and follow-up

ICF concept		EQ-5D Usual Activities (eg. work, study, housework, family or leisure activities) at baseline	EQ-5D Usual Activities at 6 month
d230	LDQ Q2 Is drinking or taking drugs more important than anything else you might do during the day? (range 0-3; 0 is 'never')	0.15*	0.14*
d230	LDQ Q4 Do you plan your days around getting and taking drink or drugs?	0.13*	0.15*
d760	SSQ Q7 7. How satisfied are you with your closest relationship in life (eg. spouse, partner, lover, parent, best friend)? (range 0-3; 0 is 'very dissatisfied')	-0.03	-0.08
d760	SSQ Q8 How satisfied are you with your relationship with your family (include children and other relatives)?	-0.02	-0.12
d850	SSQ Q3 How satisfied are you with your employment situation? (Please answer this question even if you are unemployed or a full-time homemaker)	-0.06	0.04
d920	SSQ Q5 How satisfied are you with the amount of time you are able to go out?	-0.07	-0.19**
d920	SSQ Q6 How satisfied are you with the amount of time you see your friends?	-0.10	-0.15*

*: $p < 0.05$; **: $p < 0.001$

3.5 Conclusions and Discussion

The aim of this chapter has been to evaluate the content of EQ-5D by comparing it with other outcome measures. This has been achieved first by using ICF, the content comparison technique developed by the WHO (2001), to examine whether or not EQ-5D covers the same concepts as other outcome measures used in the drug misuse intervention studies identified in the previous chapter.

ICF identifies a range of different concepts across 4 components that provide a comprehensive framework for examining individuals' well-being. However, EQ-5D only covers concepts in 2 of those components: b (body functions) and d (activities and participation). This indicates first that EQ-5D only partially maps onto the WHO's framework. Second, and more importantly, it reveals one of the major limitations of using EQ-5D as the only outcome measure for drug misuse studies, as the other outcome measures considered also cover concepts in the third ICF component, e (environmental factors) and cover concepts that do not map onto those identified by the ICF. There are 53 such concepts that EQ-5D does not cover that are covered by the other measures.

The other measures also cover 51 different concepts in ICF component b and 92 in ICF component d, whereas EQ-5D only covers 2 concepts in component b and 12 in component d. All the concepts covered by EQ-5D were also covered by the other measures, but there were a great number of concepts that EQ-5D did not cover that were covered by the other measures. At first this might seem to suggest that it would be inadequate to use EQ-5D as a single outcome measure, however, closer examination revealed that this is not quite the case. Even though EQ-5D did not have a lot of overlapping concepts with the other outcome measures in components b and d, there was a high level of agreement at the first level of the ICF chapter. The first level of the ICF chapter denotes the general concern that is addressed in the questionnaire, such as self-care (d5). It is only at the second level of the ICF chapter, which is much more detailed, that EQ-5D did not cover the same concepts. This means that although EQ-5D was not covering exactly same concepts as other measures it was frequently covering similar concepts and there was a great extent of general agreement in the content between the measurers.

Even though there was a general amount of content agreement between EQ-5D and the other measures within components b and d, this only indicates that EQ-5D might be an adequate single outcome measure for drug misuse studies if the interest is only with outcomes of drug misuse interventions related to body functions (b) and activities and participation (d). EQ-5D fails to take into account outcomes related to environmental factors (d) and other concepts not included in the ICF concepts, such as suicide, which other outcome measures consider.

A further limitation of using EQ-5D as the only outcome measure is that even when it does cover the same concepts as other outcome measures, it is not clear that patients will necessarily respond to different questions covering the same concept in the same way. If patients did respond to different questions covering the same concept in the same way then strong correlation would be expected between questions in EQ-5D and other measures that cover the same concepts. However, the analysis of the RESULT study (Raistrick et al, 2008) has shown that there is often not strong correlation between the questions in overlapping concepts between EQ-5D and the other measures. These results themselves are limited, as there was only a small number of overlapping concepts between EQ-5D and the measures in the RESULT study. Nevertheless, they tentatively suggest that if EQ-5D is to be used as a single outcome measure, it is important to realise that it may not provide the same patient responses as other measures that cover the same concepts. To reveal whether or not these findings are more widely applicable it would be beneficial if future studies could examine the correlation between questions in EQ-5D and other outcome measures with which it has more overlapping concepts, such as SF-36 or WHODAS II.

If EQ-5D covered the same concepts as other outcome measures and if patients could be expected to give the same responses to different questions within the same concept, then it may not be necessary to use as many questionnaires as are currently used in drug misuse intervention studies. In addition NICE (2008) recommends using the EQ-5D instrument with UK population values to measure health outcomes in the UK. There are advantages for policy makers if they can use a single generic outcome measure, however, this chapter and the previous one have questioned whether EQ-5D adequately reflects the other outcome measures used in drug misuse intervention studies by comparing the content of the measures and examining whether there are trends between their results. The 2 chapters have highlighted the limitations with using EQ-5D, or indeed any single

outcome measure, to reflect the range of different outcome measures that should be taken into account to provide a comprehensive evaluation of the individual level outcomes for drug misuse policy.

Chapter 4 Systematic Review for drug misuse intervention on the individual patient level of the monetary outcome

4.1 Background

The previous two chapters have examined whether EQ-5D is an adequate outcome measure for drug misuse intervention studies by comparing it with other non-monetary outcomes. However, it is also important to consider the monetary (or the social cost) outcome in the economic evaluation of drug misuse interventions. One of the advantages of evaluating the monetary outcome is that a wide range of dimensions can all be presented in commensurate units of measurement. In addition the monetary outcome for health interventions may also be compared with interventions outside of the health sector where the results are all measured in monetary units. However, which monetary dimensions are measured depends on the perspectives and interests of those undertaking the research. Different regulatory authorities in different countries recommend different perspectives (Claxton et al, 2010). In the UK, the NHS recommends the inclusion of the difference of the resources used or the resources saved (Kelly et al, 2005). The resources used show what resources the individual patient has used, whereas the resources saved show the estimated savings to society from the patient receiving the intervention compared with patients not receiving the intervention.

For drug misuse research it is especially important to estimate the societal cost. Drug misuse is regarded as being closely related to the social resource use, especially within the criminal justice system and with respect to the health burden of hepatitis and HIV (Cartwright, 1998; Cartwright, 2008; Garfein et al, 1996; Godfrey, 2006; Hser and Anglin, 1991; Joseph, 1988; Mark et al, 2001; Masson et al, 2002; Neale et al, 2006; Sweeney et al, 2009; Wiessing et al, 2004). A wide range of outcome categories for economic evaluations in drug misuse interventions have been developed, which cover areas like resource use in health care, crime, social care, and productivity loss (Godfrey, 2006; Simoens et al, 2006; McCollister and French, 2003). However, there are only a few common methods for estimating the monetary benefit within these categories. For instance, the social costs related to crime can be based on the cost incurred by the victims, or the resource use within the criminal justice system.

This review is based on the dimensions of the monetary outcome categorised by Godfrey (2006). Although there are other ways of categorising dimensions (for example Cartwright, 1998), the advantage of using the dimensions categorised by Godfrey (2006) is that they are based on the economic evaluation theory suggested by M. F. Drummond and colleagues (2005), which is employed throughout this thesis. The study by Godfrey (2006) categorises monetary dimensions in 2 domains: resources saved and other value created. In the resources saved domain there are 3 dimensions: the health care cost, the criminal justice cost, and the social care cost. As interventions are primarily aimed at the drug misuse patients' health it is very important to measure the health care cost. The social care services cost is also important, given that drug misuse patients are very likely to use services such as shelters in the case of homeless drug users or counselling in the case of unemployed drug users. Given that drug misuse patients are also likely to commit crime, the criminal justice cost is another important measure.

In the other value created domain there are a further 5 dimensions: increased productivity; the value from reduced accidents and deaths to third parties; the value to communities from reduced drug related problems, the reduced risk to third parties of the spread of infectious diseases and the potential impact on future drug use and harms. Increased productivity is important given that healthy individuals will contribute to the productivity of society. The value from reduced accidents/ deaths to third parties is important to consider because drug misuse patients are likely to endanger the health of others, for example from accidents caused by driving under the influence of drugs. The value to the community from reduced drug related problems is particularly important given that drug users may commit crime and therefore the fear of crime and cost to the victims should be taken into account. The reduced risk to third parties of infectious diseases like HIV and hepatitis is especially considerable among injecting drug users. Although interventions might be effective in the short-term the patient might relapse later in life, therefore it is also important to measure the potential impact on future drug use and harms. For a comprehensive economic evaluation, then, the outcomes in both the resources saved and other value created domains should all be measured.

4.2 Objectives

The purpose of this review is to examine which dimensions of the monetary outcome have been chosen in the individual level patient data of the economic evaluation of drug

misuse interventions. The review examines the monetary dimensions that have been included in previous intervention research and how these are measured.

The first objective of this review is to identify the studies that have estimated the monetary outcome for drug misuse interventions and examine which dimensions of the monetary outcome have been measured. This will provide an overview of the current development of economic evaluations of drug misuse interventions and the limitations with existing studies. The second objective is to investigate how the dimensions are determined within each outcome category. This will illustrate whether or not there is a common understanding within economic evaluations of how to estimate monetary dimensions. The results of the review will provide an overview of the monetary burden to the society arising from drug misuse, from which the implications for policy makers will be analysed.

4.3 Methods

The most common method for measuring the monetary outcome in economic evaluations is by conducting a cost-benefit analysis. A cost-benefit analysis compares all the costs and the benefits of different interventions in monetary terms, and therefore allows policy makers to assess directly whether or not an intervention is worthwhile, without recourse to any other standard in the analysis (Drummond, M.F. et al, 2005). However, this review focuses on all of the studies that have measured the individual level outcome in monetary terms and not just those that conducted a cost-benefit analysis.

4.3.1 Inclusion Criteria for this review

Type of studies: Studies measuring the monetary outcome at one point of time, at different points of time, or changes between points of time will be included. There will be no intervention comparison restriction in the searching criteria, because comparing different interventions is not the main interests of this review. Studies considering one or more interventions will be included.

Type of intervention: Studies of interventions primarily aimed at reducing drug misuse problems will be included. All types of intervention delivered to the individual drug user or potential drug users will be considered. Studies of interventions delivered solely to the

drug users' family/ partner will not be included as the focus here is only on the outcome of the individual drug users.

Type of participants: People who misuse substances, including any type of illegal substance. Studies of people with only alcohol addiction or smoking problems will be excluded. Only studies collecting individual patient level data will be included.

Outcome: Outcomes have to be measured in monetary terms and have to consider the impact of the intervention on others in society. Studies that consider some dimensions of the monetary outcome as well as other clinical or economic outcomes will also be included. Studies only measuring intervention costs or only measuring clinical effectiveness will not be included.

Comparison: Studies considering at least one intervention will be included. Studies that measure outcomes either at one point of time, at different points of time, or the changes between points of time will be included.

4.3.2 Data sources and search strategy

Electronic and manual searches are undertaken to identify studies.

Search strategy:

The search was performed in June 2010. Studies which meet the inclusion criteria are identified from the following sources. There is no restriction for language or the year of publication.

Econlit (1969 – to June 2010)

EMBASE (1980–June 2010)

MEDLINE (1950 –June 2010)

PsycINFO (1806 –June 2010)

CRD (Centre for Reviews and Dissemination) databases

The Cochrane Library

The Cochrane Central Register of Controlled Trials (CENTRAL)

Current Controlled Trials Register

Example of searching strategy: MEDLINE; 1950 –June 2010:

[(drug misuse or drug dependen* or substance misuse or substance abuse or substance dependen* or addict* or illegal drug* or illicit drug* or inject* drug* or methadone or heroin or opiat* or opium or cocaine or crack cocaine or ecstasy or LSD or magic mushroom* or amphetamine or cannabis or marijuana or ketamine) and (economic evaluation)] and [(cost* or resource use* or soci* cost)]

4.4 Results

4.4.1 Description of included studies and dimensions of monetary outcome included

The purpose of this section is to identify the studies that measured the monetary outcome. Of 425 studies that were reviewed, 50 studies that are related to drug misuse treatment have been included. Most of the excluded studies only estimated the treatment costs or were modelling studies.

The interventions used in the included studies were mainly treatment types of intervention like methadone maintenance treatment, outpatient treatment and residential treatment. There were also some prevention programmes such as drug testing, and crime-related interventions like drug courts.

Only one of the included studies is a cross-sectional study (Neale et al, 2006), whereas the rest of the studies all followed the patients for a certain period of time, from 2 weeks up to 10 years. The number of participants in the included studies also ranged widely. The smallest sample size was 25 patients (Mauser, VanStelle and Moberg, 1994), and the largest sample size was 3.9 million (Berger, 2003). Most of the studies estimated the outcome from the societal perspective, and 11 studies estimated the outcome from the health care service provider/ government's perspective. 4 studies estimated the outcome from the perspective of the tax-payer (Daley et al, 2000; French, Fang and Fretz, 2010; Longshore et al, 2006; McCollister et al, 2009).

Most of the included studies were conducted in the USA and 6 studies were conducted in the UK. There was also 1 Norwegian study, 1 Dutch study, 1 German study, 1 Taiwanese study and 2 Australian studies. Details of each included study are listed in Table 4.4.1 and Appendix 4.

46 of the included studies measure monetary dimensions in either the resources saved domain, the other value created domain or both domains. Of these 23 are cost-benefit analyses, which apply the human capital approach for estimating the monetary outcome. The human capital approach values life and health foregone in terms of lost productivity. The other 23 studies are either cost-utility analyses or cost-effectiveness analyses with additional estimations for the monetary outcome, or studies designed to measure the monetary outcome alone. There are a further 4 studies, however, that do not measure the monetary outcome in terms of the dimensions within the 2 domains (Bishai et al, 2008; Borisova and Goodman, 2003 and 2004; Tang et al, 2007; Zarkin, Cates and Bala, 2000). These are all cost-benefit analyses that adopt the willingness-to-pay approach, which uses hypothetical questions to estimate values of how much individuals are willing to pay to improve their life quality and quantity. The merits of this approach remain contested and there are reservations about adopting it (Drummond, M.F. et al, 2005). Given that most of the included studies measure monetary dimensions in at least one of either the resources saved or other value created domain, these alone will provide the focus for the remainder of the analysis in this chapter and the willingness-to-pay studies will be examined no further.

Table 4.4.2 shows the different monetary dimensions measured, categorised by resources saved and other value created, which provides an overview of the dimensions of the monetary outcome that are covered in the included studies. All of the studies measured at least one dimension from the resources saved domain. However, of the 46 studies identified, 10 did not measure the health care cost, 26 did not measure the social care services cost, and 10 did not measure the criminal justice cost. Only 17 studies measured all 3 of the costs from the resources saved domain. In addition, only 32 of the 46 identified studies measured any dimensions in the other value created domain. Of these 23 measured productivity and 19 measured the value to communities from reduced drug related problems, but none of the other outcomes in this domain were measured at all. Of the 17 studies that measured all 3 costs in the resources saved domain, 8 measured either productivity or the value to communities from reduced drug related problems in the other value created domain, but only 4 measured both (Ettner et al, 2006; Koenig et al, 2005; Mark et al, 2001; Miller and Hendrie, 2009).

Table 4.4.1 Description of included studies

Study, country	Population	Intervention	Follow-up	Study perspective	Approach to estimate monetary outcome
Abou-Saleh et al, 2003; Abou-Saleh et al, 2008 (HEPC), UK	33 injecting drug users (IDUs), recruited from drug treatment centres	Trial enhanced HIV prevention counselling intervention -Stay Safe Therapy (SST; 4 sessions) -Simple Educational Counselling (SEC; 1 session)	12 months	Societal perspective	Monetary outcomes converted from Service Use Questionnaire (SUQ) -Resource saved: health care costs, criminal justice costs and social care costs
Ates et al, 2005, Germany	57 drug misuse patients	Three groups: -Specialised integration project (Mudra e.V.) -Standard work projects -Graduates of work projects	1 year	Societal perspective	Human capital approach -Resource saved: health care costs, criminal justice costs and social care costs -Other value created: increased productivity
Avants et al, 1999, USA	291 opioid dependent patients	Two groups -Day treatment -Enhanced standard methadone maintenance programme	6 months	Societal perspective	Human capital approach -Resource saved: health care costs, criminal justice costs and social care costs -Other value created: increased productivity
Barnett et al, 2006, USA	126 IDUs	Patients in methadone treatment	6 months	Health care system	-Resource saved: health care costs
Berg, 1997, Norway	61 patients who have used several substance (heroin, amphetamine, hashish, painkillers, benzodiazepines and/or alcohol)	Residential detoxification and counselling for 3 weeks -Completer -Non-completer	2 weeks since the detoxification started	Societal perspective	Human capital approach -Resource saved: health care costs -Other value created: increased taxes from taxable income
Berger, 2003, USA	3.9 million pregnant	Universal drug	1 year estimate	Societal	-Resource saved: health care

	women	misuse screening	based on data from existing literature	perspective	costs
Bishai et al, 2008, USA	241 heroin addicts	Before entering a methadone maintenance treatment	N/A	Health care provider perspective	Willingness-to-pay (WTP) approach -Heroin addicts' willingness-to-pay for the methadone maintenance treatment
Borisova and Goodman, 2003 and 2004, USA	303 drug misuse patients	Methadone maintenance treatment	N/A	Health care provider perspective	WTP approach -Drug misuse patients' willingness-to-pay and willingness-to-accept of the travel time required to obtain methadone maintenance treatment
Conover et al, 2006, USA	1,138 patients with HIV/AIDS, chronic mental illness and substance misuse	Two groups: -Employed -Unemployed	30 days	Societal perspective	Human capital approach -Resource saved: social care costs -Other value created: income
Daley et al, 2000, USA	439 pregnant drug misuse patients	Public funded drug misuse treatment	90, 180 and 270 days	Taxpayer perspective	-Resource saved: criminal justice costs -Other value created: victim costs
Davies et al, 2009 (Drug treatment outcomes research study; DTORS), UK	1,545 drug misuse patients	Patients received structured drug misuse treatment: community-based drug treatment or residential drug treatment	1 year	Societal perspective	-Resource saved: health care costs, criminal justice costs and social care costs -Other value created: victim costs
Dijkgraaf et al, 2005, Netherlands	430 Heroin addicts	Two groups: -Methadone plus heroin -Methadone alone	12 months	Societal perspective	Monetary outcomes converted from the European version of Addiction Severity Index

					(EuropASI) -Resource saved: health care costs and criminal justice costs -Other value created: victim costs
Dismuke et al, 2004 (PETS; The Persistent Effects of Treatment Study), USA	1,326 drug misuse patients from PETS	Drug misuse programmes from Chicago Target Cities Project	6, 24, 36 and 48 months	Societal perspective	Monetary outcomes converted from Addiction Severity Index (ASI), human capital approach -Resource saved: health care costs and criminal justice costs -Other value created: income
Drummond et al, 2004; Drummond, C. et al, 2005 (UKCBTMM), UK	60 opiate addicts, recruited from 10 community based clinics	Two groups: -Cognitive behaviour therapy (CBT) plus methadone maintenance treatment (MMT) -MMT alone	6 and 12 months	Societal perspective	Monetary outcomes converted from SUQ -Resource saved: health care costs, criminal justice costs and social care costs
Ettner et al, 2006 (CalTOP; California Treatment Outcome Project), USA	2,567 drug misuse patients	43 drug misuse treatment for CalTOP	3 and 9 months	Social planner/ government perspective	Monetary outcomes converted from ASI, human capital approach -Resource saved: health care costs, criminal justice costs and social care costs -Other value created: income and victim costs
Fals-Stewart, O'Farrell and Birchler, 1997, USA	80 drug misuse male patients from married or cohabiting couple	Two groups: -Behavioural couples therapy (BCT) -Individual-based drug misuse treatment (IBT)	12 months	Operation/ government perspective	-Resource saved: health care costs, criminal justice costs and social care costs

Finigan, 1996, USA	1,267 drug misuse patients	Two groups: -Drug misuse treatment (outpatient, residential and methadone) -No treatment	3 years data from existing database	Societal perspective	-Resource saved: health care costs, criminal justice costs and social care costs -Other value created: victim costs
Finigan, Carey and Cox, 2007, USA	11,102 offenders	Two groups: -Drug court -Traditional court	10 years data from existing database	Societal perspective	-Resource saved: criminal justice costs -Other value created: victim costs
Flynn et al, 1999 (DATOS; Drug Abuse Treatment Outcome Studies), USA	502 cocaine dependent patients	Two groups: -Long-term residential treatment (LTR) -Outpatient drug-free treatment (ODF)	12 months	Societal perspective	Human capital approach -Resource saved: criminal justice costs -Other value created: crime career/productivity loss and victim costs
French et al, 2000, USA	263 addiction treatment patient	Two groups: -Outpatient substance abuse treatment (PC) -Residential substance abuse treatment (FC)	9 months	Societal perspective	Monetary outcomes converted from ASI, human capital approach -Resource saved: health care costs and criminal justice costs -Other value created: income
French et al, 2002a (PAAM; Pregnant Addicts/Addicted Mothers), USA	121 pregnant drug misuse patients	Two groups: -Specialty residential treatment -Standard residential treatment	6 months	Societal perspective	Monetary outcomes converted from ASI, human capital approach -Resource saved: health care costs and criminal justice costs -Other value created: income
French et al, 2002b, USA	186 patients from homeless shelters and psychiatric hospitals	Two groups: -Treatment-as-usual (TAU) -Modified therapeutic	12 months	Societal perspective	Human capital approach -Resource saved: health care costs and criminal justice costs

		community treatment (TC)			-Other value created: income and victim costs
French et al, 2002c, USA	178 drug misuse patients	3 outpatient drug-free programmes	7 months	Societal perspective	Monetary outcomes converted from ASI, human capital approach -Resource saved: health care costs and criminal justice costs -Other value created: income
French, Salome, and Carney, 2002, USA	222 drug misuse patients	9 adult substance residential treatments	6 months	Societal perspective	Monetary outcomes converted from ASI, human capital approach -Resource saved: health care costs and criminal justice costs -Other value created: income
French et al, 2003, USA	600 adolescent cannabis users aged 12 to 18	5 programmes of CYT study (Cannabis Youth Treatment)	3, 6, 9, 12 months	Societal perspective	-Resource saved: health care costs, criminal justice costs and social care costs
French, Fang and Fretz, 2010, USA	571 criminal offenders	Two groups: -Pre-release substance treatment -No treatment	1 year after release	Tax-payer perspective	Human capital approach -Resource saved: criminal justice costs -Other value created: wage loss and victim costs
Godfrey, Stewart and Gossop, 2004 (NTORS; National Treatment Outcome Research Study), UK	549 drug misuse patients	Patient from 54 residential and community treatment programmes	1 and 2 years	Societal perspective	-Resource saved: health care costs, criminal justice costs and social care costs -Other value created: victim costs
Harris, Gospodarevskaya and Ritter, 2005, Australia	139 heroin dependent patients	Two groups: -Buprenorphine -Methadone	3, 6, and 12 months	Societal perspective	-Resource saved: health care costs and criminal justice costs
Hartz et al, 1999, USA	102 opioid-addicted patients	Two groups: -Methadone treatment with contingency	6 months	Government perspective	-Resource saved: health care costs

		contracting -Methadone treatment (control group)			
Harwood et al, 1988 (TOPS; Treatment Outcome Prospective Study), USA	11,000 drug users from TOPS	41 drug misuse treatment of outpatient methadone, residential and outpatient drug-free programme	12 months	Societal perspective	Human capital approach -Resource saved: criminal justice costs -Other value created: crime career/productivity loss, income and victim costs
Healey et al, 1998, (NTORS), UK	1,075 drug misuse patients	Patient from 54 residential and community treatment programmes	12 months before treatment	Societal perspective	-Resource saved: health care costs, criminal justice costs and social care costs -Other value created: victim costs
Koenig et al, 2005 (PETS), USA	595 drug misuse patients	Drug misuse programme (methadone, residential rehabilitation, intensive overnight, outpatient)	6, 12, 24, 30 months	Societal perspective	Human capital approach -Resource saved: health care costs, criminal justice costs and social care costs -Other value created: income and victim costs
Levine, Stoloff and Spruill, 1976, USA	15,000 drug misuse patients	45 public drug misuse treatment programmes	4 years data from existing database	Government perspective	-Other value created: victim costs
Logan et al, 2004, USA	745 offenders	Three groups of drug court programme: -Graduated clients -Terminated clients -Assessed clients	12 months	Societal perspective	Human capital approach -Resource saved: health care costs, criminal justice costs and social care costs -Other value created: income
Longshore et al, 2006 (SACPA; The California Substance Abuse and Crime Prevention Act), USA	130,152 offenders	Two groups: -Probation with drug misuse treatment -Incarceration/probation without treatment	12 and 30 months data from existing database	Taxpayer perspective	Human capital approach -Resource saved: health care costs and criminal justice costs -Other value created: income and sale taxes

Mark et al, 2001, USA	600,000 heroin addicts	Cost-of-illness of heroin dependence	1 year data from existing literature	Societal perspective	Human capital approach -Resource saved: health care costs, criminal justice costs and social care costs -Other value created: productivity due to premature mortality, income and victim costs
Masson et al, 2002, USA	3,147 opioid dependent patients	Two groups: -Opioid dependent patients -General patient population	2 years	Health care provider perspective	-Resource saved: health care costs
Mauser, VanStelle and Moberg, 1994 (TAP; Treatment Alternative Program), USA	25 patients	Treatment alternative programmes	6 months	Societal perspective	Human capital approach -Resource saved: health care costs and criminal justice costs -Other value created: increased productivity and victim costs
McCollister et al, 2009, USA	119 young offenders aged 12 to 17	Four different drug court interventions	4 and 12 months	Tax-payer perspective	-Resource saved: criminal justice costs -Other value created: victim costs
McGlothlin and Anglin, 1981, USA	187 drug misuse patients	Two groups: -Patients from a closed down methadone treatment clinic (Bakersfield) -Patients from a continuing methadone treatment (Tulare)	25-26 months after discharge	Societal perspective	-Resource saved: criminal justice costs and social care costs
Miller and Hendrie, 2009, USA	0.4-1.1 million young drug users aged 12 to 14	Drug misuse prevention	1 year estimate based on data	Societal perspective	Human capital approach -Resource saved: health care

			from existing literature		costs, criminal justice costs and social care costs -Other value created: productivity loss (due to premature death, illness related to substance or incarceration and criminal careers) and victim costs
Neale et al, 2006, UK	75 injecting drug users	Patients recruited from existing needle exchange programmes in large city, small town, and medium town	N/A	Societal perspective	Monetary outcomes converted from SUQ -Resource saved: health care costs, criminal justice costs and social care costs
Robertson, Grimes and Rogers, 2001, USA	293 young offenders aged 11 to 17	Two groups: -Community-based intensive supervision and monitoring (ISM) -Cognitive behavioural intervention (CB)	6, 12 and 18 months	Public policy perspective	-Resource saved: criminal justice costs
Salome et al, 2003, USA	2,665 addiction patients	Addiction treatment from 19 treatment facilities	6 months	Societal perspective	Monetary outcomes converted from ASI, human capital approach -Resource saved: health care costs and criminal justice costs -Other value created: income and victim costs
Scanlon, 1976, USA	37,184 drug misuse patients	Drug misuse treatment from 6 facilities	5 years	Societal perspective	Human capital approach -Resource saved: health care costs and social care costs -Other value created: income
Sirotnik and Bailey,	285 heroin addicts	5 community drug	9 months	Societal	Human capital approach

1975, USA		misuse treatment programmes		perspective	-Resource saved: health care costs, criminal justice costs and social care costs -Other value created: productivity loss
Sweeney et al, 2009, Australia	393 IDUs	Treatment for injecting-related injuries and diseases	12 months	Public health system perspective	-Resource saved: health care costs
Tang et al, 2007, Taiwan	1,817 members of general public	Drug misuse treatment	N/A	Societal perspective	WTP approach -Willingness-to-pay of the general public for the drug misuse treatment
Yu et al, 1991, USA	123 drug misuse patients	Drug misuse treatment in workplaces	2 years	Health insurance perspective	-Resource saved: health care costs
Zarkin, Cates and Bala, 2000, USA	393 members of general public	Drug misuse treatment	N/A	Societal perspective	WTP approach -Willingness-to-pay of the general public for the drug misuse treatment

Table 4.4.2 List of dimensions of the monetary outcome in the included studies

Study	Resource saved			Other value created	
	Health care costs	Criminal justice costs	Social care costs	Increased productivity	Value to communities from reduced drug related problems
Abou-Saleh et al, 2003; Abou-Saleh et al, 2008 (HEPC)	✓	✓	✓		
Ates et al, 2005	✓	✓	✓	✓	
Avants et al, 1999	✓	✓	✓	✓	
Barnett et al, 2006	✓				
Berg, 1997	✓			✓	
Berger, 2003	✓				
Conover et al, 2006			✓	✓	
Daley et al, 2000		✓			✓
Davies et al, 2009 (DTORS)	✓	✓	✓		✓
Dijkgraaf et al, 2005	✓	✓			✓
Dismuke et al, 2004 (PETS)	✓	✓		✓	
Drummond et al, 2004; Drummond, C. et al, 2005 (UKCBTMM)	✓	✓	✓		
Ettner et al, 2006 (CalTOP)	✓	✓	✓	✓	✓
Fals-Stewart, O'Farrell and Birchler, 1997	✓	✓	✓		
Finigan, 1996	✓	✓	✓		✓
Finigan, Carey and Cox, 2007		✓			✓
Flynn et al, 1999 (DATOS)		✓		✓	✓
French et al, 2000	✓	✓		✓	
French et al, 2002a (PAAM)	✓	✓		✓	
French et al, 2002b	✓	✓		✓	✓
French et al, 2002c	✓	✓		✓	
French, Salome, and Carney, 2002	✓	✓		✓	
French et al, 2003	✓	✓	✓		
French, Fang and Fretz, 2010		✓		✓	✓
Godfrey, Stewart and Gossop, 2004 (NTORS)	✓	✓	✓		✓

Harris, Gospodarevskaya and Ritter, 2005	✓	✓			
Hartz et al, 1999	✓				
Harwood et al, 1988 (TOPS)		✓		✓	✓
Healey et al, 1998	✓	✓	✓		✓
Koenig et al, 2005 (PETS)	✓	✓	✓	✓	✓
Levine, Stoloff and Spruill, 1976					✓
Logan et al, 2004	✓	✓	✓	✓	
Longshore et al, 2006 (SACPA)	✓	✓		✓	
Mark et al, 2001	✓	✓	✓	✓	✓
Masson et al, 2002	✓				
Mausser, VanStelle and Moberg, 1994 (TAP)	✓	✓		✓	✓
McCollister et al, 2009		✓			✓
McGlothlin and Anglin, 1981		✓	✓		
Miller and Hendrie, 2009	✓	✓	✓	✓	✓
Neale et al, 2006	✓	✓	✓		
Robertson, Grimes and Rogers, 2001		✓			
Salome et al, 2003	✓	✓		✓	✓
Scanlon, 1976	✓		✓	✓	
Sirotnik and Bailey, 1975	✓	✓	✓	✓	
Sweeney et al, 2009	✓				
Yu et al, 1991	✓				

4.4.2 Estimation methods for different dimensions of monetary outcome

In the previous section, the different dimensions of the monetary outcome have been identified and categorised. This section examines how monetary dimensions are estimated and whether there are common methods between the studies. As shown in Table 4.4.3, there are 2 main methods for estimating monetary dimensions in the included studies.

The first method estimates the outcome by multiplying the unit cost and the frequency of the social cost events. Of the 46 studies included, 39 estimated the monetary outcome by the first method. All of the studies acquire the unit cost either from the existing literature or from government reports or from both. The unit cost may be varied within the existing literature because drug misuse policies are varied between different countries and even different states in some countries. The economic burden caused by drug misuse patients will not be the same between different countries.

Questionnaires are used to estimate the frequency of the social cost events, however the type of questionnaire used varies between studies. Some studies (11 of the 39) used a standardised questionnaire, like ASI or EuropASI (McLellan et al, 1980; Kokkevi and Hartgers, 1995, respectively), or the Service Use Questionnaire (SUQ) designed by Godfrey and colleagues originally for the UKATT trial (UKATT research team, 2001 and 2005). The advantage of using a standardised questionnaire to estimate the frequency of the social cost events is that it provides a standard way between countries to measure the same dimensions.

The design of ASI and EuropASI are very similar, as EuropASI is actually the revised version of ASI for European research. Both include questions about the patient's use of various resources: medical services; employment/ support services; services related to alcohol problems; services related to drug problems; resources used for criminal justice; resources used relating to family and social relationships; and psychology services (McLellan et al, 1980; Kokkevi and Hartgers, 1995). The questionnaire estimates the improvement of the individual's health state and social functioning state by calculating the health resources saved, the social care resources saved and the increased productivity. It also estimates the value of the prevented crime by calculating the criminal justice resources saved following the intervention.

SUQ is another type of standardised questionnaire which was used in 3 of the studies that estimate the monetary outcome: the hepatitis C intervention trial (Abou-Saleh et al, 2003; Abou-Saleh et al, 2008), the UKCBTMM trial (Drummond et al, 2004; Drummond, C. et al, 2005), and a cross-sectional study of injecting drug users in needle exchange programmes (Neale et al, 2006). SUQ includes questions about the patient's use of health services; use of other social services (which includes individual's employment status); use of drug related services; and use of criminal justice services. The purpose of SUQ is to evaluate the resources used by drug misuse patients. It estimates the value of the individual's health state and social functioning state improvement by calculating the health resources saved and the social care resources saved. Like ASI and EuropASI, it also estimates the value of the prevented crime by calculating the criminal justice resources saved.

The other 28 studies use non-standardised questionnaires, which differ from one another. Most of these also estimate the value of the individual's health state and social functioning state improvement by calculating the health resources saved and the social care resources saved. However, they might also include the other types of value arising from prevented crime, such as the victim costs.

The second method for estimating the monetary outcome does not use the frequency of the social cost events at all. Instead it uses the overall estimates for the sum of the resource use among the population and the percentage of the resource use that is attributed to a particular group in society, in this case drug misuse patients. These estimates are taken from either government reports or the literature. The main problem with this method is that it is difficult to accurately attribute social resource use to a specific group within society. 7 of the 46 studies used this method. 2 of these were focused on estimating the value created from prevented crime and considered criminal justice resources saved and the victim cost (Finigan, Carey and Cox, 2007; Levine, Stoloff and Spruill, 1976). 3 of the studies estimated the value of increased productivity and 5 estimated the value of the improvement of the individual's health state, by considering the health care resources saved.

Even within the 2 methods different studies estimate the monetary outcome differently by considering different dimensions. This will depend on the perspective of those conducting the research. However, as the 2 different methods in many cases measure the same dimensions, it is important to recognise that when comparing the studies they may not be using the same method to estimate the value within the same dimensions.

Table 4.4.3 Estimation of societal resource use in the included studies

Source/methods	Study
Unit cost * frequency	<p>-Use EuropASI or ASI to estimate outcomes: Dijkgraaf et al, 2005; Dismuke et al, 2004; Ettner et al, 2006; French et al, 2000; French et al, 2002a; French et al, 2002c; French, Salome, and Carney, 2002; Salome et al, 2003</p> <p>-Use SUQ to estimate outcomes: Abou-Saleh et al, 2003; Abou-Saleh et al, 2008; Drummond et al, 2004; Drummond, C. et al, 2005; Neale et al, 2006</p> <p>-Others: Ates et al, 2005; Avants et al, 1999; Barnett et al, 2006; Berg, 1997; Conover et al, 2006; Daley et al, 2000; Davies et al, 2009; Fals-Stewart, O'Farrell and Birchler, 1997; Flynn et al, 1999; French et al, 2002b; French et al, 2003; French, Fang and Fretz, 2010; Godfrey, Stewart and Gossop, 2004; Harris, Gospodarevskaya and Ritter, 2005; Hartz et al, 1999; Harwood et al, 1988; Healey et al, 1998; Koenig et al, 2005; Logan et al, 2004; Masson et al, 2002; Mauser, VanStelle and Moberg, 1994; McCollister et al, 2009; McGlothlin and Anglin, 1981; Robertson, Grimes and Rogers, 2001; Scanlon, 1976; Sirotnik and Bailey, 1975; Sweeney et al, 2009; Yu et al, 1991</p>
Estimate of average resource use from the database or literature	Berger, 2003; Finigan, 1996; Finigan, Carey and Cox, 2007; Levine, Stoloff and Spruill, 1976; Longshore et al, 2006; Mark et al, 2001; Miller and Hendrie, 2009

4.5 Conclusions and Discussion

The aim of this chapter has been to identify the economic evaluations of drug misuse interventions and to examine whether or not they share a common method for evaluating the monetary benefits of the intervention. The results of the review have provided an overview of the different dimensions of the monetary outcome measured in existing studies.

The results of this chapter, however, have shown that existing studies do not offer a comprehensive estimate of the monetary outcome. The dimensions of the monetary outcome may be classified in 2 domains. It is important to take into account all of the dimensions in the resources saved domain as they will all influence the monetary impact on the society. However, only 17 of the 46 studies considered all 3 dimensions. A further 5 dimensions have been identified in the other value created domain. All of these dimensions are important and should be considered as they represent the potential impact on others in society. However, only 32 of the studies measured any of the dimensions in the value created domain at all, and these only covered 2 of the 5 dimensions. Only 4 of the studies considered all 3 of the dimensions in the resources saved domain and 2 of the dimensions in the value created domain. None of the studies provide a comprehensive estimate of the costs from the societal perspective and therefore policy makers might be misled when they make decisions if they assume that the studies do represent a comprehensive estimate.

It is important that when policy makers use the existing research they are aware of the limitations within it. It is difficult for economic evaluations to take into account all of the dimensions in each domain, especially given the amount of information that is required to estimate the different dimensions. Few studies have the resources to conduct the analysis from a broad enough perspective to provide a comprehensive estimate of the societal monetary outcome and policy makers should be aware of these limitations and be able to justify which dimensions of the monetary outcome they think should be prioritised.

If policy makers are only concerned with a certain problem, such as the health of the individual drug users, then it might be acceptable to adopt a narrow perspective, providing that the policy makers are both aware of the limitations of that perspective and

of the dimensions that they are neglecting, which would influence the monetary impact on society. If specific problems are targeted then it is also important that policy makers examine the costs of each dimension of the monetary outcome and not just the overall figure, as this may have important implications for who pays for the drug misuse intervention. For instance, if one intervention is directed at reducing the levels of crime committed, this may be paid for by the criminal justice department, whereas an intervention directed at reducing health care resources used may be paid for by the health department, such as the NHS in the UK.

A more general consideration when measuring the monetary outcome is its relationship with specific individual patients' characteristics and individual level outcomes, such as QALYs. Even though many of the studies included in the review used a standardised questionnaire for estimating the monetary outcome, none of them examined which type of drug user is more likely to use each type of resource, such as the health care services or criminal justice services. Given that the studies reviewed did not include all of the monetary dimensions it is all the more important to know whether or not there are specific relationships between different dimensions and patient characteristics as this might reveal potential bias within those studies if they exclude dimensions which relate more strongly to specific groups of drug misuse patient. In addition, if a profile of different types of drug user could be developed then this would provide useful information for policy makers as they would be able to direct specific types of intervention at specific types of drug misuse patient and allocate resources accordingly. The relationship between the monetary dimensions and the characteristics of individual drug users is examined in the next chapter.

Chapter 5 Problems of resource use estimation in drug misuse interventions

5.1 Background

In the previous chapter the methods that have been used to estimate the monetary outcome in economic evaluations of drug misuse interventions were examined. This chapter focuses on the resource use of drug misuse patients. The resource use is a category of the monetary outcome that estimates the cost of the services that drug misuse patients use within the public sector. The difference between the costs of the resources of a drug misuse patient as a result of drug misuse intervention from that of a patient who did not receive the intervention is called the resources saved, which was one of the 2 domains of the monetary outcome categorised in the previous chapter. This chapter, therefore, is only concerned with the resources saved domain and not the other value created domain.

One of the problems that emerged from the analysis in the previous chapter was that most drug misuse studies do not consider whether different types of patients use some resources more than others; indeed this is a problem with most drug misuse studies and not just those that measure the monetary outcome. The results from most existing studies only indicate the amount of resources used by either the total drug misuse patients or the average patient. However, this does not indicate whether or not some types of patient use more of one type of resource than another. For example, the results do not show which type of patients are most likely to commit crime or have a higher health care resource use. The results only show the overall or average figures, which does not account for variation within the sample of drug misuse patients surveyed. It might be that some types of patient have a high health care resource use and commit a low amount of crime, whereas over patients commit a lot of crime but have a low health care resource use. However, from the overall or average results it is impossible to conclude whether or not this is the case.

Identifying the relationship between the types of drug users and the resource use may help policy makers decide about the allocation of resources, as they might be able to target specific interventions at specific types of drug users. It is important to understand which

factors are related to high societal costs and whether or not these vary between different types of drug misuse patients, especially when there is a financial incentive to minimise the burden to society.

Some studies have attempted to capture the characteristics of different types of drug misuse patients by considering their gender, age and location (Daley et al, 2000; Neale et al, 2006). However, these might not be the only significant characteristics, and it is also important to consider whether or not other characteristics affect drug misuse, such as patients' employment status, physical health status and whether they use other substances like cigarettes.

5.2 Objectives

The aim of this chapter is to use an existing data sample to examine whether or not a profile can be developed of the resource use in the public domain, by distinguishing between drug misuse patient characteristics.

The first objective is to cluster the patients together according to the distribution of their costs within their various social cost categories and to identify the statistically significant characteristics of the patients in each cluster. The statistically significant social costs for the clusters will also be identified.

The second objective is to examine whether or not there are any patterns between the significant characteristics and the significant social costs across the clusters. For example, if the patients have high health care costs whether or not they are also more likely to have high addiction and crime costs, or whether there is any relationship between employment status and social costs. If relationships can be identified across the clusters then a profile of different types of drug misuse patients may be identified.

5.3 Methods

5.3.1 Problems of using the mean average in highly skewed data

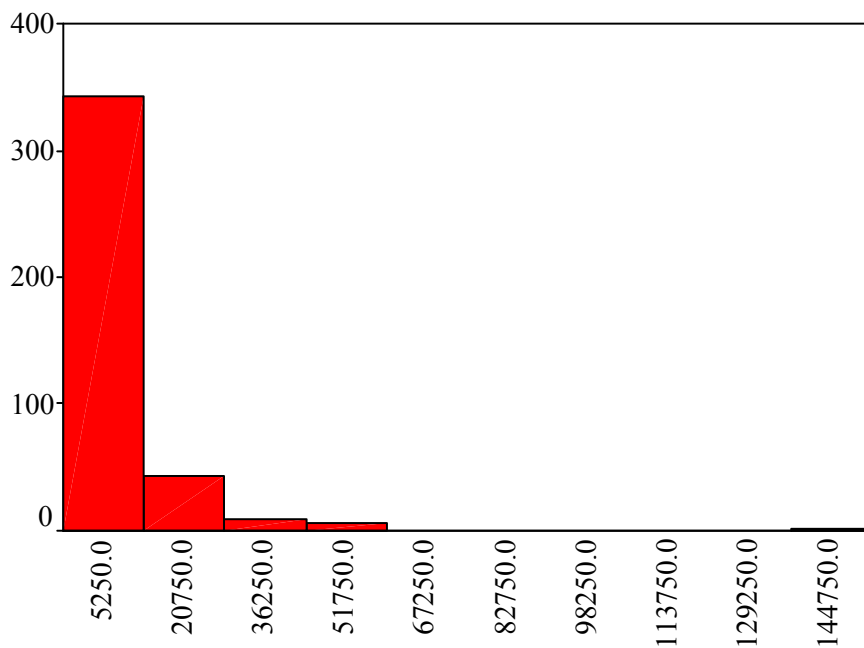
This chapter uses data from RESULT (Raistrick et al, 2008), which uses the Service Use Questionnaire (SUQ) originally designed by Godfrey and colleagues for the UKATT trial (UKATT research team, 2001 and 2005). This is used to determine patients' resource use in 4 main categories: health care services, addiction related services, social care services, and criminal justice services.

In each category a wide range of events are listed and the patients are asked in the interview whether or not they have experienced these events, such as a visit to the GP in the last 6 months. Based on the data of the frequency and unit cost of each event, the resource use of the 4 main categories and the overall resource use are estimated. As shown in Table 5.3.1 and Table 5.3.2, at the baseline the mean of resource use in health care services, addiction services and social care services are all lower than £1,000, and both the resource use in criminal justice and the overall resource use are higher than £4,500. In Table 5.3.2 there are similar findings at the 6 month follow-up period showing that both the crime costs and the overall societal costs are over £2,000, whereas the costs in the other 3 categories are much lower.

Table 5.3.1 and Table 5.3.2 reveal that the data of all 4 social cost categories and the overall societal costs are highly positively skewed at both baseline and the 6 month follow-up period. For instance, Figure 5.3.1 and Figure 5.3.2 show that in the RESULT sample patients' overall resource use is within the lowest clusters of the social costs at both baseline and 6 month follow-up. In addition, Table 5.3.1 and Table 5.3.2 show that over 55% of patients at baseline do not use any resources relating to addiction services, social care services and criminal justice services. Similarly, over 65% of patients do not have any costs relating to social care services and criminal justice services. The results of kurtosis show that the sample has a highly leptokurtic distribution at both baseline and the 6 month follow-up period. This shows that the majority of patients' social costs are clustered in a small cost range. The results of skewness and kurtosis show that the societal costs of patients in the RESULT sample are mainly clustered at the lowest end of the societal cost ranges.

Table 5.3.1 Description of the sample at baseline

Baseline	N	% of Patients with £0	Mean; £	S.D. of mean	Skewness	Kurtosis
health care costs	402	24.1%	940.54	3838.68	10.15	122.85
addiction service costs	402	70.5%	422.79	1932.80	7.64	65.09
social care costs	402	68.0%	85.12	294.09	5.93	43.25
crime costs	402	55.1%	4580.51	10545.21	7.61	94.54
total societal cost	402	8.7%	6028.96	11803.32	5.94	59.94



Baseline total societal cost

Figure 5.3.1 Distribution of total societal costs at baseline

Table 5.3.2 Description of the sample at 6 month follow-up

6 month	N	% of Patients with £0	Mean; £	S.D. of mean	Skewness	Kurtosis
health care costs	268	9.0%	1,197.74	5210.52	13.77	205.63
addiction service costs	268	4.1%	757.48	2000.75	8.67	85.15
social care costs	268	66.0%	93.51	302.08	5.44	36.12
crime costs	268	73.9%	2084.51	4788.98	2.71	7.40
total societal cost	268	2.2%	4133.24	7242.09	5.36	47.11

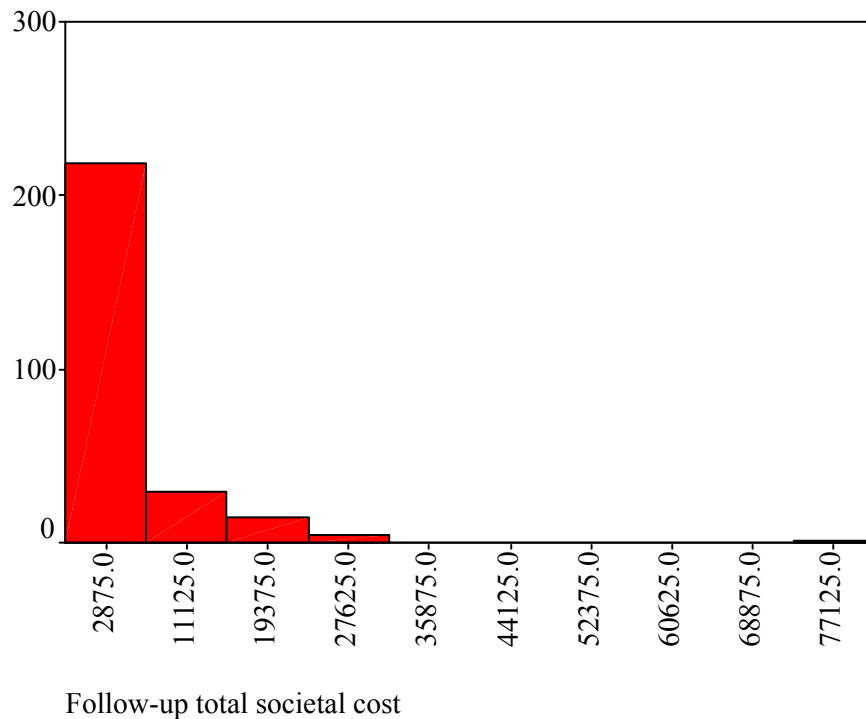


Figure 5.3.2 Distribution of total societal costs at follow-up

In order to examine how different factors are related to the social cost, a range of different values is needed. When the data is highly positively skewed, it reveals a lack of variance in the sample. For instance, when the majority of the patients in the sample have £0 in the health care services category, their age, gender and other characteristics make no difference. It would, therefore, be impossible to use general statistical techniques to determine whether age, gender and any other characteristics are relevant factors for predicting the health care services cost. When the data is more normally distributed across a wider range of different health care service costs, it is possible to examine whether there are any factors related to the different range of health care costs, for example, whether or not the older patients have higher health care costs. Due to the highly skewed data, this chapter will pursue a different approach by using clustering techniques and examining the relationship between social costs and patients' characteristics within the subgroup in the RESULT sample.

5.3.2 Cluster analysis

Cluster analysis allows researchers to establish subgroups within the sample and then analyse the group membership (Garson, 2009). The distance between each case in the

sample is examined and the cases with the lowest distance are grouped into homogenous groups and distinct clusters (Garson, 2009; Tryfos, 1998). Once the subgroups have been identified, the relationship between social costs and patients' characteristics may be examined within each cluster later in the chapter.

The two-step cluster analysis is chosen to identify the subgroups in the RESULT sample. The two-step cluster analysis is a type of clustering technique and is considered to be a better technique than hierarchical clustering and k-mean clustering for a large sample because it scales more efficiently (Garson, 2009). The two-step cluster analysis allows researchers to handle mixed type attributes and automatically determine the number of clusters (Bacher, Wenzig and Vogler, 2004). The cases have minimised distances between each other in one cluster, and each cluster has the maximum variance (Garson, 2009).

The two-step cluster analysis aims to analyse the relationship between patients' characteristics and the social costs in the RESULT study. RESULT has a relatively large sample (n=401) and the patients' characteristics cover a range of both continuous and categorical variables, hence it is appropriate to use the two-step cluster analysis. K-mean cluster analysis is also good for handling a large number of cases, but it is necessary to define the number of clusters (k) in advance (Garson, 2009). The cases in the RESULT study are highly skewed and it is difficult to decide the ideal number of clusters. It is therefore a better option to use the two-step cluster analysis as the number of clusters is automatically determined.

All 4 categories of social costs as well as the total societal cost are included in the two-step cluster analysis. This allows the homogeneous subgroups to be clustered together and makes it easy to compare the differences between the cost categories. In a hypothetical cluster, for example, the mean of the health care cost may be the lowest among all the clusters, but the cluster may have the highest mean of the crime cost. Combining these results with patients' characteristics would provide a profile for this particular group of patients. The results of the clustering analysis will provide an overview of the distribution of the higher and lower cost clusters within each social cost category, which will provide a brief mapping of the societal cost clusters and a basis for later sections.

5.3.3 Factors related to the social costs within the subgroups

In section 5.3.2 all patients were divided into different clusters, based on the results of the two-step clustering analysis. Within each cluster, the patients' characteristics are examined, such as gender, age, smoking habit, employment status, having children or not, the types of drug that they have taken, and their recent social resource use such as hospital visits, drug treatment and prescriptions for medication. Patients' individual level outcomes, such as QALYs, dependence, physical and psychological health status and social satisfaction are also considered as variables. Whether or not they complete the follow-up interview after 6 months will also be examined. The exploratory analysis of the missing patients will provide a brief overview of how drop-outs in drug misuse research are related to the different social costs. The descriptive results at baseline and the 6 month follow-up period are presented as a percentage of the patients within each cluster. Taking a hypothetical cluster for example, 200 patients are grouped into cluster 1 and 60% of these patients have children and the other 40% do not. The results would thus illustrate the characteristics of the patients in each societal cost cluster and provide an exploratory description of the different cost clusters.

Using the chi-square test for the categorical variables and the t-test for the continuous variables as a simple statistical technique, the statistical significance of each factor will also be tested within the cluster. The test will show whether or not the patients' characteristics are statistically significant factors for forming the clusters.

5.3.4 Factors related to the social costs changes

The previous sections show how the social cost clusters will be determined at both baseline and the follow-up period, and compare the significance of different factors for the formation of each social cost cluster. Using a similar approach, the aim of this section is to obtain a profile of the changes of social costs between baseline and the follow-up period. In section 5.3.2, all categories of social costs are included in the clustering process. Similarly, the changes within all categories of social costs are included in the two-step cluster analysis in this section. Patients with the least variance are clustered in the same social cost cluster. The results provide a descriptive profile of patients' social cost changes between baseline and the 6 month follow-up period. Within each cluster, the

results indicate whether or not each category of social cost has increased or decreased between the 2 time points.

The RESULT study (Raistrick et al, 2008) is not a clinical trial. It is an observational study between 2 time points that are 6 months apart, during which the patients receive drug misuse interventions. The treatment episodes of each individual patient are not clear, thus it is not possible to examine the differences before and after the treatment. The large number of participants in the RESULT study, however, provides a broader overview of the drug misuse patients in treatment than is provided by most clinical trials. The results of this section therefore provide a description of the characteristics of patients who have higher and lower costs at the baseline while receiving drug misuse treatment, which could be used as a profile of drug misuse patients for future studies.

5.4 Results

There are 2 types of patient characteristics that are examined in the cluster analysis. The categorical variables include age, gender, employment status, whether or not the patients have a child, whether or not they smoke, whether or not they take heroin, methadone or crack, whether or not they have received treatment for drug problems, visited hospital, or had a prescription in the last 6 months. The continuous variables are age, and results for EQ-5D, LDQ, CORE, SSQ, and SCL. EQ-5D is the health related utility measure, LDQ measures the drug dependence outcome, CORE measures the psychological health of the patient, SSQ measures the patients' satisfaction regarding social relationships, and SCL measures the physical health outcome.

5.4.1 Results at baseline

As described in section 5.2.1, the two-step clustering is performed to analyse the distribution of the societal cost among the patients in the RESULT study. The total societal cost and the social costs of all 4 categories are included in the analysis: health care services, addiction services, social care services and crime costs.

As shown in Table 5.4.1 and Table 5.4.2, at baseline 401 patients are included in the two-step cluster analysis and 13 patients are excluded, due to missing data in one or more of

the variables. 3 clusters are determined: 50.1% of patients are grouped in cluster 1 and 40.7% of patients are in cluster 2, with the remainder of the patients (6%) in cluster 3.

Table 5.4.1 shows the characteristics of patients within each cluster at baseline. Within cluster 1 none of the patients have taken methadone and this is the most statistically significant categorical variable, although other variables such as follow-up completion (43.1%), whether they take heroin (59.4%), whether they have recently received drug treatment (17.8%), and whether they are unemployed (71.8%) are also statistically significant. None of the continuous variables are statistically significant. Table 5.4.2 shows the mean social cost categories at baseline. The statistically significant costs are health (£335.22), addiction (£105.15) and total social cost (£4,302.60).

Within cluster 2 the only statistically significant categorical variables are whether patients have completed the follow-up evaluation (100%), taken methadone (92.7%), or taken heroin (93.3%). There are no statistically significant continuous variables. The statistically significant mean costs are addiction (£248.25), crime (£3,289.18) and total social cost (£4,316.50). The addiction cost is over twice that of cluster 1, whereas the total cost is only marginally higher (£13.90) than cluster 1.

Within cluster 3 only 2 categorical variables are statistically significant: whether the patient has received treatment for drug problems (75%) and whether they have visited the hospital in the last 6 months (75%). There are no statistically significant continuous variables. The only statistically significant mean cost is the total societal cost (£33,587.09), which is the highest among the clusters.

With the results for all 3 clusters at baseline set out some conclusions may be drawn. To draw strong conclusions about the character profile of patients that are likely to have higher or lower costs the same characteristics must be statistically significant variables in more than one cluster and there must be comparable statistically significant mean costs. If there are no such comparable statistically significant results across the clusters then no conclusions can be drawn about the relationship between individual characteristics, both with one another and with the different types of social costs.

None of the characteristics were significant variables in all 3 clusters, however, in clusters 1 and 2 the percentage of patients that take both methadone and heroin were statistically significant. In cluster 1 the results were 0% and 59.4% respectively compared with 92.7% and 93.3% respectively in cluster 2. The total societal cost between the 2 clusters was not particularly different: £4,302.60 in cluster 1 compared with £4,316.50 in cluster 2. However, the addiction cost in cluster 1 was £105.15, whereas in cluster 2 it was £248.25, over twice as much. This indicates, as might be expected, that patients who take methadone or heroin are likely to use more addiction resources, even if their societal cost is not that different from other drug misuse patients.

Table 5.4.1 Patient characteristics within each cluster at baseline

Baseline		Total (n=390)	Cluster 1 (n=202)	Cluster 2 (n=164)	Cluster 3 (n=24)
complete follow-up	Yes (n=263)	67.4%	43.1%*	100.0%*	50.0%
Age	Mean	30.70	31.15	30.00	31.75
	S.D.	6.89	7.12	6.63	6.63
Sex	Male (n=283)	72.6%	80.2%	65.2%	58.3%
Employment	Have job (n=312)	20.0%	28.2%*	12.8%	0.0%
Have child	Yes (n=208)	53.3%	57.4%	48.8%	50.0%
Smoker	Yes (n=369)	94.6%	91.6%	98.2%	95.8%
Taking methadone	Yes (n=232)	40.5%	0.0%*	92.7%*	25.0%
Taking heroin	Yes (n=291)	74.6%	59.4%*	93.3%*	75.0%
Taking crack	Yes (n=382)	2.1%	4.0%	0.0%	0.0%
Treatment for drug problem in last 6 months	Yes (n=271)	30.5%	17.8%*	39.6%	75.0%*
Visited hospital in last 6 months	Yes (n=270)	30.8%	23.3%	33.5%	75.0%*
Prescriptions in last 6 months	Yes (n=258)	33.8%	30.2%	36.0%	50.0%
EQ-5D ^a baseline overall score	Mean	0.74	0.76	0.73	0.62
	S.D.	0.27	0.23	0.30	0.37
LDQ ^a baseline overall score	Mean	16.24	15.65	16.95	16.33
	S.D.	8.09	7.89	8.34	7.87
CORE ^a baseline overall score	Mean	56.47	56.26	57.02	54.42
	S.D.	23.76	24.00	23.54	24.19
SSQ ^a baseline overall score	Mean	13.68	13.92	13.94	10.00
	S.D.	5.72	5.63	5.63	6.03
SCL ^a baseline overall score	Mean	15.63	15.25	15.99	16.29
	S.D.	7.88	8.22	7.44	8.12

*: p<0.05

a: The higher scores of EQ-5D and SSQ represent the better outcomes. The higher scores of LDQ, CORE and SCL represent the worse outcomes.

Table 5.4.2 Mean costs within each cluster at baseline

Baseline	N	health care costs		addiction service costs		social care costs		crime costs		total societal cost	
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Cluster 1	202	335.22*	867.44	105.15*	499.83	56.67	177.01	3805.55	6657.02	4302.60*	6756.81
Cluster 2	164	710.02	1702.87	248.25*	597.10	69.06	217.92	3289.18*	5986.69	4316.50*	6229.95
Cluster 3	24	7851.78	13269.82	4428.05	6516.04	459.49	859.19	20847.78	31143.81	33587.09*	29649.09
Total	402	955.39	3895.47	431.35	1960.56	86.67	298.18	4637.16	10611.45	6110.57	11893.78

*: p<0.05

5.4.2 Results at the 6 month follow-up period

Table 5.4.3 and Table 5.4.4 show that at the 6 month follow-up period 268 patients are included in the cluster analysis. 25% of patients are excluded because of missing patient information. 4 clusters are formed: 31.3% of patients are in cluster 1, 14.2% in cluster 2, 19.0% in cluster 3 and 10.04% in cluster 4.

The characteristics of patients within each cluster are shown in Table 5.4.3. Within cluster 1 all of the patients have a child and this is the most statistically significant categorical variable, although whether the patients have taken heroin (92.9%) or methadone (79.8%) are also statistically significant variables. The only statistically significant continuous variable is the average age of the patients (33.02 years old). Table 5.4.4 shows the mean cost of each cluster at the 6 month follow-up period. In cluster 1, however, there are no statistically significant mean costs.

Within cluster 2, whether the patients take methadone (0%), heroin (15.8%), or crack (13.2%), as well as how many are unemployed (47.4%) are all significantly statistic categorical variables. There are no statistically significant continuous variables. The statistically significant mean costs are addiction (£85.57) and social care (£36.61).

Within cluster 3, whether the patients have visited hospital (3.9%) or received prescriptions in the last 6 months (19.6%), as well as whether they have a child (2%) are the statistically significant categorical variables. There are 2 statistically significant continuous variables: the average age of the patients (25.49 years old) and the average EQ-5D score (0.91). The statistically significant mean costs are health (£468.58), addiction (£445.05) and the total societal cost (£2,294.56).

Within cluster 4, whether the patients have a child (3.6%), gender (100% male), and whether they have visited hospital (75%) or received prescriptions in the last 6 months (71.4%) are the statistically significant categorical variables. Average CORE and SSQ scores (61.36 and 12.36 respectively) are both significantly statistically continuous variables However, the only statistically significant cost is social care (£27.38)

It is very difficult to draw any conclusions from the results at the 6 month follow-up period as there are only a few statistically significant results in the same characteristics and cost categories across the clusters. There is only one statistically significant characteristic across 3 of the 4 clusters (whether the patient has a child), however there are no comparable statistically significant mean costs for those 3 clusters.

Table 5.4.3 Patient characteristics within each cluster at follow-up

6 month		Total (n=201)	Cluster 1 (n=84)	Cluster 2 (n=38)	Cluster 3 (n=51)	Cluster 4 (n=28)
Age	Mean	30.79	33.02*	31.12	25.49*	33.31
	S.D.	7.25	6.60	7.94	3.56	8.40
Sex	Male (n=140)	69.7%	56.0%	78.9%	68.6%	100.0%*
Employment	Have job (n=163)	18.9%	15.5%	52.6%*	9.8%	0.0%
Have child	Yes (n=108)	53.7%	100.0%*	57.9%	2.0%*	3.6%*
Smoker	Yes (n=195)	97.0%	98.8%	89.5%	98.0%	100.0%
Taking methadone	Yes (n=121)	60.2%	79.8%*	0.0%*	58.8%	85.7%
Taking heroin	Yes (n=148)	73.6%	92.9%*	15.8%*	78.4%	85.7%
Taking crack	Yes(n=195)	2.5%	0.0%	13.2%*	0.0%	0.0%
Treatment for drug problem in last 6 months	Yes (n=197)	98.0%	100.0%	92.1%	100.0%	96.4%
Visited hospital in last 6 months	Yes (n=124)	38.3%	40.5%	52.6%	3.9%*	75.0%*
Prescriptions in last 6 months	Yes (n=115)	42.8%	45.2%	47.4%	19.6%*	71.4%*
EQ-5D ^a 6 month overall score	Mean	0.79	0.77	0.79	0.91*	0.61
	S.D.	0.30	0.30	0.30	0.14	0.42
LDQ ^a 6 month overall score	Mean	8.63	9.13	5.89	7.63	12.64
	S.D.	7.94	8.29	6.01	7.97	7.70
CORE ^a 6 month overall score	Mean	44.43	47.57	34.74	37.20	61.36*
	S.D.	24.01	23.61	20.27	22.64	22.07
SSQ ^a 6 month overall score	Mean	15.44	15.02	17.37	16.37	12.36*
	S.D.	5.24	5.20	5.60	4.66	4.44
SCL ^a 6 month overall score	Mean	11.98	13.07	8.21*	10.14	17.18
	S.D.	8.17	7.94	6.75	7.40	8.90

*: p<0.05

a: The higher scores of EQ-5D and SSQ represent the better outcomes. The higher scores of LDQ, CORE and SCL represent the worse outcomes.

Table 5.4.4 Mean costs within each cluster at follow-up

6 month	N	health care costs		addiction service costs		social care costs		crime costs		total societal cost	
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Cluster 1	84	1116.44	1346.74	760.17	819.73	144.41	410.34	1832.45	3726.56	3853.46	4444.80
Cluster 2	38	2630.83	13018.13	85.57*	183.02	36.61*	87.19	1334.58	4271.32	4087.59	13432.79
Cluster 3	51	468.58*	593.95	445.05*	402.53	60.24	238.79	1320.69	3543.97	2294.56*	3656.76
Cluster 4	28	1035.11	742.27	2493.58	5634.09	27.38*	76.36*	4372.41	7691.43	7928.49	8752.61
Total	268	1227.03	5727.03	794.15	2267.63	86.37	298.12	1962.30	4611.38	4069.85	7627.13

*: p<0.05

5.4.3 Results of the clustering for the changes

The previous section has covered the results of clustering analysis of social costs at both baseline and the 6 month follow-up period. In this section a similar clustering analysis is performed to determine the profile of the social cost change clusters and the factors relating to the changes.

Table 5.4.6 shows that 268 patients are included in the two-step cluster analysis, whereas 68 cases are excluded due to missing data. 4 clusters are identified: 20.9% of patients are within cluster 1, 29.5% of patients are in cluster 2, 3.4% are in cluster 3 and 20.9% of patients are grouped in cluster 4.

Patients' characteristics within each social cost cluster are shown in Table 5.4.5. In cluster 1 the only statistically significant categorical variables are the unemployment level (62.5%), and whether they take methadone (10.7%) or heroin (14.3%). There are no statistically significant continuous variables. Table 5.4.6 shows the mean cost changes within each cluster. The only statistically significant cost change is addiction, where the cost increased by £46.86.

Within cluster 2 there is a wide range of statistically significant categorical variables: whether the patients take methadone (87.3%) or heroin (98.7%), the unemployment rate (94.9%), gender (53.2% male), and whether they have visited hospital (62%) or received a prescription in the last 6 months (67.1%). There are no statistically significant continuous variables or cost changes.

Within cluster 3 the only statistically significant categorical variables are the amount of smokers (77.8%) and the amount that do not take crack (77.8%). Again, there are no statistically significant continuous variables or cost changes.

Within cluster 4 the statistically significant categorical variables are whether the patients have taken heroin (100%), and whether they have visited hospital (0%) or received a prescription in the last 6 months (0%). Average age is the only statistically significant continuous variable (28.61 years old), and there are no statistically significant cost changes.

As there is only one statistically significant cost change across all the clusters it is difficult to compare the different characteristics with the different social costs. The only comparisons that are statistically significant are those between different characteristics. For example, there is a close relation between the percentage of patients that take methadone and heroin. The results in cluster 1 are 10.7% and 14.3% respectively, and 87.3% and 98.7% in cluster 2 respectively. Similarly, the percentage of patients visiting hospital and receiving prescriptions is very close. The results in cluster 1 are 62% and 67.1% respectively, and 0% for both in cluster 4.

Table 5.4.5 Patient characteristics within each cluster at 6 month change

6 month change		Total (n=200)	Cluster 1 (n=56)	Cluster 2 (n=79)	Cluster 3 (n=9)	Cluster 4 (n=56)
Age	Mean	30.81	32.30	31.81	26.51	28.61*
	S.D.	7.26	8.27	7.37	6.61	5.22
Sex	Male (n=140)	70.0%	80.4%	53.2%*	66.7%	83.9%
Employment	Have job (n=162)	19.0%	37.5%*	5.1%*	0.0%	23.2%
Have child	Yes (n=107)	53.5%	48.2%	68.4%	11.1%	44.6%
Smoker	Yes (n=194)	97.0%	94.6%	98.7%	77.8%*	100.0%
Taking methadone	Yes (n=120)	60.0%	10.7%*	87.3%*	66.7%	69.6%
Taking heroin	Yes (n=147)	73.5%	14.3%*	98.7%*	55.6%	100.0%*
Taking crack	Yes (n=195)	2.5%	5.4%	0.0%	22.2%*	0.0%
Treatment for drug problem in last 6 months	Yes (n=196)	98.0%	94.6%	100.0%	88.9%	100.0%
Visited hospital in last 6 months	Yes (n=123)	38.5%	39.3%	62.0%*	66.7%	0.0%*
Prescriptions in last 6 months	Yes (n=115)	42.5%	51.8%	67.1%*	33.3%	0.0%*
EQ-5D ^a overall score change	Mean	0.03	0.00	0.03	0.03	0.05
	S.D.	0.15	0.15	0.16	0.12	0.14
LDQ ^a overall score change	Mean	-7.34	-7.00	-8.71	-8.00	-5.64
	S.D.	8.94	7.51	10.47	5.02	8.24
CORE ^a overall score change	Mean	-10.77	-11.21	-8.96	-24.00	-10.75
	S.D.	23.68	23.07	26.57	27.07	18.84
SSQ ^a overall score change	Mean	1.21	0.54	1.34	5.22	1.04
	S.D.	5.45	4.84	6.17	4.12	4.94
SCL ^a overall score change	Mean	-3.72	-3.18	-2.96	-9.67	-4.36
	S.D.	7.97	9.65	7.43	10.76	5.84

*: p<0.05

a: Patients' outcome score changes for EQ-5D, LDQ, CORE, SSQ, SCL = (follow-up score) – (baseline score), If change >0, patients' scores at follow-up is higher than scores at baseline. The higher scores of EQ-5D and SSQ represent the better outcomes. The higher scores of LDQ, CORE and SCL represent the worse outcomes.

Table 5.4.6 Mean costs within each cluster at 6 month change

6 month change	N	health care costs difference ^a		addiction service costs difference ^a		social care costs difference ^a		crime costs difference ^a		total societal cost difference ^a	
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Cluster 1	56	65.60	1225.22	46.86*	377.93	4.59	132.82	-644.64	3800.04	-527.60	4109.35
Cluster 2	79	260.47	2503.12	511.51	1007.14	-5.91	573.91	-1523.98	6123.86	-757.90	6778.44
Cluster 3	9	4311.70	31649.15	3778.34	12672.26	-31.50	68.55	-17130.33	45557.38	-9071.79	57946.28
Cluster 4	56	172.97	724.21	224.59	1667.17	32.03	177.23	-592.54	6046.00	-162.96	6510.37
Total	268	363.71	6635.38	448.08	2867.67	6.50	378.36	-1719.25	11120.61	-900.96	13137.61

*: p<0.05

a: Cost difference = (cost of follow-up) - (cost of baseline). If change > 0, patients' social costs increase at follow-up.

5.5 Conclusions and Discussion

One of the problems in most existing drug misuse research is that it is unclear whether or not different types of drug misuse patients are more likely to use different social resources. Very few studies have examined the relationship between dimensions of the monetary outcome and patient characteristics or the relationship between the different dimensions of the monetary outcome. This information may prove important for policy makers because if different characteristics of patients can be identified that relate to specific dimensions of the monetary outcome then different patients can be targeted with specific interventions.

The aim of this chapter has been to use an existing data sample to cluster patients by the resources they use and to attempt to build a profile of drug misuse patients within these clusters. Although the statistically significant characteristics of the patients in each cluster have been identified and described, it has proved difficult to compare these characteristics with the different social cost categories across the clusters. One exception was identified in clusters 1 and 2 at baseline, where patients who take methadone or heroin have a much higher mean addiction service cost than those who do not, even though there is little difference between the mean total societal costs.

The reason that it has not proved possible to identify more relationships is that only very few statistically significant characteristics and costs were identified in the different clusters. Where characteristics were identified, they were often not the same across the clusters, therefore they could not be compared to see whether or not they consistently lead to different social costs. This is because the results do not identify any significant characteristic that can be used to describe the patients across all the clusters. In addition, in many cases there were also no statistically significant costs.

The main limitation with the RESULT sample used in this chapter is that it is not an intervention study, therefore the patients within the sample did not all start the treatment at the same time. This might affect how much of the resources they use, and this may partly explain why it was difficult to identify common characteristics between the patients. Future

studies that aim to identify a patient profile may benefit from having all the patients start the treatment at the same time.

There is also a limitation with using clustering techniques as the clusters are only hypothetical groups based on a given set of characteristics. However, if other characteristics were used then the cluster groups would be different and it is possible that more statistically significant characteristics would be identified. In this chapter 16 single characteristics were used to determine the clusters without finding any significant results. This indicates that clustering analysis may be inadequate for determining the profile of drug misuse patients.

These limitations aside, the fact that there were few statistically significant characteristics suggests that the profile of drug misuse patients might be more complex than expected. The data used in this chapter sampled over 400 patients and still failed to identify many statistically significant characteristics. In addition, a national UK study, NTORS (Godfrey, Stewart and Gossop, 2004), has also found that no specific characteristics can be used to explain the monetary outcome in their sample, while using a regression technique that examines multi-variable characteristics. This indicates that the difficulties with identifying statistically significant characteristics might not be primarily due to the limitations of the sample in the RESULT study or the clustering technique used in this chapter, but rather simply due to the complexity of the different characteristics of drug misuse patients. Although it is important for policy makers to know whether they can target interventions at specific groups of drug misuse patients, this chapter has revealed the main limitations with identifying the relevant characteristics.

Chapter 6 Systematic Review for decision analytic models in the economic evaluation of drug misuse interventions

6.1 Background

The previous chapters have shown that outcomes in the economic evaluation of drug misuse interventions involve a complex of dimensions and cannot be predicted by patient characteristics alone. Furthermore, despite drug misuse being considered as a chronic condition (Zarkin et al, 1994), there are very few studies which follow the patients for longer than 24 months, even though it is important that policy makers consider long-term outcomes (NICE, 2008).

One way of potentially taking into account the complexity of drug misuse patients and estimating their long-term outcomes is by developing modelling studies. A decision analytic modelling study is an analytical approach that is developed to synthesize the costs and the outcomes of interventions (Buxton et al, 1997). It provides a structural framework for decision making under conditions of uncertainty. It provides the full structure of the possible prognoses of the individuals, brings together the relevant evidence from different resources, and translates the relative evidence into estimates of cost and effectiveness to predict outcomes in the long-term (Drummond, M.F. et al, 2005).

There are different types of structuring techniques for decision analytic models. The decision tree model and the Markov model are the 2 most frequently used types of structuring technique. The decision tree model is probably the most common structure for decision analytic models in economic evaluations (Drummond, M.F. et al, 2005). The decision tree provides a visual illustration of the prognoses of the individuals after the interventions. By following the pathway of the individuals throughout the intervention the decision tree model illustrates the possible outcomes and costs at each chance point (the point at which the patient's outcome can go down one of many pathways), as well as predicting the costs and outcomes at the end point of the model. The structure of the Markov model represents a series of 'states' that a patient can occupy at any given point of time (Drummond, M.F. et al,

2005). The Markov model estimates the probability that a patient could be in any given 'state' over a period of time.

Using decision analytic models in economic evaluations helps decision makers to understand the costs and outcomes of the interventions involved. The decision tree model in drug misuse interventions can provide comprehensive estimates of the possible prognoses in both the interventions of interest and alternative intervention strategies. The Markov model can provide the probability of the patients being in any given health state after receiving the drug misuse interventions. However, there are only a limited number of studies that have applied decision analytic models in the economic evaluation of drug misuse interventions, and very few studies have reviewed the applications of doing so. This chapter will therefore examine the current development of decision analytic models in economic evaluation studies of drug misuse interventions.

6.2 Objectives

The purpose of this review is to explore the different methods of estimating costs and outcomes that have been applied in decision analytic modelling studies of drug misuse interventions. The previous chapters have examined the short-term outcomes derived from the patient-level data in the economic evaluation for drug misuse interventions. This review, by contrast, will focus on the long-term outcomes and provide information about what outcomes have been chosen in the modelling studies in the previous treatment or prevention research, how the outcomes are translated into monetary terms and the theoretical constructs of the models. This chapter focuses on the extent to which modelling studies are able to overcome the problems and limitations identified in the previous chapters with other types of drug misuse intervention studies. In particular, it is therefore concerned to examine whether or not existing modelling studies provide comprehensive evaluations of drug misuse interventions from the societal perspective that consider the patients outcomes over a long period of time.

The first objective of this review is to identify the studies in which decision analytic models have been conducted, particularly those that have applied the decision tree model and Markov model techniques to estimate the costs and outcomes for drug misuse interventions. This will reveal the current applications of the decision analytic modelling techniques in the drug misuse research. The second objective is to assess the quality of these models by adopting a quality assessment checklist developed by Philips and colleagues (2004) to examine the theoretical structures and data synthesis techniques in the identified models. The checklist is a comprehensive guideline of good practice for all types of health related economic evaluation models, thus this chapter focuses on the aspects of the guideline that are especially relevant for drug misuse models in order to evaluate the benefits and limitations of modelling studies for drug misuse interventions.

The results of this review will provide an overview of how long-term costs and outcomes are estimated through the decision analytic modelling techniques in the current drug misuse modelling research. This will complete the methodological examination of existing drug misuse interventions that has been carried out throughout the thesis. With the methodological critique complete, the following chapter will then propose a model that attempts to take into account both the long-term outcomes and the other outcomes of drug misuse interventions discussed previously.

6.3 Methods

6.3.1 Inclusion Criteria for this review

The first objective of this chapter is to identify the economic evaluation studies that have applied the decision analytic model in drug misuse research, which is achieved by using the searching strategies detailed in this section and section 6.3.2 to identify these studies.

Type of studies: The main inclusion criterion is that only studies which conducted decision analytic modelling methods to estimate the costs and outcomes in the economic evaluation will be included. The studies should give a full description of their model, including details

of which predictive variables have been chosen, which outcomes have been measured, how the outcomes are translated into the surrogate and monetary outcomes in the long-term and the theoretical constructs of the decision analytic models.

Type of intervention: All types of intervention delivered to the individual drug user or potential drug users and primarily aimed at reducing problems related to drug misuse will be considered. Studies on intervention delivered to the drug users' family/ partner will not be included.

Type of participants: Only studies modelling individual drug users or potential user data of drug misuse intervention are included.

Outcome: Only studies with outcomes from the economic evaluation will be included. Outcome data must be from the data synthesis within the modelling studies, instead of the data from the actual individual drug users in a trial or research.

Comparison: To provide scope for comparison only studies considering at least 2 alternatives will be included, for instance, intervention versus no intervention or 2 different types of intervention in the model.

6.3.2 Data sources and search strategy

Electronic and manual searches are undertaken to identify studies.

Search strategy:

The search was performed in July 2010. Studies which meet the inclusion criteria are identified from the following sources. There is no restriction for language or the year of publication.

Econlit (1969 – to July 2010)

EMBASE (1980–July 2010)

MEDLINE (1950 –July 2010)

PsycINFO (1806 –July 2010)

CRD (Centre for Reviews and Dissemination) databases

The Cochrane Library

Example of searching strategy: MEDLINE; 1950 –July 2010:

[(drug misuse or drug dependen* or substance misuse or substance abuse or substance dependen* or addict* or illegal drug* or illicit drug* or inject* drug* or methadone or or buprenorphine or heroin or opiat* or opium or cocaine or crack cocaine or ecstasy or LSD or magic mushroom* or amphetamine or cannabis or marijuana or ketamine or tranquiliser* or tranquilizer* or club drug*) and (economic evaluation or cost-benefit analysis or cost-effectiveness analysis or cost-utility analysis)] and [(decision analytic model* or decision tree or Markov or Monte Carlo)]

6.3.3 Quality assessment of the included models

The second objective of this chapter is to examine the quality and structures of the decision analytic models in economic evaluations of drug misuse interventions. The quality assessment checklist for decision analytic models has been developed by Philips and colleagues (2004), which was published by the Health Technology Assessment (HTA) programme of the NHS in the UK. This HTA report establishes the guideline for good practice of decision analytic models (Philips et al, 2004). Therefore, in order to examine the quality of the included models, this chapter will adopt the checklist as the guideline for the review. The checklist identifies 3 general components of a model (Philips et al, 2004):

1. Structure of a model: quality assessment related to the structure of the model has 9 dimensions, including objectives, scope and perspective of the model, rationales and assumptions for the structure, the strategies for comparison in the model, model types, time horizon, disease pathway, and the cycle length of the model.
2. Data of the model: quality assessment for the data used in the model covers 4 dimensions: the identification of data in the model, modelling the data (treatment effects, costs, and

utilities), data incorporation, and the assessment of the uncertainty for methodology, structure, heterogeneity, and parameters.

3. Consistency of the model: assessment of the internal and external consistency of the model.

Details of the dimensions will be discussed while the included models are examined in the later sections of this chapter. The third dimension, the consistency of the model, will not be examined among the included models. This is because none of the included models have examined the internal and external consistency/ validity. The review will focus on the dimensions of the guideline that are particularly important for drug misuse modelling studies, rather than those that are only of more general relevance for health related models. The results of this section will provide an overview of the current development and problems with decision analytic models in the economic evaluation of drug misuse interventions. This will provide the basis to make recommendations about the application of decision analytic models in drug misuse research for policy makers and for future research.

6.4 Results

The first objective of this review is to identify the decision analytic models in the economic evaluation studies of drug misuse interventions. Using the searching strategies described in section 6.3.1 and 6.3.2, 42 studies were identified and 19 studies using decision-analytic modelling were included. Most excluded studies are related to opiate treatment for the pain symptoms of cancer patients. 3 of the included studies are sub-studies of 2 models; hence, 16 models were identified in this review. Among the 16 models, there are 6 decision tree models and 7 Markov models. The other 3 models combine the decision tree model and Markov models in their studies. Details of each included model are listed in the Table 6.4.1.

6 of the included models are conducted with the population in the UK and 4 models are conducted with the population in the United States. There are also 2 models that consider the population in Italy, 1 in Canada, 1 in France, 1 in Spain, and 1 in New Zealand. There are 2 main types of interventions which are examined in the included modelling studies. 8 of the

16 models examined the first type of intervention, which examines the costs and outcomes of the screening of injecting drug users, such as screening for hepatitis C, HIV and tuberculosis. The other 8 models examined the second type of intervention, which examines the costs and outcomes of the drug misuse treatment, such as maintenance treatment and needle exchange programmes.

Among the 16 models, 6 were cost-utility analysis models, which measure QALYs; 4 were cost-benefit analysis models, which calculate the ratio between the costs and benefits; and 6 were cost-effectiveness analysis models, of which 5 measure the life years saved and 1 measures the number of HCV (hepatitis C infection) cases identified. 11 of the models used a hypothetical cohort and 5 used a real cohort.

Table 6.4.1 Description of the included studies

Study, country	Type of model and population	Intervention/ scenarios	Period of prediction	Study perspective	Costs and outcome of economic evaluation in the model
Adi et al, 2007, UK	Decision tree model with Monte Carlo simulation for a hypothetical cohort of 10,000 opioid dependent drug users	Two scenarios: -Oral naltrexone for relapse prevention -Placebo	12 months	-NHS and Personal Social Service (PSS) -Societal perspective (for costs)	Simulation with 2004 value (not discounted) Costs (NHS perspective) -Treatment cost: naltrexone, counselling, and urine tests -Health care costs: GP, A&E, hospital stays, mental health service visits Costs (societal perspective) -Criminal justice system cost: drug arrests, acquisitive crime arrests, held in custody, court appearance, imprisonment -Victim cost of crime Outcome of the model: -From NHS perspective, ICER= £42,500 per QALY -From the societal perspective, Naltrexone dominates placebo in ICER (placebo is more costly and less effective)
Barnett, 1999, USA	Markov model of a hypothetical cohort of 1,000 25-year-old heroin addicts (when entering methadone treatment)	Two scenarios: -Methadone treatment -Drug-free treatment	Lifetime	Societal perspective	Simulation with 1996 value (3% discount rate) Costs: cost of treatment Outcome of the model: cost-effectiveness ratio= \$5,915/life-year gained

<p>Connock et al, 2007, UK</p>	<p>Decision tree model with Monte Carlo simulation for a hypothetical cohort of 10,000 opioid dependence patients</p>	<p>Three scenarios: -Methadone maintenance therapy (MMT) -Buprenorphine maintenance therapy (BMT) -No treatment</p>	<p>12 months</p>	<p>-NHS and PSS -Societal perspective (for costs)</p>	<p>Simulation with 2004 value (not discounted)</p> <p>Costs (NHS perspective) -Treatment cost: pharmacological treatment, counselling, and urine tests -Health care costs: GP, A&E, hospital stays, mental health service visits</p> <p>Costs (societal perspective) -Criminal justice system cost: drug arrests, acquisitive crime arrests, held in custody, court appearance, imprisonment -Victim cost of crime</p> <p>Outcome of the model -From NHS perspective, MMT vs. no treatment ICER= £13,697 per QALY; BMT vs. no treatment ICER=£26,429 per QALY -From the societal perspective, MMT dominates BMT and 'no treatment' group in ICER, and BMT dominates 'no treatment' group</p>
<p>Gold et al, 1997, Canada</p>	<p>Decision tree type model of incidence outcome for a cohort of 275 IDUs</p>	<p>Two scenarios: -Needle exchange programme along with related harm-reduction services (counselling and referral, HIV testing, hepatitis B vaccination, provision of condoms</p>	<p>5 years</p>	<p>Societal perspective</p>	<p>Simulation with 1995 value (5% discount rate)</p> <p>Cost: -Cost of interventions: operating cost of the programme, costs</p>

		and dental dams) -No programme			for the time contributed by the community volunteers and the pharmacists -Health care costs related to HIV: inpatient and outpatient hospital costs, physician services and medication costs Outcome of the model: Needle exchange programme prevents 24 HIV infection over 5 years, and \$1.3 million cost-saving. The ratio of cost savings to costs is 4:1.
Leal, Stein and Rosenberg, 1999, UK	Markov model for 5,600 IDUs in South and West health region	Screening for hepatitis C	30 years	NHS	Simulation with 1995 value (6% discount rate) Costs: -Intervention costs: cost of hep C screening, counselling, liver biopsy -Treatment cost: cost of 12 or 40 weeks interferon α (IFN α) treatment, cost of post-treatment testing -Cost of adverse events -Cost of monitoring Outcome of the model: cost-utility ratio=£9,300 per QALY
Loubiere, Rotily and Moatti, 2003, France	Decision tree model with Markov model for a hypothetical	Four scenarios of screening: -No screening and no treatment for HCV -‘Wait and treat cirrhosis’: HCV	Lifetime	Health care system	Simulation with 1998 value (3% discount rate) Costs

	<p>cohort of 1,000 patients with hepatitis C infection (HCV)</p>	<p>treatment after the diagnosis of cirrhosis</p> <ul style="list-style-type: none"> -‘Two EIA’ screening test (enzyme immunoblot assay): a EIA test followed a positive EIA test -‘EIA+PCR(polymerase chain reaction)’: PCR test followed a positive EIA test 		<ul style="list-style-type: none"> -Cost of screening tests: cost of PCR, cost of EIA -Cost of HCV treatment: cost of pre-treatment testing, Interferon costs, Ribavirin costs -Cost of HCV management: cost of remission, cost of chronic hepatitis, cirrhosis, hepatocellular carcinoma, transplantation <p>Outcome of the model</p> <p>For IDUs (prevalence=80%):</p> <ul style="list-style-type: none"> -Intervention of ‘wait and treat’ dominates -‘Two EIA’, ICER=\$4,513 per life-years saved -‘EIA+PCR’, ICER=\$4,897 per life-years saved <p>For general population (prevalence=1.2%):</p> <ul style="list-style-type: none"> -‘Wait and treat’, ICER=\$4,102 per life-years saved -Intervention of ‘two EIA’ dominates -‘EIA+PCR’, ICER=\$5,821 per life-years saved <p>For transfusion recipients (prevalence=7%):</p> <ul style="list-style-type: none"> -‘Wait and treat’, ICER=\$18,054 per life-years saved -Intervention of ‘two EIA’
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					dominates -‘EIA+PCR’, ICER=\$283,495 per life-years saved
Martinez-Raga et al, 2010, Spain	Decision tree model of budgetary impact analysis with for 86,017 opioid addicted patients	Two scenarios: -Suboxone (Buprenorphine/Naloxone) -Methadone as an agonist opioid treatment	3 years	NHS in Spain	Simulation with 2007 value (discount rate is not presented) Costs: cost of medication, logistics, dispensing, medical and pharmacy personnel, and counselling Outcome of the model: incremental cost (Suboxone - methadone)=EUR 791,418 in year 1, EUR480,226 in year 2, EUR492,671 in year 3
Masson et al, 2004, USA	Markov model for 179 opioid addicted patients	Two scenarios: -Enriched 180-day methadone detoxification (with psychosocial services and drug-free substance misuse treatment) -Standard methadone maintenance treatment	Lifetime	Health care system	Simulation (3% discount rate) Costs -Cost of the treatment provided by study -Health care utilisation: costs of hospitalisation, A&E, substance misuse and mental health treatment Outcome of the model: -ICER= \$16,967 per life-year gained -ICER= \$19,997 per QALY (if heroin has very large effect on quality of life; deduct 0.03 utilities)
Perlman et al,	Decision tree type	Three scenarios:	5 years	Societal	Simulation (not discounted)

2001, USA	model for a hypothetical cohort of 10,000 IDUs at a syringe-exchange programme	<ul style="list-style-type: none"> -Tuberculosis (TB) screening and directly observed preventive therapy -TB screening only -No intervention 		perspective	<p>Costs: screening costs, treatment costs(directly observed preventive therapy), monitoring costs, and hepatotoxicity costs</p> <p>Outcome: costs prevented of TB</p> <p>Outcome of the model:</p> <ul style="list-style-type: none"> -If isoniazid preventive therapy (INH) efficacy rate is 0.65 Net savings of 'no intervention'= \$53,094 Net savings of 'TB screening only'= \$49,336 Net savings of 'TB screening plus treatment'= \$46,226 -If isoniazid preventive therapy (INH) efficacy rate is 0.90 Net savings of 'no intervention'= \$129,950 Net savings of 'TB screening only'= \$126,192 Net savings of 'TB screening plus treatment'= \$123,081
Sheerin, Green and Sellman, 2004, New Zealand	Markov model for a cohort of 1,000 IDUs in methadone maintenance treatment (MMT)	<p>Methadone maintenance treatment (MMT) and antiviral therapy for Hepatitis C</p> <p>Six scenarios:</p> <ul style="list-style-type: none"> -MMT only -MMT31: 5% Receive conventional combination therapy (COT) after stabilising on MMT 	Lifetime	Perspective of tax payers	<p>Simulation with 2000 value (3% discount rate)</p> <p>Costs</p> <ul style="list-style-type: none"> -Treatment cost of MMT: operating cost of methadone treatment, prescription cost of methadone, cost of assessment and basic counselling

		<p>at age 31</p> <p>-MMT31+COT: all patients receive COT after stabilising on MMT at age 31</p> <p>-MMT26+COT: same as 'MMT31+COT', but stabilising on MMT at age 26</p> <p>-MMT31+PEG: all patients receive PEG (pegylated interferon combined with ribavirin) after stabilising on MMT at age 31</p> <p>-MMT26+PEG: same as 'MMT31+PEG', but stabilising on MMT at age 26</p>			<p>-Treatment cost of COT: screening cost, follow-up appointment costs, cost of liver biopsy and laboratory tests, cost of pharmaceuticals</p> <p>-Treatment cost of PEG: cost of pharmaceuticals</p> <p>Outcome of the model with lower rate of disease progression, ICER for 'MMT31+COT', 'MMT26+COT', 'MMT31+PEG', 'MMT26+PEG':</p> <p>If the presented value is in (), value<0</p> <p>-For non-Maori men, ICER are \$New Zealand 22,305, \$NZ(10,774), \$NZ26,201, \$NZ(2,723) per LYS respectively</p> <p>-For Maori men, ICER are \$NZ 34,825, \$NZ(8,551), \$NZ37,904, \$NZ(1,621) per LYS respectively</p> <p>-For non-Maori women, ICER are \$NZ 19,044, \$NZ(11,157), \$NZ22,929, \$NZ(3,048) per LYS respectively</p> <p>-For Maori women, ICER are \$NZ 23,268, \$NZ(20,757), \$NZ27,260, \$NZ(10,500) per LYS respectively</p>
Stein et al, 2002,	Markov model	Screening for hepatitis C among	50 years	NHS	Simulation with 2001 value

Stein et al, 2003 and Stein et al, 2004, UK	with a hypothetical cohort of IDUs	<p>IDUs</p> <p>Two scenarios:</p> <ul style="list-style-type: none"> -Screening in drug services -Screening in genitourinary medicine clinics (GUM) clinic 			<p>(costs and QALYs at 6% and 1.5% discount rate, respectively)</p> <p>Costs</p> <ul style="list-style-type: none"> -Cost of interventions: staff cost (cost of assessing and counselling eligibility), cost for ELISA(enzyme-linked immunosorbent assay) and PCR(polymerase chain reaction) tests, cost of liver biopsy -Health care resource use: cost of hospitalisation, GP, outpatient visit, , cost of liver transplant and follow-up care, cost of cost of HCV related therapy <p>Outcome of the model</p> <ul style="list-style-type: none"> -Cost-utility ratio of screening in drug services=£28,120 per QALY -Cost-utility ratio of screening in GUM clinics=£84,570 adherence to medication
Sutton, Edmunds and Gill, 2006, UK	Decision tree model with Markov model for a hypothetical cohort of 1,000 IDUs in prison	<p>Detecting cases of chronic hepatitis C infection on reception into prison</p> <p>Five scenarios:</p> <ul style="list-style-type: none"> -Scenario 1: verbally screen for 'ever had a positive HCV test' and 'ever injected illicit drugs' -Scenario 2: verbally screen for 	15 years (until 2017)	Health care provider	<p>Simulation with 2004 value (3.5% discount rate)</p> <p>Costs:</p> <ul style="list-style-type: none"> -Intervention costs cost of screening, cost of doctor and nurse, staff cost

		<p>‘ever had a positive HCV test’ only</p> <ul style="list-style-type: none"> -Scenario 3: verbally screen for ‘ever injected illicit drugs’ only -Scenario 4: no verbal screening -Scenario 5: no verbal screening and no testing 			<p>Outcome of the model Comparing to scenario 5 (no interventions):</p> <ul style="list-style-type: none"> -Scenario 1, ICER=£2,102 per HCV case identified -Scenario 5 dominates scenario 2, scenario 2 is the least cost-effective -Scenario 3, ICER=£16,625 per HCV case identified -Scenario 4, ICER=£6,388 per HCV case identified
Thompson Coon et al, 2006, UK	Decision tree model with Markov model for a hypothetical cohort of 10,000 former IDUs	<p>Two scenarios:</p> <ul style="list-style-type: none"> -Systematic case finding strategy (‘population’ or ‘targeted’ approach) for hepatitis C in primary care -Non-case-finding strategy 	Lifetime	NHS	<p>Simulation with 2004 value (costs and QALYs at 6% and 1.5% discount rate, respectively)</p> <p>Costs</p> <ul style="list-style-type: none"> -Intervention costs: cost of hepatitis C testing, liver biopsy, counselling, referral; -Health care costs: health care cost of patients with Hep C and Hep C related conditions, waiting list for liver transplant, health care costs of liver transplant and post-transplant <p>Outcome of the model:</p> <ul style="list-style-type: none"> -For population approach, ICER=£15,493 per QALY -For targeted approach, ICER=£16,493 per QALY
Tramarin et al, 2008, Italy	Markov model for two cohorts: 9,460	<p>Two scenarios:</p> <ul style="list-style-type: none"> -HCV screening to enable early 	Lifetime	societal perspective	Simulation with 2007 value (3% discount rate)

	IDUs, and 4,738,313 IWSs (individuals with surgery related to risk of HCV infection.)	treatment of hepatitis C -No screening			Costs -Cost of screening -Health care cost: costs of cirrhosis, cost of transplantation in HCC (hepatocellular carcinoma), cost of acute and chronic therapy Outcome of the model: -For IDUs cohort, ICER= EUR - 3,132, per QALY (HCV screening dominates that it is less costly and more effective) -For IWSs cohort, ICER=EUR 918,147 per QALY
Villari et al, 1996, Italy	Markov model for a hypothetical cohort of IDUs	Four scenarios: -No HIV screening -HIV screening -Delayed early treatment (DEA) which starts 5 years after infection) -Early treatment (EA) started immediately after seroconversion	Lifetime	NHS in Italy	Simulation with 1991 value (5% discount rate) Costs -Cost of HIV screening: costs of laboratory tests, counselling, basic medical follow-up for asymptomatic HIV-positive patients -Cost of early antiviral therapy: costs of ZDV (zidovudine) -Health care costs: costs of HIV-positive symptomatic patients, costs of AIDS patients treated with ZDV, and costs of untreated AIDS patients

					<p>Outcome of the model:</p> <ul style="list-style-type: none"> -Low HIV prevalence scenario (5%): ICER of HIV-testing shows that it is less costly and more effectively than the scenario without HIV-testing. ICER of DEA and EA are Lire (L) 41,079,810 per life-years saved (LYS) and L 54,923,198 per LYS, respectively. -Medium HIV prevalence scenario (30%): ICER of HIV-testing, DEA and EA are L 13,995,242 per LYS , L 38,502,063 per LYS and L 44,335,492 per LYS, respectively -High HIV prevalence scenario (60%): ICER of HIV-testing, DEA and EA are L 55,800,000 per LYS , L 39,222,657 per LYS and L 42,505,898 per LYS, respectively
Zarkin et al, 1994, Zarkin et al, 2005, USA	Decision tree model with Monte Carlo simulation for a hypothetical cohort of 1 million heroin users and non-users	<p>Four scenarios:</p> <ul style="list-style-type: none"> -Scenario 1(baseline): current drug misuse and treatment environment -Scenario 2: 100% increase that heroin users going to methadone treatment -Scenario 3: 25% increase of length of stay in methadone treatment for heroin users -Scenario 4: Heroin users do not 	Lifetime	Societal perspective	<p>Simulation with 2001 value (3% discount rate)</p> <p>Costs</p> <ul style="list-style-type: none"> -Costs of intervention: methadone treatment costs <p>Economic benefits:</p> <ul style="list-style-type: none"> -Crime costs: costs per crime, costs per arrest, costs per

		receive methadone treatment			<p>incarceration which occurred at the beginning, monthly costs of incarceration</p> <ul style="list-style-type: none"> -Earning from employment -Health care costs: costs of inpatient service use for non-users and heroin users, costs of outpatient service use and A&E <p>Outcome of the model</p> <ul style="list-style-type: none"> -For scenario 2, incremental benefit-cost ratio=76.02 -For scenario 3, no significant benefit or cost changes -For scenario 4, incremental benefit-cost ratio=37.72
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6.4.1 Quality assessment of the included models: dimensions related to the model structure

The second objective of this chapter is to examine the quality and structure of the decision analytic models included in this review using the quality assessment checklist (Philips et al, 2004). As the checklist is of general application for health related economic evaluation models, some of the dimensions of the guideline are more relevant and instructive for drug misuse models than others. Rather than comprehensively evaluating each model against each dimensions of the checklist, this review instead focuses on the specific dimensions and models that reveal the problems and limitations with modelling drug misuse interventions. The results thus provide an overview of the models paying particular attention to the problems of modelling a range of outcomes that have been discussed previously in the thesis and the limitations of modelling long-term outcomes.

Dimensions of structure

S1: Statement of decision problem/ objective

The first dimension is the structure of the model. The guideline recommends that for a good decision analytic model there should be a clear statement of the decision problems and that the objective of both the evaluation and the model should be defined (Philips et al, 2004). As shown in Table 6.4.1, all of the treatment and screening intervention models have stated the decision problems and the objectives for their models.

Most of the included treatment models are designed to examine the costs and effectiveness of methadone maintenance treatment (MMT) or to compare methadone treatment to alternative treatments like buprenorphine maintenance therapy or Suboxone for opioid-dependent patients (Barnett, 1999; Connock et al, 2007; Martinez-Raga et al, 2010; Masson et al 2004; Zarkin et al, 2005) Other models aim to compare the costs and effectiveness of other interventions such as adding the anti-viral therapy for hepatitis C to current MMT (Sheerin, Green and Sellman, 2004), relapse prevention intervention with oral naltrexone (Adi et al, 2007) and the needle exchange programme to prevent HIV transmission among injecting drug users (Gold et al, 1997).

Most of the included screening models aim to examine the costs and effectiveness of the screening for hepatitis C infection among injecting drug users. 2 of the models are designed to examine the costs and effectiveness of the screening for tuberculosis (Perlman et al, 2001) and the screening of HIV (Villari et al, 1996) among injecting drug users.

S2: Statement of scope/perspective

The second dimension of the quality assessment of the decision analytic model is that the statement of scope and perspective should be stated clearly in the model and the data input of the model should be consistent with the stated perspective and objectives (Philips et al, 2004). This is especially important given the emphasis that previous chapters have placed on considering a wide range of both non-monetary (chapter 2) and monetary outcomes (chapter 4) to provide a comprehensive evaluation of drug misuse interventions. Table 6.4.1 shows that all included models have clearly stated the perspective of the study and the scope of the model.

3 of the drug misuse treatment models stated that their intention is to examine the costs and outcomes from the societal perspective, of which 2 examined the costs of interventions as well as the societal costs of the drug users in the model. The model by Gold and colleagues (1997) examined the health care costs of HIV-related illness as the cost-saved for society from providing needle exchange programmes. Although the study claims to be from a societal perspective, it only considers one dimension of the monetary benefit, and therefore may be incomprehensive. The other model (Zarkin et al, 1994; Zarkin et al, 2005) provides a more comprehensive societal perspective as it examined the costs of crime, health care, and individuals' earning from the increased employment of the drug users to calculate the economic benefit of the methadone treatment. However, it also omitted important dimensions of the monetary outcome, such as those related to the cost of social care resources that the drug misuse patients may use, which would greatly influence the monetary impact on society. The model developed by Barnett (1999) states that it is based on the societal perspective, however, only the costs of methadone maintenance treatment therapy are defined. No other types of costs from the societal perspective are measured in this study, such as crime related costs.

Only 2 of the preventative intervention models state that they are based on the societal perspective. The model by Perlman and colleagues (2001) has taken into account the cost of the screening as well as the costs of the prevented tuberculosis (TB) cases for the TB screening. Similarly, the other model (Tramarin et al, 2008) has considered the cost of the screening of hepatitis C infection, and the health care costs of hepatitis C related diseases. Both models only consider the health care costs and omit other costs such as criminal justice costs, which are important considerations from the societal perspective, the omission of which might lead to an incomplete estimation of the interventions.

11 of the included models stated that their aim is to examine the outcomes and costs from the perspective of the health care system. All of these models examined the intervention costs, as well as the health care costs of related health conditions. However some of the models only considered a narrow perspective of health care costs. For example, the model by Martinez-Raga and colleagues (2010) examined treatment costs, as well as the health care resource consumption related to the treatment, such as the costs of psychiatric supervision and social worker supervision, but did not consider other types of health care costs, such as GP visits or A&E visits. In addition, 2 of the models from the health care system perspective also stated that their aim is to evaluate the costs from the societal perspective and have accordingly estimated the broader monetary effect of the interventions, including the criminal justice system costs and the victim costs of crimes (Adi et al, 2007; Connock et al, 2007). However, these may not be comprehensive as neither of the studies have taken into account any social care costs.

There is only one model that is based on the perspective of the tax payers. Sheerin and colleagues (2004) have developed the model from the perspective of the tax payers in New Zealand and only the costs of the interventions are considered as the financial burden for the tax payers. Previous chapters of this thesis, however, have stressed the complexity of drug misuse, which is related to a range of other health or psychological problems that would lead to high health care costs, which would be funded by the taxpayer. By neglecting these costs the economic impact of the interventions for the taxpayer may be misjudged. Of the 16 models in total, only 7 aimed to provide a societal perspective. Although most of the models consider some dimensions of the monetary

outcome, none of them take into account all of the important dimensions identified in chapter 4.

This section also includes the scope of the study. As shown in Table 6.4.1, 10 of the included models examine the costs and effectiveness for a hypothetical cohort and the number of the cohort varies from 1,000 to 1 million patients. However, how these scopes are chosen for these models is not clearly described. The other 6 models examine the actual cohort, based on the prevalence of the targeted population, such as injecting drug users. The smallest sample size of these models is 179 opioid addicted patients in the study by Masson and colleagues (2004). The largest sample size is over 4.7 million patients who are at risk of hepatitis C infection in a population simulation modelling study in Italy (Tramarin et al, 2008). All of the included models have stated the scope of the sample, with the exception of 2 models that do not describe the sample (Stein et al, 2002; Villari et al, 1996).

S3 Rationale for structure

The guideline recommends that the model structure should be consistent with a coherent theory and that the treatment pathway of the model should reflect the health condition under consideration (Philips et al, 2004). All of the 16 included models have developed the structures of treatment pathway based on the progression of the drug misuse problems.

Of the 16 models, 5 use decision tree models alone. The 2 UK studies (Adi et al, 2007; Connock et al, 2007) have constructed a decision tree based on whether the patients stayed in or dropped out of the treatment for opioid dependents. The structure of the decision tree model by Gold and colleagues (1997) is based on whether or not the patients are infected with HIV after having received a needle exchange programme. The structure of the Spanish decision tree model (Martinez-Raga et al, 2010) is based on the transmission of adherence-related groups within the maintenance treatment, and the decision tree model by Perlman and colleagues (2001) has followed patients' pathways regarding whether or not they have received the primary tuberculosis testing and then the further screening.

7 of the included models have used the Markov model alone. These models are all based on more complicated dynamics of patients' states and how the patients move between the different states. 2 of these models (Barnett, 1999; Masson et al, 2004) are based on the survival rate of the patients in the treatments from the time point when they enter the treatment. The model by Sheerin and colleagues (2004) is based on the patients' transition of different possible states of HCV-related liver disease after receiving the additional hepatitis C treatment along with methadone maintenance treatment. 2 studies (Leal, Stein and Rosenberg, 1999; Stein et al, 2002) developed the Markov model based on whether patients have received the primary HCV screening and confirmatory screening and biopsy, as well as whether the patients have received the treatments. Tramarin and colleagues (2008) developed a Markov model of the patients' transition between different states based on the probability of their acceptance of HCV screening and the treatment, as well as whether they have developed HCV-related diseases. The Markov model by Villari and colleagues (1996) is based on the probability of patients in different states related to their HIV infection states, such as HIV positive or HIV-positive asymptomatic.

The final 4 models combined decision tree and Markov models. The decision tree of the model by Zarkin and colleagues (1994 and 2005) is based on the probability of whether or not the patients continue using drugs after receiving treatment. The Markov model then examines the patients' transition between 5 different states, with each state based on whether or not they continue using drugs and whether or not they are in jail. The study by Thompson Coon and colleagues (2006) has developed a decision tree model based on whether or not the patients have received the HCV screening and treatment and whether they have positive results of the screening. The Markov model in this study is based on the patients' transitions between different states of HCV-related diseases. The decision tree model by Loubiere and colleagues (2003) is not presented; however, the authors have stated that the decision tree structure is based on the patients' life expectancy and lifetime expenditure for each of the alternative strategies. As with the model by Thompson Coon and colleagues, the Markov model in this study is based on the probability of patients being in different states of HCV-related diseases. Sutton and colleagues (2006) have developed the decision tree model based on whether or not the patients have ever injected drugs and whether the patients have positive HCV screening results to identify the possible intervention scenarios. The Markov model of this study is then based on the probability of which different scenarios the patients are in.

S4 Structural assumptions

The guideline recommends that it is good practice for a decision analytic model to justify the assumptions for the structure and that these should be transparent and reasonable according to the objective, perspective, and scope of the study (Philips et al, 2004). All of the 16 included models have justified the structural assumptions based on either the current practice of the interventions or based on the evidence from related literature, and have related their justification to their objectives. For example, the UK treatment model for oral naltrexone (Adi et al, 2007) has assumed that the compliance rates are not enhanced by contingent management rewards based on the current practice. The USA treatment model for methadone maintenance treatment (Barnett, 1999), by contrast, made assumptions based on the evidence from the literature for risks of death in methadone treatment and drug-free treatment.

S5 Strategies/ comparators

The guideline recommends that there should be a clear definition of the strategies in the model and that the model should evaluate all feasible and practical strategies (Philips et al, 2004). Most of the 8 included treatment models only consider a few alternatives in their models because their objective is to examine the effectiveness of the specific intervention. The model by Adi and colleagues (2007) aims to evaluate the costs and effectiveness of the oral naltrexone as an intervention to prevent relapse, hence, it is only compared with the alternative routine care. Similarly, the model by Gold and colleagues (1997) aims to examine the effectiveness of a needle exchange programme and is only compared with the scenario without the needle exchange programme. All of the other 6 models aimed to examine the effectiveness of the alternative maintenance treatment; hence, these interventions are compared with standard methadone treatment.

Among the 8 preventive models, 6 were designed to examine the effectiveness of the screening of hepatitis C infection, hence they are mainly compared with the alternative scenario of no screening. The study by Leal and colleagues (1999) only examined the outcomes of the hepatitis C screening and is not compared with any other options. The French study (Loubiere, Rotily and Moatti, 2003), however, also examined the scenarios

when patients receive treatment after being diagnosed for hepatitis C. Similarly, the model by Perlman and colleagues (2001) examined the costs and effectiveness of tuberculosis (TB) screening, as well as the options when patients receive the screening and treatment. Villari and colleagues (1996) developed a model to compare the costs and effectiveness of HIV screening, as well as the options of early HIV treatment and delayed treatment. Overall, most of the preventive models considered possible alternatives.

S6 Model type

The guideline recommends that the chosen type of model should be related to the stated decision problem and the choice should be based on the causal relationship within the model (Philips et al, 2004). As detailed previously (S1 and S3), among the 16 models there are 5 decision tree models, 7 Markov models, and 4 models combining decision tree and Markov models. All of the studies have chosen the appropriate type of model based on their decision problems. For instance, Villari and colleagues (1996) have chosen the Markov model to evaluate the costs and effectiveness of the HIV screening, because the transition of HIV patients between different states of the disease is very complicated and is difficult to examine in a decision tree model.

S7 Time horizon

The guideline recommends that the time horizon should be sufficient to reflect all of the important differences between the included strategies in the model (Philips et al, 2004). This is an especially important consideration given that one of the reasons for conducting this review was that the drug misuse intervention studies examined in previous chapters only measure outcomes in the short-term. However, 2 of the models only estimated the costs and outcomes of the cohort over 12 months. Adi and colleagues (2007) justified this as there is no information for the model's long-term outcome parameters and the treatment (oral naltrexone) is only available for a short period of time. Connock and colleagues (2007) developed the model of maintenance treatment based on the meta-analysis from the short-term outcomes of the trials literature as the study failed to identify any long-term trial literature. These justifications reflect a major problem with drug misuse modelling studies, which is that there is often insufficient information to set parameters for estimating longer-term outcomes. However, it is unlikely that the time

horizons used would be sufficient to reflect all of the important effects arising from the intervention, especially given the dimensions of the monetary outcomes that the models consider. It may be longer than 12 months before many of the costs that are considered in the model occur. For example some of the criminal justice costs, such as the costs associated with trials, will not be realised until many months after a crime is committed. These models therefore fail to meet the time horizon requirement as both of the interventions modelled will have long-term effects, which the models cannot take into account.

The model by Gold and colleagues (1997) only followed the patients receiving the needle exchange programme for 5 years because it is difficult to predict the status of HIV prevention and treatment beyond this period. Perlman and colleagues (2001) also followed the patients in TB screening for 5 years, because the data in the model is from a 5-year follow-up study. Another model followed the study cohort for 3 years (Martinez-Raga et al, 2010) because it only aimed to evaluate the budgetary impact of the three-year treatment programme of Suboxone, and the study by Sutton and colleagues (2006) predicted the outcomes in 2017 of HCV screening for injecting drug users in prison. These models are all less likely to be affected by the problems that the first 2 models faced, providing that the changes arising from the intervention do not take longer than the trial period to come into effect. However, the models provide little indication of whether or not this would be the case, for example the study by Sutton and colleagues (2006) gives no reason for its time horizon and therefore it is unclear whether it would meet this requirement.

8 of the remaining models followed the patients up over their lifetime, as these studies consider that drug misuse is a chronic condition and that the interventions will have a long-term impact. Similarly, 2 of the models also followed the patients in HCV screening for 30 and 50 years (Leal, Stein and Rosenberg, 1999; Stein et al, 2002, respectively) for the same reasons. Even though most of the prevention models followed the patients up over a long period of time, which appears to meet the time horizon requirement, it is important to stress that these models used parameters based on short-term studies. However, the longer the time horizon the more uncertain the model becomes because the parameters are less precise, a problem that is discussed in more detail below in D4, Assessment of uncertainty.

S8 Health/ disease states/ pathways

The guideline recommends that the health states or pathways should reflect all of the appropriate states related to the health condition with which the model is concerned (Philips et al, 2004). The disease states or pathways of all of the 16 included models are developed according to the prognoses of the drug misuse related health problems, and were discussed previously in section S3 Rationale for structure.

S9 Cycle length

The guideline recommends that the cycle length should be the minimum interval over which the pathology or symptoms are expected to alter (Philips et al, 2004). 2 of the models examined the costs and outcomes over an irregular cycle at weeks 2, 6, 13, 25 and then after 12 months, which they justified as the patient's drop-out rate is higher during these periods of time as more patients drop-out towards the beginning of the intervention (Adi et al, 2007; Connock et al, 2007). The costs and outcomes were only estimated at the end of the model as there is insufficient information at the earlier time points.

One model examined the costs and outcomes of patients in methadone maintenance treatment over a monthly cycle (Zarkin et al, 2005), even though the maintenance programme is long-term. The rationale for doing so was that the model aimed to consider employment status, which could possibly change over a monthly cycle. Another model applied a 3-month cycle length (Thompson Coon et al, 2006), based on the stated assumption of the progression states of HCV-related diseases.

6 models examined chronic health care problems such as opioid addiction (Martinez-Raga et al, 2010; Masson et al, 2004), drug-related HIV infection (Gold et al, 1997; Villari et al, 1996), or drug-related hepatitis C (Stein et al, 2002; Tramarin et al, 2008). As these models were interested in long-term outcomes they adopted an annual cycle length. 6 of the models did not describe the cycle length and therefore do not meet this requirement.

Dimensions of data

D1 Data identification

The guideline recommends that the methods of data identification should meet the objectives of the model, and there should be justification for the reasons for the choices of the data sources, as well as the quality assessment of the data (Philips et al, 2004). All of the included studies have clearly identified the sources of the data which are used in the model, which are all from the relevant literature. As there are considerable differences between the drug misuse policies of different countries, most of the models considered evidence from studies conducted in the same country. For instance, the UK model developed by Adi and colleagues (2007) mainly adopted data from the UK literature.

D2 Data modelling

The guideline recommends that the data modelling methodology should be based on justifiable statistical and epidemiological techniques (Philips et al, 2004). These include application of the half-cycle correction to both costs and outcomes and justification of how the short-term results are extrapolated to simulate the final outcomes in the model. The costs of the model should follow the appropriate guideline of economic evaluation and if the quality of life weights have been applied, they should be justified and applied appropriately in the model.

All of the included models justified the statistical methods that they used to derive the data from the literature in order to estimate the costs and effectiveness of the interventions. The data from the literature are synthesised through a simple mathematical model. Only 3 of the included models applied the half-cycle corrections for adjustment of costs (Adi et al, 2007; Connock et al, 2007; Masson et al, 2004).

The data in the model are mainly from clinical trials. As there are time constraints regarding time and resources when conducting clinical trials, they can only examine short-term outcomes. Only one model was able to identify evidence from a 5-year follow-up HIV study (Perlman et al, 2001). As there is not enough evidence from longitudinal studies, the data adopted in the model have to be extrapolated, which leads to problems of uncertainty considered below in D4, Assessment of uncertainty. All of the included

models applied simulation methods to extrapolate the costs and outcomes of the interventions.

The types of costs and outcomes of the included model are based on the type of economic evaluation adopted in the model. All of the models justified the costs and outcomes. 7 of the models carried out a cost-utility analysis where QALYs (quality-adjusted life years) are considered as the main outcome in the economic evaluation. 6 of the included models were cost-effectiveness analysis models, of which 5 considered life-years saved and 1 considered the number of identified HCV cases (Sutton, Edmunds and Gill, 2006). None of the models considered non-health related non-monetary outcomes such as outcomes related to social integration, the importance of which was discussed in chapter 2. The other 4 included models carried out cost-benefit analyses of dimensions of the monetary outcome, such as the costs saved by the interventions. The limitations of the dimensions of the monetary outcome measured based on the perspective of the study were discussed in S2, Statement of scope/ perspective.

D3 Data incorporation

The guideline recommends that all of the data used in the model should be described and referenced and the inconsistent data should be justified (Philips et al, 2004). All of the 16 included models referenced and provided a description of the data they used. The data were then modified into the unit costs, unit effectiveness, or the parameters for the model. When a number of different data sources were available for use in the model, most models adopted the most conservative estimates so as not to overestimate the effect of the intervention. For example, in the model by Gold and colleagues (1997), 5 different HIV prevalence rates for injecting drug users before commencing the intervention were available, ranging from 3% to 11.1%. The model adopted the lowest rate of 3%, which would mean that there was not a high prevalence rate before the intervention, thus it would be harder to prove that the intervention decreased the prevalence rate.

D4 Assessment of uncertainty: methodological, structural, heterogeneity, parameter

The guideline identifies 4 main types of uncertainty that models should assess through sensitivity analysis: methodological, structural, heterogeneity, and parameter (Philips et al,

2004). Of these types of uncertainty, the included models are mainly concerned with the uncertainty regarding parameters and all of the models conducted sensitivity analyses to address this problem. However, only 3 of the models conducted a probabilistic sensitivity analysis (Adi et al, 2007; Connock et al, 2007; Thompson Coon et al, 2006). The probabilistic sensitivity analysis applies all the different possible parameters at each stage of the model to generate all the possible outcomes and costs, and then calculates the probability for each outcome and cost. This is the most comprehensive way to account for the uncertainty of the parameters. All sensitivity analyses are based on the assumptions of the study, as well as the availability of the parameter data from the literature, and the limitations of the parameters thus encompass some of the problems that have been highlighted already.

The main problem regarding parameters occurs for models that attempt to estimate long-term outcomes, which usually have to use parameters based on short-term studies as few longitudinal studies have been conducted for drug misuse interventions. Problems will arise if the data regarding the costs and outcomes of the intervention over a short-term period are likely to be different from the data for subsequent years. If this is the case then parameters based on data extracted from short-term studies may be inappropriate for long-term models, as biases may arise when the short-term costs and outcomes are extended into longer-term models.

This problem is illustrated in the model developed by Masson and colleagues (2004), which conducted a 12 month trial comparing the costs and effectiveness of 2 types of methadone treatment. The differences between the 2 treatments over the final 6 months of the trial were used to set the parameters for the model, which they applied over 10 years. At this point they assumed that the effects would diminish and used the findings to project lifetime costs and outcomes. However, the parameters would only be appropriate if the differences observed in the final 6 months of the trial could be expected to apply for the remainder of the first 10 years. It is not clear that this would be the case with all the costs estimated, such as the cost of mental health visits. If the treatment is effective then it may take longer than a year before the mental health benefits are realised and the model may therefore overestimate the mental health care costs over the 10 years.

Another problem with setting parameters is that the data on which they are based often has to be extracted from a number of different studies. Although models attempt to extract data from similar studies, such as studies all from the same country, there may still be differences between the studies that affect the parameters, and it is therefore important to test different parameters from different studies. For example, the study by Gold and colleagues (1997) used HIV prevalence rates at baseline taken from Canadian studies. However, as there were no satisfactory Canadian studies for the HIV prevalence rate among injecting drug-users without the needle exchange programme, this data was extracted from studies conducted in the USA. One limitation of this model, therefore, is that bias may occur if the drug misuse patients from Canada and the USA have different HIV prevalence rates, which is likely given that different countries have different drug taking cultures.

A final problem regarding parameters with respect to treatment models is worth mentioning. In many cases researchers want to know the effects of giving drug misuse patients a certain treatment compared with not giving them that treatment. For example, Barnett (1999) aims to compare methadone treatment to drug-free treatment, and Gold and colleagues (1997) aim to compare the effectiveness of a needle exchange programme to no programme. However, real-world estimates are unavailable to set the parameters for both models as it would be unethical to give one group of drug misuse patients a treatment, yet deny access to treatment to the control group. Parameters concerning the effect of a given treatment compared to a control group usually have to be estimated without support from real-world data.

6.5 Conclusions and Discussion

Although decision analytic models are widely applied for other health care interventions, only a limited number have been developed for drug misuse interventions. This chapter has identified 16 models, of which 8 were designed to estimate the costs and effectiveness of the drug misuse treatment and 8 were designed to examine screening interventions. The quality of these models has been reviewed using a guideline developed by Philips and colleagues (2004). Although most of the identified models met most of the criteria for a good model, a number of limitations and problems have been identified. The main problem for modelling studies is choosing appropriate parameters for the model under

conditions of uncertainty. A number of limitations with choosing parameters have been identified throughout the chapter but the most important relate to the time horizons that the model aims to cover and the perspective adopted by the study range and thus the outcomes with which it is concerned.

One of the potential advantages of modelling studies is that a range of outcomes can be modelled to provide a comprehensive evaluation of drug misuse interventions. Of the 16 models, 7 aimed to provide a societal perspective. However, many of the models omitted dimensions of the monetary outcome that would prove important for estimating the monetary impact on society, and therefore face the same limitations as the drug misuse intervention studies that were discussed in chapter 4. It is important to measure a wider range of dimensions, such as criminal justice costs, social care services costs, and addiction services costs, however, none of the models conducted from a societal perspective take into account the social care services cost.

One reason that models often omit certain dimensions is that the more dimensions that are modelled the more complex the model becomes. If lots of dimensions are taken into account there will be a greater amount of parameters required. However, decision tree models frequently have to be simplified so that they are not too complicated to handle. This proves to be especially problematic for drug misuse models given that the prognoses of drug misuse patients are particularly complicated. As previous chapters have detailed, there are a range of both monetary and non-monetary outcomes that need to be taken into account to consider the societal impact of drug misuse interventions. The results of this chapter show that most of the included decision analytic models are simplified, thus the models may misjudge the costs and outcomes.

Another of the potential benefits of modelling studies is that they can estimate outcomes over a longer time period. As drug misuse is often considered as a chronic condition (van het Loo, van Beusekom and Kahan, 2002), it is necessary to consider the long-term outcomes of the interventions in order to provide all the relevant information for policy makers. Of the 16 models reviewed, 2 only adopted a time horizon of 12 months, and 3 others only considered time horizons of up to 5 years. The 2 short-term models extracted their data from clinical trials, and these are rarely longer than 24 months. Indeed there are very few longitudinal drug misuse studies available from which models can extract data

to set their parameters. Given this, any longer-term models have to make assumptions about how the patients' pathways will develop over time, even though there is little real-world evidence to support these assumptions. One of the major limitations of long-term models, therefore, is that there may not be enough information to justify the parameters that they use. If the parameters are based on data extracted from short-term studies then the model must assume that these parameters will continue to apply over a longer period of time. However, given that many of the effects and costs of drug misuse interventions may not have taken effect in the short-term period upon which the parameters were based, these parameters may not prove to be appropriate in the long-term.

As parameters are uncertain over the long-term, models tend to use sensitivity analyses to address these problems. One way of doing this is to apply a different set of parameters to the model to examine the effect of the results, or to use a probabilistic sensitivity analysis to calculate the probability of different outcomes and costs if a range of estimates are available. As only 3 of the models reviewed used a probabilistic sensitivity analysis, this would be a way that other models could attempt to address the uncertainty of their parameters. However, the problem with all long-term models is that they are more complex and so have to make more simplifications as not all pathways can be modelled, which might still lead to the results being biased. The uncertainty regarding how parameters might change over the long-term cannot be fully addressed unless there are more longitudinal drug misuse studies, which would provide real life experience to check the estimates used in the model against.

The limitations with drug misuse modelling studies identified in this chapter indicate that policy makers should be aware of the uncertainty regarding the outcomes and costs predicted by the models and the lack of realism that they might reflect. The more comprehensive the model attempts to be, the more assumptions and simplifications it has to make, which could distort the results. Long-term models need to be supported by data from longitudinal studies, however, few of these are available for drug misuse models. Nevertheless, given that drug misuse is usually considered to be a chronic condition and that there are rarely the resources to conduct long-term clinical trials, modelling may still prove to be the best way to estimate long-term costs and outcomes, despite its limitations. If long-term models are to provide a comprehensive evaluation of drug misuse interventions they must take into account a greater range of outcomes and costs than those

considered by the models reviewed in this chapter. To examine the limitations and problems with developing a model that estimates a wide range of long-term outcomes it is therefore necessary to build more drug misuse models, an example of which is developed in the next chapter.

Chapter 7 Drug testing in schools: illustration of outcomes in modelling studies

7.1 Background and objectives

The preceding chapters of this thesis have provided a methodological critique of current drug misuse intervention studies. A number of different problems have been highlighted, but for present purposes two may be stressed. The first is that many drug misuse studies that use individual patient level data fail to consider the long-term outcomes of the intervention. The second is that many existing studies do not measure a wide enough range of dimensions of the monetary outcome to provide a comprehensive evaluation of the societal impact of drug misuse interventions. In the previous chapter existing modelling studies for drug misuse were reviewed, and although many of these state that they consider the long-term societal perspective, they all omit important dimensions of the monetary outcome. The criteria for good modelling studies have been examined and the limitations for applying these to drug misuse models revealed. This provides the background for the model that is developed in this chapter, which attempts to redress many of the problems that have been identified with existing drug misuse studies throughout the thesis.

This chapter aims to build a drug testing in schools model in order to examine the benefits and limitations of developing a long-term drug misuse model that takes into account a wide range of outcomes to provide a comprehensive evaluation of the intervention from the societal perspective. The drug testing in schools model is an innovative approach as there is a need to capture multiple outcomes over a long time period. It is also an area where there has been debate and conclusions drawn about this policy without a full economic evaluation.

The development of the drug testing in schools model illustrates the structure of the possible scenarios when introducing random drug testing in schools and the rationales for including certain outcomes, which has only been discussed at a theoretical level previously. The estimated outcomes for drug testing in schools provides an example of how different outcome domains from the societal perspective are determined, and

secondly how individual level outcomes, such as drug misuse, transform into monetary outcomes for society in the long-term.

Adolescent drug misuse is regarded as a social problem with many studies showing that such use is related to delinquency, poorer health status and lower educational outcomes in schools (Godfrey et al, 2002b; Godfrey et al, 2004; McCrystal, Higgins and Percy, 2006). Current policy directed at reducing the misuse of illegal drugs among young people across the UK involves a range of general information and more targeted initiatives. The question considered in this chapter is whether random drug testing in schools would be a useful part of the overall drug intervention strategy. Most prevention programmes are directed at providing information and advice to young people. Drug testing, by contrast, can be seen to be part of a more regulatory approach, particularly if positive tests are associated with some sort of punishment. The hypothesis is that drug testing programmes will deter drug misuse.

Random drug testing in schools has been applied in many middle schools and high schools in the U.S.A. The nature of the policies and incentives or disincentives for pupils and their parents vary. Some schools require students to take drug tests before issuing them with a parking permit etc. (DuPont, Campbell, and Mazza, 2002), whereas others have restricted testing to a specific group, such as adolescent athletes (Goldberg et al, 2003; Goldberg et al, 2007).

In 2004 the UK government also declared support for random drug testing in schools, which was then applied in 2005 by a school in Kent and Hucknall (BBC News, 2006; Gerada and Gilvarry, 2005), but there has not been widespread adoption of such policies. A previous Joseph Rowntree Foundation supported review suggested that there was very limited evidence to support the wide scale introduction of drug testing in schools (McKeganey, 2005). However, drug prevention policies with even limited levels of effectiveness can be shown to be cost-effective (Caulkins et al, 1999). The social costs associated with problematic drug misuse are very high and therefore expensive programmes that prevent some young people from becoming problematic drug users could prove to be good value for money. In the absence of primary data collection, an alternative research design is to construct a simulation model of the potential beneficial and adverse effects of drug testing in schools.

In order to evaluate the impact on the student cohort after introducing drug testing, a simulation model is developed to compare two groups of pupils: one cohort in a school with random drug testing and one cohort in a school without random drug testing. These two groups are assumed to have similar characteristics, in order to avoid other factors which might be related to drug misuse among pupils, such as alcohol use and smoking. The model was designed to simulate the cost-effectiveness of introducing random drug testing in a secondary school compared to the alternative of no such random testing.

2 outcome domains are considered at the end point of this model: drug misuse and educational outcomes. In the drug testing in schools model the number of pupils using drugs may differ from those in the model of no testing, based on the assumption that random drug testing in schools has some deterrent effect. This is related to the probability of pupils who become recreational drug users or problematic users in the end point of the model and their lifetime cost of being drug users. The other main focus in this model is the educational outcome. Random drug testing in schools may increase exclusions and influence pupils' truancy behaviour which in turn could lower pupils' educational outcomes. Poor educational outcomes are also associated with considerable lifetime social costs.

The first stage in estimating the cost-effectiveness of introducing random drug testing in schools is to construct the conceptual model indicating the different pathways individual pupils may experience as a result of different outcomes associated with the drug testing regime. This model will of course be dependent on the type of policy within which the random drug testing is embedded. The next stage is to find the best estimates for the different parameters of the conceptual model from the evidence base and UK data sources. Once the best sources for all data requirements are found, results can be generated. By changing key parameters the sensitivity of the model and the results for the cost effectiveness of drug testing can be presented.

7.2 Structure of the model

The model was constructed as a decision analytic model, with the primary question being whether the introduction of random drug testing in schools was cost-effective against the alternative where there was no random drug testing.

Building the conceptual model is made of up of the following stages:

- Determining the nature of the random testing regime
- Determining the nature of policies in the school arm with no drug testing
- Determining the time period, scope and implementation of the testing within the simulated model and time horizon of the outcomes
- Determining the different outcomes states
- Determining the different pupil pathways in both arms of the model

The full model and different pathways for both the school with drug testing and without drug testing are reproduced in Appendix 5.

7.2.1 Simulated random drug testing regime

It is assumed that the initial test will use non-invasive methods such as saliva or sweat tests. Parents and pupils will be informed about random drug testing and the non-invasive testing methods, and will be asked for their consent for being tested and providing samples. However, they will not be informed about the specific date of testing in order to prevent possible absence on the testing day. Testing is assumed to take place each year from Year 7 through to Year 11.

If pupils' initial test results are positive, the school will inform pupils' parents or guardians and advise pupils to take confirmatory tests in hospitals. The confirmatory tests will use invasive methods such as blood or urine tests. If pupils have negative results in the confirmatory test, they will return to the same school and will not receive any penalties or punishment. If pupils' confirmatory test results are positive, they may be excluded from the school for a fixed period of time (suspension). The school may also provide a consultation programme for pupils who have been caught using drugs.

If pupils refuse to participate in random drug testing or in the later confirmatory test, they may receive fixed period exclusion or even permanent exclusion from school, depending on the school policy. Within this model, it is assumed that if pupils refuse to participate in random drug testing or in the later confirmatory test, they may receive fixed period exclusion (suspension). Pupils that are suspended and then return to the same school will still enter the next random drug testing cycle.

If pupils have positive results in the confirmatory test, they may be excluded from school permanently or suspended for a period of time, depending on the school policy. The DfES (Department for Education and Skills) drug guidance for schools (2004) recommends that schools inform pupils' parents or guardians when they find out that pupils have used drugs. If these are illegal drugs, the guideline suggests that the school may inform the local police. However, it is questionable whether or not the school will actually inform the local police about the pupils' illegal drug usage, due to their concern with their reputation. The next step is that the school will need to identify the needs for the appropriate disciplinary action or referral to other services, such as consultation programmes for the pupils.

Within this model, once the pupils are confirmed as having used drugs they are suspended. If the school decides to only suspend the pupil, the school will need to provide or refer the pupil to an appropriate consultation programme. The pupils will still enter the next cycle for random drug testing. In reality, if the school's policy recommends permanent exclusion, the pupils may enter another school, or a special programme provided by different educational authorities, or they may start working.

Pupils refusing to participate in random drug testing or the confirmatory test could receive different penalties, depending on the school's policy. The school may assume that pupils who refuse to participate in the test may have been taking drugs. Therefore, pupils may be suspended for a fixed period of time.

If pupils exclude themselves from school at any point of the drug testing process, the school and local educational authorities may need to take certain action regarding pupils' truancy. Depending on the school's truancy policy, a pupil's teacher will try to contact the parents or guardians about the truancy and ask the self-excluded pupil to return to the

school. The head teacher of the school and truancy officer from the local education authorities may be involved in the pupils' truancy problem. If pupils decide to come back to the same school, they will then enter the next random drug test cycle.

If the self-excluded pupils decide not to return to the same school, they may choose to go to another school without random drug testing, or join special educational programmes, or they may decide to leave the education system and start working. If the pupils decide not to return to the original school where random drug testing in schools is introduced, it would be very difficult to trace the cost and consequences of their long-term educational and drug outcome within this model. In this model, if the pupils decide to leave the school their final outcome at age 16 is estimated based on simple assumptions.

It is believed that all types of exclusion may affect pupils' educational outcomes. (Brookes, Goodall and Heady, 2007). Some research even shows that exclusion may be related to pupils' drug misuse and delinquency (McCrystal, Higgins and Percy, 2006) and missed time at school may affect their educational outcomes. Therefore, it is assumed that pupils who self-exclude or are suspended from school may have a higher probability of having lower educational outcomes and may also have a higher probability of becoming a problematic drug user within this model.

7.2.2 Control group model: no drug testing in schools

In the control group model the school relies on the existing school detection and disciplinary system for drug misuse prevention. It is assumed that the majority of pupils in the school never use drugs (as in both simulated schools based on UK population figures) but that some of them have been using drugs for recreational purposes. If pupils are recreational drug users, it is assumed that none of them have been caught. This is a simplifying assumption as the model could be extended to allow for some drug misuse discoveries and potential exclusions in the control model. At the age of 16 these pupils will either stop using drugs, continue using drugs recreationally, or become problematic drug users. Although these pupils will remain in the same school and the normal education system, any drug misuse may affect their educational outcomes. They may also have a higher probability of becoming problematic drug users.

7.2.3 Outcome domains and end states

To undertake an economic evaluation, outcomes have to be expressed either in monetary terms or by focussing on a single primary outcome. For example, the model could be constructed in terms of the net cost per reduction in drug misuse or by the number of problem drug users. An alternative approach is to seek monetary values for all outcomes and express the model in terms of net benefits or net costs, which is the additional cost or gain from introducing a policy compared with the alternative.

In constructing potential pathways and outcomes at the end of the model cycles, 2 main outcome domains were identified: drug misuse and educational outcome at age 16. Previous economic studies based on English and Welsh data had also yielded monetary values of the costs of being either a problematic drug user (Godfrey et al, 2004) or having poor educational outcomes (Godfrey et al, 2002b). The study estimates the annual cost of being a problematic drug user or recreational user. With parameter values of the length of a drug using career these estimates can be used to determine the lifetime costs of a problem drug user at age 16. The second study estimated the lifetime costs of not being in education, employment or training (NEET) at age 16-18 compared with the non NEET population at the same age.

Depending on the availability of these data pupils will be categorised into six different outcome groups, based on their educational status and their drug usage status. These six states are:

- Drug free and normal educational attainment
- Recreational drug user and normal educational attainment
- Problem drug user and normal educational attainment
- Drug free and NEET
- Recreational drug user and NEET
- Problem drug user and NEET

7.2.4 Time period and scope

In the model presented below it is assumed that pupils participate in random drug testing throughout their secondary school career. The model takes a cohort through their school

career from 11 to 16, such that those in the school with random drug testing will be likely to have a test every year if they continue at the school. It is assumed that there will be 500 pupils in the whole school cohort for both arms – drug testing school and the control group.

7.3 Building the random drug testing in schools model

The simulation model starts from the decision node, where 1000 pupils are divided into 2 different scenarios: the random drug testing in schools model and the no testing model. The decision node is usually shown as a square (\square) and the chance node as a circle (\circ). Different probabilities are needed for each branch of the chance node and the sum of these probabilities must equal 1. In the first stage of the model, it is assumed that 50% of pupils are allocated to the no drug testing model and 50% of pupils are allocated to the random drug testing in schools model.

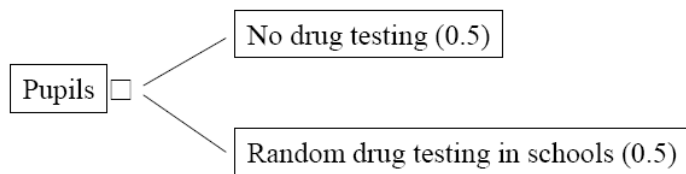


Figure 7.3.1 Decision node

The rest of this section sets out the different pathways through decision and chance nodes for these two different branches with the full model being reproduced in the following section.

7.3.1 No drug testing model

Looking at the no drug testing branch first, pupils enter the model at age 11 and it is assumed that they could either be recreational drug users or drug free. It is assumed that in the no drug testing model, the recreational users will never be caught for using drugs and both recreational users and pupils who are drug free will stay in the same school.

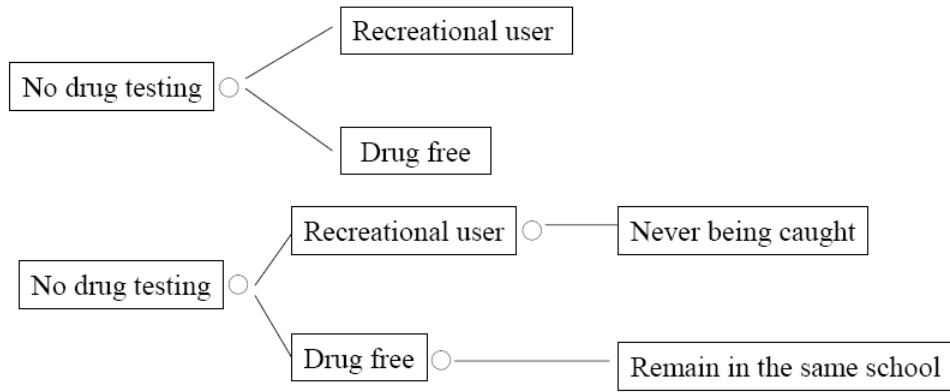


Figure 7.3.2 Scenario of no drug testing

If pupils are never caught for using drugs, they might stop using drugs or continue using drug recreationally or become a problematic user at age 16.

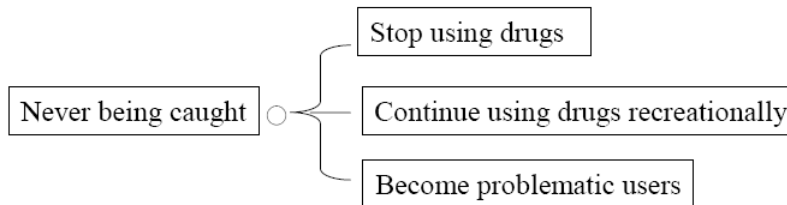


Figure 7.3.3 Recreational user pathway

Depending on pupils' status, the terminal or end stage node at age 16 will be presented according to their drug status (drug free, recreational user or problematic user) and their education status (NEET or normal education).

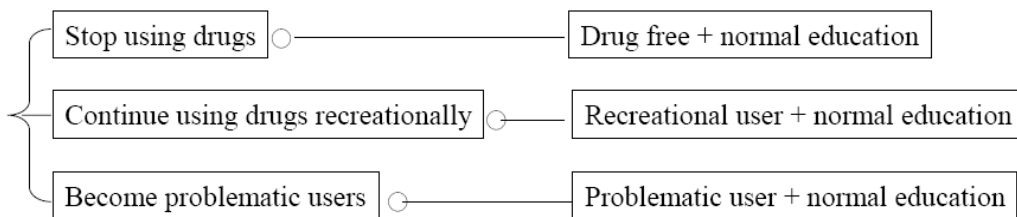


Figure 7.3.4 Recreational user end node

Those pupils who are originally drug free and remain in the same school might still change their drug usage status and become a recreational user or a problematic user by the end.

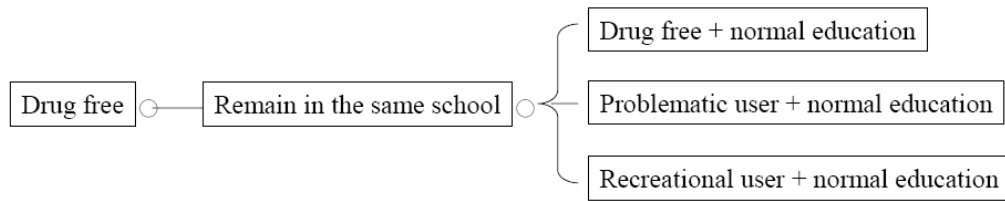


Figure 7.3.5 Non-user pathway

7.3.2 Random drug testing in schools model

The pathways for the random testing in schools model are more complex and individual pupils cycle through the drug testing programme each year they remain in the school. Pupils may have different reactions towards random drug testing. They may participate in the testing regime, self-exclude themselves and decide not to go back to school, or they may refuse to participate in the testing.

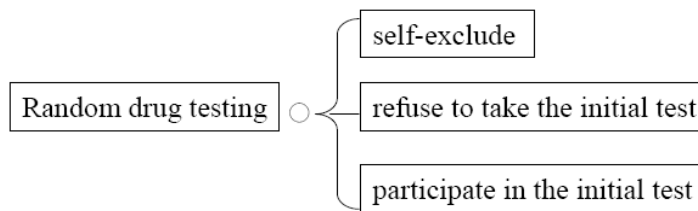


Figure 7.3.6 Random drug testing scenario

Self exclusion arm

If pupils self-exclude themselves the school may have policies in place, such as contacting with parents or guardians. After a period of self-exclusion, pupils may come back to the same school afterwards, or they may decide to leave the school.

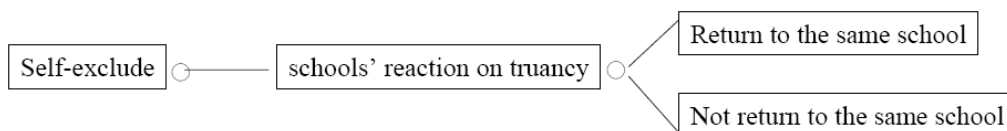


Figure 7.3.7 Self-exclusion pathway

When pupils go back to the same school, they might still enter the next cycle of random drug testing. When they get to age 16, they may have a different drug status but they would all have completed normal education.

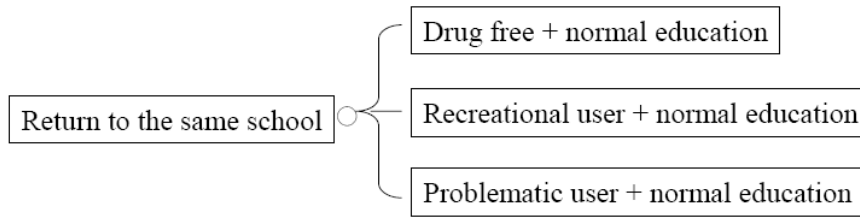


Figure 7.3.8 Self-exclusion end node

If pupils decide not to go back to the same school, they might end up going to another school or special educational programme and stay in education, or they might decide to leave the education system. If pupils leave the original school they would also leave the random drug testing model and their final outcomes will only be estimated when they are 16.

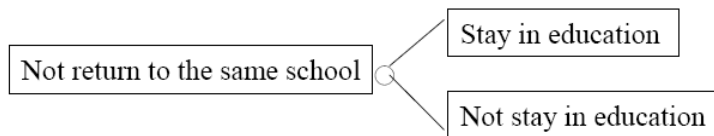


Figure 7.3.9 Permanent exclusion pathway

If pupils decide to leave the original school but still stay in the education system their final outcomes at age 16 will be estimated based on their educational status (normal education) and their drug status. If pupils decide to leave the education system completely, they might start working without any qualification and they might become NEET.

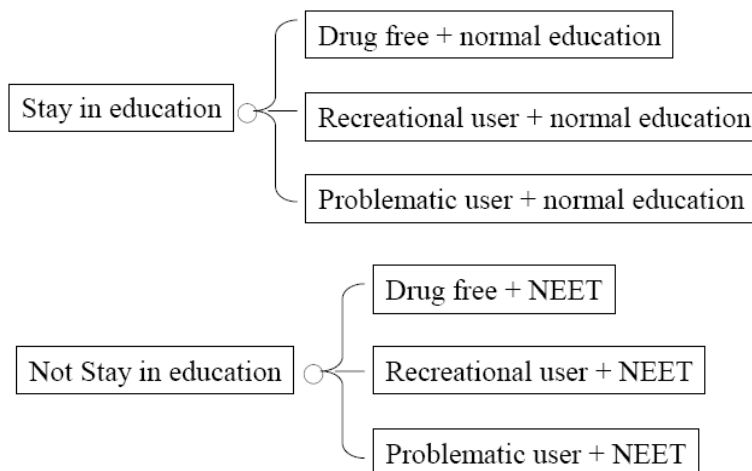


Figure 7.3.10 Permanent exclusion end node

Refusal of initial test arm

If pupils decide to refuse the initial test, it is assumed that they will receive some punishment, such as suspension. It is assumed that they will return to the same school afterwards and enter the next random drug testing cycle. Their outcome will be based on the drug and education status at age 16.

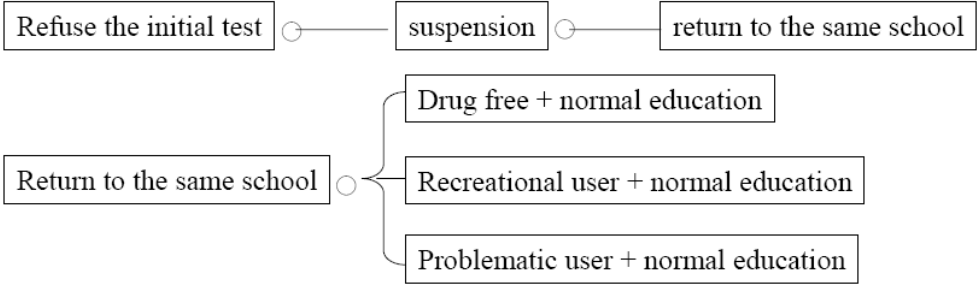


Figure 7.3.11 Initial test refusal pathway

Participation in test arm

If pupils decide to participate in the initial test, they may have positive or negative test results. The probability of having positive or negative test results depends on the sensitivity and specificity of the test.

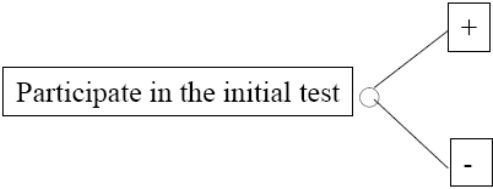


Figure 7.3.12 Initial test participation pathway

If pupils have negative initial test results they will remain in the same school and enter the next cycle of random drug testing. However, there is still a chance that they might either remain drug free, become a recreational user or a problematic user at age 16.

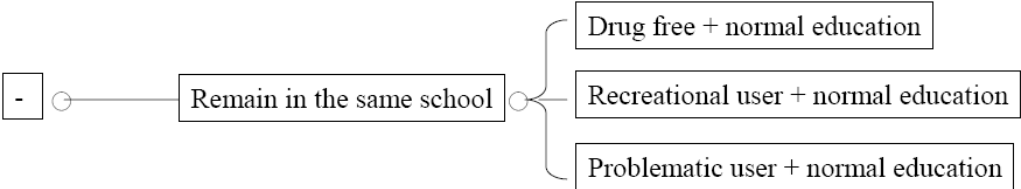


Figure 7.3.13 Initial test negative results

If pupils have positive initial test results, their parents or guardians will be informed and the pupil will be advised to take the confirmatory test (blood test) at the local hospital with their parents or guardians. When they are advised to take the confirmatory test, there may still be some chance that they refuse to take it.

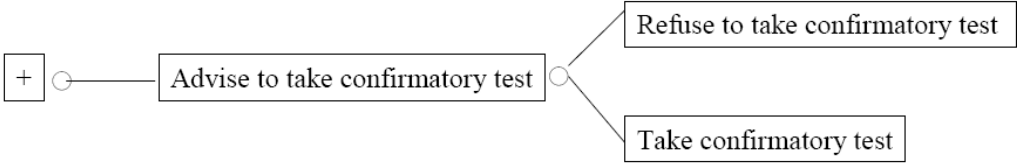


Figure 7.3.14 Initial test positive results

As with the situation for refusal of the initial tests, if pupils decide to refuse to take the confirmatory test it is assumed that they will be suspended for a fixed period of time. They will return to the same school after suspension and enter the next cycle of random drug testing. The final outcome will be based on their drug and education status (normal education) when they are 16.

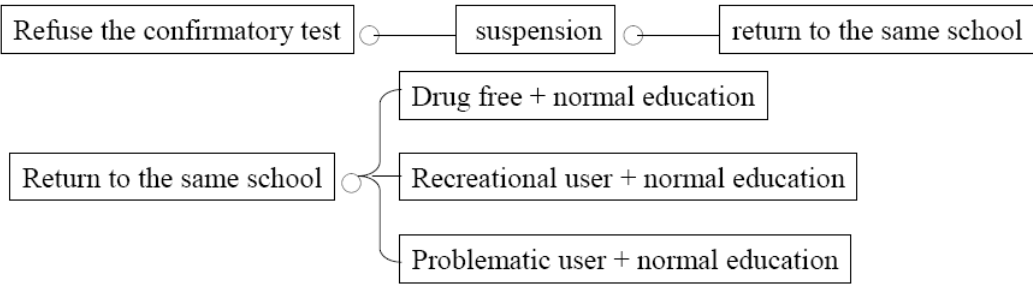


Figure 7.3.15 Initial test positive results pathway

The confirmatory test should be more effective at detecting drug usage among pupils. Pupils may have positive or negative result in the confirmatory test.

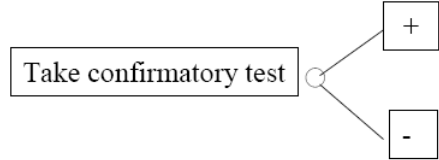


Figure 7.3.16 Confirmatory test pathway

If pupils have a positive confirmatory test result, they may receive some punishment from school, such as suspension. When they come back to the same school, they may need a

related counselling programme. They may still enter the next cycle of random drug testing in schools. Their outcomes will be based on their drug and educational status.

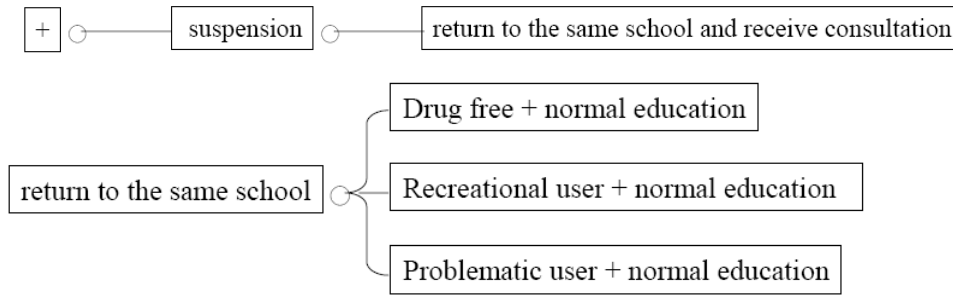


Figure 7.3.17 Confirmatory test positive results pathway

If pupils have a negative confirmatory test result, they may not have used drugs. However, like all the drug tests, there might be some false negative cases in the confirmatory tests. This may happen if the test sample is too dilute to be examined properly.

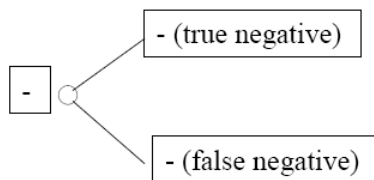


Figure 7.3.18 Confirmatory test negative results pathway

Pupils who have a negative result and have not used drugs will stay in the same school and enter the next cycle of testing. Their final outcomes will be estimated, based on their drug and educational status.

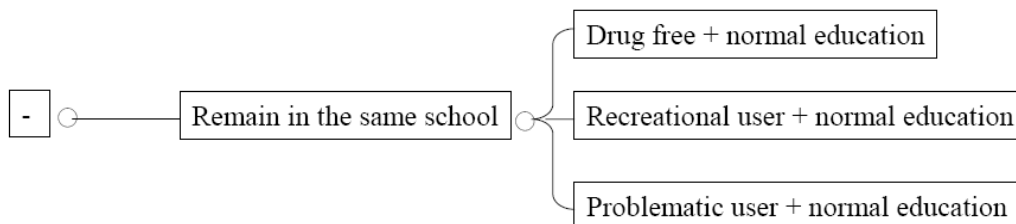


Figure 7.3.19 Confirmatory test negative results end node

If pupils have used drugs but are not caught in the confirmatory test, they will still remain at the same school and enter the next cycle. The invasive confirmatory test, such as the blood test, is usually more effective in detecting drug usage. Pupils' final outcomes at age 16 will be calculated, depending on their drug and educational status.

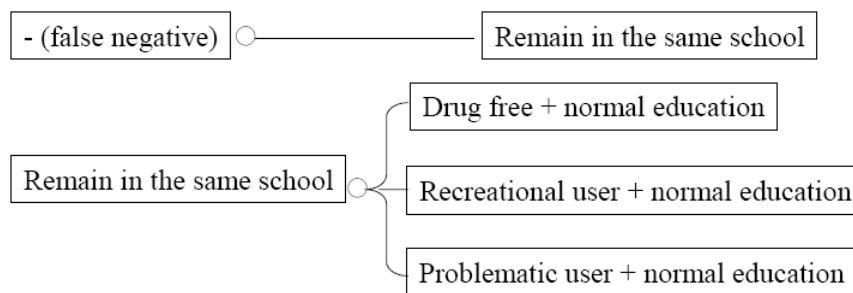


Figure 7.3.20 Confirmatory test false negative results pathway

The pathways of the full model can be seen in Appendix 5.

7.4 Parameters of the model

This section explains the development of the parameters and how the individual level outcomes relate to the social costs, which has been discussed in previous chapters. The parameters for the model are in two main forms: monetary amounts and probability estimates. For monetary parameters there are the costs of the drug testing interventions and the estimated costs for each of the 6 final outcome domains. The probability estimates are required to determine the proportion of the overall cohort split into the various pathways as set out in Appendix 5. In this section the sources of data and parameters used in the model are set out. The model takes a societal perspective, including all costs wherever they are borne and all costs are in 2005/6 UK prices.

7.4.1 Estimating the costs of drug testing

This section lists all the costs which may have occurred while introducing random drug testing in schools. These include the unit cost of random drug testing in schools (the initial test) and the unit cost for the confirmatory test. The cost of the reaction to pupil's truancy from their schools or local authorities will also be considered. If pupils are advised to participate in the confirmatory test in hospital, the costs for travel and the time of the pupils' parents or guardians will also be included.

No direct information about the cost of random drug testing in schools in the UK is available. Existing literature was searched for potential UK examples. One study

identified was a review of drug testing within a workplace setting. It shows the costs of drug testing in the workplace based on the market price and level of usage (Joseph Rowntree Foundation, 2004). A potential model related Home Office study used a bottom-up approach to costing within a public sector type intervention (Matrix Research and Consultancy and Institute for Criminal Policy Research, 2007). In this study, the unit cost of a test varied between different sites because of different levels of usage and the setting up costs. Assuming within a school setting, there is likely to be a greater number of tests, the unit cost could be predicted more accurately and would be lower than the Home Office reported price.

In a Joseph Rowntree Foundation study of drug testing in the workplace (Joseph Rowntree Foundation, 2004), it is reported that one of the drug testing companies, Altrix, charges between £30 and £35 for an initial test and £52 for the confirmation test. In the Home Office Report about Drug Interventions Programme pilots for children and young people, costs for drug tests in 5 different sites between November 2003 and September 2005 are reported (Matrix Research and Consultancy and Institute for Criminal Policy Research, 2007). The set-up cost includes personnel, training, overheads and equipment costs. The cost of drug testing cartridge kits is included in the overheads costs within this Home Office study. The running costs breakdown into personnel, training, premises and overheads costs. The unit cost of this particular study varies between £57 to £62 per test, or £100 to £121 per test from the 5 different sites, depending on the number of tests taken in each site. These tests took place at police stations or other similar settings rather than schools.

In the simulation model presented below, the price from the Home Office 2007 report (Matrix Research and Consultancy and Institute for Criminal Policy Research, 2007) is used, instead of the market price of drug testing. It is assumed that the setting within the Home Office 2007 report is closer to the model than commercial testing in workplaces. It is also assumed that the school will use the school nurse, or hire external staff from hospitals or a nurse from the local health centre to take samples and to run random drug testing within the school. The average unit cost from the lowest 2 costs from the Home Office 2007 study have been taken and converted to 2005/06 prices with GDP deflators (HM Treasury, 2007, accessed on 29 June 2007) to get £61.89 per test as the unit cost of the initial test for the random drug testing in schools model, as shown in Table 7.4.1.

The confirmatory test would be a one-off test conducted in a health care setting. A recent study of UK offender populations has compared the cost of saliva and urine tests among UK offenders (Bird, Pearson and Strang, 2002). The average unit cost for a urine test from this study is converted into 2005/06 prices to get the unit cost of a confirmatory test within the model between £122.34 and £133.46 per test.

Table 7.4.1 Unit cost of drug test

Type of drug test	2005/06 price *	Source
Initial test	£61.89	£57-£62 per test (Matrix Research and Consultancy and Institute for Criminal Policy Research, 2007)
Confirmatory test	£122.34-£133.46	£110-£120 per urine test (Bird, Pearson and Strang, 2002)

*: All prices are converted into 2005/06 prices with GDP deflators (HM Treasury, 2007).

7.4.2 Parents' time and travel cost

Within this model it is assumed that the school will inform pupils' parents or guardians if pupils have positive results for their initial drug testing. The school will then advise the parents or guardians to take their children to the hospital for the confirmatory test. The confirmatory test will use invasive methods such as blood or urine tests and it may require consent from the pupils' parents or guardians. The confirmatory test may take place during the normal office hours on weekdays. If the parents or guardians have a full-time job, it is likely that they will need to take at least a few hours off for the confirmatory test of their children.

The model calculates the approximate time for taking a confirmatory test and calculates the cost of the parents' or guardians' time. This cost is supposed to be equal to parents' hourly wage rate multiplied by the duration of the confirmatory test and travel time. It is assumed that the parents or guardians of pupils who have positive initial test results all have a full-time job, and the average wage rate in the UK, 2005/06 is used to calculate the cost of time for pupils' parents or guardians.

According to the Annual survey of hours and earning of labour market trend (National Statistics, 2005), the median hourly earnings of all full-time employees in 2004 were between £10.00 to £10.60 across all industries and services in the UK. The midpoint of these is taken as the hourly earning in 2004 of £10.30 and converted into 2005/06 prices with GDP deflators (HM Treasury, 2007) to get £10.80 as the average hourly earning for the cost of parents' or guardians' time within the model.

It is assumed that the total length of time of the parents' or guardians' involvement during the confirmatory test is approximately 1 to 1.5 hours, including the time of travelling from the pupil's house to the hospital where the test takes place. The total length of time for parents' involvement may be underestimated, depending on different situations, for instance, the traffic and the distance between the pupil's house and the hospital. It is assumed that the result will be sent to the school and to the pupil's house through the post. It is estimated that the cost of the parents or guardians' involvement for the confirmatory test is between £10.80 and £16.20 per person.

It is assumed that the pupils and their parents or guardians travel to hospital either by car, bus or by foot. The single bus fare is £1.60 per person per journey in 2007 according to the information provided by a nationwide bus company (First Group, 2007) and the average distance between a pupil's house and the hospital is 3 miles. The car running cost information from AA.com (2007) is used for the travel cost by car. It is estimated that the running cost per mile is between £0.16 and £0.29. Therefore, it is assumed that the travel cost by car is £0.48 to £0.87 per test. If the pupil and parent walk to the hospital, there would be no travel cost.

Table 7.4.2 Cost of parents' involvement

	Unit	Source
Total length of Parents' involvement (hours)	1-1.5	Based on study assumption
Average hourly earning (2005/06 price)*	£10.80	Average earning: £10.30 per hour in 2004 (National Statistics, 2005)
Cost of parents' involvement (per person)	£10.80-£16.20	Calculated

*: Price is converted into 2005/06 prices with GDP deflators (HM Treasury, 2007).

Table 7.4.3 Travel cost

Mode of travel	Per person per journey	Source
By car	£0.48-£0.87	Average distance between the hospital and the pupil's house(assume 3 miles)*running cost per mile (AA.com, 2007)
By bus	£1.60	Price listed on First Group (2007)
Walk	£0	N/A

7.4.3 Cost of truancy and exclusion

If pupils self-exclude themselves from school in order to avoid the drug test during the whole drug testing in school process, the school and perhaps the local educational authorities will need to react to pupils' truancy. Pupils' teachers may need to work overtime or visit pupils at home or visit pupils' parents or guardians to understand the reasons for truancy and try to convince pupils to come back to school. If pupils' teachers are not able to convince pupils to return to the same school, the school may report to the local educational authorities and let the education welfare services become involved. The cost of tackling the truancy problems will be included within the random drug testing in schools model.

It is quite difficult to determine how much money the school, local educational authorities and education welfare services spend on tackling the truancy problems. In a recent report of the costs of truancy and exclusion by Brookes and colleagues (2007) it is estimated, based on the costs of educational welfare services, that the cost per truant is about £706 per person per annum in 2005 prices. They also estimated £676 per person for the cost of managing the process of exclusion and £19,434 per person or £7,181 per person per annum in 2005 prices for the alternative education costs, including pupil referral unit, college, special school, mainstream school, home/ alternative education etc. They estimated that the total exclusion cost is £20,110 per person.

Due to the limited information and difficulties of determining the cost of truancy, estimates are taken from Brookes and colleagues (2007) on the truancy cost within the random drug testing in schools model and only the cost of truancy per annum is calculated due to the difficulties of predicting the length of truancy.

Table 7.4.4 Cost of truancy and exclusion

Type of cost	2005/06 price	Source
Truancy (per person per annum)	£706	£706 per truant per annum in 2005 price (Brookes, Goodall and Heady, 2007)
Exclusion (per person)	£20,110	£676 managing the process of exclusion + £19434 (per person in 2005 price) alternative education cost (Brookes, Goodall and Heady, 2007)

Table 7.4.5 Cost of random drug testing in schools

Type of cost	2005/06 price
Initial test (per test)	£61.89
Confirmatory test (per test)	£122.34-£133.46
Cost of parents' involvement (per person)	£10.8-£16.2
Cost of travel by foot (per person per journey)	£0
By car (per journey)	£0.48-£0.87
By bus (per person per journey)	£1.60
Truancy (per person per annum)	£706
Exclusion (per person)	£20110

7.5 Costs of different outcomes

7.5.1 Drug domain outcome: cost and transition of different groups

The drug domain outcome in this study is categorised into 3 different groups: drug free, recreational user and problematic user. The lifetime cost of crime and health care at age 16 of being in these 3 different groups is estimated. The data for the cost of crime and cost of health care is extracted from a study by Godfrey and colleagues (2004). The average social cost per drug user includes the costs of health care, crime (including criminal justice resources used and victim costs), driving, work, deaths and child care. It shows that the average social cost per young recreational user is £65 per annum, including £2 of health care costs, £54 of cost of deaths and £8 of crime costs.

The cost of crime and the cost of health care and deaths of the young drug users are included and converted into 2005/06 prices with GDP deflators (HM Treasury, 2007) to get the lifetime cost of being a recreational drug user at age 16. The mean cost of crime of a recreational user is estimated as £8.38 and the cost of health care and deaths as £60.11

per user per annum. Therefore, the total cost of recreational user is £68.49 per user per annum.

In this model, it is assumed that there is no difference in the social costs of being a young problematic drug user and being a problematic adult drug user. It is estimated that the annual social cost per problematic drug user is £44,232, where £1,413 is from the cost of health care, £2,663 from the cost of deaths and £39,956 from the cost of crime in the updated study by Godfrey and colleagues (2004).

Within the random drug testing in schools model, the cost of crime, the cost of health care and deaths to estimate the cost of being a problematic drug user at age 16 are included and converted into 2005/06 prices using a GDP deflator (HM Treasury, 2007). It is estimated that the cost of crime of a problematic user is £41,875 and the cost of health care and death is £4,375 per user per annum. Therefore, the total costs for a problematic user would be £46,250 per user per annum.

It is assumed that drug free pupils will not have any cost of crime or drug-related health care and deaths, although in reality there might be transition between the drug free pupils, the recreational users and the problematic users. Due to the limited information about this transition, it is assumed that there will not be any transition between these three different groups within the model after the end of the simulation period.

Table 7.5.1 Drug domain outcome

Type of cost*	Drug free	Recreational user	Problematic user
Cost of crime*	£0	£8.38	£41,875.70
Cost of health care an deaths*	£0	£60.11	£4,375.17
Total (per person per annum)	£0	£68.49	£46,250.87

*: All prices are converted into 2005/06 prices with GDP deflators (HM Treasury, 2007). Source: study by Godfrey and colleagues (2004); the updated social costs of Class A drug use in England and Wales from a Home Office research study (Godfrey et al, 2002a).

7.5.2 Education domain outcome

The educational outcome domain in this model includes normal education and NEET. Pupils who remain in their original school or change to another secondary school will have no education cost within this model.

In the drug testing model, if pupils decided to leave the education system and start working without any qualification or training, they may suffer from being unemployed and become NEET. The 2002 DfES research report (Godfrey et al, 2002b) estimates that the lifetime cost of being NEET is approximately £45,000 per capita for resource costs and £52,000 per capita for public finance costs in 2002.

In the DfES 2002 NEET study (Godfrey et al, 2002b) the lifetime costs of being NEET at age 16 to 18 included current costs, medium-term costs and long-term costs. The current costs include educational underachievement, unemployment, inactivity, teenage mothers, crime, poor health and substance misuse. The medium-term costs include educational underachievement (over 40 years), unemployment (over 40 years), early motherhood, (over 10 years) crime (over age 19-30), poor health (total for 40 years) and substance misuse (over 10 years). The long-term costs include pension differences. In the model, most of the costs within the DfES 2002 NEET study except the direct and indirect tax forgone are considered and the 2002 NEET costs are converted into 2005/06 prices with GDP deflators (HM Treasury, 2007). The resource cost of being NEET is £450,999 and £523,616 for public finance cost per person per annum. Therefore, the total cost of being NEET is £97,460.

Table 7.5.2 Education domain outcome

Type of cost*	Normal education	NEET
Resource cost	£0	£45,099
Public finance cost	£0	£52,361
Total	£0	£97,460

*: All prices are converted into 2005/06 prices with GDP deflators (HM Treasury, 2007).
Source: 2002 DfES research report (Godfrey et al, 2002b)

7.5.3 The 6 final outcomes

In the final cycle of the drug testing model, all pupils will be categorised into 6 different outcome groups, based on their educational status and their drug usage status. Pupils may

receive normal education until age 16 and remain drug free. Alternatively they may continue in normal education as a recreational drug user or a problematic user. It is also assumed that the different drug status may affect the pupils' educational performances in the school.

If pupils are self-excluded or excluded at different stages of random drug testing in schools and leave the normal education system and become NEET, their drug status may vary from drug free to problematic drug user. It is also assumed that if pupils become NEET, they may have a higher probability of becoming a problematic drug user. The cost of each group is estimated in Table 8.

Table 7.5.3 Final outcomes

Description (per person per annum)	Drug outcome	Education outcome	Total (2005/06 price)
Drug free and normal education	£0	£0	£0
Drug free and NEET	£0	£97,500	£97,500
Recreational drug user and normal education	£68	£0	£68
Recreational drug user and NEET	£68	£97,500	£97,568
Problematic drug user and normal education	£46,300	£0	£46,300
Problematic drug user and NEET	£46,300	£97,500	£143,800

7.6 Probability Parameters

7.6.1 Parameters: description

Due to the limited information regarding random drug testing in UK schools, probabilities from similar studies and government reports in the UK and the USA are used in the model (Barnes et al, 2003; Levy et al, 2007; Matrix Research and Consultancy and Institute for Criminal Policy Research, 2007).

It is assumed that 1,000 pupils enter the model at age 11, and 500 pupils are tested, while the other half will stay in the scenario without testing. Within the scenario of no testing, it is assumed that pupils might have already been recreational drug users or are drug free. According to the report of Smoking, drinking and drug usage among young people in

England (National Centre for Social Research, 2007), about 24% of pupils have ever taken drugs and 2% of pupils have taken Class A drugs in the last month. It is assumed that 24% of pupils are recreational users when they enter the non drug testing model. Among these pupils, 2% of them become problematic users, 24% of them remain as recreational users and the rest become drug free at age 16. It is assumed that if pupils are drug free when they enter the non drug testing model they will have the same outcome probabilities as recreational users.

In the drug testing model, it is assumed that pupils may participate in the test, refuse the test or self-exclude themselves in order to avoid testing. Due to the limited information about random drug testing in schools, the probabilities of testing among young offenders are used (Matrix Research and Consultancy and Institute for Criminal Policy Research, 2007). The report shows that 97% of tests are completed from 5 different sites among young people for the initial test, and less than 0.5% of young people refused to participate in the initial test.

It is assumed that within the testing model, 97% of pupils will participate in the initial test and the participation rate will remain the same through the whole period of random drug testing in schools. It is assumed that 0.5% of pupils may refuse to participate in the test and may then receive punishment, such as suspension or permanent exclusion. The rest of the pupils may self-exclude themselves from school. If pupils are only suspended for refusing the initial test, they will return to the same school and enter the next initial test.

If pupils self-exclude themselves, their teachers and the local educational authorities may react to the unauthorised absence. According to the DfES statistics (DfES, 2006), about 0.12% of pupils were permanently excluded from schools. The study by Brookes and colleagues (2007) shows that 6% of excluded children do not receive any education after exclusion. It is assumed that in the drug testing model 0.12% of the self-excluded pupils will not decide to come back to the same school, and these pupils will then not be included in the random drug testing in schools model thereafter. Among these pupils, it is assumed that 6% of them will not stay in the education system, and the rest of them may go to another school or receive alternative education.

The report of Smoking, drinking and drug usage among young people in England (National Centre for Social Research, 2007) shows that the proportion of pupils who have taken drugs in the previous month differs by age. For instance, 3% of pupils at age 11 have taken drugs in the last month and 17% of pupils at age 15 have taken drugs in the last month. Overall, 10% of pupils between the ages of 11 to 15 have taken drugs in the last month. These percentages are used to calculate the positive rate for the initial test results.

In the model, the pupils who have positive results are advised to take the confirmatory test in hospitals accompanied by their parents or guardians. The pupils who have negative results remain in the same school and may enter the next test. It is assumed that the refusal rate of confirmatory tests is the same as the refusal rate of the initial test and about 0.005% of pupils refuse to participate in the confirmatory test (Matrix Research and Consultancy and Institute for Criminal Policy Research, 2007). If pupils refuse to take the confirmatory test they would be suspended.

According to the study by Barnes and colleagues (2003) the sensitivity of the detection in oral fluid test is 82.9%. It is assumed that the positive rate for the initial test and the confirmatory test will be the sensitivity of the saliva test multiplied by the overall percentage of pupils who have taken drugs in the last month (confirmatory test positive rate: $82.9\% * 10\% = 8.29\%$).

In the random drug testing study by Levy and colleagues (2007) results showed that 6% of negative urine samples were too dilute to interpret and they may be false-negative cases. It is assumed that 6% of the pupils who have got negative results for the confirmatory test may have had a false negative result.

Table 7.6.1 Parameters

Variable: proportion	Value	Value deterrent effect (-0.24)	Source
Random drug testing	0.50	0.50	-
Recreational user	0.24	0.18	proportions of pupils who have ever taken drugs, 2006 (National Centre for Social Research, 2007)
Recreational then problematic user	0.02	0.01	proportions of pupils who have taken any Class A drugs in the last month, 2006 (National Centre for Social Research, 2007)
Participate initial test	0.97	0.97	Total test completed from 5 sites among young people (Matrix Research and Consultancy and Institute for Criminal Policy Research, 2007)
Refuse initial test (non self-exclude)	0.005	0.005	Total test refused from 5 sites among young people= ≤ 1 , less than 0.5% (Matrix Research and Consultancy and Institute for Criminal Policy Research, 2007)
Initial test positive	0.10	0.08	proportions of pupils who have taken drugs last month, 2006 (National Centre for Social Research, 2007)
11 years old	0.03	0.02	proportions of pupils who have taken drugs in the last month, by age, 2006 (National Centre for Social Research, 2007)
12 years old	0.03	0.02	
13 years old	0.06	0.05	
14 years old	0.13	0.10	
15 years old	0.17	0.13	
Refuse confirmatory test	0.005	0.005	Total test refused from 5 sites among young people= ≤ 1 , less than 0.5% (Matrix Research and Consultancy and Institute for Criminal Policy Research, 2007)
Confirmatory test positive	0.08	0.06	sensitivity (82.9%), specificity (98.7%) and efficiency (95.6%) of the Cozart Microplate EIA Opiate Oral Fluid Kit for Detection of Codeine and Metabolites in Oral Fluid at different immunoassay/GC-MS Cutoffs (Cutoff (ug/L)=20/20) (Barnes et al, 2003)
False negative	0.06	0.06	Found substantial proportion (6%) of urine samples were negative, but too dilute to interpret and it could have led to false-negative (Levy et al, 2007)
Truant not return to the same school	0.0012	0.0012	0.12% of pupils in schools were permanently excluded from primary, secondary and all special schools in 2004/05 (DfES, 2006)
Do not receive any education after leaving the original school	0.06	0.06	6% of excluded children have no education (including any alternative education). (Brookes, Goodall and Heady, 2007)

7.6.2 Parameters: deterrent effect

Reduction of drug users in schools

Some research suggests that random drug testing in schools will reduce the drug usage among pupils (Goldberg et al, 2003; Goldberg et al, 2007). Although it is difficult to determine what makes pupils take drugs, it is normally suggested that peer influence may be one of the reasons. It may affect pupils' behaviour by excluding or punishing the pupils who have used drugs.

There is very limited information on the deterrent effect in the previous studies of random drug testing in schools. Goldberg and colleagues (2003) studied the deterrent effect on the past 30 days illicit drug use. The study was conducted in 2 high schools with similar characteristics in Oregon, USA in autumn 1999, using the self-report survey. In order to find the impact of random drug testing among athletes, such as students in football or swimming teams, the study participants are divided into athletes and non-athletes, and each contains the control group (no drug testing) and the treatment group (random drug testing).

The Goldberg study (2003) used the self-report drug misuse index. It shows that the pre-test score of past 30-day illicit drug use is 0.074 and the post-test score is 0.053 among the athlete group. Among the non-athlete group, the pre-test score is 0.327 and the post-test score is 0.266. In this report no clear explanation of the score of the drug index was provided. However, in their later study published in 2007 (Goldberg et al, 2007), the drug index range is between 0 and 3, where 0 means no drug misuse and 3 means heavy use. The study by Goldberg and colleagues (2007) found the deterrent effect only in the past year of drug misuse.

The outcome data from the study by Goldberg and colleagues (2003) for the deterrent effect is used for the model. The drug misuse index score for illicit drugs decreased by 28% among the athlete group and by 19% among the non-athlete group. The average, 24%, is taken as the deterrent effect in the model.

Table 7.6.2 Parameters: deterrent effect

Variable: deterrent effect	Value	Source
Deterrent effect from literature (athlete)	-0.28	Difference of pre-test mean and post-test mean for past 30-day illicit drug use index(Goldberg et al, 2003) For Treatment Group among athletes students: pre-test mean is 0.074; post-test mean is 0.053.(significant $p < .05$) For Treatment Group among non-athletes
Deterrent effect from literature (non-athlete)	-0.19	students: pre-test mean is 0.327; post-test mean is 0.266. (significant $p < .10$)

7.7 Results

7.7.1 Comparing cost and outcomes of the two scenarios

The model was run for both random drug testing in schools and non drug testing in schools for 5 years and the final outcome when pupils are at age 16 was calculated. The total cost and outcomes of both models is shown in Table 7.7.1.

The costs include the cost of truancy and the cost of exclusion if pupils self-exclude themselves. The truancy and exclusion costs both include the administration costs. The exclusion cost also includes the alternative education costs.

Costs of drug testing include the unit cost of both the initial test and the confirmatory test, the cost of parents' time and the travel costs for both the pupil and his or her parent. These costs are varied, depending on how the pupils and their parents travel to the hospital from their house and how long it takes if pupils are advised to take the confirmatory test. Hence, the highest cost and the lowest cost of testing are calculated. The cost of testing occurs every year, and it is assumed that there will only be one random drug testing in school every year.

The outcomes within this model are presented in monetary terms. The outcome has 2 different domains according to pupils' drug usage status and educational status at age 16. Pupils might become drug free, recreational users or problematic users at age 16, while they may receive normal education or may not receive any qualification and become NEET. The outcomes within the drug status domain include the cost of crime and the cost of health care of being drug free, recreational users or problematic users. The educational

outcomes are presented as the cost of being NEET and the cost of receiving normal education. For instance, in the model of random drug testing in schools, if a pupil is a recreational user and has stayed in normal education until age 16, his or her outcome will be -£68. The outcome is presented as a negative value, since it is the cost to society.

The number of pupils in the 6 different final outcome groups is then multiplied by the cost to society. For instance, in the baseline model, the final outcome of each pupil who is a recreational user and stays in normal education is -£68 and the total number of pupils in this outcome group is 120 within the random drug testing in schools model. Within the non drug testing in schools model, the total number of pupils who are recreational users and stay in normal education is 120. The outcome for pupils who are in this particular group can then be compared between the random drug testing in schools model and the non drug testing in schools model. The total outcome for recreational users who stay in normal education is -£8,200 in the testing model, and -£8,200 in the non-testing model. There is no difference between the 2 models. Outcomes of -£8,200 represents the cost to society when introducing random drug testing in schools.

The total outcome sum (A) of the 6 outcome groups in both models is then calculated. In the testing model the total outcome is -£471,200, and in the non-testing model the total outcome is -£471,600. The difference between the 2 models is -£400 for the whole cohort of pupils. If it is assumed that there is a deterrent effect of 24%, the total outcome is -£360,900 in random drug testing in schools model, and in the non-drug testing model the total outcome remains the same, -£471,200. The difference between the 2 models is £110,300 for the whole cohort of pupils, when there is a 24% deterrent effect.

Costs of random drug testing are varied due to the difference in travel costs and unit costs of testing. The sum of the highest total costs (B) and the lowest total costs (B') among the whole cohort of pupils in both models are calculated. In the non-drug testing model, the total cost of testing is 0, while in the random drug testing in schools model the highest total cost of testing is £226,700 or £222,800 for the lowest total cost of testing. The highest total cost of testing is £219,400 or £216,400 for the lowest total cost of testing when there is a 24% deterrent effect.

The net benefit is total outcome minus total benefit (A-B or A-B'). It shows that within the random drug testing in schools model, the net benefit is between -£694,400 and -£698,300 in the baseline model or between -£577,300 and -£580,300 when there is a deterrent effect. In the non-drug testing in schools model, the net benefit is -£471,200 and it does not change according to the deterrent effect. The difference of net benefit between the 2 models is between £223,200 and £227,100 at baseline, or between -£106,100 and -£109,100 when there is a deterrent effect.

The cost of testing and net benefit for each individual pupil is then calculated. This shows that the highest total cost of testing per pupil is £453 and the lowest total cost of testing per pupil is £446 at baseline. The total cost per pupil is between £439 and £433 when there is a 24% deterrent effect in the testing model and there is no cost per pupil in the non-testing model. The costs include truancy costs and exclusion costs. The net benefit per pupil is between -£1,397 and -£1,389 at baseline or between -£1,161 and -£1155 with a deterrent effect in the testing model and -£942 per pupil in the non-drug testing model. The difference per pupil between the 2 models is between -£454 and -£446 at baseline or between -£218 and -£212 with a 24% deterrent effect.

It is often suggested that random drug testing in schools may affect pupils' behaviour and may reduce the drug usage among young people (Goldberg et al, 2003; Goldberg et al, 2007). However, this random drug testing simulation model indicates that any deterrent effect of random drug testing in schools is not cost-effective. In fact it is about 16 times more costly than the non-testing in schools scenario.

Table 7.7.1 Total cost and outcomes of baseline model (number rounded)

Outcome(£)	Number of pupils(no test)	Number of pupils(drug testing in schools)	No drug test (outcome) (£)	Drug testing in schools (outcome) (£)	Difference(£)
drug free and normal education (a)	370.0	370.0	0	0	0
recreational user and normal education (b)	120.0	120.0	-8200	-8200	0
problematic user and normal education (c)	10.0	10.0	-463000	-463000	0
drug free and NEET (d)	0.0	0.0	-	-325	-325
recreational user and NEET (e)	0.0	0.0	-	-105	-105
problematic user and NEET (f)	0.0	0.0	-	-13	-13
Total outcome (A=a+b+c+d+e+f)	-	-	-471200	-471600	-400
Total cost of testing, highest (B)	-	-	0	226700	226700
Total cost of testing, lowest (B')	-	-	-	222800	222800
Net benefit (A-B)	-	-	-471200	-698300	-227100
Net benefit (A-B')	-	-	-	-694400	-223200
Cost per pupil, highest (=B/500)	-	-	0	453	453
Cost per pupil, lowest (=B'/500)	-	-	-	446	446
Net benefit per pupil (=A-B)/500)	-	-	-942	-1397	-454
Net benefit per pupil (=A-B')/500)	-	-	-	-1389	-446

Table 7.7.2 Total cost and outcomes of model with a deterrent effect of 24% (number rounded)

Outcome	Number of pupils(no test)	Number of pupils(drug testing in schools)	No drug test (outcome) (£)	Drug testing in schools (outcome) (£)	Difference(£)
drug free and normal education (a)	370.0	400.5	0	0	0
recreational user and normal education (b)	120.0	91.8	-8200	-6200	2000
problematic user and normal education (c)	10.0	7.7	-463000	-354200	108800
drug free and NEET (d)	0.0	0.0	-	-325	-325
recreational user and NEET (e)	0.0	0.0	-	-105	-105
problematic user and NEET (f)	0.0	0.0	-	-13	-13
Total outcome (A=a+b+c+d+e+f)	-	-	-471200	-360900	110300
Total cost of testing, highest (B)	-	-	0	219400	219400
Total cost of testing, lowest (B')	-	-	-	216400	216400
Net benefit (A-B)	-	-	-471200	-580300	-109100
Net benefit (A-B')	-	-	-	-577300	-106100
Cost per pupil, highest (=B/500)	-	-	0	439	439
Cost per pupil, lowest (=B'/500)	-	-	-	433	433
Net benefit per pupil (=A-B)/500)	-	-	-942	-1161	-218
Net benefit per pupil (=A-B')/500)	-	-	-	-1155	-212

7.7.2 Sensitivity analysis

This model was constructed using a variety of data. In particular there was limited evidence regarding the deterrent effect. A sensitivity analysis was therefore conducted to investigate different deterrent effects and compare the difference between the outcomes, such as the net benefit and total costs (Table 7.7.3 and Table 7.7.4). The sensitivity analysis shows that the difference of net benefit between the no-testing model and the testing model gradually decreases when there is a higher deterrent effect.

The deterrent effect was also calculated to determine the breakeven point of random drug testing, where the difference between no drug testing and random drug testing will be close to 0. The breakeven point will need to have around 45.3% deterrent effect. However, in reality, as the finding in the study by Goldberg and colleagues (2003) shows, the deterrent effect is between 19% and 28%.

Different prevalence rates are used to estimate the net benefit in both the random drug testing model and the no drug testing model. The proportion of pupils who have taken class A drugs in the last month (2%) is used as the probability of problematic users in the model (National Centre for Social Research, 2007). Different proportions are used, including pupils who have taken class A drugs in the last month (2%), in the last year (4.3%) and ever taken them (5.4%) as the probability of problematic users in the sensitivity analysis. The difference between no deterrent effect and deterrent effect of 24% is also compared. This shows that the higher the proportion of problematic users, the greater the difference is between the 2 models. Furthermore, comparing the difference between the baseline model and the model with deterrent effect reveals that the deterrent effect will also interact with the prevalence rate. Under the scenario of a 24% deterrent effect, the random drug testing model is more likely to be beneficial than the no testing model, when there is a higher prevalence of problematic users (Tables 7.7.5 to Table 7.7.8).

The proportion of pupils who have taken any drugs in the last month by age are used as the probability of positive results in the initial test (National Centre for Social Research, 2007). In the sensitivity analysis, different proportions are used as the probability of problematic users, such as pupils who have taken any drugs in the last month, in the last

year and ever taken drugs. All probabilities vary according to age. Furthermore, the difference between no deterrent effect and a deterrent effect is compared. This shows that when there is a higher percentage of positive results for the initial test, the difference is greater between the non-testing model and the drug testing model. However, there is only very little difference between the different scenarios. The baseline model and the model with the deterrent effect are also compared, which shows that the deterrent effect is interacted with the prevalence of the positive result for the initial test (Tables 7.7.5 to Table 7.7.8).

Finally, in terms of sensitivity analyses, different self-exclusion rates are used to compare the difference between outcomes. The self-exclusion rate is reduced until it gets to no self-exclusion. The sensitivity analysis shows that there is only very little difference of outcomes between the different self-exclusion rates (Tables 7.7.9 and 7.7.10).

Table 7.7.3 Sensitivity analysis: deterrent effect on number of pupils

Deterrent effect	Recreational user no. (non-NEET) (no testing)	Problematic user no. (non-NEET) (no testing)	Recreational user no. (non-NEET) (drug testing)	Problematic user no. (non-NEET) (drug testing)
0.00	120.0	10.0	120.0	10.0
-0.19	120.0	10.0	97.2	8.1
-0.24	120.0	10.0	91.8	7.7
-0.28	120.0	10.0	86.4	7.2
-0.30	120.0	10.0	84.0	7.0
-0.40	120.0	10.0	72.0	6.0
-0.45	120.0	10.0	66.0	5.5
-0.453	120.0	10.0	65.7	5.5
-0.50	120.0	10.0	60.0	5.0

Table 7.7.4 Sensitivity analysis: deterrent effect on net benefits

Deterrent effect	Net benefit: no test (C)	Net benefit: drug test (D)	Net benefit: drug test (D')	Difference (=D-C)	Difference (=D'-C)	Net benefit per pupil: no test (=C/500)	Net benefit per pupil: drug test (=D/500)	Net benefit per pupil: drug test (=D'/500)	Difference (=D-C)/500)	Difference (=D'-C)/500)
0.00	-471200	-698300	-694400	-227100	-223200	-942	-1397	-1389	-454	-446
-0.19	-471200	-602500	-599400	-131300	-128200	-942	-1205	-1199	-263	-256
-0.24	-471200	-580300	-577300	-109100	-106100	-942	-1161	-1155	-218	-212
-0.28	-471200	-557400	-554600	-86200	-83400	-942	-1115	-1109	-172	-167
-0.30	-471200	-547400	-544600	-76200	-73400	-942	-1095	-1089	-152	-147
-0.40	-471200	-497200	-494900	-26000	-23700	-942	-994	-990	-52	-47
-0.45	-471200	-472100	-470000	-900	1200	-942	-944	-940	-2	2
-0.453	-471200	-470600	-468500	600	2700	-942	-941	-937	1	5
-0.50	-471200	-447000	-445100	24200	26100	-942	-894	-890	48	52

Table 7.7.5 Sensitivity analysis: number of pupils applied different prevalence with no deterrent effect

Prevalence (no deterrent)	Recreational user no. (non-NEET) (no testing)	Problematic user no. (non-NEET) (no testing)	Recreational user no. (non-NEET) (drug testing)	Problematic user no. (non-NEET) (drug testing)
problematic user=taken class A drugs in last month (0.02)	120.0	10.0	120.0	10.0
problematic user=taken class A drugs in last year (0.043)	120.0	21.5	120.0	21.5
problematic user=ever taken class A drugs (0.054)	120.0	27.0	120.0	27.0
Initial test positive= have taken any drugs in last month, by age	120.0	10.0	120.0	10.0
Initial test positive= have taken any drugs in last year, by age	120.0	10.0	120.0	10.0
Initial test positive=ever taken any drugs, by age	120.0	10.0	120.0	10.0

Table 7.7.6 Sensitivity analysis: net benefits applied different prevalence with no deterrent effect

Prevalence (no deterrent)	Net benefit: no test (C)	Net benefit: drug test (D)	Net benefit: drug test (D')	Difference (=D-C)	Difference (=D'-C)	Net benefit per pupil: no test (=C/500)	Net benefit per pupil: drug test (=D/500)	Net benefit per pupil: drug test (=D'/500)	Difference (=D-C)/500)	Difference (=D'-C)/500)
problematic user=taken class A drugs in last month (0.02)	-471200	-698300	-694400	-227100	-223200	-942	-1397	-1389	-454	-446
problematic user=taken class A drugs in last year (0.043)	-1002600	-1229700	-1225800	-227100	-223200	-2005	-2459	-2452	-454	-446
problematic user=ever taken class A drugs (0.054)	-1257000	-1484100	-1480200	-227100	-223200	-2514	-2968	-2960	-454	-446
Initial test positive=have taken any drugs in last month, by age	-471200	-698300	-694400	-227100	-223200	-942	-1397	-1389	-454	-446
Initial test positive=have taken any drugs in last year, by age	-471200	-723700	-716500	-252500	-245300	-942	-1447	-1433	-505	-491
Initial test positive=ever taken any drugs, by age	-471200	-750200	-739700	-279000	-268500	-942	-1500	-1479	-558	-537

Table 7.7.7 Sensitivity analysis: number of pupils applied different prevalence with 24% deterrent effect

Prevalence (-24% deterrent effect)	Recreational user no. (non-NEET) (no testing)	Problematic user no. (non-NEET) (no testing)	Recreational user no. (non-NEET) (drug testing)	Problematic user no. (non-NEET) (drug testing)
problematic user=taken class A drugs in last month (0.02)	120.0	10.0	91.8	7.7
problematic user=taken class A drugs in last year (0.043)	120.0	21.5	91.8	16.5
problematic user=ever taken class A drugs (0.054)	120.0	27.0	91.8	20.7
Initial test positive= have taken any drugs in last month, by age	120.0	10.0	91.8	7.7
Initial test positive= have taken any drugs in last year, by age	120.0	10.0	91.8	7.7

Table 7.7.8 Sensitivity analysis: net benefits applied different prevalence with 24% deterrent effect

Prevalence (-24% deterrent effect)	Net benefit: no test (C)	Net benefit: drug test (D)	Net benefit: drug test (D')	Difference (=D-C)	Difference (=D'-C)	Net benefit per pupil: no test (=C/500)	Net benefit per pupil: drug test (=D/500)	Net benefit per pupil: drug test (=D'/500)	Difference (=D-C)/500)	Difference (=D'-C)/500)
problematic user=taken class A drugs in last month (0.02)	-471200	-580300	-577300	-109100	-106100	-942	-1161	-1155	-218	-212
problematic user=taken class A drugs in last year (0.043)	-1002600	-986900	-983900	15700	18700	-2005	-1974	-1968	31	37
problematic user=ever taken class A drugs (0.054)	-1257000	-1181500	-1178500	75500	78500	-2514	-2363	-2357	151	157
Initial test positive=have taken any drugs in last month, by age	-471200	-580300	-577300	-109100	-106100	-942	-1161	-1155	-218	-212
Initial test positive=have taken any drugs in last year, by age	-471200	-599700	-594200	-128500	-123000	-942	-1199	-1188	-257	-246

Table 7.7.9 Sensitivity analysis: different self-exclusion rate with no deterrent effect

Self-exclusion rate (= 1-rate of initial test participate-rate of refuse to participate) (Baseline)	Total number of exclusion (NEET)	Problematic user no. (non-NEET) (no testing)	Problematic user no. (non-NEET) (drug testing)	Net benefit: no test (C)	Net benefit: drug test (D)	Net benefit: drug test (D')	Difference (=D-C)	Difference (=D'-C)	Net benefit per pupil: no test (= C/500)	Net benefit per pupil: drug test (= D/500)	Net benefit per pupil: drug test (= D'/500)	Difference (= (D-C)/500)	Difference (= (D'-C)/500)
0.025	0.1	10.0	7.7	-471200	-580300	-577300	-109100	-106100	-942	-1161	-1155	-218	-212
0.020	0.1	10.0	7.7	-471200	-571600	-568600	-100400	-97400	-942	-1143	-1137	-201	-195
0.015	0.0	10.0	7.7	-471200	-563300	-560300	-92100	-89100	-942	-1127	-1121	-184	-178
0.010	0.0	10.0	7.7	-471200	-555000	-552000	-83800	-80800	-942	-1110	-1104	-168	-162
0.005	0.0	10.0	7.7	-471200	-546700	-543500	-75500	-72300	-942	-1093	-1087	-151	-145
0	0.0	10.0	7.7	-471200	-538400	-535300	-67200	-64100	-942	-1077	-1071	-134	-128

Table 7.7.10 Sensitivity analysis: different self-exclusion rate with 24% deterrent effect

Self-exclusion rate (= 1 - rate of initial test participate - rate of refuse to participate) (24% deterrent effect)	Total number of exclusion (NEET)	Problematic user no. (non-NEET) (no testing)	Problematic user no. (non-NEET) (drug testing)	Net benefit: no test (C)	Net benefit: drug test (D)	Net benefit: drug test (D')	Difference (= D-C)	Difference (= D'-C)	Net benefit per pupil: no test (= C/500)	Net benefit per pupil: drug test (= D/500)	Net benefit per pupil: drug test (= D'/500)	Difference (= (D-C)/500)	Difference (= (D'-C)/500)
0.025	0.1	10.0	10.0	-471200	-698300	-694400	-227100	-223200	-942	-1397	-1389	-454	-446
0.020	0.1	10.0	10.0	-471200	-689600	-685700	-218400	-214500	-942	-1379	-1371	-437	-429
0.015	0.0	10.0	10.0	-471200	-681300	-677400	-210100	-206200	-942	-1363	-1355	-420	-412
0.010	0.0	10.0	10.0	-471200	-673000	-669100	-201800	-197900	-942	-1346	-1338	-404	-396
0.005	0.0	10.0	10.0	-471200	-664700	-660800	-193500	-189600	-942	-1329	-1322	-387	-379
0	0.0	10.0	10.0	-471200	-656500	-652500	-185300	-181300	-942	-1313	-1305	-371	-363

7.8 Conclusion and discussion

The aim of the chapter has been to develop a drug testing in schools model to provide an example of a long-term drug misuse modelling study that considers a wide range of dimensions of the monetary outcome in order to comprehensively evaluate the intervention from the societal perspective. Having developed the model, it is worth briefly summarising its findings and examining the extent to which it overcomes the limitations of other modelling studies discussed in the previous chapter.

The results of the model illustrate that although drug testing in schools may reduce the number of recreational and problematic users, the testing itself is very costly. The sensitivity analysis shows that even if there is a very large deterrent effect, the net benefit of the random drug testing model would still be lower than the model of no testing. The break even point, where the costs of drug testing are equal to the potential benefits, requires a 45.3% deterrent effect, well above any realistic rate. The sensitivity analysis also indicates that when there is higher prevalence of problematic users, the random drug testing model will be more beneficial. This indicates that the model is more likely to be cost-effective in those schools with greater drug problems.

One of the main problems identified in the previous chapter with existing long-term drug misuse models was that there are very few longitudinal studies of drug misuse interventions from which data can be extracted. The drug testing in schools model attempted to overcome this problem by combining an intervention period of only 5 years with long-term estimates of costs and outcomes for drug users extracted from existing literature. This assumes, however, that all of the effects of the intervention will have materialised by the time the pupils are 16. Although this approach may be justified in the case of the drug testing in schools model it may not be applicable for other drug misuse models, which expect the effects of the intervention to continue for a longer period of time, as is the case with many drug misuse treatment models.

One of the other principal advantages of the drug testing in schools model is that it considers a wide range of dimensions of the monetary outcome. In chapter 4 it was shown that many drug misuse intervention studies do not consider a number of dimensions in both the resources saved and other value created domain which would influence the overall monetary impact on society, and this was also true of the modelling studies reviewed in chapter 6. By contrast, the drug testing in schools model considered the health care costs, crime costs, and social care services costs (especially those related to education costs) in the resources saved domain. In the other value created domain the model considered a wide range of relevant dimensions including the value to third parties from reduced drug related crime and the impact on productivity, both whether or not the pupils become NEET and the costs of parents' time while accompanying the pupils for confirmatory tests.

One of the limitations of considering such a wide range of costs, however, is that the model had to assume a number of estimates. For example, after introducing drug testing in schools more pupils may exclude themselves, which is an important cost to take into account. However, there is no real-world evidence to indicate the increased amount of self-exclusion from the programme, which would support the estimates used in the model. The model thus faces one of the major problems identified in the previous chapter, which is that there is often insufficient real-world data on which to base the estimates used in the model.

The problem of there being insufficient real-world evidence is not only related to estimating costs, but also to setting the parameters for the model. As there is no evidence regarding the refusal rate for drug testing in schools in the UK, the model used refusal rates from a drug testing study among the UK young offender population (Matrix Research and Consultancy and Institute for Criminal Policy Research, 2007). Although random drug testing in schools may have a similar effect to mandatory drug testing, the refusal rate among school pupils might still be higher than among the arrestees who are supervised by a police officer.

Another major limitation due to the lack of available information concerned the transition between drug free pupils, recreational users and problematic users. As there was no applicable real-world evidence regarding the transition between these states, the model

assumed that no transition occurred. However, in real life it is likely that there would be some transition between these states and random drug testing in schools may affect the pattern of this transition. Transition between states would be one of the most important parameters for the model, thus further research would be required before these parameters could be accurately estimated in order to make the model more realistic.

The problem of setting parameters was further increased due to the complexity of the model as many simplifications had to be made. For example, in the no testing scenario it was assumed that recreational users will not be caught. Although in reality this may be unlikely, it would have been too complex to factor this into the model. Similarly, it was assumed that both recreational drug users and drug free pupils entering the model have the same probabilities of becoming problematic drug users at age 16, which does not take into account the possibility that recreational drug users might be more likely to start using hard drugs. Consequently, the model may underestimate the total costs and outcomes within the non drug testing in schools scenario.

In addition to making simplifying assumptions, in some cases data had to be extracted from different sources as there were no available UK studies. Some of the probabilities from random drug testing studies in the USA were used to calculate the proportion of positive test results. These may underestimate the positive results in drug testing among young people in the UK. The proportion of recreational drug misuse may be higher in the UK because the general attitude of the public and the government is more open towards soft drugs, such as marijuana and other Class C drugs. The problem of having to use studies from different countries when there is insufficient data available from one country alone was encountered by models reviewed in the last chapter, and this model faces the same problem.

The development of the drug testing in schools model has demonstrated that it is possible to consider a wide range of outcomes in the long-term. In doing so, the model has attempted to overcome 2 of the major limitations with many existing drug misuse intervention studies: that they do not consider a broad enough perspective and that they do not estimate the long-term outcomes of the intervention. However, in overcoming these problems, the model has proven

susceptible to a number of the other limitations with modelling studies identified in the previous chapter. Indeed this chapter has illustrated that in modelling a range of long-term outcomes, drug misuse models are likely to face more problems. This provides a performative example of one of the major problems with modelling. The more comprehensive a model attempts to be, the more complex it becomes and the more real-world data it requires. Consequently, the model has to make more simplifications and assumptions, and is more likely to encounter problems regarding the lack of real-world information on which the parameters and estimates of outcomes are based.

The main advantage of developing a model is that it can hypothetically consider the long-term outcomes of an intervention, when the time and resources would be unavailable to examine this in real life. However, the model is likely to be uncertain if there is no real-world data available, such as data from longitudinal studies in the case of drug misuse. This poses something of a dilemma for policy makers. If there is not the time and resources to invest in longitudinal studies that follow patients up over many years then modelling studies may prove the best way to estimate the long-term costs and outcomes of a given intervention. However, as the model has to make assumptions and set parameters based on estimates of what will happen in real life, the results of the model will be more uncertain and less reliable to the extent that there is a lack of real-world data that they can apply. The main problem with modelling studies, therefore, is one of limited data, which can only be rectified if the limitations with other drug misuse intervention studies examined throughout this thesis are addressed.

Chapter 8 Conclusion

The purpose of this thesis has been to examine and evaluate the measurement of outcomes in economic evaluations of drug misuse interventions. The importance of economic evaluations is that they provide an analysis of the costs and effectiveness of different interventions, which policy makers can then take into account.

It is important to know which outcomes should be measured in the economic evaluation, and which of these are the most significant. Economic evaluations of cost-effectiveness or cost utility design can only take into consideration one outcome at a time, such as QALYs. Policy makers usually take into consideration generic outcomes so that they can compare different policies across different fields. In contrast, cost benefit analysis involves measuring individual and social outcomes in monetary terms.

This thesis has examined the different outcomes that have been taken into account in economic evaluations of drug misuse interventions, identified the rationales for choosing outcomes and addressed the problems of using generic outcomes to evaluate drug misuse interventions. The aim of this chapter is to summarise the main findings of the thesis, and to consider their limitations and the implications for future research and drug misuse policy.

8.1 Summary of findings

This thesis has examined 3 different aspects of measuring outcomes in the economic evaluation of drug misuse interventions. The first focused on non-monetary outcomes at the individual patient level, the second focused on monetary outcomes within studies using individual patient level data, and the third focused on long-term outcomes, either monetary or non-monetary. These aspects were each examined in turn.

In chapters 2 and 3 the non-monetary individual patient level outcomes were evaluated. Within the UK, NICE (2008) requires that QALYs, a health utility measure, are used as the standard health measure for evaluating interventions and policy making. Furthermore, it

strongly recommends that the EQ-5D instrument with UK population values should be used to evaluate QALYs. However, EQ-5D is a generic measure and is not specifically designed to measure the outcomes of drug misuse patients. It is therefore important to know whether the results from using the EQ-5D measure are supported by the results of measures that are designed specifically for drug misuse patients, and whether they measure the same concepts as each other. For example, if the results from EQ-5D show that a patient's QALYs have improved after receiving the treatment, it is important to know whether or not other specific outcomes such as the patient's dependence have also improved. If the results from EQ-5D reveal the same trends as specific drug misuse measures then EQ-5D may be an adequate generic measure that policy makers can use, however, if it does not, this might suggest that policy makers need to consider specific drug misuse measures as well as, or instead of, EQ-5D.

Chapter 2 examined the evaluation studies that have considered both EQ-5D and other outcome measures together when evaluating drug misuse interventions. These studies each include an economic evaluation that uses EQ-5D to measure QALYs and also include other individual level patient outcomes, such as dependence. The chapter reviewed these evaluation studies to identify which outcomes have been measured and whether or not they have similar trends to EQ-5D. The review only identified 8 evaluation studies. However, in addition to EQ-5D, 16 relevant outcomes measures were identified over 3 different dimensions, which indicates that current researchers consider it important to take into account a wide range of outcomes to evaluate the effectiveness of any given intervention.

As the outcome scores in the different studies were all presented differently, they were first standardised so that they could be compared with one another. With the exception of a few individual measures, the results revealed that EQ-5D generally did not reflect the same trends as most of the other measures across all 3 dimensions of non-monetary outcomes. Indeed there was a wide divergence of trends among the included studies, which reveals that it may be inappropriate to use any single measure to provide a comprehensive evaluation of drug misuse interventions.

Where chapter 2 was concerned with comparing the outcomes measured by EQ-5D and other specific drug misuse measures, chapter 3 was concerned with the concepts measured in the different outcomes. If EQ-5D does not cover the same concepts as the other outcome measures then any similarity between them may only be contingent. The chapter followed the WHO's ICF guideline to categorise the different concepts that can be measured, such as the physical and psychological health of the patients. The guideline identified a wide range of different concepts across 4 different categories.

EQ-5D only covers some of the concepts from 2 of the 4 categories. The other specific drug misuse measures cover some of the concepts from 3 of the categories, including the 2 that are covered by EQ-5D. All of the concepts that are covered in EQ-5D are also covered by most of the other outcome measures, even though there are many concepts covered by the other measures that EQ-5D does not cover. In the 2 categories that EQ-5D covers there is a large extent of content agreement with the other measures, even if they do not cover exactly the same concepts. However, there are also a large number of concepts in other categories that EQ-5D does not cover, which is a major limitation of using EQ-5D as a single outcome measure. In addition, even where EQ-5D and other measures cover the same concepts, it is not clear that patients respond consistently to questions within the same concept, which indicates a wide range of questionnaires may be necessary to capture all of the aspects of patients' responses to any intervention. Taken together, chapters 2 and 3 thus expose the problems with using EQ-5D as a generic outcome measure for drug misuse intervention studies as NICE recommends.

Having considered non-monetary outcomes in the previous two chapters, chapters 4 and 5 turned to examine the individual level monetary outcome. One of the advantages of this approach is that a wide range of monetary dimensions can potentially be evaluated in commensurate units of measurement, which may allow policy makers to make informed decisions about the economic benefit to society. The aim of the chapters was to identify which monetary dimensions have been measured in drug misuse interventions and to evaluate the limitations of the existing studies.

The first aim of chapter 4 was simply to identify the drug misuse studies that have measured social outcomes and the monetary dimensions that have been measured. The chapter followed Godfrey (2006) in identifying the dimensions that it is important to measure for drug misuse policy, which were divided into 2 domains: resources saved and other value created. Given that drug misuse is associated with many social problems, it is important that a wide range of dimensions are included in economic evaluations, as otherwise the figures that policy makers work with might neglect some of the determining factors of the overall monetary impact on society.

The review identified 46 drug misuse studies. Although most of the studies claimed to be conducted from a societal perspective, many of them only measured a limited number of monetary dimensions. Most of the studies considered the monetary dimensions related to the resources that patients use, especially those relating to health care and criminal justice resources. However, many studies neglected the social care resources, which drug misuse patients are likely to use, and only a few of the studies measured all of the dimensions in the resource use domain and any in the other value created domain. None of the studies measured all of the dimensions identified in both domains. This indicates a major limitation when policy makers base their decisions on existing studies, as they do not take into account all of the relevant factors that might impact on the overall monetary outcome of drug misuse interventions, thus the figure that the policy makers work with may be misleading. A further limitation was also identified in the chapter. It is not clear whether specific types of drug misuse patient use more of certain resources than other types of patients, which might influence how policy makers target their interventions.

The aim of chapter 5 was to see whether or not a profile of different types of drug misuse patients could be developed. This would provide valuable information for policy makers as they would then be able to target different types of intervention at different types of drug misuse patient. The chapter used an existing data sample, RESULT (Raistrick et al, 2008), to attempt to develop this profile. The first step was to use a clustering technique to cluster the patients into different groups. These clusters could then be analysed to try to identify

relationships between different patient characteristics and different dimensions of the monetary outcome, or just between different monetary dimensions.

The chapter failed, however, to identify any strong relationships between the different patient characteristics and the different monetary dimensions. It would therefore be difficult to develop a profile based on any single patient characteristic. The reason that this proved to be so difficult was that when the data sample was run through the clustering technique only very few characteristics and monetary dimensions that determined the different clusters were statistically significant. In addition, where there were statistically significant characteristics, they often varied between the different clusters, which meant that the clusters could not be compared with one another to determine the influence of any single patient characteristic. This indicates that the profile of different types of drug misuse patient might be more complicated than expected and very difficult to capture using economic evaluations of the monetary outcome. Although it would be beneficial if policy makers could target the interventions at particular groups of drug misuse patient, the chapter revealed the problems with estimating the monetary outcome for different groups, on which such decisions would have to be based.

One problem with using clinical trials to estimate the individual level outcome is that they do not usually have the resources to follow the patients up over a period of more than 2 years. However, as drug misuse is usually considered to be a chronic condition it is important that policy makers are aware of the long-term effects of the interventions. This is a problem not just in drug misuse policy but in a wider range of health care problems. The only way to estimate the long-term outcomes is by economic modelling. The possibilities and limitations of doing this for drug misuse interventions were explored in chapters 6 and 7, by using the decision analytic model. The decision analytic model identifies the possible pathways of the patients who receive the intervention compared with the pathways of those who do not receive it. This suggests a possible range of outcomes for the patient based on the existing evidence that is entered into the model. The various endpoints of the model can then be compared to assess the effectiveness and the benefits of the intervention.

Chapter 6 reviewed the existing decision analytic models that have been conducted for drug misuse interventions. Having identified the relevant models, their quality was then assessed using the checklist of good practice developed by Phillips and colleagues (2004). This provided the basis for evaluating the limitations of using modelling for drug misuse interventions.

The review identified 16 models and most met the standard of good practice for a decision analytic model in most dimensions. However, a number of limitations were also identified. One of the limitations was that there is a lack of detailed parameters, especially from longitudinal studies, which would render the estimates more plausible and reflect real-world experience. As there are no longitudinal studies available for drug misuse interventions, assumptions have to be based on trials that have only followed up the patients over a few years, which may not reflect their potential longer-term outcomes. Another limitation with the existing models is that the pathways are usually simplified to prevent the model from becoming overly complex, yet this may result in the model misjudging the outcomes and the costs involved. One of the most significant limitations is that although many studies claim to be estimating societal outcomes they do not include a wide range of dimensions of the monetary outcome, for instance none of the models reviewed took into account the social care services cost.

Given the limitations identified with modelling studies in chapter 6, the aim of chapter 7 was to indicate how some of these might be overcome by building a model illustrating the possible outcomes of a drug misuse intervention, while also taking into account the limitations of existing drug misuse studies identified throughout the thesis. To this extent chapter 7 explored the limitations of trying to address the problems highlighted throughout the thesis within a single intervention study. To do this a drug testing in schools model was built, which aimed to examine the potential pathways and benefits to society, by following a hypothetical population of 1000 pupils over the course of their secondary school education. At the endpoint the real life estimates that had been extracted from the literature for drug free, recreational and problematic drug users aged 16 were entered into the model to estimate the long-term outcomes of the drug testing in schools intervention.

To some extent the model proved successful. The model took into account the most important individual level outcomes for the pupils, including their education outcomes and their drug misuse outcomes. By combining the model with real life estimates of the monetary outcome, the study was able to estimate the long-term monetary outcome of the intervention, even though the intervention was only followed over 5 years. This indicates one way of estimating long-term outcomes even when there are no longitudinal studies of drug misuse interventions available.

The drug testing in schools model therefore offers one way of addressing the limitations of existing drug misuse models; however, there were further limitations with doing so. As the drug testing in schools model attempted to take into account a wide range of outcomes it necessarily became more complex. The more complex a model becomes, the more assumptions and simplifications have to be made, which increases the level of uncertainty. The drug testing in schools model also faced one of the main problems encountered by other drug misuse models, which is that there was insufficient real-world evidence to support the parameters and estimates used in the model. A more general problem with drug misuse models was thus revealed. Such models are developed as the resources to follow patients up over a long period of time are rarely available. However, if there is a lack of real-world evidence to support the models then the extent to which their results will reflect real life experiences is uncertain. This problem can only be rectified if the limitations with existing drug misuse intervention studies discussed in earlier chapters are addressed, yet this would require a great deal of time and resources.

8.2 Limitations of research and implications for future research

Although this thesis has attempted to conduct a comprehensive analysis of different economic evaluations of drug misuse interventions, there are a number of limitations to the findings. In many cases these were due to having to work with existing drug misuse intervention studies, which were not always concerned with the same objectives as this thesis. It is worth summarising these limitations by chapter, as they also indicate where future

research should be conducted, before considering a couple of general limitations of the research taken as a whole.

In chapter 2 the focus was on EQ-5D as it is the recommended measure of QALYs by NICE in the UK. However, it is important to recognise that EQ-5D is not the only measure of QALYs and a more comprehensive review should take into account other measures of QALYs, which may well lead to different results. In addition, only studies that measured both EQ-5D and other individual level outcome measures were included in the review, as the objective was to compare EQ-5D with those measures. However, there are many outcome measures that have not been studied alongside EQ-5D and the results of the chapter therefore do not indicate whether or not EQ-5D has similar trends to these outcome measures. A final limitation was that the standardised mean score that was used to examine the trends of EQ-5D was extracted from existing research. As a result, it was impossible to calculate the variance across the data, which means there could have been a lot of outlying results that were not taken into account. It would have been better to use the Z score, which takes into account standard deviation, but this was not possible as the individual patient scores were unavailable.

In chapter 3 the WHO's ICF was used to map the concepts between EQ-5D and other outcome measures. ICF is a generic outline developed for any concepts related to individual well-being, however, there had not previously been an ICF mapping study for drug misuse specific outcome measures and so this had to be conducted for the first time. Future research should try to identify the concepts in drug misuse specific outcome measures to map onto ICF, which could then be compared with the mapping exercise conducted in the chapter.

The mapping found that most of the concepts covered by EQ-5D were also covered by other drug misuse specific outcome measures but not vice versa. There are 2 limitations that follow from this. The first is that even where there are overlapping concepts, this only indicates a probable cause of the correlation. However, greater analysis would be required to prove that the correlation was certainly not contingent. In addition, a more sophisticated analysis, such as factor analysis, might be required to examine the relationship between the non-overlapping

concepts; those covered by other outcome measures but not EQ-5D. A final limitation of chapter 3 was that where in other fields a content comparison of the outcome measures used a gold standard, this is not available for drug misuse studies. There is therefore no accepted standard with which the content of EQ-5D and other outcome measures can be compared.

In chapter 4 the guideline by Godfrey (2006) was used to identify the different dimensions of the monetary outcome that should be measured in economic evaluations of drug misuse interventions. However, there is no common agreement about how the individual dimensions are calculated. For example, for health care resource saved, some studies might take into account the costs of the prescriptions whereas other might not. This could distort the overall monetary outcome when comparing interventions. It is also worth stressing that although studies were reviewed from different countries, it proves difficult to compare these with one another as the drug misuse policies vary between countries and thus the societal cost will be different for the same type of drug misuse patient in different countries.

In chapter 5 a clustering technique was used to cluster the patients into different groups based on the available characteristics from the RESULT sample used. However, the clustering results would have varied greatly if different characteristics had been taken into consideration. The results therefore rested on assumptions about which characteristics might prove to be the most important. A further limitation of the RESULT sample is that it is an original data set, which only considers the intervention over a 6 month follow-up period and the patients do not begin receiving the intervention at the same time. All these factors might have contributed to the complexity of patients' characteristics and the difficulty of identifying statistically significant characteristics across the clusters.

One of the limitations of chapter 6 was simply the lack of modelling studies identified by the review, which made it difficult to assess whether modelling is a satisfactory approach for drug misuse intervention studies. Although the checklist designed by Phillips and colleagues (2004) was used to assess the quality of the decision analytic models reviewed, it remains difficult to conclude whether or not models are realistic as there is no empirical data of real-

world experience with which they can be compared. If the model is not realistic then policy makers may be misled by the findings of the modelling study.

There are a number of limitations with the drug testing in schools model that was developed in chapter 7. These were discussed in detail in the chapter and some of the problems have been summarised in section 8.1. However, there were also limitations with the implications of the modelling study for the objectives of the thesis. The drug testing in schools model was developed to try to overcome the limitations within existing drug misuse intervention studies identified throughout the thesis. However, the problems that were addressed in the drug testing in schools model would probably not be of application to other drug misuse intervention studies, especially treatment studies. Prevention studies are primarily concerned with preventing individuals from becoming drug users, whereas treatment studies are aimed at changing the behaviour of existing drug misuse patients. Where the deterrent effect of drug testing in schools will only apply during the period of the intervention, treatment studies would expect to affect the behaviour and health status of the drug misuse patient beyond the duration of the intervention. Such interventions would therefore not be able to use real-world estimates to predict the long-term societal costs at the end of the intervention period. Even though the drug testing in schools model overcomes some of the shortcomings identified with existing studies, it therefore fails to provide a model that could suitably be adopted for other drug misuse intervention studies.

In addition to the limitations of the individual chapters, there are more general limitations of the thesis as a whole that are worth indicating. This thesis has only examined economic evaluation studies and has focused on individual level interventions rather than population level interventions, such as drug legalisation. In addition, there are other considerations that policy makers might want to consider when framing policy that are not covered by economic evaluations, such as ethical considerations.

8.3 Conclusions, discussion and the implications for policy makers

This thesis has provided an overview of the existing methods of economic evaluation of drug misuse interventions and identified many of the shortcomings and limitations within existing studies. The main problems highlighted in the thesis may be broadly summarised in two points. The first is simply that only a relatively small number of economic evaluations of drug misuse interventions have been carried out to date. The second is that these studies have many limitations, especially regarding the lack of studies that follow patients up over a long period of time. It is important to recognise that the limitations of these studies are not simply criticisms of them, but rather that they reflect the complexity and difficulty of conducting economic evaluations in this field.

Given the wide range of effects that drug misuse has on society many different outcomes should be measured in economic evaluations, and furthermore there are many dimensions that may determine the monetary outcome. However, this being the case, to provide a comprehensive evaluation of the benefits and drawbacks of any given intervention proves particularly difficult, as not only the benefits to the individual drug user but also the wider impact on society must be considered. It is often simply unfeasible to take into account all of these considerations in any given study. In addition, the outcomes for drug misuse patients prove especially impractical to measure. Drug misuse is considered to be a chronic condition, however, given the characteristics of drug misuse patients it is often unfeasible to follow them up over a long enough period of time that would be necessary to estimate the realistic societal outcomes.

In the studies that have been examined different perspectives have been adopted and it is important to recognise that these may be in tension with one another, for example research can be conducted from the perspective of the health care system or the societal perspective. This is especially important to bear in mind in states like the UK where the priorities are often set by the NHS, as it cannot be assumed that the NHS priorities reflect the best outcomes when considered from the wider societal perspective.

In addition to identifying the limitations with existing research, this thesis has attempted to draw out recommendations for policy makers and future research. However, there has only

been mixed success in doing this. One of the strongest conclusions relates to the use of EQ-5D as a generic outcome measure as recommended by NICE in the UK. Chapters 2 and 3 have demonstrated that in many respects EQ-5D is inadequate at reflecting the trends and measuring the concepts of other drug misuse specific measures. If EQ-5D is used as the only outcome measure in drug misuse intervention studies then many important drug-related outcomes may be neglected. However, other chapters were unable to arrive at such strong conclusions. For example, the attempt to develop a patient characteristic profile of the different monetary outcomes in chapter 5 proved largely unsuccessful. Although it would be beneficial for policy makers to target interventions at specific types of drug misuse patient, the findings have only highlighted the difficulties with identifying the relevant characteristics and indicate the complexity of characteristics among drug misuse patients.

If there is a lesson to be drawn for policy makers from this thesis, it is to approach the existing studies with caution. In many cases there is insufficient evidence or data to provide a comprehensive economic evaluation of the different drug misuse interventions, and if policy makers adopt the results from these without bearing in mind the limitations they may be misled. The importance of this thesis, then, is primarily in highlighting those limitations. In addition, policy makers need to be able to justify their priorities when considering drug misuse interventions. In some cases the intervention might have different effects on different individual level outcomes. This is well illustrated in the drug testing in schools model, where it was estimated that if the programme was adopted then the drug population among 16 year olds would decrease, but the school drop-out rate would increase. In such circumstances policy makers have to decide which outcome they want to prioritise. This is indicative of a wider problem that different outcomes might conflict with one another, and the intervention that is in the best interest of the individual drug misuse patient might not be considered to be in the best interest of society more generally.

This thesis has exposed many of the limitations of measuring outcomes in economic evaluations of drug misuse interventions and identified the problems with conducting such studies. It is important that policy makers are aware of these limitations when framing drug policy. The thesis has attempted to identify relationships between different types of outcome

measures that might help to overcome the existing limitations. However, at best the relationships identified have proved tentative, and at worst no such relationships have been identified. This only goes to indicate further the complexity of designing adequate drug misuse interventions and the problems that face future research. It is certainly important to be aware of the limitations of existing studies, however, the somewhat disquieting conclusion of this thesis, is that even when the limitations are known it still proves very difficult to design evaluations and interventions that can take them into account.

Appendices

Appendix 1 Description of outcome measure

Brief Symptom Inventory (BSI)

BSI, a shorter version of the Symptom Checklist-90, was developed by Derogatis and Melisaratos (1983). It is a validated questionnaire and includes 53 items that assess individuals' psychological status. It consists of 9 dimensions: somatisation, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism. The rating of the individuals' psychological status ranges between 0 and 4, where 4 is the worst status. It produces 3 global indices: global severity index, positive symptom distress index, and positive symptom total. The global severity index is the average rating of all of the 53 items. The positive symptom distress index is the average rating of all of the symptoms complained of (items rated higher than 0). The positive symptom total is the number of symptoms complained about regarding individuals' psychological status.

Composite International Diagnostic Interview (CIDI)

Developed by WHO (WHO, 1990), CIDI is an outcome measure that covers 41 different dimensions related to individuals' well-being, such as depression, mania, panic disorder, phobia, anxiety disorder, suicidality, personality, alcohol and illegal substance use, chronic conditions, tobacco use, eating disorders, obsessive compulsive disorder, psychosis, employment, finances, and childhood. Each dimension covers questions related to the specific life area of the participants. Only the illegal substance use dimension of CIDI is used in the included studies for this thesis. The CIDI illegal substance use section consists of 65 questions related to individuals' past and current severity of addiction, functioning status related to substance misuse problems and consumption of substance. Individuals need to answer the questions to indicate their history regarding the specific substance misuse related problems, the severity of the problems and the frequency of the problems.

Clinical Outcomes in Routine Evaluation (CORE)

The outcome measure, CORE, discussed in this thesis is CORE Outcome Measure (CORE-OM). CORE-OM is a validated self-completed outcome measure which was developed in 1998 (Barkham et al, 1998; Evans et al, 2000; Evans et al, 2002). It consists of 34 items related to individuals' psychological health status in 4 dimensions: well-being, symptoms, functioning, and risk. The score ranges from 0 to 4, where 4 indicates that individuals experience the specified psychological problems all of the time. To calculate the overall CORE score of the individuals the mean item score is multiplied by 10.

European Addiction Severity Index (EuropASI)

EuropASI, developed by Kokkevi and Hartgers (1995), is the modified version of the original ASI (McLellan et al, 1980). EuropASI is a validated semi-structured interview among the substance misuse population in Europe. It covers a wide range of dimensions related to individuals' current problems regarding substance misuse: medical, employment and education, alcohol use, drug use, family and social relations, forensic and legal, and psychiatric (Koeter and Hartgers, 1997). The composite scores from each domain are derived from the key questionnaire items related to recent problems and severity. The composite score ranges from 0 to 1, where the higher score indicates more problems and greater severity.

Hospital Anxiety and Depression scale (HADS)

Developed by Zigmond and Snaith (1983), HADS is a specific validated questionnaire that assesses individuals' psychological health status during their hospitalisation. Individuals are asked how often they have experienced the 14 different specified states of depression and anxiety. The overall score ranges from 0 to 42. Individuals who scored 0-7 are classified as non-cases and those who scored 8-10 are classified as borderline cases. Individuals who scored more than 11 are classified as cases with depression and anxiety.

Injecting Drug User Quality of Life Scale (IDUQoL)

IDUQoL (Brogly et al, 2003; Hubley, Russell and Palepu, 2005) is a validated questionnaire designed to assess both the health and non-health related quality of life of injecting drug users. Based on the WHO-QoL definition of quality of life, it consists of 21 life area questions: being useful, drugs, drug treatment, education, family, feeling good, friends, harm

reduction, health, health care, housing, independence, leisure activities, money, neighbourhood safety, partners, resources in the community, sex, spirituality, transportation and treatment by others. Each question is presented on a picture card with a description. Each area is given a score weighting its importance by the participant by placing small plastic chips. The score ranges from 0 to 3, where 0 is not at all important. It also measures the satisfaction score for each area given by the participant and the score ranges from 1 to 7, where 7 means very satisfied. The overall quality of life score is estimated based on the importance weighting and the satisfaction score of each area.

Injecting Risk Questionnaire (IRQ)

Developed by Stimson and colleagues (1998), IRQ consists of 18 questions and is a validated questionnaire that assesses individuals' retrospective (last 4 weeks) injecting behaviour and sharing risk. Individuals are asked how often they have experienced the specified risky injecting behaviours, such as sharing equipment or the number of people they share equipment with, based on a 4-point scale.

Leeds Dependence Questionnaire (LDQ)

LDQ, developed by Raistrick and colleagues (1994), is a 10-item validated questionnaire that is designed to assess individuals' substance dependence status. Individuals are asked about how frequently they have experienced the specified description related to drug misuse, based on a 4-point scale. The overall LDQ score ranges from 0 to 30, where 30 represents those who have the highest dependence severity.

Manchester Short Assessment of Quality of Life (MANSA)

MANSA, derived from the Lancashire Quality of Life Profile (Oliver, 1991-1992), is a 16-item validated questionnaire designed to assess quality of life among patients with mental illness (Priebe et al, 1999). It is a shorter and modified version of the Lancashire Quality of Life Profile. It consists of 4 YES/NO questions about relationships with friends and criminal activity, and 12 questions about satisfaction of life, job, financial situation, friendships, leisure activities, accommodation, personal safety, people lived with, sex life, family

relationships, physical health, and mental health. The score for satisfaction ranges from 1 to 7, where 1 represents the worst state.

Maudsley Addiction Profile (MAP)

MAP, developed by Marsden and colleagues (1998), is a validated questionnaire to assess the outcomes for substance misuse patients. It consists of 4 dimensions: substance use, high risk behaviour, physical and psychological health, and personal/ social functioning. In the substance use domain, the results are presented as frequency of substance use in the past month, and as the total amount of substance consumed across the day. In the high risk behaviour domain, the results are presented as the frequency of risky injecting behaviour and risky sexual behaviour. The physical and psychological health domain measures the frequency of problems experienced in 10 items related to physical health problems and 10 items related to anxiety and depression. The total composite score of physical and psychological health each ranges from 0 to 40, where 40 represents the worst health status. The personal/social functioning domain measures the frequency of contacts and conflicts with family and friends, days of being in employment/unemployment, and the estimated frequency of crime committed.

Opiate Treatment Index (OTI)

Developed by Darke and colleagues (1991b), OTI is a validated structured interview designed to measure the effectiveness of drug treatments. OTI consists of a wide range of dimensions: drug use, HIV risk-taking behaviour, social functioning, criminality, health status and psychological functioning. Drug use measure is derived from the calculation of a quantity/frequency estimate of drug use (Q score), and the higher score indicates greater drug use consumption. OTI produces the composite scores in the other dimensions, based on the questions about frequency of the specified incidents. In the dimensions of HIV risk-taking behaviour, social functioning dimension, criminality and psychological function, the maximum scores are 55, 48, 16 and 28, respectively. The higher scores indicate that individuals have more problems in these areas. In the health status domain, the composite score is derived from individuals' responses to the questions about whether or not they have

the listed symptoms/diseases or not. The highest score for a female is 50 and 48 for a male and the higher score indicates the worse health status.

HIV Risk-Taking Behaviour Scale (RTBS)

Developed by Darke and colleagues (1991a), RTBS is a validated questionnaire to measure the HIV risk behaviours in 2 dimensions: injecting risk and sexual risk. The highest composite score attainable for injecting risk behaviour is 30, and for sexual risk behaviour it is 25. The highest overall score is 55, and a higher score indicates a higher incidence of risk behaviour.

Symptom Checklist-90 (SCL-90)

SCL-90, developed by Derogatis and Cleary (1977), is a 90-item validated self-completed questionnaire that assesses the individuals' psychological health status. As with the shorter version, BSI, SCL-90 consists of 9 dimensions of psychological symptoms. The rating scale for each item is from 0 to 4, where 4 represents the worst status. It produces the same 3 global indices as BSI, where the global severity index is the average rating of all 90 items.

Severity of Dependence Scale (SDS)

Developed by Gossop and colleagues (1995), SDS is a validated 5-item questionnaire designed to assess the degree of drug dependence of individuals. The rating scale of each item is from 0 to 3 and the total score ranges from 0 to 15. The highest scores indicate the highest levels of dependence severity.

SF-12 and SF-36

SF-36 (Ware et al, 1993; Ware, Kosinski and Keller, 1994) is a validated questionnaire that assesses individuals' health-related quality of life. It consists of 8 dimensions: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. It produces 2 composite scores: MCS (mental component summary) and PCS (physical component summary) and the scores of MCS and PCS each range from 0 to 100. Similarly, SF-12, the shorter version of SF-36, also consists of questions

within the 8 dimensions and produces the MCS and PCS scores (Ware, Kosinski and Keller, 1995 and 1996).

Social Satisfaction Questionnaire (SSQ)

SSQ (Raistrick et al, 2007; Tober et al, 2000) is a validated questionnaire, which is designed to assess individuals' satisfaction towards different areas related to social integrations, such as employment and social relationships. SSQ consist of 8 questions and individuals are asked about their degree of satisfaction towards to the specified area. SSQ scores range from 0 to 24, where 24 represents that the individuals have the highest degree of satisfaction towards the specified areas of social integration.

Timeline Follow Back (TLFB)

TLFB (Sobell and Sobell, 1996; Sobell et al, 1996) is a validated questionnaire designed to estimate individuals' consumption of different substances. The overall scores are presented as the percentage of days being abstinent of the specific drugs (PDA).

WHO's Disability Assessment Schedules II (WHODAS II)

WHODAS II (WHO, 2000), is a validated questionnaire designed to assess individuals' health status. The version discussed in this thesis is the 12-item WHODAS II. It consists of questions from 6 dimensions: understanding and communicating, getting around, self care, getting along with people, life activities, and participation in society. The score of each item ranges from 1 to 5, where 1 indicates that individuals do not experience any difficulty for the specified health-related motilities and social functioning

Appendix 2 Kappa coefficient of inter-observer agreement

Appendix 2.1 Kappa coefficient of inter-observer agreement in the outcome measures included in chapter 2

	component	Chapter 1st level	2nd level	3rd level	4th level
EQ-5D	1.00**	1.00**	0.79**		
BSI	0.27**	0.93**	0.80**	1.00**	1.00
CIDI	0.92**	0.96**	0.99**	0.95**	
EuropASI	0.60**	0.95**	0.98**	1.00**	
HADS	0.62**	1.00**	0.55**	0.33	
IDUQoL	0.71**	0.94**	0.94**	1.00**	
IRQ	1.00**	0.04	0.40		
MANSA	0.61**	1.00**	0.86**	1.00**	
MAP	0.46**	1.00**	0.81**	0.80**	1.00*
OTI	0.60**	0.81**	0.73**	1.00**	1.00
RTBS	1.00**	0.46**	1.00**	1.00**	
SCL-90	0.26**	0.78**	0.78**	0.95**	1.00*
SDS	1.00**	1.00**	1.00**	0.71*	
SF-12	0.89**	1.00**	1.00**	1.00**	
SF-36	0.91**	1.00**	0.95**	1.00**	
TLFB	0.85**	1.00**	1.00**	1.00**	
WHODAS II	0.66**	0.94**	0.87**	1.00**	
Overall	0.75**	0.89**	0.91**	0.97**	1.00**

*: $p < 0.05$

** : $p < 0.001$

Appendix 2.2 Kappa coefficient of inter-observer agreement in RESULT

	component	Chapter 1st level	2nd level	3rd level	4th level
CORE	0.35**	0.86**	0.61**	0.77*	
EQ-5D	1.00**	1.00**	0.79**		
LDQ	0.51**	0.44*	0.69*	1.00	
SCL	1.00**	1.00**	1.00**	0.79**	1.00*
SSQ	0.64*	1.00**	0.77**	0.84*	
Overall	0.61**	0.90**	0.81**	0.80**	1.00*

*: $p < 0.05$

** : $p < 0.001$

Appendix 3 ICF mapping results

Appendix 3.1 ICF mapping results for outcome measures in the continuation of illegal substance use and abuse dimension

Appendix 3.1.1 ICF mapping results for outcome measures in the continuation of illegal substance use and abuse dimension: body functions component

ICF category	EQ-5D	CIDI	EuropASI	EuropASI Drug	IDUQoL	IRQ	OTI	OTI-drug	RTBS	SDS	TLFB-cannabis	TLFB-heroin, methadone
b126 Temperament and personality functions			1				1					
b1262 Conscientiousness							1					
b1263 Psychic stability							3					
b1265 Optimism							1					
b1266 Confidence					1		2					
b1267 Trustworthiness							2					
b1300 Energy level							1					
b1303 Craving		3								1		
b1304 Impulse control		6	1							2		
b134 Sleep functions			1	1								
b1340 Amount of sleep			1	1			1					
b1342 Maintenance of sleep							1					
b140 Attention functions			2									
b1442 Retrieval of memory		4	2									
b152 Emotional functions	1	3	9	1			3			2		
b156 Perceptual			1									

functions												
b160 Thought functions			9	1								
b1603 Control of thought			1									
b164 High-level cognitive function			6	1								
b280 Sensation of pain	1											
b28010 Pain in head and neck							2					
b5500 Body temperature							1					
Total ICF concepts	2	16	34	5	1	0	19	0	0	5	0	0

Appendix 3.1.2 ICF mapping results for outcome measures in the continuation of illegal substance use and abuse dimension: activities and participation component

ICF category	EQ-5D	CIDI	EuropASI	EuropASI Drug	IDUQoL	IRQ	OTI	OTI-drug	RTBS	SDS	TLFB-cannabis	TLFB-heroin, methadone
d177 Making decisions					1		1					
d2102 Undertaking a single task independently					1							
d2202 Undertaking multiple tasks independently					1							
d230 Carrying out daily routine	1	2					1					
d240 Handling stress and other psychological demands							1					
d2400 Handling responsibilities		1					2					
d2401 Handling stress							1					
d350 Conversation		4										
d355 Discussion		1										
d4 Mobility	1											
d450 Walking	1											
d470 Using transportation					1							
d475 Driving			1									
d4750 Driving human-powered transportation		1										
d4751 Driving motorized vehicles		1	2									
d498 Mobility, other specified-confined to bed	1											
d5 Self-care	2											

d510 Washing oneself	1											
d540 Dressing	1											
d550 Eating			1									
d570 Looking after one's health		1	1									
d5702 Maintaining one's health			3	3		12			9			
d620 Acquisition of goods and services			1	1							1	2
d6200 Shopping		1										
d640 Doing housework	1	1										
d6402 Cleaning living area		1										
d660 Assisting others			1									
d710 Basic interpersonal interactions			2		1							
d720 Complex interpersonal interactions			2		1	4	1					
d7200 Forming relationships		1										
d730 Relating with strangers			1									
d740 Formal relationships			1									
d750 Informal social relationships		1	4									
d7500 Informal relationships with friends			3									
d7501 Informal relationships with neighbours			1									
d7503 Informal relationships with co-inhabitants			3									
d760 Family relationships	1	2	5		1							

d7600 Parent-child relationships		1	2		1							
d7601 Child-parent relationships		1	4		1							
d7602 Sibling relationships		1	2		1							
d7603 Extended family relationships			1									
d770 Intimate relationships			3									
d7701 Spousal relationships			3		1							
d7702 Sexual relationships			2		1	1		5				
d779 Particular interpersonal relationships, other specified and unspecified			1			1						
d810 Informal education					1							
d820 School education		1	1		1							
d830 Higher education			1									
d839 Education, other specified and unspecified-study	1		1		1							
d850 Remunerative employment	1	4	7		1							
d855 Non-remunerative employment			2		1							
d860 Basic economic transactions			2				1					
d865 Complex economic transactions			1				1					
d870 Economic self-sufficiency					1							

d8700 Personal economic resources			7									
d8701 Public economic entitlements			5									
d910 Community life		1										
d920 Recreation and leisure	1				1							
d9201 Sports		1										
d9205 Socializing		1	2									
d930 Religion and spirituality					1							
d940 Human rights					1							
Total ICF concepts	13	29	79	4	21	18	9	0	14	0	1	2

**Appendix 3.1.3 ICF mapping results for outcome measures in the continuation of illegal substance use and abuse dimension:
environmental factors component**

ICF category	EQ-5D	CIDI	EuropASI	EuropASI Drug	IDUQoL	IRQ	OTI	OTI-drug	RTBS	SDS	TLFB-cannabis	TLFB-heroin, methadone
e1100 Food			17	13			5	5				
e1101 Drugs		72	45	37	1		51	50		3	3	7
e165 Assets			1				1					
e1651 Tangible assets					1							
e310 Immediate family			7									
e315 Extended family			3									
e320 Friends			3		1	1						
e325 Acquaintances, peers, colleagues, neighbours and community members			2			1						
e345 Strangers						1						
e355 Health professionals		4										
e540 Transportation services, systems and policies					1							
e5458 Civil protection services, systems and policies, other specified			8				4					
e5500 Legal services			12									
e570 Social security services, systems and policies			1									
e5700 Social security services			1		1							
e5750 General social support services		2	2									

e5800 Health services		5	11	5	1							
e590 Labour and employment services, systems and policies			2									
Total ICF concepts	0	83	115	55	6	3	61	55	0	3	3	7

Appendix 3.1.4 ICF mapping results for outcome measures in the continuation of illegal substance use and abuse dimension: concepts not covered in ICF

ICF category	EQ-5D	CIDI	EuropASI	EuropASI Drug	IDUQoL	IRQ	OTI	OTI-drug	RTBS	SDS	TLFB-cannabis	TLFB-heroin, methadone
hc-AIDS			1									
hc-chronic medical problems			1									
hc-health problems			1									
hc-hepatitis B			1									
hc-hepatitis-C			1									
hc-HIV			2									
hc-medical problems			4									
hc-medical problems (o.d.'s, d.t.'s)			1									
hc-pelvic inflammatory disease			1									
hc-tuberculosis			1									
hc-venereal diseases			1									
nc-abuse			3									
nc-conflict			1									
nc- neighbourhood safety					1							
nc-physical abuse			1									
nc-sexual abuse			1									
nc-suicide			4				4					
nd-gh					1		2					
nd-mh			5		1							
nd-period of consumption							11	11				
nd-QoL			1									
nd-satisfaction			3				1					
Total ICF concepts	0	0	34	0	3	0	18	11	0	0	0	0

Appendix 3.2 ICF mapping results for outcome measures in the improvement of medical conditions dimension

Appendix 3.2.1 ICF mapping results for outcome measures in the improvement of medical conditions dimension: body functions component

ICF category	EQ-5D	BSI	EuropASI Medical	EuropASI Psychiatric	HADS	IDUQoL	MANSA	MAP-HSS	OTI- psychological health	SCL-90	SF-12	SF-36	WHODASII
b1 Mental functions													1
b126 Temperament and personality functions				1					1	1			
b1262 Conscientiousness									1				
b1263 Psychic stability		2			3				3	3		1	
b1265 Optimism									1	1			
b1266 Confidence		1				1			2	1			
b1267 Trustworthiness		1							2	1			
b1300 Energy level					1				1	1	1	4	2
b1301 Motivation		1								1			
b1302 Appetite		1			1			1		1			
b1304 Impulse control		3		1						3			
b1340 Amount of sleep									1	1			
b1341 Onset of sleep		1								1			

b1342 Maintenance of sleep					1				1				
b1343 Quality of sleep					1					1			
b140 Attention functions		1		2						1			
b1400 Sustaining attention		1								1			1
b1442 Retrieval of memory		1		2						1			
b152 Emotional functions	1	18		5	5				3	29	4	7	1
b156 Perceptual functions				1									
b1560 Auditory perception										1			
b160 Thought functions		2	1	4	1					1			
b1602 Content of thought		3								4			
b1603 Control of thought		1		1	1					6			
b164 High-level cognitive function			1	1									
b2401 Dizziness		1								2			
b265 Touch function		1						1		1			
b280 Sensation of pain	1										1	2	1
b2800 Generalized pain								1					
b28010 Pain in head and neck									2	1			

b28011 Pain in chest		1						1		1			
b28012 Pain in stomach or abdomen								1					
b28013 Pain in back										1			
b28016 Pain in joints								1					
b340 Alternative vocalization functions										1			
b4100 Heart rate										1			
b4101 Heart rhythm					1								
b440 Respiration functions								1					
b4401 Respiratory rhythm		1								1			
b4552 Fatiguability								1					
b460 Sensations associated with cardiovascular and respiratory functions										1			
b5350 Sensation of nausea		1						1		1			
b5500 Body temperature		1							1	1			
b640 Sexual functions										1			
b6400 Functions										1			

of sexual arousal phase													
b730 Muscle power functions		1								1			
b7301 Power of muscles of one limb										1			
b7651 Tremor								1		1			
b780 Sensations related to muscles and movement functions										1			
Total ICF concepts	2	44	2	18	15	1	0	10	19	78	6	14	6

Appendix 3.2.2 ICF mapping results for outcome measures in the improvement of medical conditions dimension: activities and participation component

ICF category	EQ-5D	BSI	EuropASI Medical	EuropASI Psychiatric	HADS	IDUQoL	MANSA	MAP-HSS	OTI- psychological health	SCL-90	SF-12	SF-36	WHODASII
d Activities and Participation											1		
d155 Acquiring skills													1
d177 Making decisions		1				1			1	1			
d2 General tasks and demands										2			
d2102 Undertaking a single task independently						1							
d2202 Undertaking multiple tasks independently						1							
d230 Carrying out daily routine	1				1				1		2	3	5
d2303 Managing one's own activity level													2
d240 Handling stress and									1	2			

other psychological demands													
d2400 Handling responsibilities									2				
d2401 Handling stress									1				
d355 Discussion		1								1			
d4 Mobility	1												
d4102 Kneeling												1	
d4104 Standing													1
d4105 Bending												1	
d4154 Maintaining a standing position													1
d430 Lifting and carrying objects											1	2	
d4300 Lifting												1	
d4451 Pushing											1		
d4454 Throwing										1			
d450 Walking	1												
d4500 Walking short distances												2	
d4501												1	1

Walking long distances													
d4551 Climbing										1	2		
d4552 Running											1		
d470 Using transportation					1				1				
d498 Mobility, other specified-confined to bed	1												
d5 Self-care	2												
d510 Washing oneself	1										1		
d5101 Washing whole body													1
d540 Dressing	1										1		1
d550 Eating				1					2				
d560 Drinking									1				
d570 Looking after one's health									2				1
d5702 Maintaining one's health													1
d6200 Shopping									1		1		
d640 Doing housework	1									1	2		1
d660 Assisting others											1		

d710 Basic interpersonal interactions						1							
d7100 Respect and warmth in relationships		2								2			
d7102 Tolerance in relationships		1								1			
d7103 Criticism in relationships		1								2			
d7105 Physical contact in relationships		1								1			
d720 Complex interpersonal interactions		2				1				3			
d7203 Interacting according to social rules		1								1			
d730 Relating with strangers													1
d7500 Informal relationships with friends							1						1
d7503 Informal relationships with co-inhabitants							3						

d760 Family relationships	1					1	1						
d7600 Parent-child relationships						1	1						
d7601 Child-parent relationships						1							
d7602 Sibling relationships						1							
d7701 Spousal relationships						1							
d7702 Sexual relationships						1	1						
d810 Informal education						1							
d820 School education						1							
d839 Education, other specified and unspecified-study	1					1	1						
d840 Apprenticeship (work preparation)							1						
d850 Remunerative employment	1					1	1				3	4	
d855 Non-remunerative employment						1	1						

d859 Work and employment, other specified and unspecified													2
d870 Economic self-sufficiency						1	1						
d8701 Public economic entitlements				1			1						
d9 Community, social and civic life					1								
d910 Community life													1
d920 Recreation and leisure	1					1	1				1	1	1
d9201 Sports											1	2	
d9202 Arts and culture										1		1	
d9204 Hobbies												1	
d9205 Socializing							1				1	2	
d930 Religion and spirituality						1							1
d940 Human rights						1							
Total ICF concepts	13	10	0	2	2	21	15	0	6	25	13	31	23

Appendix 3.2.3 ICF mapping results for outcome measures in the improvement of medical conditions dimension: environmental factors component

ICF category	EQ-5D	BSI	EuropASI Medical	EuropASI Psychiatric	HADS	IDUQoL	MANSA	MAP-HSS	OTI-psychological health	SCL-90	SF-12	SF-36	WHODASII
e1100 Food				1									1
e1101 Drugs			1	1		1							1
e1200 General products and technology for personal indoor and outdoor mobility and transportation										1			
e1650 Financial assets							1						
e1651 Tangible assets						1	2						
e320 Friends						1	1						
e540 Transportation services, systems and policies						1							
e570 Social security services, systems and policies				1									
e5700 Social			1			1							

security services													
e5800 Health services			4	2		1							
Total ICF concepts	0	0	6	5	0	6	4	0	0	1	0	0	2

Appendix 3.2.4 ICF mapping results for outcome measures in the improvement of medical conditions dimension: concepts not covered in ICF

ICF category	EQ-5D	BSI	EuropASI Medical	EuropASI Psychiatric	HADS	IDUQoL	MANSA	MAP-HSS	OTI- psychological health	SCL-90	SF-12	SF-36	WHODASII
hc												1	
hc-AIDS			1										
hc-chronic medical problems			1										
hc-health problems			1										
hc-hepatitis B			1										
hc-hepatitis-C			1										
hc-HIV			2										
hc-medical problems			4										
hc-medical problems (o.d.'s, d.t.'s)			1										
hc-pelvic inflammatory disease			1										
hc-tuberculosis			1										
hc-venereal diseases			1										
nc-life													2
nc-neighbourhood safety						1							
nc-physical				1									

abuse													
nc-safety							1						
nc-sexual abuse				1									
nc-suicide		2		4	1				4	2			
nc-violence							1						
nd-blame oneself										1			
nd-blame others										1			
nd-gh						1	1		2		3	8	2
nd-guilt		1											
nd-mh				4		1	1						
nd-moderate activities												1	
nd-QoL			1				1						
nd-satisfaction							1		1				
nd-vigorous activities												1	
pf-crime							1						
Total ICF concepts	0	3	16	10	1	3	7	0	7	4	3	11	4

Appendix 3.3 ICF mapping results for outcome measures in the social integration dimension

Appendix 3.3.1 ICF mapping results for outcome measures in the social integration dimension: body functions component

ICF category	EQ-5D	CIDI	EuropASI Employment	EuropASI Family/Other	EuropASI Legal	IDUQoL	MANSA	MAP-crime	OTI-crime
b1266 Confidence						1			
b1303 Craving		3							
b1304 Impulse control		6							
b1442 Retrieval of memory		4							
b152 Emotional functions	1	3		3					
b160 Thought functions			1	1	1				
b164 High-level cognitive function			1	1	1				
b280 Sensation of pain	1								
Total ICF concepts	2	16	2	5	2	1	0	0	0

Appendix 3.3.2 ICF mapping results for outcome measures in the social integration dimension: activities and participation component

ICF category	EQ-5D	CIDI	EuropASI Employment	EuropASI Family/Other	EuropASI Legal	IDUQoL	MANSA	MAP-crime	OTI-crime
d177 Making decisions						1			
d2102 Undertaking a single task independently						1			
d2202 Undertaking multiple tasks independently						1			
d230 Carrying out daily routine	1	2							
d2400 Handling responsibilities		1							
d350 Conversation		4							
d355 Discussion		1							
d4 Mobility	1								
d450 Walking	1								
d470 Using transportation						1			
d475 Driving			1						
d4750 Driving human-powered transportation		1							
d4751 Driving motorized vehicles		1			2				
d498 Mobility, other specified-confined to bed	1								
d5 Self-care	2								
d510 Washing oneself	1								
d540 Dressing	1								
d570 Looking after one's health		1	1						
d6200 Shopping		1							
d640 Doing housework	1	1							
d6402 Cleaning living area		1							
d660 Assisting others			1						
d710 Basic interpersonal interactions				2		1			
d720 Complex interpersonal interactions				1	1	1			1

d7200 Forming relationships		1							
d730 Relating with strangers				1					
d740 Formal relationships				1					
d750 Informal social relationships		1		4					
d7500 Informal relationships with friends				3			1		
d7501 Informal relationships with neighbours				1					
d7503 Informal relationships with co-inhabitants				3			3		
d760 Family relationships	1	2		5		1	1		
d7600 Parent-child relationships		1		2		1	1		
d7601 Child-parent relationships		1		4		1			
d7602 Sibling relationships		1		2		1			
d7603 Extended family relationships				1					
d770 Intimate relationships				3					
d7701 Spousal relationships				3		1			
d7702 Sexual relationships			1		1	1	1		
d779 Particular interpersonal relationships, other specified and unspecified				1					
d810 Informal education						1			
d820 School education		1	1			1			
d830 Higher education			1						
d839 Education, other specified and unspecified-study	1		1			1	1		
d840 Apprenticeship (work preparation)							1		
d850 Remunerative employment	1	4	7			1	1		
d855 Non-remunerative employment			2			1	1		
d860 Basic economic transactions					2				1

d865 Complex economic transactions					1			1	1
d870 Economic self-sufficiency						1	1		
d8700 Personal economic resources			7						
d8701 Public economic entitlements			4				1		
d910 Community life		1							
d920 Recreation and leisure	1					1	1		
d9201 Sports		1							
d9205 Socializing		1		2			1		
d930 Religion and spirituality						1			
d940 Human rights						1			
Total ICF concepts	13	29	27	39	7	21	15	1	3

Appendix 3.3.3 ICF mapping results for outcome measures in the social integration dimension: environmental factors component

ICF category	EQ-5D	CIDI	EuropASI Employment	EuropASI Family/Other	EuropASI Legal	IDUQoL	MANSA	MAP-crime	OTI-crime
e1100 Food				3					
e1101 Drugs		72		3	3	1		1	1
e165 Assets					1			4	1
e1650 Financial assets							1		
e1651 Tangible assets						1	2		
e310 Immediate family			1	6					
e315 Extended family			1	2					
e320 Friends			1	2		1	1		
e325 Acquaintances, peers, colleagues, neighbours and community members				2					
e355 Health professionals		4							
e540 Transportation services, systems and policies						1			
e5452 Civil protection policies								5	
e5458 Civil protection services, systems and policies, other specified			2	1	5				4
e5500 Legal services					12				
e5700 Social security services						1			
e5750 General social support services		2		2					
e5800 Health services		5				1			
e590 Labour and employment services, systems and policies			2						

Total ICF concepts	0	83	7	21	21	6	4	10	6
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Appendix 3.3.4 ICF mapping results for outcome measures in the social integration dimension: concepts not covered in ICF

ICF category	EQ-5D	CIDI	EuropASI Employment	EuropASI Family/Other	EuropASI Legal	IDUQoL	MANSA	MAP-crime	OTI-crime
nc-abuse				3					
nc-conflict				1					
nc- neighbourhood safety						1			
nc-safety							1		
nc-violence							1		
nd-gh						1	1		
nd-mh				1		1	1		
nd-QoL							1		
nd-satisfaction				3			1		
pf-crime							1		
Total ICF concepts	0	0	0	8	0	3	7	0	0

Appendix 3.4 ICF mapping results for outcome measures in RESULT

Appendix 3.4.1 ICF mapping results for outcome measures in RESULT: body functions component

ICF category	EQ-5D	CORE	LDQ	SCL (MAP-HSS)	SSQ
b1263 Psychic stability		2			
b1265 Optimism		2			
b1266 Confidence		1			
b1300 Energy level		1			
b1302 Appetite				1	
b1303 Craving			3		
b1304 Impulse control			1		
b1341 Onset of sleep		1			
b1342 Maintenance of sleep		1			
b1442 Retrieval of memory		1			
b152 Emotional functions	1	11			
b1602 Content of thought		2			
b1603 Control of thought			1		
b1645 Judgement			1		
b265 Touch function				1	
b280 Sensation of pain	1	1			
b2800 Generalized pain				1	
b28011 Pain in chest				1	
b28012 Pain in stomach or abdomen				1	
b28016 Pain in joints				1	
b440 Respiration functions				1	
b4552 Fatiguability				1	
b5350 Sensation of nausea				1	
b7651 Tremor				1	
Total ICF concepts	2	23	6	10	0

Appendix 3.4.2 ICF mapping results for outcome measures in RESULT: activities and participation component

ICF category	EQ-5D	CORE	LDQ	SCL (MAP-HSS)	SSQ
d175 Solving problems		1			
d177 Making decisions			2		
d230 Carrying out daily routine	1		2		
d240 Handling stress and other psychological demands		1			
d2400 Handling responsibilities		1			
d2401 Handling stress			1		
d4 Mobility	1				
d450 Walking	1				
d498 Mobility, other specified-confined to bed	1				
d5 Self-care	2				
d510 Washing oneself	1				
d540 Dressing	1				
d560 Drinking			1		
d610 Acquiring a place to live					1
d640 Doing housework	1				
d710 Basic interpersonal interactions		2			
d7100 Respect and warmth in relationships		1			
d7101 Appreciation in relationships		1			
d7103 Criticism in relationships		1			
d7202 Regulating behaviours within interactions		1			
d7500 Informal relationships with friends					1
d7503 Informal relationships with co-inhabitants					1
d760 Family relationships	1				2
d7600 Parent-child relationships					1
d7601 Child-parent relationships					1
d770 Intimate relationships					1
d7700 Romantic relationships					1
d7701 Spousal relationships					1
d839 Education, other specified and unspecified-study	1				
d850 Remunerative employment	1				1
d855 Non-remunerative employment					1
d870 Economic self-sufficiency					1
d920 Recreation and leisure	1				1
d9205 Socializing					1
Total ICF concepts	13	9	6	0	15

Appendix 3.4.3 ICF mapping results for outcome measures in RESULT: environmental factors component

ICF category	EQ-5D	CORE	LDQ	SCL (MAP-HSS)	SSQ
e1101 Drugs			1		
e3 Support and relationships		1			
e320 Friends		1			
Total ICF concepts	0	2	1	0	0

Appendix 3.4.4 ICF mapping results for outcome measures in RESULT: concepts not covered in ICF

ICF category	EQ-5D	LDQ	SSQ	CORE	SCL (MAP-HSS)
nc-achievement				1	
nc-hurt oneself				1	
nc-suicide				2	
Total ICF concepts	0	0	0	4	0

Appendix 4 Description of the outcome measures for the included human capital approach studies in chapter 4

Study, country	Population	Intervention	Benefit outcome measures and cost-benefit outcomes
Abou-Saleh et al, 2003; Abou-Saleh et al, 2008 (HEPC), UK	33 injecting drug users (IDUs), recruited from drug treatment centres	Trial enhanced HIV prevention counselling intervention -Stay Safe Therapy (SST; 4 sessions) -Simple Educational Counselling (SEC; 1 session)	Monetary outcomes converted from Service Use Questionnaire (SUQ) Resource saved -Health care costs: costs of A&E (visit and overnight), emergency ambulance, inpatient stay, day care patient, GP(surgery visit and home visit), practice nurse (surgery visit and home visit), CPN home, NHS direct, walk-in centre, prescriptions, outpatient and inpatient drug services, counselling, residential treatment, after-care hostel, other agency, street agency, needle-exchange scheme and day programme -Criminal justice costs: costs of crime arrests (drug possession/drug offences, drink driving, other motoring, prostitution, other sex offences) and costs per offences (violence/assault, robbery, burglary, shoplifting, vehicle theft, criminal damage) -Social care costs: costs of housing benefit advisor, social worker, occupational therapist, citizens advice, RELATE counselling, alternative medical practitioner, debt advisor, homeless person agency and employment advisor Cost-benefit outcome -Changes of resource use between baseline and follow-up for SST group and SEC group are £5,239 and £-3,968 per patient, respectively
Ates et al, 2005, Germany	57 drug misuse patients	Three groups: -Specialised integration project (Mudra e.V.) -Standard work projects	Resource saved -Health care costs: costs of hospital stays, inpatient and outpatient detoxification and substitution -Criminal justice costs: costs of law enforcement,

		-Graduates of work projects	<p>criminal justice system, probation and prison</p> <p>-Social care costs: cost of unemployment social assistance</p> <p>Other value created</p> <p>-Increased productivity</p> <p>Cost-benefit outcome</p> <p>-Net benefit of Mudra e.V. at 1 year follow-up is EUR4,446.39</p>
Avants et al, 1999, USA	291 opioid dependent patients	<p>Two groups</p> <p>-Day treatment</p> <p>-Enhanced standard methadone maintenance programme</p>	<p>Resource saved</p> <p>-Health care costs: costs of medical primary care, medical hospitalisation, emergency room, mental health services, psychiatric/drug hospitalisation and transfer payment (administrative costs)</p> <p>-Criminal justice costs: costs of incarceration</p> <p>-Social care costs: cost of vocational counselling and legal counselling</p> <p>Other value created</p> <p>-Increased productivity</p> <p>Cost-benefit outcome</p> <p>-Mean difference of total societal costs at 6 month between two groups is \$661 per patient</p>
Barnett et al, 2006, USA	126 IDUs	<p>Patients in methadone treatment</p> <p>-Group 1: usual care</p> <p>-Group 2: case management</p> <p>-Group 3: voucher for free substance treatment</p> <p>-Group 4: case management plus voucher</p>	<p>Resource saved</p> <p>-Health care costs: costs of case management, long-term methadone maintenance, methadone detoxification, residential substance abuse treatment, other substance abuse treatment, outpatient mental health care, inpatient mental health care, hospital care, emergency department care and outpatient medical care</p>

			<p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Total resource use for group 1-4 are \$5,620, \$7,400, \$13,087, \$10,411 per patient, respectively
Berg, 1997, Norway	61 patients who have used several substance (heroin, amphetamine, hashish, painkillers, benzodiazepines and/or alcohol)	Residential detoxification and counselling for 3 weeks -Completer -Non-completer	<p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: decline in costs of future detoxifications and reduction in necessary treatment sessions (GP and hospital) <p>Other value created</p> <ul style="list-style-type: none"> -Increased productivity: increased taxes from taxable income <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Net benefit of completer and non-completer are NKR 19,000 (\$2,920) and NKR 69,000 per patient, respectively
Berger, 2003, USA	3.9 million pregnant women	Universal substance misuse screening	<p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: reduced substance abuse and reduced need for medical/ health care services (hospital costs of drug exposed new born, hospital costs of boarder babies, health care costs of postnatal exposure, avoided infant lives saved) <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Assuming 5.6% CPS (child protective services) reporting rate, net benefit of the universal substance misuse screening is from \$-44.09 to \$-126.89 per pregnant woman -Assuming 4.1% CPS reporting rate, net benefit of the programme is from \$40.98 to \$50.03
Bishai et al, 2008, USA	241 heroin addicts	Before entering a methadone maintenance treatment	<p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Estimated programme costs is \$82 per week -Patients are willing to pay for a median weekly fee from \$7.3 (3 months heroin-free effects) to \$17.11

			(24 months heroin-free effects) -Median WTP of case management is \$5.64 per week
Borisova and Goodman, 2003 and 2004, USA	303 substance misuse patients	Methadone maintenance treatment	Cost-benefit outcome -Mean WTP and willingness-to-accept (WTA) of the travel time required to obtain methadone maintenance treatment are \$7.32 and \$8.65 per hour, respectively -Median wage of the employed patients is \$10.04 per hour -Average value of travel time is \$5.49 per hour
Conover et al, 2006, USA	1,138 patients with HIV/AIDS, chronic mental illness and substance misuse	Two groups: -Employed -Unemployed	Resource saved -Social care costs: unemployment/ workers compensation, public assistance/ AFDC/ welfare, child support/ alimony and pension/ benefits/ social security Other value created -Increased productivity: income Cost-benefit outcome -Average societal costs related to income is \$447 -Average societal costs of employed patients and unemployed patients are \$247 and \$479, respectively
Daley et al, 2000, USA	439 pregnant substance misuse patients	Public funded treatment -Group 1: detoxification -Group 2: methadone -Group 3: residential -Group 4: outpatient -Group 5: residential/ outpatient	Resource saved -Criminal justice costs: costs of police investigation, illegal earnings, stolen property, other crime, incarceration, adjudication and parole Other value created -Victim costs Cost-benefit outcome

			<p>-Avoided crime costs for group 1-5 are \$2,151, \$1,867, \$5,184, \$983, \$1,692, \$2,642 per patient, respectively</p> <p>-Benefit-cost ratio for group 1-5 are 1.14, 1.54, 2.11, 1.72, 2.10, 1.54, respectively</p>
Davies et al, 2009 (Drug treatment outcomes research study; DTORS), UK	1,545 drug misuse patients	Patients received structured drug misuse treatment: community-based drug treatment or residential drug treatment	<p>Resource saved</p> <p>-Health care costs: costs of GP visits, community nurse, social worker, other professional services, A&E, Day hospital, general medical and surgical, other services, psychiatry, non-psychiatric, psychiatric services, substance misuse treatment, other unstructured drug treatment services, needle exchange and drug related advice services</p> <p>-Criminal justice costs: costs of offending behaviour (shoplifting, begging, buying and selling stolen goods, drug dealing, prostitution, theft of vehicle, theft from vehicle, house burglary, business burglary, violent theft, bag snatch, other stealing, cheque or credit card fraud, benefit fraud, and other violent crime)</p> <p>-Social care costs: costs of children in care, accommodation (hostel, night-time drop-in centres)</p> <p>Other value created</p> <p>-Victim costs</p> <p>Cost-benefit outcome</p> <p>-Average net benefit of drug misuse treatment is £7,301</p> <p>-Benefit-cost ratio is 2.5:1</p>
Dijkgraaf et al, 2005, Netherlands	430 Heroin addicts	Two groups: -Methadone plus heroin -Methadone alone	<p>Monetary outcomes converted from the European version of Addiction Severity Index (EuropASI)</p> <p>Resource saved</p>

			<p>-Health care costs: costs of GP, physiotherapist, psychiatrist/ psychologist/ therapist, company physician, alternative/ traditional medicine, other addiction care programmes, general hospital (outpatient and inpatient), psychiatric hospital (outpatient and inpatient), regional agency for mental health care, crisis intervention centre (outpatient and inpatient) and addiction care centre (physical and psychiatric)</p> <p>-Criminal justice costs: police arrests and official report, conviction (prosecution and adjudication), imprisonment and probation</p> <p>Other value created</p> <p>-Victim costs: company (theft and burglary) and civilian</p> <p>Cost-benefit outcome</p> <p>-Benefit of methadone plus heroin and methadone are EUR 19,533 and EUR 49,002, respectively</p> <p>-Net benefit difference between methadone plus heroin and methadone is EUR -12,793</p>
Dismuke et al, 2004 (PETS; The Persistent Effects of Treatment Study), USA	1,326 substance misuse patients from PETS	Substance misuse programmes from Chicago Target Cities Project	<p>Monetary outcomes converted from Addiction Severity Index (ASI)</p> <p>Resource saved</p> <p>-Health care costs: days experience medical problem, days in inpatient medical treatment, emergency room visits, clinic or physician visits, days experience psychological problems, days in inpatient psychiatric treatment and days in outpatient psychiatric treatment</p>

			<p>-Criminal justice costs: drug offence, forgery, burglary, robbery, assault, arson, rape, homicide, prostitution, drug deal, illegal gambling, vehicle theft and receiving/selling stole property</p> <p>Other value created</p> <p>-Increased productivity: income received from employment</p> <p>Cost-benefit outcome</p> <p>-Total societal costs are \$18,187, \$9,051, \$7,402, \$3,319, \$3,726 per patient at baseline, 6, 24, 36, 48 months follow-up, respectively</p>
Drummond et al, 2004; Drummond, C. et al, 2005 (UKCBTMM), UK	60 opiate addicts, recruited from 10 community based clinics	<p>Two groups:</p> <p>-Cognitive behaviour therapy (CBT) plus methadone maintenance treatment (MMT)</p> <p>-MMT alone</p>	<p>Monetary outcomes converted from Service Use Questionnaire (SUQ)</p> <p>Resource saved</p> <p>-Health care costs: costs of A&E (visit and overnight), emergency ambulance, inpatient stay, outpatient visit, day care patient, GP(surgery visit and home visit), practice nurse, CPN, NHS direct, walk-in centre, prescriptions, inpatient drug services, residential treatment, after-care hostel, street agency, day care programme and residential drug care</p> <p>-Criminal justice costs: costs of crime arrests (drug possession/drug supply), costs per offences (violence/assault, robbery, burglary, shoplifting, prostitution and other criminal offence)</p> <p>-Social care costs: benefit advisor, social worker, occupational therapist, citizens advice, RELATE counselling, alternative medical practitioner, debt advisor, homeless person agency, employment advisor and other advice</p>

			<p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Changes of resource use between baseline and 12-month follow-up for MMT&CBT group and MMT group are £-9,028.45 and £-2,064.68 per patient, respectively
Ettner et al, 2006 (CalTOP; California Treatment Outcome Project), USA	2,567 drug misuse patients	43 drug misuse treatment for CalTOP	<p>Monetary outcomes converted from ASI</p> <p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of hospital nights for medical problems, emergency room visits and inpatient and outpatient mental health services -Criminal justice costs: costs of criminal activities and incarceration -Social care costs: unemployment, disability/retirement and other services <p>Other value created</p> <ul style="list-style-type: none"> -Increased productivity: money received from employment -Victim cost <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Average net benefit is \$9,903 per patient. -Benefit-cost ratio is 7:1
Fals-Stewart, O'Farrell and Birchler, 1997, USA	80 substance misuse male patients from married or cohabiting couple	<p>Two groups:</p> <ul style="list-style-type: none"> -Behavioural couples therapy (BCT) -Individual-based substance misuse treatment (IBT) 	<p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: outpatient counselling programmes and intensive ambulatory care, hospital-based programmes (28-day inpatient and detoxification) and long-term residential facilities (halfway houses, sober houses and therapeutic communities) -Criminal justice costs: costs of crime arrests, incarceration, legal supervision (parole and

			<p>probation) and illegal income (trafficking, robbery and selling stolen property)</p> <p>-Social care costs: cost of general cash assistance and food stamps</p> <p>Cost-benefit outcome</p> <p>-Net benefit of BCT and IBT are \$4,856.01 and \$544.95 per patient, respectively</p> <p>-Benefit-cost ratio of BCT and IBT are 5.01 and 1.37, respectively</p>
Finigan, 1996, USA	1,267 substance misuse patients	<p>Two groups:</p> <p>-Substance misuse treatment (outpatient, residential and methadone)</p> <p>-No treatment</p>	<p>Resource saved</p> <p>-Health care costs: costs of inpatient and outpatient medical care, emergency medical care, inpatient and outpatient mental health care</p> <p>-Criminal justice costs: costs of police protection services, prosecution, adjudication, public defence and correction (incarceration, parole and probation)</p> <p>-Social care costs: food stamps, emergency assistance, public disability payment and other public assistance</p> <p>Other value created</p> <p>-Victim cost: victim expenditures on medical care, repairs of damaged property, lost time from work that results from predatory crimes and value of property or money stolen during a crime</p> <p>Cost-benefit outcome</p> <p>-Total net benefit of substance misuse treatment is \$83,147</p>
Finigan, Carey and Cox, 2007, USA	11,102 offenders	<p>Two groups:</p> <p>-Drug court</p> <p>-Traditional court</p>	<p>Resource saved</p> <p>-Criminal justice costs: costs of arrests, bookings, court, imprisonment, probation</p>

			<p>Other value created -Victim cost</p> <p>Cost-benefit outcome -Cost-benefit ratio of drug court is 1: 2.63</p>
Flynn et al, 1999 (DATOS; Drug Abuse Treatment Outcome Studies), USA	502 cocaine dependent patients	<p>Two groups:</p> <ul style="list-style-type: none"> -Long-term residential treatment (LTR) -Outpatient drug-free treatment (ODF) 	<p>Resource saved</p> <ul style="list-style-type: none"> -Criminal justice costs: costs of criminal justice system (aggravated assault, burglary, theft, robbery, forgery, fencing, gambling, prostitution and drug lay violation) <p>Other value created</p> <ul style="list-style-type: none"> -Increased productivity: crime career/productivity loss -Victim cost (aggravated assault, burglary, theft, and robbery) <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Cost of crime of LTR group is from \$18,461 to \$30,092 and cost of crime of ODF group is from \$1,891 to \$4,638 -Benefit-cost ratio of LTR is from 1.68 to 2.73 and benefit-cost ratio of ODF is from 1.33 to 3.26
French et al, 2000, USA	263 addiction treatment patient	<p>Two groups:</p> <ul style="list-style-type: none"> -Outpatient substance misuse treatment (PC) -Residential substance misuse treatment (FC) 	<p>Monetary outcomes converted from ASI</p> <p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of days experiencing medical problems, overnight hospitalisation, emergency room visits, clinic or physician visits, days experiencing psychological problems, inpatient and outpatient psychiatric treatment and hospital outpatient psychiatric treatment -Criminal justice costs: costs of criminal activities

			<p>Other value created</p> <ul style="list-style-type: none"> -Increased productivity: income received from employment <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Net benefit of PC and FC are \$11,173 and \$17,833, respectively -Benefit-cost ratio of PC and FC are 23.33 and 9.70, respectively
French et al, 2002a (PAAM; Pregnant Addicts/Addicted Mothers), USA	121 pregnant substance misuse patients	<p>Two groups:</p> <ul style="list-style-type: none"> -Specialty residential treatment -Standard residential treatment 	<p>Monetary outcomes converted from ASI</p> <p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of days experiencing medical problems, overnight hospitalisation, emergency room visits, clinic or physician visits, days experiencing psychological problems, inpatient and outpatient psychiatric treatment and hospital outpatient psychiatric treatment -Criminal justice costs: costs of criminal activities <p>Other value created</p> <ul style="list-style-type: none"> -Increased productivity: income received from employment <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Net benefit of specialty residential treatment and standard residential treatment are \$17,143 and \$8,090, respectively -Benefit-cost ratio of specialty residential treatment and standard residential treatment are 3.1 and 6.5, respectively
French et al, 2002b, USA	186 patients from homeless shelters and psychiatric hospitals	<p>Two groups:</p> <ul style="list-style-type: none"> -Treatment-as-usual (TAU) -Modified therapeutic 	<p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of other therapeutic community treatment, emergency room visits,

		community treatment (TC)	<p>hospital detoxification, short-term residential treatment, non-residential treatment, outpatient treatment, individual psychotherapy, methadone maintenance treatment, outpatient and inpatient psychological treatment</p> <p>-Criminal justice costs: costs of criminal justice system (alcohol offence, drug law violation, forgery/ fraud, fencing, gambling/ running numbers, prostitution/ pimping, burglary/ GTA, other theft, robbery, violent assault, and other/ miscellaneous)</p> <p>Other value created</p> <p>-Increased productivity: income</p> <p>-Victim costs</p> <p>Cost-benefit outcome</p> <p>-Net benefit of TAU and TC are \$85,257 and \$253,337, respectively</p> <p>-Benefit-cost ratio of TAU and TC are 5.19 and 13.44, respectively</p>
French et al, 2002c, USA	178 substance misuse patients	3 outpatient drug-free programmes	<p>Monetary outcomes converted from ASI</p> <p>Resource saved</p> <p>-Health care costs: costs of inpatient medical care, inpatient psychiatric care, and inpatient addiction treatment, days of experiencing medical problems and days of experiencing psychiatric problems</p> <p>-Criminal justice costs: costs of criminal activities</p> <p>Other value created</p> <p>-Increased productivity: income received from employment</p> <p>Cost-benefit outcome</p>

			<p>-Average net benefit is from \$1,939 to \$14,307</p> <p>-Average benefit-cost ratio is from 9 to 56</p>
French, Salome, and Carney, 2002, USA	222 substance misuse patients	9 adult substance residential treatments	<p>Monetary outcomes converted from ASI</p> <p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of inpatient medical care, inpatient psychiatric care, and inpatient addiction treatment, days of experiencing medical problems and days of experiencing psychiatric problems -Criminal justice costs: costs of criminal activities <p>Other value created</p> <ul style="list-style-type: none"> -Increased productivity: income received from employment <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Average net benefit is from \$4,673 to \$90,839 -Average benefit-cost ratio is from 1.63 to 25.89
French et al, 2003, USA	600 adolescent cannabis users aged 12 to 18	<p>5 programmes of CYT study (Cannabis Youth Treatment):</p> <ul style="list-style-type: none"> -Motivational enhancement treatment/cognitive behaviour therapy (MET/CBT) 5 sessions -MET/CBT 12 sessions -Family support network (FSN) -Adolescent community reinforcement approach (ACRA) -Multidimensional family therapy (MDFT) 	<p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of inpatient hospital days, emergency room visit, outpatient clinic/ doctor's office visit, days bothered by health/ medical problems, days bothered by psychological problems, detoxification programmes, inpatient substance abuse treatment, long-term residential programmes, intensive and regular outpatient substance abuse programmes -Criminal justice costs: costs of crime arrests, probation, parole, prison/jail, juvenile detention -Social care costs: costs of schools truancy, lost income for stressful days of parents <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Net benefit of MET/CBT5, MET/CBT12, FSN,

			ACRA and MDFT are \$1,113, \$1,185, \$3,246, \$1,408 and \$2,012, respectively
French, Fang and Fretz, 2010, USA	571 criminal offenders	Two groups: -Pre-release substance treatment -No treatment	Resource saved -Criminal justice costs: costs of arrests, convictions, incarceration Other value created -Increased productivity: wage loss -Victim costs Cost-benefit outcome -Total cost of crime for treatment group and control group are \$7,678 and \$11,985, respectively
Godfrey, Stewart and Gossop, 2004 (NTORS; National Treatment Outcome Research Study), UK	549 substance misuse patients	Patient from 54 residential and community treatment programmes	Resource saved -Health care costs: costs of substitute prescribing, substance misuse hospital inpatient, residential rehabilitation, medical inpatient hospital, A&E, GP, psychiatric inpatient hospital, community psychiatric care and street agency -Criminal justice costs: costs of criminal justice system (shoplifting, burglary, robbery, fraud and drug offences) -Social care costs: costs of social care services Other value created -Victim costs Cost-benefit outcome -Average benefit-cost ratio is from 9.5:1 to 18:1
Harris, Gospodarevskaya and Ritter, 2005, Australia	139 heroin dependent patients	Two groups: -Buprenorphine -Methadone	Resource saved -Health care costs: costs of other prescription drugs, over-the-counter drugs, prescribe visits, inpatient hospital, outpatient and emergency services, ambulance, psychiatric counselling, Allied Health

			<p>and pathology</p> <p>-Criminal justice costs: costs of criminal activities (property crime, fraud, credit card fraud and violent crime) and police investigation</p> <p>Cost-benefit outcome</p> <p>-Total societal costs of buprenorphine group and methadone group are AUD16,614 and AUD10,131, respectively</p>
Hartz et al, 1999, USA	102 opioid-addicted patients	<p>Two groups:</p> <p>-Methadone treatment with contingency contracting</p> <p>-Methadone treatment (control group)</p>	<p>Resource saved</p> <p>-Health care costs: costs of medications (analgesics, antibiotics, cardiac, cold/ respiratory, psychotropic and miscellaneous) and procedures (minor surgery, radiology, laboratory analysis), emergency room visit, outpatient visit and inpatient hospitalisation</p> <p>Cost-benefit outcome</p> <p>-Total health care resource use of treatment group and control group are \$397.51 and \$1329.69, respectively</p> <p>-Benefit-cost ratio is 4.87:1 between two groups</p>
Harwood et al, 1988 (TOPS; Treatment Outcome Prospective Study), USA	11,000 drug users from TOPS	41 drug misuse treatment of outpatient methadone, residential and outpatient drug-free programme	<p>Resource saved</p> <p>-Criminal justice costs: costs of criminal justice system (police protection services, prosecution, adjudication, public defence and correction services)</p> <p>Other value created</p> <p>-Increased productivity: crime career/ productivity loss and legal earnings</p> <p>-Victim costs: medical services, property destruction and lost work and household productivity</p> <p>Cost-benefit outcome</p>

			<ul style="list-style-type: none"> -Benefit-cost ratio of residential treatment, methadone treatment and drug-free treatment are 2.01, 0.92 and 4.28, respectively (benefits in reduced costs to society) -Benefit-cost ratio of residential treatment, methadone treatment and drug-free treatment are 3.84, 4.04 and 1.28, respectively (benefits in reduced costs to law-abiding citizens)
Healey et al, 1998, (NTORS), UK	1,075 substance misuse patients	Patient from 54 residential and community treatment programmes	<p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of general medical inpatient, psychiatric inpatient, A&E, GP visits, community mental health/ outpatient, drug dependency inpatient treatment, residential rehabilitation, methadone treatment provided in hospitals or by community drug teams or by GP, Alcoholics and Narcotics Anonymous and street agency -Criminal justice costs: costs of criminal justice system (burglary, robbery, shoplifting and vehicle theft, drug possession, drug supply, fraud, soliciting and other) -Social care costs: costs of social care services <p>Other value created</p> <ul style="list-style-type: none"> -Victim costs <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Total societal cost is £12.2 million over 1 year and the average total societal cost is £11,404 per patient
Koenig et al, 2005 (PETS), USA	595 substance misuse patients	Substance misuse programme (methadone, residential rehabilitation, intensive overnight, outpatient)	<p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of doctor's office visits, emergency room visit and psychiatric hospital -Criminal justice costs: police enforcement, adjudication, prosecution and corrections -Social care costs: costs of unemployment

			<p>compensation, government assistance, supplemental security income, disability pay and food stamps</p> <p>Other value created</p> <ul style="list-style-type: none"> -Increased productivity: income -Victim costs <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Average benefit-cost ratio of single treatment and multiple treatment admission at 30 month is 9.9 and 2.9, respectively -Average benefit-cost ratio of the sample is 4.1
Levine, Stoloff and Spruill, 1976, USA	15,000 substance misuse patients	45 public drug misuse treatment programmes	<p>Other value created</p> <ul style="list-style-type: none"> -Victim costs of property crime <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Benefits to victims of reduced crime is \$129,430 per year
Logan et al, 2004, USA	745 offenders	<p>Three groups of drug court programme:</p> <ul style="list-style-type: none"> -Graduated clients -Terminated clients -Assessed clients 	<p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of inpatient and outpatient mental health care and accidents -Criminal justice costs: costs of prison, jail, parole, probation, convictions, charges -Social care costs: costs of child support services <p>Other value created</p> <ul style="list-style-type: none"> -Increased productivity: income <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Benefit-cost ratio at 12 months for graduated clients and terminated clients are 3.81 and 1.13, respectively -Average benefit-cost ratio at 12 months for all clients is 2.71

<p>Longshore et al, 2006 (SACPA; The California Substance Abuse and Crime Prevention Act), USA</p>	<p>130,152 offenders</p>	<p>Two groups: -Probation with drug misuse treatment -Incarceration/ probation without treatment</p>	<p>Resource saved -Health care costs: costs of medical care services and addiction services -Criminal justice costs: costs of prison, jail, parole, probation, arrests and convictions</p> <p>Other value created -Increased productivity: income and sale taxes</p> <p>Cost-benefit outcome -First year of SACPA: average benefit-cost ratio at 30 months is 2.44:1 -Second year of SACPA: average benefit-cost ratio at 12 month is 2.3:1 -Benefit-cost ratio of treatment completer at 30 months is 4:1</p>
<p>Mark et al, 2001, USA</p>	<p>600,000 heroin addicts</p>	<p>Cost-of-illness of heroin dependence</p>	<p>Resource saved -Health care costs: costs of general hospital inpatient and outpatient, emergency room, physician office, medical complications from heroin addiction (AIDS, tuberculosis, hepatitis B, hepatitis C, pregnancy problems), health insurance administration, heroin addiction treatment and specialty substance misuse facilities -Criminal justice costs: costs of incarceration, policing, legal -Social care costs: costs of social welfare costs</p> <p>Other value created -Increased productivity: productivity due to premature mortality and income -Victim costs</p> <p>Cost-benefit outcome</p>

			-Total societal costs is \$21, 872
Masson et al, 2002, USA	3,147 opioid dependent patients	Two groups: -Opioid dependent patients -General patient population	Resource saved -Health care costs: costs of ambulatory care visits, emergency department visits and inpatient admissions Cost-benefit outcome -Average health care resource use of opioid dependent patients and general patient population are \$13,393 and \$5,440, respectively
Mauser, VanStelle and Moberg, 1994 (TAP; Treatment Alternative Program), USA	25 patients	Treatment alternative programmes	Resource saved -Health care costs: costs of doctor visits, hospitalisation and psychologist -Criminal justice costs: costs of police services, jail, probation, parole and courts Other value created -Increased productivity -Victim costs (medical care expenses and property damage losses) Cost-benefit outcome -Average societal costs is from \$58 to \$81 at baseline, and from \$47 to \$50 at 6 months -Benefit-cost ratio is from 1.4:1 to 3.3:1
McCollister et al, 2009, USA	119 young offenders aged 12 to 17	Four groups: -Family court with community services (FC) -Drug court with community services (DC) -Drug court with evidence-based treatment (DC/MST) -Drug court with evidence-based treatment enhanced	Resource saved -Criminal justice costs: costs of criminal activities (public disorder, theft and crimes against persons) and crime career costs Other value created -Victim costs and intangible costs associated with victims' pain and suffering

		with contingency management (DC/MST/CM)	Cost-benefit outcome -Average total crime-related societal costs at baseline, 4 months and 12 months are \$86,477, \$67,444 and \$54,099, respectively
McGlothlin and Anglin, 1981, USA	187 substance misuse patients	Two groups: -Patients from a closed down methadone treatment clinic (Bakersfield) -Patients from a continuing methadone treatment (Tulare)	Resource saved -Criminal justice costs: costs of crime arrests, court processing, incarceration, legal supervision, property crime -Social care cost: costs of welfare income Cost-benefit outcome -Average societal costs of patients at Bakersfield before, during and after methadone are \$120, \$61 and \$52 per year, respectively -Average societal costs of patients at Tulare before, during and after methadone are \$176, \$82 and \$56 per year, respectively
Miller and Hendrie, 2009, USA	0.4-1.1 million young drug users aged 12 to 14	Substance misuse prevention	Resource saved -Health care costs: costs of speciality treatment and prevention services, treatment of medical consequences -Criminal justice costs: costs of criminal justice system and criminal activities -Social care costs: costs of education Other value created -Increased productivity: productivity loss due to premature death, illness related to substance or incarceration and criminal careers -Victim costs Cost-benefit outcome -Total societal costs is \$151.4 billion -Benefit-cost ratio is from \$7.7:1 to \$36:1

Neale et al, 2006, UK	75 injecting drug users	Patients recruited from existing needle exchange programmes in large city, small town, and medium town	<p>Monetary outcomes converted from Service Use Questionnaire (SUQ)</p> <p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of A&E, emergency ambulance, inpatient and patient hospital, day care, GP, practice nurse, CPN, NHS direct, NHS walk-in centre, prescription, psychologist, psychiatrist, methadone, addiction problem treatment in hospital, key worker, social worker, addiction residential treatment, after care hostel, other addiction treatment facility, street agency, needle exchange and addiction day programme -Criminal justice costs: costs of arrests, probation, magistrates court, crown court and prison -Social care costs: cost of benefit advisor, social worker, occupational therapist, citizens advice, RELATE, alternative medical practitioner, debt or legal advisor, homeless persons agency, employment advisor and other advice <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Total resource use in Large city, small town and medium town are £6,299, £8,170 and £3,563 per patient, respectively
Robertson, Grimes and Rogers, 2001, USA	293 young offenders aged 11 to 17	<p>Two groups:</p> <ul style="list-style-type: none"> -Community-based intensive supervision and monitoring (ISM) -Cognitive behavioural intervention (CB) 	<p>Resource saved</p> <ul style="list-style-type: none"> -Criminal justice costs: costs of criminal justice systems <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Average net benefit is \$1,435 per offender at 18 months -Benefit-cost ratio is 1.96
Salome et al, 2003, USA	2,665 addiction patients	Addiction treatment from 19	Monetary outcomes converted from ASI

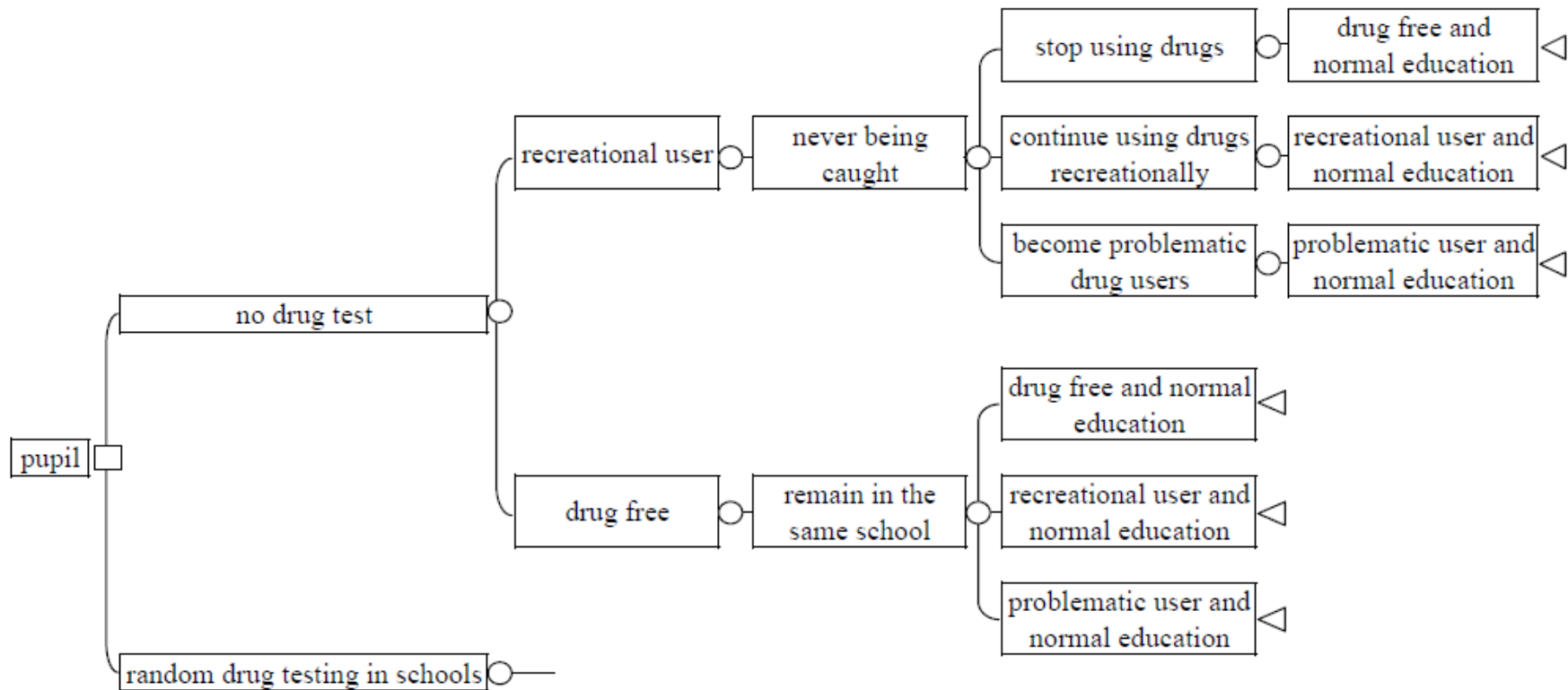
		treatment facilities	<p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of days experiencing medical problems, inpatient medical treatment, emergency room visits, clinic or physician visits, days experiencing psychological problems, inpatient and outpatient psychiatric treatments -Criminal justice costs: costs of criminal activities (drug offence, forgery, burglary, robbery, assault, arson, rape, homicide, prostitution, drug deal, illegal gambling, vehicle theft and receiving/ selling stolen property) <p>Other value created</p> <ul style="list-style-type: none"> -Increased productivity: income -Victim costs <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Average net benefit is \$6,325 -Average benefit-cost ratio is 4.26
Scanlon, 1976, USA	37,184 drug misuse patients	Drug misuse treatment from 6 facilities	<p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of opiate addiction and non-opiate addiction -Social care costs: costs of welfare <p>Other value created</p> <ul style="list-style-type: none"> -Increased productivity: income <p>Cost-benefit outcome</p> <ul style="list-style-type: none"> -Average benefit-cost ratio is 17:1
Sirotnik and Bailey, 1975, USA	285 heroin addicts	5 community drug misuse treatment programmes	<p>Resource saved</p> <ul style="list-style-type: none"> -Health care costs: costs of health care services -Criminal justice costs: costs of arrests, court and incarceration

			<p>-Social care costs: costs of unemployment and welfare</p> <p>Other value created</p> <p>-Increased productivity: productivity loss</p> <p>Cost-benefit outcome</p> <p>-Net benefit is \$3,359,919</p>
Sweeney et al, 2009, Australia	393 IDUs	Treatment for injecting-related injuries and diseases	<p>Resource saved</p> <p>-Health care costs: costs of community based treatment, public hospital emergency departments, hospital admissions</p> <p>Cost-benefit outcome</p> <p>-Total health care resource use is between AUD 16.3 million and AUD 27.6 million</p>
Tang et al, 2007, Taiwan	1,817 members of general public	Drug misuse treatment	<p>Cost-benefit outcome</p> <p>-General public are willing to pay from NT\$81 to NT\$95 per month for a drug misuse treatment, while the benefits of the treatment are estimated around NT\$12.8-15.0 billion</p>
Yu et al, 1991, USA	123 substance misuse patients	Substance misuse treatment in workplaces	<p>Resource saved</p> <p>-Health care costs: costs of medical care services</p> <p>Cost-benefit outcome</p> <p>-Net benefits for patients with drug misuse and with alcohol and drug misuse are \$1,097 and \$95, respectively</p>
Zarkin, Cates and Bala, 2000, USA	393 members of general public	Drug misuse treatment	<p>Cost-benefit outcome</p> <p>-General public are willing to pay \$37.12 or \$30.90 when 100 or 500 drug users are successfully treated</p> <p>-General public are willing to pay \$40.56 or \$41.42 when 100 or 500 women drug users are successfully treated</p>

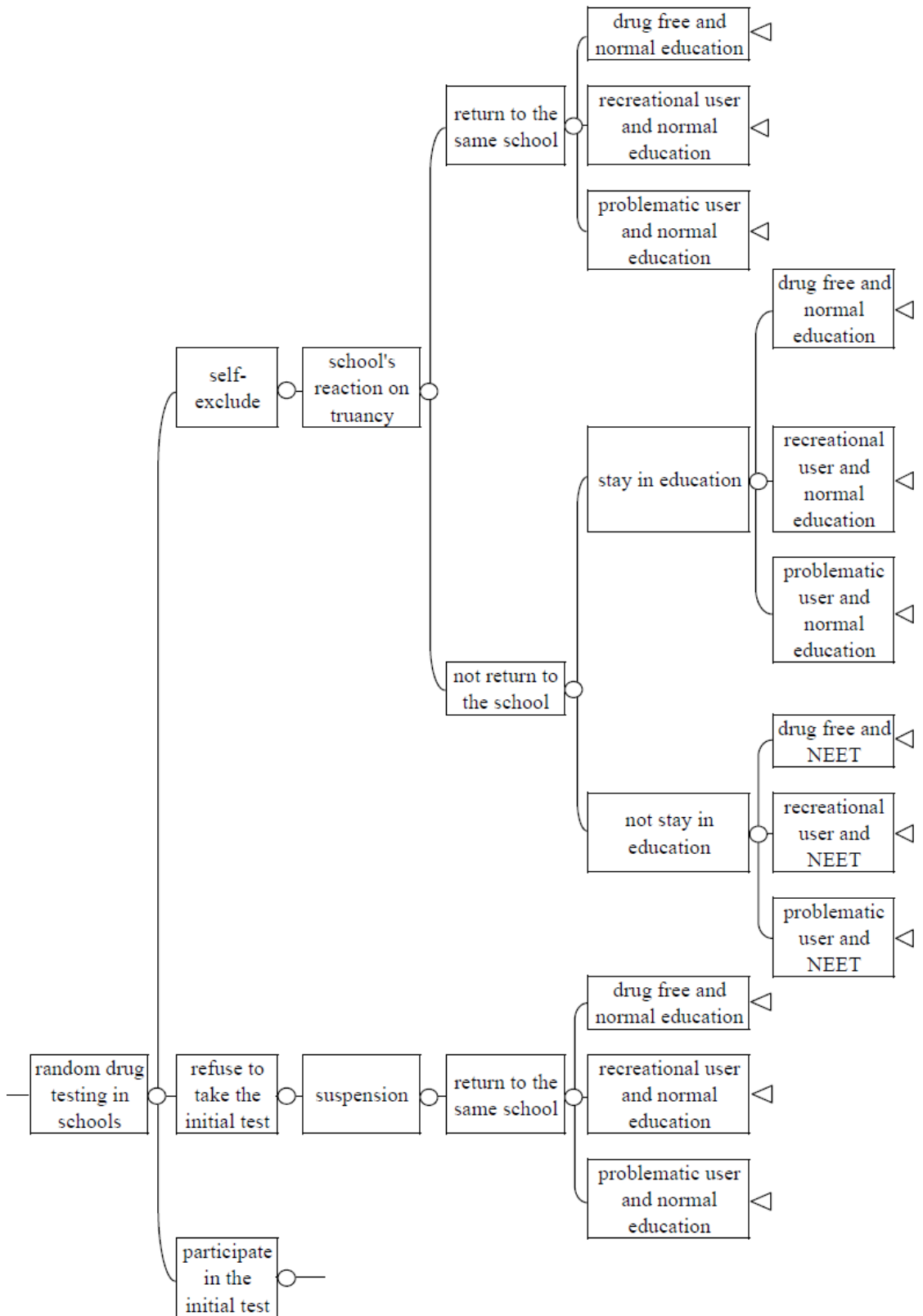
Appendix 5 Decision tree of drug testing in schools model

Appendix 5.1 Decision tree of drug testing in schools model part 1

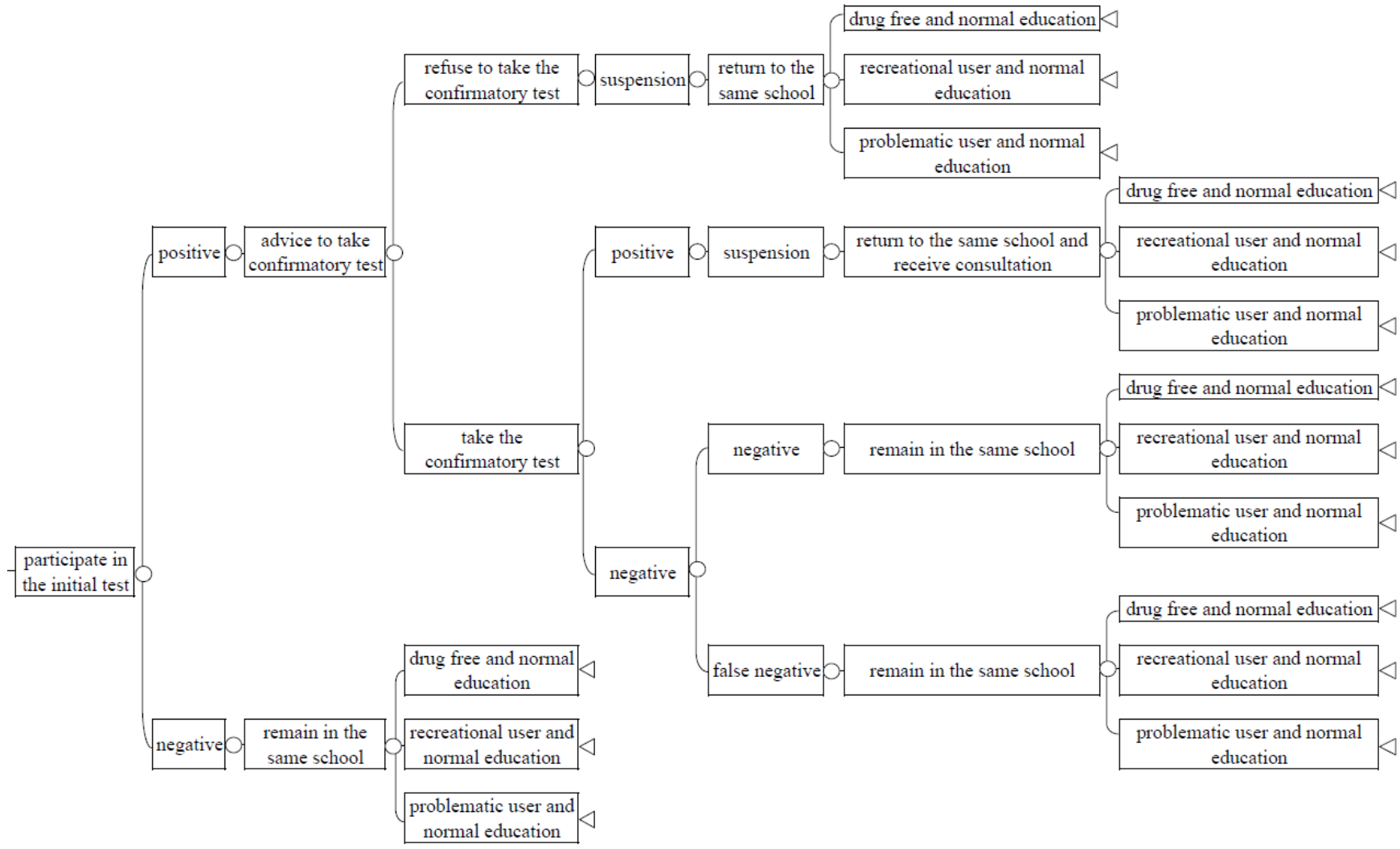
□: decision node; ○: chance node; △: terminal node



Appendix 5.2 Decision tree of drug testing in schools model part 2



Appendix 5.3 Decision tree of drug testing in schools model part 3



References

AA.com. (2007) *Running cost for petrol car* [online]. Available at: http://www.theaa.com/allaboutcars/advice/advice_rcosts_petrol_table.jsp [Accessed 26 August 2007].

Abou-Saleh, M., Checinski, K., Davis, P., Drummond, C., Ghodse, H., Godfrey, C., Maxwell, D., Oyefeso, A., Porter, S., Rice, P. and Tibbs, C. (2003) *The efficacy of enhanced prevention counselling in the primary prevention of hepatitis C among injecting drug users: a randomised controlled trial*. London: Department of Health.

Abou-Saleh, M., Davis, P., Rice, P., Checinski, K., Drummond, C., Maxwell, D., Godfrey, C., John, C., Corrin, B., Tibbs, C., Oyefeso, A., de Ruiter, M. and Ghodse, H. (2008) The effectiveness of behavioural interventions in the primary prevention of hepatitis C amongst injecting drug users: a randomised controlled trial and lessons learned. *Harm Reduction Journal*. 5, article number 25.

Adi, Y., Juarez-Garcia, A., Wang, D., Jowett, S., Frew, E., Day, E., Bayliss, S., Roberts, T. and Burls, A. (2007) Oral naltrexone as a treatment for relapse prevention in formerly opioid-dependent drug users: a systematic review and economic evaluation. *Health Technology Assessment*. 11(6), 1-85.

Almond, S., Knapp, M., Francois, C., Toumi, M. and Brugha, T. (2004) Relapse in schizophrenia: costs, clinical outcomes and quality of life. *British Journal of Psychiatry*. 184(4), 346-351.

Altman, D.G. (1991) *Practical statistics for medical research*. London: Chapman and Hall.

Amato, L., Minozzi, S., Davoli, M., Vecchi, S., Ferri, M. and Mayet, S. (2008) Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. *Cochrane Database of Systematic Reviews*. (4), article number CD004147.

Ates, T., Langer, B., Erbas, B., Tretter, F. and Wehner, B. (2005) Assessment of cost-benefit analysis in integration projects on drug addiction. *Gesundheitswesen*. 67(2), 159-162.

Avants, S.K., Margolin, A., Sindelar, J.L., Rounsaville, B.J., Schottenfeld, R., Stine, S., Cooney, N.L., Rosenheck, R.A., Li, S.H. and Kosten, T.R. (1999) Day treatment versus enhanced standard methadone services for opioid-dependent patients: a comparison of clinical efficacy and cost. *American Journal of Psychiatry*. 156(1), 27-33

Bacher, J., Wenzig, K. and Vogler, M. (2004) SPSS Two Step Cluster– a first evaluation. In: *RC33 Sixth International Conference on Social Science Methodology*. Amsterdam, Netherlands. 16-20 August, 2004.

Barkham, M., Evans, C., Margison, F., McGrath, G., Mellor-Clark, J., Milne, D. and Connell, J. (1998) The rationale for developing and implementing core batteries in service settings and psychotherapy outcome research. *Journal of Mental Health*. 7(1), 35-47.

Barnes, A.J., Kim, I., Schepers, R., Moolchan, E.T., Wilson, L., Cooper, G., Reid, C., Hand, C. and Huestis, M.A. (2003) Sensitivity, specificity, and efficiency in detecting opiates in oral fluid with the Cozart Opiate Microplate EIA and GC-MS following controlled codeine administration. *Journal of Analytical Toxicology*. 27 (7), 402-407.

Barnett, P.G. (1999) The cost-effectiveness of methadone maintenance as a health care intervention. *Addiction*. 94(4), 479-488.

Barnett, P.G., Masson, C.L., Sorensen, J.L., Wong, W. and Hall, S. (2006) Linking opioid-dependent hospital patients to drug treatment: health care use and costs 6 months after randomization. *Addiction*. 101(12), 1797-1804.

BBC News (2006) *School drug testing 'a success'* [online]. Available at: <http://news.bbc.co.uk/1/hi/england/nottinghamshire/5010554.stm> [Accessed 25 June 2007]

Berg, J.E. (1997) Completers from a detoxification unit: Some cost-benefit considerations after using psychometric tests. *Substance Abuse*. 18(3), 105-112.

Berger, L.M. (2003) Estimating the benefits and costs of a universal substance abuse screening and treatment referral policy for pregnant women. *Journal of Social Service Research*. 29(1), 57-84.

Bird, S.M., Pearson, G. and Strang, J. (2002) Rationale and cost-efficiency compared for urine or saliva testing and behavioural inquiry among UK offender populations: injectors, arrestees and prisoners. *Journal of Cancer Epidemiology and Prevention*. 7(1), 37-47.

Bishai, D., Sindelar, J., Ricketts, E.P., Huettner, S., Cornelius, L., Lloyd, J.J., Havens, J.R., Latkin, C.A. and Strathdee, S.A. (2008) Willingness to pay for drug rehabilitation: implications for cost recovery. *Journal of Health Economics*. 27(4), 959-972.

Borchers, M., Cieza, A., Sigl, T., Kollerits, B., Kostanjsek, N. and Stucki, G. (2005) Content comparison of osteoporosis-targeted health status measures in relation to the International Classification of Functioning, Disability and Health (ICF). *Clinical Rheumatology*. 24(2), 139-144.

Borisova, N.N. and Goodman, A.C. (2003) Measuring the value of time for methadone maintenance clients: willingness to pay, willingness to accept, and the wage rate. *Health Economics*. 12(4), 323-334.

Borisova, N.N. and Goodman, A.C. (2004) The effects of time and money prices on treatment attendance for methadone maintenance clients. *Journal of Substance Abuse Treatment*. 26(1), 345-352.

Brazier, J., Roberts, J., Tsuchiya, A. and Busschbach, J. (2004) A comparison of the EQ-5D and SF-6D across seven patient groups. *Health Economics*. 13(9), 873-884.

Broekman, T.G., Schippers, G.M., Koeter, M.W.J. and van den Brink, W. (2004) Standardized assessment in substance abuse treatment in the Netherlands: The case of the Addiction Severity Index and new developments. *Journal of Substance Use*. 9(3-4), 147-155.

Brogly, S., Mercier, C., Bruneau, J., Palepu, A. and Franco, E. (2003) Towards more effective public health programming for injection drug users: development and evaluation

of the Injection Drug User Quality of Life Scale. *Substance Use and Misuse*. 38(7), 965-992.

Brookes, M., Goodall, E. and Heady, L. (2007) *Misspent youth: The costs of truancy and exclusion, a guide for donors and funders*. London: New Philanthropy Capital.

Brownstein, M.J. (1993) A brief history of opiates, opioid peptides, and opioid receptors. *Proceedings of the National Academy of Sciences of the United States of America*. 90(12), 5391-5393.

Buxton, M.J., Drummond, M.F., van Hout, B.A., Prince, R.L., Sheldon, T.A., Szucs, T. and Vray, M. (1997) Modelling in economic evaluation: an unavoidable fact of life. *Health Economics*. 6(3), 217-227.

Byford, S., Knapp, M., Greenshields, J., Ukoumunne, O.C., Jones, V., Thompson, S., Tyrer, P., Schmidt, U. and Davidson, K. (2003) Cost-effectiveness of brief cognitive behaviour therapy versus treatment as usual in recurrent deliberate self-harm: a decision-making approach. *Psychological Medicine*. 33(6), 977-986.

Carpentier, P.J., Krabbe, P.F., van Gogh, M.T., Knapen, L.J., Buitelaar, J.K. and de Jong, C.A. (2009) Psychiatric comorbidity reduces quality of life in chronic methadone maintained patients. *American Journal on Addictions*. 18(6), 470-480.

Cartwright, W.S. (1998) Cost-benefit and cost-effectiveness analysis of drug abuse treatment services. *Evaluation Review*. 22(5), 609-636.

Cartwright, W.S. (2008) Economic costs of drug abuse: financial, cost of illness, and services. *Journal of Substance Abuse Treatment*. 34(2), 224-233.

Castillo, I.I. (2008) Injection Drug User Quality of Life scale (IDUQoL): psychometric assessment of the Spanish version. *Adicciones*. 20(3), 281-294.

Caulkins, J.P., Rydell P., Everingham, S.S., Chiesa, J. and Bushway, S. (1999) *An ounce of prevention, a pound of uncertainty: the cost-effectiveness of school-based drug prevention programs*. Santa Monica: Drug Policy Research Center, RAND.

Cieza, A., Brockow, T., Ewert, T., Amman, E., Kollerits, B., Chatterji, S., Ustun, T.B. and Stucki, G. (2002) Linking health-status measurements to the international classification of functioning, disability and health. *Journal of Rehabilitation Medicine*. 34(5), 205-210.

Cieza, A., Geyh, S., Chatterji, S., Kostanjsek, N., Ustun, B. and Stucki, G. (2005) ICF linking rules: an update based on lessons learned. *Journal of Rehabilitation Medicine*. 37(4), 212-218.

Cieza, A. and Stucki, G. (2005) Content comparison of health-related quality of life (HRQOL) instruments based on the international classification of functioning, disability and health (ICF). *Quality of Life Research*. 14(5), 1225-1237.

Claxton, K., Sculpher, M. and Drummond, M.F. (2002) A rational framework for decision making by the National Institute For Clinical Excellence (NICE). *Lancet*. 360(9334), 711-715.

Claxton, K., Walker, S., Palmer, S. and Sculpher, M. (2010) Appropriate perspectives for health care decisions. *Centre for Health Economics Research Paper 54*, York: Centre of Health Economics.

Cohen, J. (1960) A coefficient of agreement for nominal scales. *Educational and Psychological Measurement*. 20(1), 37-46.

Connock, M., Juarez-Garcia, A., Jowett, S., Frew, E., Liu, Z., Taylor, R.J., Fry-Smith, A., Day, E., Lintzeris, N., Roberts, T., Burls, A. and Taylor, R.S. (2007) Methadone and buprenorphine for the management of opioid dependence: a systematic review and economic evaluation. *Health Technology Assessment*. 11(9), 1-171.

Conover, C.J., Arno, P., Weaver, M., Ang, A. and Ettner, S.L. (2006) Income and employment of people living with combined HIV/AIDS, chronic mental illness, and substance abuse disorders. *Journal of Mental Health Policy and Economics*. 9(2), 71-86.

Daley, M., Argeriou, M., McCarty, D., Callahan, J.J. Jr., Shepard, D.S. and Williams, C.N. (2000) The costs of crime and the benefits of substance abuse treatment for pregnant women. *Journal of Substance Abuse Treatment*. 19(4), 445-458.

Darke, S., Hall, W., Heather, N., Ward, J. and Wodak, A. (1991a) The reliability and validity of a scale to measure HIV risk-taking behaviour among intravenous drug users. *AIDS*. 5(2), 181-185.

Darke, S., Ward, J., Hall, W., Heather, N. and Wodak, A. (1991b) *The Opiate Treatment Index (OTI) researcher's manual*. Sydney: National Drug and Alcohol Research Centre.

Davies, L., Jones, A., Vamvakas, G., Dubourg, R. and Donmall, M. (2009). *The Drug Treatment Outcomes Research study (DTORS): cost effectiveness analysis*. London: Home Office.

Department for Education and Skills (DfES). (2004) *Drugs: Guidance for schools*. (DfES/0092/2004) London: Department for Education and Skills.

Department for Education and Skills (DfES). (2006) *Statistical First Release: Permanent and fixed period exclusions from schools and exclusion appeals in England, 2004/05*. (SFR 24/2006) London: Department for Education and Skills.

Derogatis, L.R. and Cleary, P.A. (1977) Confirmation of the dimensional structure of the SCL-90: a study in construct validation. *Journal of Clinical Psychology*. 33(4), 981-989.

Derogatis, L.R. and Melisaratos, N. (1983) The Brief Symptom Inventory: an introductory report. *Psychological Medicine*. 13(3), 595-605.

Dijkgraaf, M.G., van der Zanden, B.P., de Borgie, C.A., Blanken, P., van Ree, J.M. and van den Brink, W. (2005) Cost utility analysis of co-prescribed heroin compared with methadone maintenance treatment in heroin addicts in two randomised trials. *British Medical Journal*. 330(7503), 1297-1302.

Dismuke, C.E., French, M.T., Salome, H.J., Foss, M.A., Scott, C.K. and Dennis, M.L. (2004) Out of touch or on the money: Do the clinical objectives of addiction treatment

coincide with economic evaluation results? *Journal of Substance Abuse Treatment*. 27(3), 253-263.

Dolan, P. (1997) Modeling valuations for EuroQol health states. *Medical Care*. 35(11), 1095-1108.

Dolan, P., Gudex, C., Kind, P. and Williams, A. (1995) A social tariff for EuroQoL: results from a UK general population survey. *Centre of Health Economics Discussion Paper 138*. York: Centre of Health Economics.

Drummond, C., Kouimtsidis, C., Reynolds, M., Russell, I., Godfrey, C., McCusker, M., Coulton, S., Parrott, S., Davis, P., Tarrier, N., Turkington, D., Sell, L., Merrill, J., Williams, H., Abou-Saleh, M., Ghodse, H. and Porter, S. (2004) *The effectiveness and cost effectiveness of cognitive behaviour therapy for opiate misusers in methadone maintenance treatment: a multicentre, randomised, controlled trial. UKCBTMM Study: United Kingdom Cognitive Behaviour Therapy study in Methadone Maintenance treatment*. London: Department of Health.

Drummond, C., Kouimtsidis, C., Reynolds, M., Russell, I., Godfrey, C., McCusker, M., Coulton, S., Parrott, S., Davis, P., Tarrier, N., Turkington, D., Sell, L., Merrill, J., Williams, H., Abou-Saleh, M., Ghodse, H. and Porter, S. (2005) The effectiveness and cost effectiveness of cognitive behaviour therapy for opiate misusers in methadone maintenance treatment: a multicentre, randomised, controlled trial. UKCBTMM Study: United Kingdom Cognitive Behaviour Therapy Study in Methadone Maintenance Treatment. *Drugs: Education, Prevention and Policy*. 12(Suppl 1), 69-76.

Drummond, M.F., Cooke, J. and Walley, T. (1997) Economic evaluation under managed competition: evidence from the U.K. *Social Science and Medicine*. 45(4), 583-595.

Drummond, M.F., Jonsson, J. and Rutten, F. (1997) The role of economic evaluation in the pricing and reimbursement of medicines. *Health Policy*. 40(3), 199-215.

Drummond, M.F., Sculpher, M.J., Torrance, G.W., O'Brien, B.J. and Stoddart, G.L. (2005) *Methods for the Economic Evaluation of Health Care Programmes*. Third ed. Oxford: Oxford University Press.

DuPont, R.L., Campbell, T.G. and Mazza, J.J. (2002) *Elements of a successful school-based student drug testing program*. Washington, D.C.: United States Department of Education.

Ettner, S.L., Huang, D., Evans, E., Ash, D.R., Hardy, M., Jourabchi, M. and Hser, Y.I. (2006) Benefit-cost in the California treatment outcome project: does substance abuse treatment "pay for itself"? *Health Services Research*. 41(1), 192-213.

EuroQol Group. (1990) EuroQoL-a new facility for the measurement of health-related quality of life. *Health Policy*. 16(3), 199-208.

Evans, C., Connell, J., Barkham, M., Margison, F., McGrath, G., Mellor-Clark, J. and Audin, K. (2002) Towards a standards brief outcome measure: psychometric properties and utility of the CORE-OM. *British Journal of Psychiatry*. 180(1), 51-60.

Evans, C., Mellor-Clark, J., Margison, F., Barkham, M., McGrath, G., Connell, J. and Audin, K. (2000) Clinical Outcomes in Routine Evaluation: The CORE-OM. *Journal of Mental Health*. 9(3), 247-255.

Fals-Stewart, W., O'Farrell, T.J. and Birchler, G.R. (1997) Behavioral couples therapy for male substance-abusing patients: a cost outcomes analysis. *Journal of Consulting and Clinical Psychology*. 65(5), 789-802.

Field, A. (2005) *Discovering statistics using SPSS*. Second ed. London: SAGE.

Finigan, M.W. (1996) *Societal outcomes and cost savings of drug and alcohol treatment in the state of Oregon*. Oregon: Oregon Department of Human Resources, Office of Alcohol and Drug Abuse Programs.

Finigan, M.W., Carey, S.M. and Cox, A. (2007) *Impact of a mature Drug Court over 10 years of operation: recidivism and costs*. (Document number 219225) Washington D.C.: United States Department of Justice.

First Group. (2007) *Single/return bus fare*. [online] Available at:

<http://www.firstgroup.com/ukbus/yorkhumber/york/fares/singlereturn.php> [Accessed 10 September 2007]

Flynn, P.M., Kristiansen, P.L., Porto, J.V. and Hubbard, R.L. (1999) Costs and benefits of treatment for cocaine addiction in DATOS. *Drug and Alcohol Dependence*. 57(2), 167-174.

French, M.T. and Drummond, M.F. (2005) A research agenda for economic evaluation of substance abuse services. *Journal of Substance Abuse Treatment*. 29(2), 125-137.

French, M.T., Fang, H. and Fretz, R. (2010) Economic evaluation of a prerelease substance abuse treatment program for repeat criminal offenders. *Journal of Substance Abuse Treatment*. 38(1), 31-41.

French, M.T., McCollister, K.E., Cacciola, J., Durell, J. and Stephens, R.L. (2002a) Benefit-cost analysis of addiction treatment in Arkansas: specialty and standard residential programs for pregnant and parenting women. *Substance Abuse*. 23(1), 31-51.

French, M.T., McCollister, K.E., Sacks, S., McKendrick, K. and De Leon, G. (2002b) Benefit-cost analysis of a modified therapeutic community for mentally ill chemical abusers. *Evaluation and Program Planning*. 25 (2), 137-148.

French, M.T., Roebuck, M.C., Dennis, M.L., Godley, S.H., Liddle, H.A. and Tims, F.M. (2003) Outpatient marijuana treatment for adolescents. Economic evaluation of a multisite field experiment. *Evaluation Review*. 27(4), 421-459.

French, M.T., Salome, H.J. and Carney, M. (2002) Using the DATCAP and ASI to estimate the costs and benefits of residential addiction treatment in the State of Washington. *Social Science and Medicine*. 55(12), 2267-2282.

French, M.T., Salome, H.J., Krupski, A., McKay, J.R., Donovan, D.M., McLellan, A.T. and Durell, J. (2000) Benefit-cost analysis of residential and outpatient addiction treatment in the State of Washington. *Evaluation Review*. 24(6), 609-634.

French, M.T., Salome, H.J., Sindelar, J.L. and McLellan, A.T. (2002c) Benefit-cost analysis of addiction treatment: methodological guidelines and empirical application using the DATCAP and ASI. *Health Services Research*. 37(2), 433-455.

Garfein, R.S., Vlahov, D., Galai, N., Doherty, M.C. and Nelson, K.E. (1996) Viral infections in short-term injection drug users: the prevalence of the hepatitis C, hepatitis B, human immunodeficiency, and human T-lymphotropic viruses. *American Journal of Public Health*. 86(5), 655-661.

Garson, G.D. (2009) *Cluster Analysis* [online]. Available at: <http://faculty.chass.ncsu.edu/garson/PA765/cluster.htm> [Accessed 10 January 2010]

Gerada, C. and Gilvarry, E. (2005) Random drug testing in schools. *British Journal of General Practice*. 55(516), 499-501.

Geyh, S., Cieza, A., Kollerits, B., Grimby, G. and Stucki, G. (2007) Content comparison of health-related quality of life measures used in stroke based on the international classification of functioning, disability and health (ICF): a systematic review. *Quality of Life Research*. 16(5), 833-851.

Godfrey, C. (2006) Evidence-Based Illicit Drug Policy: The Potential Contribution of Economic Evaluation Techniques. *De Economist*. 154(4), 563-580.

Godfrey, C., Eaton, G., McDougall, C. and Culyer, A. (2002a) *The economic and social costs of Class A drug use in England and Wales, 2000*. (Research Study 249) London: Home Office

Godfrey, C., Hutton, S., Bradshaw, J., Coles, B., Craig, G. and Johnson, J. (2002b) *Estimating the cost of being "Not in Education, Employment or Training" at Age 16-18*. (Research Report 346) London: Department for Education and Skills.

Godfrey, C., Stewart, D. and Gossop, M. (2004) Economic analysis of costs and consequences of the treatment of drug misuse: 2-year outcome data from the National Treatment Outcome Research Study (NTORS). *Addiction*. 99(6), 697-707.

Gold, M., Gafni, A., Nelligan, P. and Millson, P. (1997) Needle exchange programs: an economic evaluation of a local experience. *Canadian Medical Association Journal*. 157(3), 255-262.

Goldberg, L., Elliot, D., MacKinnon, D.P., Moe, E., Kuehl, K.S., Nohre, L. and Lockwood, C.M. (2003) Drug testing athletes to prevent substance abuse: background and pilot study results of the SATURN (Student Athlete Testing Using Random Notification) study. *Journal of Adolescent Health*. 32(1), 16-25.

Goldberg, L., Elliot, D., MacKinnon, D.P., Moe, E.L., Kuehl, K.S., Myeongsun, Y., Taylor, A. and Williams, J. (2007) Outcome of a prospective trial of Student Athlete Testing Using Random Notification (SATURN) study. *Journal of Adolescent Health*. 41(5), 421-429.

Gossop, M., Darke, S., Griffiths, P., Hando, J., Powis, B., Hall, W. and Strang, J. (1995) The Severity of Dependence Scale (SDS): psychometric properties of the SDS in English and Australian samples of heroin, cocaine and amphetamine users. *Addiction*. 90(5), 607-614.

Haro, J.M., Edgell, E.T., Jones, P.B., Alonso, J., Gavart, S., Gregor, K.J., Wright, P. and Knapp, M. (2003) The European Schizophrenia Outpatient Health Outcomes (SOHO) study: rationale, methods and recruitment. *Acta Psychiatrica Scandinavica*. 107(3), 222-232.

Harris, A.H., Gospodarevskaya, E. and Ritter, A.J. (2005) A randomised trial of the cost effectiveness of buprenorphine as an alternative to methadone maintenance treatment for heroin dependence in a primary care setting. *Pharmacoeconomics*. 23(1), 77-91.

Hartz, D.T., Meek, P., Piotrowski, N.A., Tusel, D.J., Henke, C.J., Delucchi, K., Sees, K. and Hall, S.M. (1999) A cost-effectiveness and cost-benefit analysis of contingency contracting-enhanced methadone detoxification treatment. *American Journal of Drug and Alcohol Abuse*. 25(2), 207-218.

Harwood, H.J., Hubbard, R.L., Collins, J.J. and Rachal, J.V. (1988) The costs of crime and the benefits of drug abuse treatment: a cost-benefit analysis using TOPS data. *National Institute on Drug Abuse Research Monograph Series*. 86, 209-235.

Healey, A., Knapp, M., Astin, J., Gossop, M., Marsden, J., Stewart, D., Lehmann, P. and Godfrey, C. (1998) Economic burden of drug dependency. Social costs incurred by drug users at intake to the National Treatment Outcome Research Study. *British Journal of Psychiatry*. 173, 160-165.

Hjorthoj, C., Fohlmann, A., Larsen, A.M., Madsen, M.T., Vesterager, L., Gluud, C., Arendt, M.C. and Nordentoft, M. (2008) Design paper: The CapOplus trial: a randomized, parallel-group, observer-blinded clinical trial of specialized addiction treatment versus treatment as usual for young patients with cannabis abuse and psychosis. *Trials*. 9, article number 42.

HM Treasury. (2007) *GDP deflators* [online]. Available at: http://www.hm-treasury.gov.uk/media/2/F/gdpdeflators_290607.xls [Accessed 29 June 2007]

Hser, Y.I. and Anglin, M.D. (1991) Cost-effectiveness of drug abuse treatment: relevant issues and alternative longitudinal modeling approaches. *National Institute on Drug Abuse Research Monograph Series*. 113, 67-93.

Hubley, A.M., Russell, L.B. and Palepu, A. (2005) Injection Drug Use Quality of Life scale (IDUQOL): a validation study. *Health and Quality of Life Outcomes*. 3, article number 43.

Jerant, A., Chapman, B.P. and Franks, P. (2008) Personality and EQ-5D scores among individuals with chronic conditions. *Quality of Life Research*. 17(9), 1195-1204.

Joseph, H. (1988) The criminal justice system and opiate addiction: a historical perspective. *National Institute on Drug Abuse Research Monograph Series*. 86, 106-125.

Joseph Rowntree Foundation. (2004) *Drug Testing in the Work Place*. York: Joseph Rowntree Foundation

- Kelly, M.P., McDaid, D., Ludbrook, A. and Powell, J. (2005) *Economic appraisal of public health interventions*. London: NHS Health Development Agency.
- Kind, P., Hardman, G. and Macran, S. (1999) UK Population norms for EQ-5D. *Centre for Health Economics Discussion Paper 172*. York: Centre of Health Economics.
- King, R.G. (1953) The Narcotics Bureau and the Harrison Act: Jailing the Healers and the Sick. *Yale Law Journal*. 62(5), 736-749.
- Koenig, L., Siegel, J.M., Harwood, H., Gilani, J., Chen, Y.J., Leahy, P. and Stephens, R. (2005) Economic benefits of substance abuse treatment: findings from Cuyahoga County, Ohio. *Journal of Substance Abuse Treatment*. 28 (Suppl 1), S41-S50.
- Koeter, M.W. and Hartgers, C. (1997). *Preliminary procedure for the computation of the EuropASI composite scores*. Amsterdam: The Amsterdam Institute for Addiction Research.
- Kokkevi, A. and Hartgers, C. (1995) EuropASI: European adaptation of a multidimensional assessment instrument for drug and alcohol dependence. *European Addiction Research*. 1(4), 208-210.
- Lamers, L.M., Bouwmans, C.A., van Straten, A., Donker, M.C. and Hakkaart, L. (2006) Comparison of EQ-5D and SF-6D utilities in mental health patients. *Health Economics*. 15(11), 1229-1236.
- Leal, P., Stein, K. and Rosenberg, W. (1999) What is the cost utility of screening for hepatitis C virus (HCV) in intravenous drug users? *Journal of Medical Screening*. 6(3), 124-131.
- Levine, D., Stoloff, P. and Spruill, N. (1976) Public Drug Treatment and Addict Crime. *Journal of Legal Studies*. 5(2), 435-462

Levy, S., Sherritt, L., Vaughan, B.L., Germak, M. and John, R.K. (2007) Results of random drug testing in an adolescent substance abuse program. *Pediatrics*. 119(4), e843-e848

Lintzeris, N., Strang, J., Metrebian, N., Byford, S., Hallam, C., Lee, S., Zador, D. and RIOTT Group. (2006) Methodology for the Randomised Injecting Opioid Treatment Trial (RIOTT): evaluating injectable methadone and injectable heroin treatment versus optimised oral methadone treatment in the UK. *Harm Reduction Journal*. 3, article number 28.

Logan, T.K., Hoyt, W.H., McCollister, K.E., French, M.T., Leukefeld, C. and Minton, L. (2004) Economic evaluation of drug court: methodology, results, and policy implications. *Evaluation and Program Planning*. 27(4), 381-396.

Longshore, D., Hawken, A., Urada, D. and Anglin, M.D. (2006) *Evaluation of the Substance Abuse and Crime Prevention Act (SACPA): cost-analysis report (first and second years)*. California: California Department of Alcohol and Drug Programs and California Health and Human Services Agency.

Loubiere, S., Rotily, M. and Moatti, J.P. (2003) Prevention could be less cost-effective than cure: the case of hepatitis C screening policies in France. *International Journal of Technology Assessment in Health Care*. 19(4), 632-645.

Mark, T.L., Woody, G.E., Juday, T. and Kleber, H.D. (2001) The economic costs of heroin addiction in the United States. *Drug and Alcohol Dependence*. 61(2), 195-206.

Marsden, J., Gossop, G., Stewart, D., Best, D., Farrell, M., Lehmann, P., Edwards, C. and Strang, J. (1998) The Maudsley Addiction Profile (MAP) A brief instrument for assessing treatment outcome. *Addiction*. 93(12), 1857-1867.

Martinez-Raga, J., Gonzalez Saiz, F., Pascual, C., Casado, M.A. and Sabater Torres, F.J. (2010) Suboxone (buprenorphine/naloxone) as an agonist opioid treatment in Spain: a budgetary impact analysis. *European Addiction Research*. 16(1), 31-42.

Masson, C.L., Barnett, P.G., Sees, K.L., Delucchi, K.L., Rosen, A., Wong, W. and Hall, S.M. (2004) Cost and cost-effectiveness of standard methadone maintenance treatment compared to enriched 180-day methadone detoxification. *Addiction*. 99(6), 718-726.

Masson, C.L., Sorensen, J.L., Batki, S.L., Okin, R., Delucchi, K.L. and Perlman, D.C. (2002) Medical service use and financial charges among opioid users at a public hospital. *Drug and Alcohol Dependence*. 66(1), 45-50.

Matrix Research and Consultancy and Institute for Criminal Policy Research, Kings College (2007) *Evaluation of Drug Interventions Programme pilots of children and young people: arrest referral, drug testing and Drug Treatment and Testing Requirements*. [online]. London: Home Office. Available at: <http://rds.homeoffice.gov.uk/rds/pdfs07/rdsolr0707.pdf> [Accessed 10 August 2007]

Mausser, E., VanStelle, K. and Moberg, D. (1994) The economic impact of diverting substance-abusing offenders into treatment. *Crime and Delinquency*. 40(4), 568-588.

McCollister, K.E. and French, M.T. (2003) The relative contribution of outcome domains in the total economic benefit of addiction interventions: a review of first findings. *Addiction*. 98(12), 1647-1659.

McCollister, K.E., French, M.T., Sheidow, A.J., Henggeler, S.W. and Halliday-Boykins, C.A. (2009) Estimating the differential costs of criminal activity for juvenile drug court participants: challenges and recommendations. *Journal of Behavioral Health Services and Research*. 36(1), 111-126.

McCrystal, P., Higgins, K. and Percy, A. (2006) Brief Report: School exclusion drug use and delinquency in adolescence. *Journal of Adolescence*. 29(5), 829-836.

McGlothlin, W.H. and Anglin, M.D. (1981) Shutting off methadone. Costs and benefits. *Archives of General Psychiatry*. 38(8), 885-892.

McKeganey, N. (2005) *Random drug testing of schoolchildren: A shot in the arm or a shot in the foot for drug prevention?* York: Joseph Rowntree Foundation

McLellan, A.T., Luborsky, L., Woody, G.E. and O'Brien, C.P. (1980) An improved diagnostic evaluation instrument for substance abuse patients. The Addiction Severity Index. *Journal of Nervous and Mental Diseases*. 168(1), 26-33.

Miller, T.R. and Hendrie, D. (2009) *Substance Abuse Prevention Dollars and Cents: A Cost-Benefit Analysis*. (SMA 07-4298) Rockville: US Dept of Health and Human Services, Substance Abuse and Mental Health Service Admin (SAMHSA)

Myers, C. and Wilks, D. (1999) Comparison of Euroqol EQ-5D and SF-36 in patients with chronic fatigue syndrome. *Quality of Life Research*. 8(1-2), 9-16.

National Centre for Social Research. (2007) *Smoking, drinking and drug use among young people in England 2006*. London: The Information Centre.

National Institute for Health and Clinical Excellence (NICE). (2008) *Guide to the methods of technology appraisal*. London: NHS NICE.

National Statistics. (2005) Annual Survey of Hours and Earnings. *Labour Market Trends*. 113(3), S64-S67.

Neale, J., Godfrey, C., Parrott, S., Tompkins, C. and Sheard, L. (2006) *Barriers to the effective treatment of injecting drug users*. London: Department of Health.

Oliver, J.P. (1991-1992) The social care directive: development of a quality of life profile for use in community services for the mentally ill. *Social Work and Social Sciences Review*. 3(1), 5-45.

Perlman, D.C., Gourevitch, M.N., Trinh, C., Salomon, N., Horn, L. and Des Jarlais, D.C. (2001) Cost-effectiveness of tuberculosis screening and observed preventive therapy for active drug injectors at a syringe-exchange program. *Journal of Urban Health*. 78(3), 550-567.

Philips, Z., Ginnelly, L., Sculpher, M., Claxton, K., Golder, S., Riemsma, R., Woolacoot, N. and Glanville, J. (2004) Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technology Assessment*. 8(36), 1-158.

Priebe, S., Huxley, P., Knight, S. and Evans, S. (1999) Application and results of the Manchester Short Assessment of Quality of Life (MANSA). *International Journal of Social Psychiatry*. 45(1), 7-12.

Prodinger, B., Cieza, A., Williams, D.A., Mease, P., Boonen, A., Kersch-Schindl, K., Fialka-Moser, V., Smolen, J., Stucki, G., Machold, K. and Stamm, T. (2008) Measuring health in patients with fibromyalgia: content comparison of questionnaires based on the International Classification of Functioning, Disability and Health. *Arthritis and Rheumatism*. 59(5), 650-658.

Raistrick, D., Bradshaw, J., Tober, G., Weiner, J., Allison, J. and Healey, C. (1994) Development of the Leeds Dependence Questionnaire. *Addiction*. 89(5), 563-572.

Raistrick, D., Tober, G., Godfrey, C., Parrott, S., Lui, S., Loftus, A., Maddox, S., Cheney, C. and Bates, E. (2008) *Cost and cost effectiveness of treatment as usual in drug misuse services*. London: Department of Health.

Raistrick, D., Tober, G., Heather, N. and Clark, J. (2007) Validation of the Social Satisfaction Questionnaire in the context of routine outcome evaluation for alcohol and drug problems treatment. *Psychiatric Bulletin*. 31, 333-336.

Rehm, J., Guggenbuhl, L. and Uchtenhagen, A. (2000) *Adequacy in Drug Abuse Treatment and Care in Europe (ADAT) Part IV: Evaluations of effectiveness and economic evaluations*. Zurich: Addiction Research Institute.

Robertson, A.A., Grimes, P.W. and Rogers, K.E. (2001) A short-run cost-benefit analysis of community-based interventions for juvenile offenders. *Crime and Delinquency*. 47(2), 265-284.

Ross, J. (1995) The use of economic evaluation in health care: Australian decision makers' perceptions. *Health Policy*. 31(2), 103-110.

- Salome, H.J., French, M.T., Scott, C., Foss, M. and Dennis, M. (2003) Investigating variation in the costs and benefits of addiction treatment: econometric analysis of the Chicago Target Cities Project. *Evaluation and Program Planning*. 26(3), 325-338.
- Scanlon, J.C. (1976) Proceedings: Cost savings/benefit analysis of drug abuse treatment. *American Journal of Drug and Alcohol Abuse*. 3(1), 95-101.
- Schafer, A., Wittchen, H.U., Backmund, M., Soyka, M., Golz, J., Siegert, J., Schafer, M., Tretter, F. and Kraus, M.R. (2009) Psychopathological changes and quality of life in hepatitis C virus-infected, opioid-dependent patients during maintenance therapy. *Addiction*. 104(4), 630-640.
- Sheerin, I.G., Green, F.T. and Sellman, J.D. (2004) What is the cost-effectiveness of hepatitis C treatment for injecting drug users on methadone maintenance in New Zealand? *Drug and Alcohol Review*. 23(3), 261-272.
- Simoens, S., Ludbrook, A., Matheson, C. and Bond, C. (2006) Pharmaco-economics of community maintenance for opiate dependence: a review of evidence and methodology. *Drug and Alcohol Dependence*. 84(1), 28-39.
- Sirotnik, K.A. and Bailey, R.C. (1975) A cost-benefit analysis for a multimodality heroin treatment project. *International Journal of the Addictions*. 10(3), 443-451.
- Sobell, L.C. and Sobell, M.B. (1996) *Timeline FollowBack user's guide: A calendar method for assessing alcohol and drug use*. Toronto: Addiction Research Foundation.
- Sobell, L.C., Sobell, M.B., Buchan, G., Cleland, P.A., Fedoroff, I. and Leo, G.I. (1996) The reliability of the Timeline Followback method applied to drug, cigarette, and cannabis use. In: *30th Annual Meeting of the Association for Advancement of Behavior Therapy*. New York, USA. November, 1996.
- Sobocki, P., Ekman, M., Agren, H., Krakau, I., Runeson, B., Martensson, B. and Jonsson, B. (2007) Health-related quality of life measured with EQ-5D in patients treated for depression in primary care. *Value in Health*. 10(2), 153-160.

Stamm, T.A., Cieza, A., Machold, K.P., Smolen, J.S. and Stucki, G. (2004) Content comparison of occupation-based instruments in adult rheumatology and musculoskeletal rehabilitation based on the International Classification of Functioning, Disability and Health. *Arthritis and Rheumatism*. 51(6), 917-924.

Stamm, T., Geyh, S., Cieza, A., Machold, K., Kollerits, B., Kloppenburg, M., Smolen, J. and Stucki, G. (2006) Measuring functioning in patients with hand osteoarthritis--content comparison of questionnaires based on the International Classification of Functioning, Disability and Health (ICF). *Rheumatology*. 45(12), 1534-1541.

Stein, K., Dalziel, K., Walker, A., Jenkins, B., Round, A. and Royle, P. (2003) Screening for hepatitis C in genito-urinary medicine clinics: a cost utility analysis. *Journal of Hepatology*. 39(5), 814-825.

Stein, K., Dalziel, K., Walker, A., Jenkins, B., Round, A. and Royle, P. (2004) Screening for Hepatitis C in injecting drug users: a cost utility analysis. *Journal of Public Health*. 26(1), 61-71.

Stein, K., Dalziel, K., Walker, A., McIntyre, L., Jenkins, B., Horne, J., Royle, P. and Round, A. (2002) Screening for hepatitis C among injecting drug users and in genitourinary medicine clinics: systematic reviews of effectiveness, modelling study and national survey of current practice. *Health Technology Assessment*. 6(31), 1-122.

Stimson, G.V., Jones, S., Chalmers, C. and Sullivan, D. (1998) A short questionnaire (IRQ) to assess injecting risk behaviour. *Addiction*. 93(3), 337-347.

Strang, J., Griffiths, P. and Gossop, M. (1997) Heroin smoking by 'chasing the dragon': origins and history. *Addiction*. 92(6), 673-683

Strang, J., Metrebian, N., Lintzeris, N., Potts, L., Carnwath, T., Mayet, S., Williams, H., Zador, D., Evers, R., Groshkova, T., Charles, V., Martin, A. and Forzisi, L. (2010) Supervised injectable heroin or injectable methadone versus optimised oral methadone as treatment for chronic heroin addicts in England after persistent failure in orthodox treatment (RIOTT): a randomised trial. *Lancet*. 375(9729), 1885-1895.

Sutton, A.J., Edmunds, W.J. and Gill, O.N. (2006) Estimating the cost-effectiveness of detecting cases of chronic hepatitis C infection on reception into prison. *BMC Public Health*. 6, article number 170.

Sweeney, R., Conroy, A.B., Dwyer, R. and Aitken, C.K. (2009) The economic burden to the public health system of treating non-viral injecting-related injury and disease in Australia (a cost of illness analysis). *Australian and New Zealand Journal of Public Health*. 33(4), 352-357.

Szende, A., Oppe, M. and Devlin, N. ed. (2007) *EQ-5D value sets: inventory, comparative review and user guide*. Dordrecht: Springer.

Tang, C.H., Liu, J.T., Chang, C.W. and Chang, W.Y. (2007) Willingness to pay for drug abuse treatment: results from a contingent valuation study in Taiwan. *Health Policy*. 82(2), 251-262.

Thompson Coon, J., Castelnovo, E., Pitt, M., Cramp, M., Siebert, U. and Stein, K. (2006) Case finding for hepatitis C in primary care: a cost utility analysis. *Family Practice*. 23(4), 393-406.

Tober, G., Brearley, R., Kenyon, R., Raistrick, D. and Morley, S. (2000) Measuring outcomes in a health service addiction clinic. *Addiction Research*. 8(2), 169-182.

Tramarin, A., Gennaro, N., Compostella, F.A., Gallo, C., Wendelaar Bonga, L.J. and Postma, M.J. (2008) HCV screening to enable early treatment of hepatitis C: a mathematical model to analyse costs and outcomes in two populations. *Current Pharmaceutical Design*. 14(17), 1655-1660.

Tryfos, P. (1998) Cluster Analysis [online]. In Tryfos, P. *Methods for business analysis and forecasting: text and case*. New York: John Wiley and Sons, Inc. Available at: <http://www.yorku.ca/ptryfos/f1500.pdf> [Accessed 15 August 2009]

Tschiesner, U., Rogers, S.N., Harreus, U., Berghaus, A. and Cieza, A. (2008) Content comparison of quality of life questionnaires used in head and neck cancer based on the

international classification of functioning, disability and health: a systematic review. *European Archives of Otorhinolaryngology*. 265(6), 627-637.

UKATT research team. (2001) United Kingdom Alcohol Treatment Trial (UKATT): hypotheses, design and methods. *Alcohol and Alcoholism*. 36(1), 11-21.

UKATT research Team. (2005) Cost effectiveness of treatment for alcohol problems: findings of the randomised UK Alcohol Treatment Trial (UKATT). *British Medical Journal*. 331(7516), 544-548.

van den Brink, W., Hendriks, V.M., Blanken, P., Koeter, M.W., van Zwieten, B.J. and van Ree, J.M. (2003) Medical prescription of heroin to treatment resistant heroin addicts: two randomised controlled trials. *British Medical Journal*. 327(7410), 310-315.

van der Zanden, B.P., Dijkgraaf, M.G., Blanken, P., de Borgie, C.A., van Ree, J.M. and van den Brink, W. (2006) Validity of the EQ-5D as a generic health outcome instrument in a heroin-dependent population. *Drug and Alcohol Dependence*. 82(2), 111-118.

van het Loo, M., van Beusekom, I. and Kahan, J.P. (2002) Decriminalization of drug use in Portugal: The development of a policy. *Annals of the American Academy of Political and Social Science*. 582, 49-63.

Viera, A.J. and Garrett, J.M. (2005) Understanding interobserver agreement: the kappa statistic. *Family Medicine*. 37(5), 360-363.

Villari, P., Fattore, G., Siegel, J.E., Paltiel, A.D. and Weinstein, M.C. (1996) Economic evaluation of HIV testing among intravenous drug users. An analytic framework and its application to Italy. *International Journal of Technology Assessment in Health Care*. 12(2), 336-357.

Ware, J.E., Kosinski, M. and Keller, S.D. (1994) *SF-36 physical and mental health summary scales: a user's manual*. Boston: The Health Institute.

Ware, J.E., Kosinski, M. and Keller, S.D. (1995) *How to score the SF-12 physical and mental health summary scales. 2nd edition*. Boston: The Health Institute.

Ware, J. E., Kosinski, M. and Keller, S.D. (1996) A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Medical Care*. 34(3), 220-233.

Ware, J.E., Snow, K.K., Kosinski, M. and Gandek, B. (1993) *SF-36 health survey manual and interpretation guide*. Boston: The Health Institute.

Wiessing, L., Roy, K., Sapinho, D., Hay, G., Taylor, A., Goldberg, D. and Hartnoll, R. (2004) Surveillance of hepatitis C infection among injecting drug users in the European Union. In Jager, J., Limburg, W., Kretzschmar, M., Postma, M. and Wiessing, L. ed. *EMCDDA Monographs 7: Hepatitis C and injecting drug use: impact, costs and policy options*. Luxembourg: European Monitoring Centre for Drugs and Drug Addiction.

World Health Organization. (1990) *Composite International Diagnostic Interview - Core Version 1.0*. Geneva: WHO

World Health Organization. (2000) *WHO's Disability Assessment Schedules II training manual: a guide to administration*. Geneva: WHO

World Health Organization. (WHO). (2001) *International classification of functioning, disability and health : ICF*. Geneva: WHO

Yu, J., Chen, P.J., Harshman, E.J. and McCarthy, E.G. (1991) An analysis of substance abuse patterns, medical expenses and effectiveness of treatment in the workplace. *Employee Benefits Journal*. 16(3), 26-30.

Zarkin, G.A., Cates, S.C. and Bala, M.V. (2000) Estimating the willingness to pay for drug abuse treatment: a pilot study. *Journal of Substance Abuse Treatment*. 18(2), 149-159.

Zarkin, G.A., Dunlap, L.J., Hicks, K.A. and Mamo, D. (2005) Benefits and costs of methadone treatment: results from a lifetime simulation model. *Health Economics*. 14(11), 1133-1150.

Zarkin, G.A., French, M.T., Anderson, D.W. and Bradley, C.J. (1994) A conceptual framework for the economic evaluation of substance abuse interventions. *Evaluation and Program Planning*. 17(4), 409-418,

Zigmond, A.S. and Snaith, R.P. (1983) The Hospital Anxiety And Depression Scale. *Acta Psychiatrica Scandinavica*. 67(6), 361-370.