PREOPERATIVE ALCOHOL & OTHER RECREATIONAL SUBSTANCE USE: RISK ANALYSIS & INTERVENTION DEVELOPMENT RESEARCH

by

Luke William Budworth

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DECLARATIONS

The candidate confirms that the work submitted is his own. The contribution of the candidate and the other authors to this work has been explicitly indicated below. The candidate confirms that appropriate credit has been given within the thesis where reference has been made to the work of others.

Chapter 3 (Study 1). Luke Budworth (LB): conceived the analysis strategy; wrote the application for data access; organised, cleaned and linked datasets; performed analyses; wrote the chapter. Andrew Scally: provided statistical guidance. Rebecca Lawton (RL), Andrew Prestwich (AP) and Ian Kellar (IK): (as with all following studies) provided critical feedback on the chapter write up and performed a supervisory role e.g., provided general guidance, contributed to the design and analysis strategy, helped interpret findings.

Chapter 4 (Study 2 and 3). LB: acted as study coordinator (Study 3); conceived the design (Study 3); conceived the analysis strategy (Study 2 and 3); collected and tabulated data (Study 3); performed analyses (Study 2 and 3); coded routine substance use measure ‘detections’ (Study 3); helped generate perioperative complication codes (Study 3); wrote the chapter. Daniel Clark: conceived the design (Study 2); collected and tabulated original data (Study 2). Sally Moore (SM) and Caroline Reynolds (CR): categorised surgeries according to i. speciality (Study 2) and ii. AXA categories (Study 3); categorised patients by ASA-PS grades (Study 3). Alwyn Kotzé (AK): categorised surgeries according to AXA categories (Study 3); categorised patients by ASA-PS grades (Study 3); provided critical logistical support; helped generate perioperative complication codes (Study 3). Sakarias Bank: performed second coding of routine substance use measure ‘detections’ (Study 3). Sheona Gillies: acted as point of contact for NHS coding; ran coding searches (Study 3). RL, AP, IK and AK: provided critical feedback on the chapter write up; performed a supervisory role.

Chapter 5 (Study 4). LB: acted as study coordinator; conceived the design and analysis strategy; developed search strategy; ran searches;

performed abstract and full-text screening; performed data extraction; coded behaviour change techniques; coded risk of bias judgments; performed the analysis; wrote the chapter. RL: performed second coder abstract and full-text screening; coded behaviour change techniques. AP: helped conceive the design and analysis strategy; checked over data extraction; checked over analyses. IK: performed second coder abstract and full-text screening; performed second coding of risk of bias judgments. RL, AP, IK and AK: provided critical feedback on the chapter write up; performed a supervisory role.

Chapter 6 (Study 5). LB: acted as study coordinator; conceived the design and analysis strategy; contributed to the formulation of questionnaire items; collected and tabulated data; performed the analysis; wrote the chapter. SM and CR: categorised surgeries according to speciality. RL, AP and IK: contributed to the formulation of questionnaire items; provided critical feedback on the chapter write up; performed a supervisory role.

Chapter 7 (Study 6). LB: acted as study coordinator; conceived the design and analysis strategy; collected (e.g., acted as interviewer) and tabulated data; performed the analysis (e.g., coding of transcripts); wrote the chapter. RL: performed second coding of transcripts; helped conceive the design and analysis strategy. RL, AP and IK: provided critical feedback on the chapter write up; performed a supervisory role.

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All other studies are being prepared for submission to peer reviewed journals.

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ABSTRACT

Perioperative substance use may catalyse perioperative complications. Nevertheless, a literature review in Chapter 2 of this thesis found little (particularly UK) research investigating the extent and detectability of this issue (risk analysis), nor methods to counteract the issue (intervention research). There are also plausible but unexplored routes through which substance use may have negative perioperative effects (e.g., mental health impacts). Through secondary data analysis, Study 1 (n = 18,508) found that (in covariate-adjusted models) hazardous preoperative alcohol use may negatively impact postoperative affect (which may catalyse complications). Across two Leeds-based preoperative assessment clinics, Study 2 and 3 (n = 196; n = 273) found that over a third of preoperative patients had alcohol use scores associated with complications in previous studies and polysubstance use was high. Routine preoperative assessment was less sensitive at detecting hazardous use versus validated measures, though postoperative complications were predicted by neither. In Study 4, a systematic review found few interventions targeting preoperative alcohol use and zero targeting other substance use alone. Effects on substance use were mixed and trial quality was low. Recommendations for future studies included the development of interventions using behavioural determinant elicitation research. In Study 5 (n = 102) a (*Capability, Opportunity, Motivation – Behaviour* [COM-B] based) questionnaire for assessing and targeting determinants of preoperative alcohol use was developed. The questionnaire had good psychometric properties and among preoperative patients, each COM-B subdomain was significantly associated with alcohol consumption (*reflective motivation, physical capability* and *physical opportunity* were predictive after controlling for all subdomains). In Study 6 (n = 36) thematic analysis of interviews with addiction service users identified several determinants (e.g., low self-efficacy) and intervention features (e.g., individualisation) for future interventions to target and incorporate. In Chapter 8 results are summarised and directions for future research and practice are suggested.

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LIST OF ABBREVIATIONS AND ACRONYMS

(M)ANOVA	(Multivariate) Analysis of Variance
95% CI	95% Confidence Interval
A&E	Accident and Emergency
ABV	Alcohol by Volume
ADHD	Attention Deficit Hyperactivity Disorder
AIC	Akaike Information Criterion
ASA-PS	American Society of Anaesthesiologist’s Physical Status
ASH	Action on Smoking and Health
ASSIST	Alcohol, Smoking and Substance Involvement Screening Test
AUC	Area under the Curve
AUDIT(-C)	Alcohol Use Disorder Identification Test (Consumption)
BAI	Beck’s Anxiety Inventory
BCT	Behaviour Change Technique
BDI	Beck’s Depression Inventory
BIC	Bayesian Information Criterion
BMI	Body Mass Index
CAPI	Computer Assisted Personal Interviewing
CCSD	Clinical Coding & Schedule Development Group
CFA	Confirmatory Factor Analysis
CFI	Comparative Fit Index
CG	Control Group
CMA	Comprehensive Meta-Analysis
COM-B	Capability, Opportunity, Motivation - Behaviour
COMET	Core Outcome Measures in Effectiveness Trials Initiative
COREQ	Consolidated Criteria for Reporting Qualitative Research

DSM	Diagnostic and Statistical Manual of Mental Disorders
DSOS	Disease Specific Outcome Score
DUDIT	Drug Use Disorders Identification Test
DV	Dependent Variable
ENT	Ear, Nose and Throat
ES	Effect Size
ESA-ESICM	European Society of Anaesthesiology and the European Society of Intensive Care Medicine
GP	General Practitioner
HADS	Hospital Anxiety and Depression Scale
HD	Hazardous Drinking
HDU	High Dependency Unit
ICU	Intensive Care Unit
IG	Intervention Group
IP	Inpatient Surgery
ISCED	International Standard Classification of Education
ISOS	International Surgical Outcomes Study
ISU	Illicit Substance Use
MDMA	3-4, Methylenedioxymethamphetamine
MOS-SF 12	Medical Outcome Sudy Short Form
MRC	Medical Research Council
NCEPOD	National Confidential Enquiry into Patient Outcome and Death
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NPV	Negative Predictive Value
Ns	Not Statistically Significant
OCD	Obsessive Compulsive Disorder
ONS	Office for National Statistics
OR	Odds Ratio
PAS	Patient Administration System

POSU	Preoperative Substance use
Ppt	Participant
PPV	Positive Predictive Value
PTSD	Post-Traumatic Stress Disorder
RC	Recovery Coordinator
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
Ref	Reference Category/Level
RMSEA	Root Mean Square Error of Approximation
RR	Risk Ratio
RTT	Referral to Treatment
SD	Standard Deviation
SE	Standard Error
SF-36	Short Form Health Survey
SHARE	Survey of Health, Ageing and Retirement in Europe
SMART	Specific, Measurable, Attainable, Realistic and Timely
SOCRATES	Stages of Change Readiness and Treatment Eagerness Scale
SORT	Surgical Outcomes Risk Tool
TAM-2	Total Activity Measure 2
TLI	Tucker Lewis Index
WHO	World Health Organisation

“Alcohol is the anaesthesia by which we endure the operation of life!”

George Bernard Shaw

CHAPTER 1. PERIOPERATIVE MEDICINE: AN INTRODUCTION

1.1 Introduction

Consuming excessive amounts of alcohol or other substances, not having a healthy diet, and not exercising frequently are all associated with poor physical and mental health and wellbeing (e.g., Stranges et al., 2014; Lozano et al., 2010; Lim et al., 2012). Indeed, it has been suggested that individual behaviours such as these are among the most prominent determinants of health alongside genetics, social circumstances, quality of medical care and one's environment (e.g., Goinvo, 2018). There are, of course, many complex routes through which these behaviours can have a deleterious impact on health, though this thesis focuses on one, perhaps lesser known route: the impact of individual behaviour on the outcomes of elective surgical operations. More specifically, this thesis focuses on one behaviour: the use of recreational substances - but particularly the substance most commonly over-used in the UK: alcohol.

This introductory chapter provides a non-technical overview of issues around surgical care for a non-medical audience, including an outline and discussion of i. surgery types and key statistics, ii. contemporary issues relevant to surgery in the UK, iii. the surgical pathway of patients, iv. the definition, assessment and impact of surgical complications and v. the impact patient factors, including lifestyle behaviours, may have on perioperative outcomes. This serves as a preface for Chapter 2 which focuses more specifically on perioperative substance use, and outlines the thesis aims and objectives.

1.2 Defining Surgery and the Incidence of Surgery

The online Oxford dictionary defines the word “*surgery*” as: “*The treatment of injuries or disorders of the body by incision or manipulation, especially with instruments*.” Naturally, such a broad conception obscures the fact that what constitutes surgery is in practice more nuanced and subject to a range of idiosyncratic definitions. Assessing the precise number of surgical operations performed each year in the UK is difficult, not just because of the complexity and scope of the NHS, but because this number differs depending on variation in how one defines the term surgery.

Perhaps the best contemporary estimates come from an analysis of NHS data by Abbot et al. (2017). Here, the authors chose to assess the yearly incidence of surgeries according to “*inclusive*”, “*intermediate*” and “*restrictive*” definitions; the first including minor interventions[1]: any invasive, including diagnostic, procedures (i.e., any procedures involving the insertion of an instrument into the body through the skin or a body orifice; as opposed to non-invasive); the second including procedures involving general (i.e., induction of controlled unconsciousness) or regional anaesthesia (i.e., numbing of a specific body area) and/or procedures performed in an operating theatre; and the third including major[2] procedures only (throughout this thesis, unless otherwise specified, the intermediate definition of surgery will be used). The authors identified a yearly average of 7,926,360 (12,537 per 100,000 head of population) inclusive; 5,104,165 (8073 per 100,000) intermediate; and 526,421 (2414 per 100,000) restrictive procedures, respectively. The authors also found that across five years these figures increased 5.3%, 4.2%, and 6.5% within each category (a worldwide trend [Weiser et al., 2015], likely associated with increases in life expectancy). Given such a high incidence, the cost of surgical care is growing and represents a large proportion (approximately 9%) of the total NHS budget (Abbot et al., 2017) - which itself is approximately 9.8% of the total UK GDP (see Appleby & Gershlick, 2017), and almost 20% - approximately £145 billion - of total government expenditure (HM Treasury, 2016). For an overview of key statistics in the UK, see Table 1.1.

Table 1.1. An Overview of Surgery in the UK.

Procedure complexity	**Annual frequency (% of total)**	**30-day mortality (%)**	**Median hospital stay (days)**	**Approximate annual cost (£)**
Minor	2,282,871 (30.4)	1.7	1	1,259,448,935
Intermediate	2,809,170 (37.4)	0.9	1	2,459,712,092
Major	1,781,877 (23.7)	0.8	2	3,042,633,330
Major plus	408,312 (5.4)	1.0	3	2,041,534,339
Complex	238,025 (3.2)	2.1	7	997,079,264
Total	7,520,256	1.2	-	9,800,407,961

Notes. Data were taken and adapted from Abbot et al. (2017), where procedures are categorised according to the BUPA system (BUPA, 2018), and 30-day mortality is reported as the average percentage across five years. Note that frequency figures here differ to the definitions provided above due to conversion between two coding systems (OPCS4 and CCSD) (see subsection 1.2.2). See the original paper for data sources and further methodology.

1.2.1 Surgical Terms

It is beyond the scope of this thesis to precisely define a host of anatomical terms, though it may be necessary to provide a general overview. The names of specific surgical procedures are generally made up by a prefix and a suffix; the prefix denotes the area of the surgery (e.g., rhino-, nose) and the suffix provides a description of the procedure (e.g., -plasty, to modify/reshape). In this example, a rhinoplasty would be a reshaping of the nose, or what is more commonly known as a *nose job*. Table A1 provides an overview of common surgical terms and can be used as a reference. Not all procedures follow this structure (e.g., coronary bypass graft) and for this thesis, which does not focus on one specific procedure, surgeries are best defined in broader categories.

1.2.2 Surgical Classification

Though surgeries may be broadly categorised by the speciality training of the surgeon undertaking a procedure (e.g., an awake craniotomy may be considered “*neurological*”, or a microdiscectomy may be considered “*spinal*” or “*orthopaedic*”) – more granularity can be achieved using a classification system. To provide a common language between clinicians, to standardise costs (e.g., for insurance claims), and to ease data collection and collation, several such classification systems exist. These include the BUPA (BUPA, 2018) and the AXA Schedule of Procedures (AXA, 2018) (which are, in turn, based on the Clinical Coding & Schedule Development Group [CCSD] codes; see CCSD, 2018). In CCSD-based systems of categorisation, surgery is categorised by the general anatomical feature or area of interest (e.g., abdomen), a more specific body area (e.g., stomach) and by surgical complexity (also referred to as *severity*): minor, intermediate, major, major plus and complex. The degree to which a surgery is categorised as increasingly complex (e.g., major versus minor, or major plus versus intermediate) reflects increasingly expensive procedures, and procedures more associated with complications (e.g., Davenport, Henderson, Khuri & Mentzer, 2005; Milad, Sokol & Chuang, 2002). Some specialities and body areas are inevitably associated with more complex and risky surgical procedures (e.g., cardiac surgery). In this thesis, surgeries are classified both by speciality (Study 2 and 5) and when more detail was deemed necessary, a CCSD-based classification system (Study 3).

1.3 Elective Surgery

As opposed to emergency surgery, that is, a procedure for an acute medical condition that needs to be addressed as soon as possible (where, without immediate intervention, a patient is at risk of significant disability or death), elective surgery is scheduled in advance. More specifically, the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) classification system, which is routinely employed, categorises surgeries into four groupings: immediate, urgent, expedited and elective (NCEPOD, n.d.). The focus throughout this thesis is on the latter.

1.3.1 The Perioperative Pathway

A patient's journey to elective surgery is often termed the *perioperative pathway*. During the pathway, interventions are often delivered to optimise the patient's recovery (see subsection 1.5.1). The typical patient pathway can be described relatively straightforwardly, though there is slight variation due to the disparity in the protocols of specific NHS trusts or sites. For a more in-depth picture of the following description, see *Figure 1.1*.

The beginning of a patient's journey to elective surgical treatment generally begins after primary care referral to a specialist in secondary care. At both stages, tests may be performed to determine whether surgery is in the patient's best interests. When it is determined that the patient does require an operation, the patient's local hospital is alerted, and the patient attends an outpatient appointment called a preoperative assessment - generally at the hospital's nurse-run (or *nurse-led*) preoperative assessment clinic (PAC). This assessment is performed by a nurse, with support from clinical support workers (see section 1.5). Each site will have exclusion criteria (e.g., high blood pressure) which, depending on whether the patient meets it, leads to a referral to either an anaesthetist or another specialist for further tests or treatments (see Appendix A for the NICE recommendations). Following the tests and treatments, the patient is judged by the exclusion criteria again – if they meet them, the patient must determine, with help from clinical staff, whether they wish to undergo treatment with significant risks to their health. Some surgeons and/or anaesthetists may even refuse to operate on and/or anaesthetise the patient due to the risks. If they pass the criteria (at either point in time), or it is decided that the benefits of surgery outweigh the risks, a preliminary surgery date, and preoperative tests dates, are agreed by both the patient and clinical staff (if a date cannot be booked, for various reasons, the patient follows a slightly different pathway – see *Figure 1.2*). The patient is subsequently given information about their procedure and instructions for best preparation. If necessary, the patient is tested for any relevant issues in the preceding weeks prior to surgery and treated/not treated as appropriate (which could delay surgery). Following satisfactory treatment or test results, the patient has their operation, with the specific procedure incurring different recovery pathways.

Pathway delay. In 2010, the NHS constitution was amended to implement a maximum 18-week window between GP referral to non-urgent, consultant-led treatment (i.e., elective surgery) (or simply *referral to treatment* or

RTT). In 2012, it became a legal requirement for the NHS to meet this target in 92% of all patients[3].The percentage of patients being admitted within this window has steadily declined since 2012, and in June 2018 this figure stood at 87.8% (QualityWatch, 2018). Alongside a delay in treatment has been a rapid increase in the number of patients on the waiting list for treatment. By 2017, this had reached over 4,000,000 patients (Iacobucci, 2017) the highest number since records began in 2007. Even more worrying, the number of patients waiting over 52 weeks since GP referral has been steadily increasing since around 2013; in June 2018 this figure stood at 3517 patients (QualityWatch, 2018).

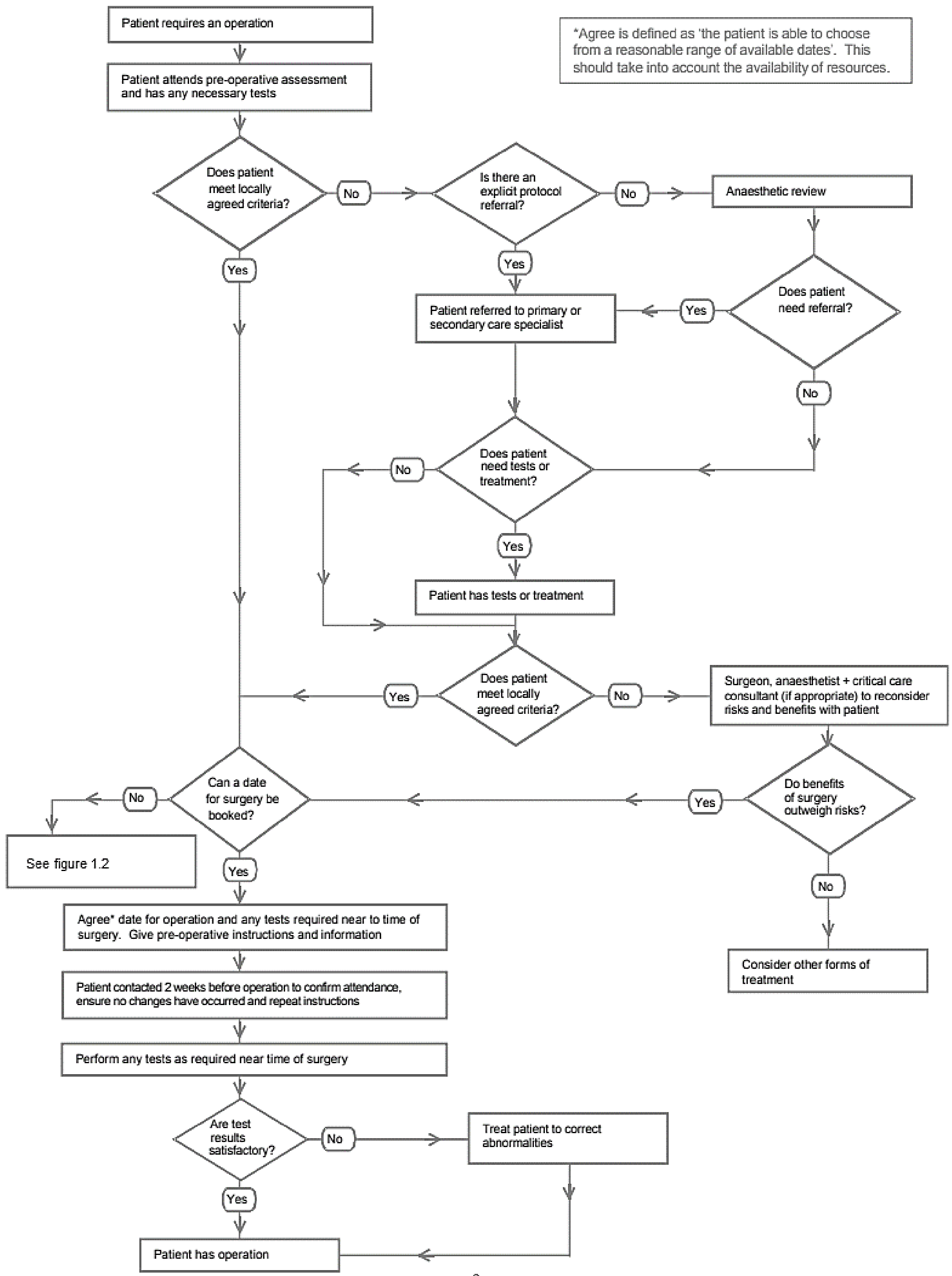

Figure 1.1. Elective Surgery Patient Pathway.

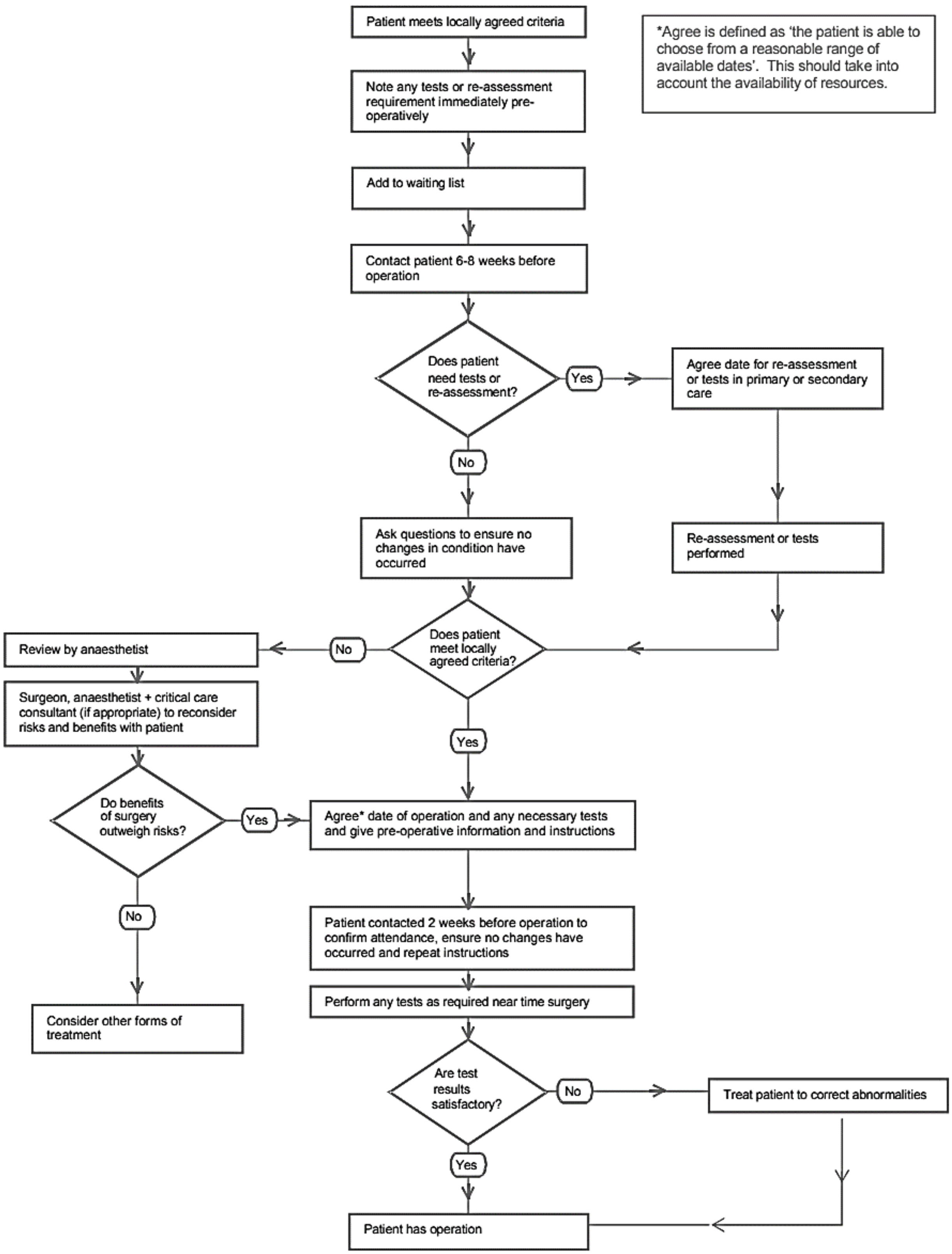

Figure 1.2. Elective Surgery Patient Pathway (Alternative).

1.4 Surgical Complications

In the sections above, there have been passing mentions to the risks of undergoing different types of surgery, including the use of term *complication*, but little further explanation. But what exactly are surgical complications? There can be both simple and more expansive answers to this question.

1.4.1 Defining Surgical Complications

Recognizing that the difficulty with proposing a definition of surgical complications is trying to parse out morbidity intrinsic to a particular surgery, and unexpected morbidity experienced during or after that surgery (and failure of a surgery to meet a specific goal, such that the harmful condition to be treated returns or persists), Clavien, Sanabria and Strasberg (1992) proposed a simple definition: *any deviation from the normal postoperative course that is not a failure to cure, or sequalae (or the after-effect) inherent to the procedure*[4]. More specifically, four increasingly hazardous grades of complications were initially proposed, though these have since been updated in 2004[5] (following extensive reliability testing with quite remarkable, almost perfect levels of between-surgeon inter-rater reliability) (Dindo, Demartines & Clavien, 2004). In 2008 Clavien and Dindo (2008) proposed that the initial definition *normal postoperative course* should be modified to *ideal postoperative course* (as it is less subject to subjective interpretation) which is arguably the most useful, popular and precise definition of surgical complications created to date.

1.4.2 Assessing Surgical Complications

In practice, there are several useful ways of assessing perioperative complications for research and other data analysis (e.g., service evaluation). A landmark review paper by the European Society of Anaesthesiology and European Society of Intensive Medicine (ESA-ESICM) joint taskforce on perioperative outcome measures provides a comprehensive overview (Jammer et al., 2015). Here, precise definitions (including clinical cut-offs) and severity gradings are provided for assessment of a wide range of individual deleterious conditions (e.g., surgical site infection), alongside best-practice composite measures (including quality of life/recovery measures). The paper recommends that all outcomes are assessed up-to 30 days post-surgery, except for mortality, which they suggest should be assessed up to 90 days (or, ideally, a year).

In reality, and as routine, the above outcomes are often not typically recorded in such detail by the relevant clinical systems (especially at the patient-level, and especially following discharge from hospital), thus require complex retrospective coding and/or prospective planning to assess, likely requiring some degree of patient follow-up (invariably at large time and monetary expense). Therefore, several useful proxy measures of complications are often used in many studies which are easier to capture (as they are recorded or can be calculated using data routinely collected on site) (e.g., see Chapter 4) but are more vulnerable to statistical noise. Such outcomes typically include: hospital readmission (for a specific condition or all-cause; and whether to A&E or a repeat surgery) within a set period (usually 30/90 days), length of hospital stay (which could indicate a delayed recovery, or the incidence of new complaints), unexpected admissions to high dependency (HDU) or intensive care units (ICU), delayed discharge, and conversion of a day case procedure to inpatient procedure (unplanned admission). Such outcomes are best to identify whether a problem exists but are less well placed to identify the nature of that problem.

1.4.3 The Incidence of Surgical Complications

Several studies have tried to estimate the incidence rate of surgical complications on a broad level (i.e., across surgeries) and at the level of categorizations outlined above (e.g., by surgical complexity and/or surgical speciality). One study by the International Surgical Outcomes Study Group (ISOS, 2016) provides an exceptional assessment of both. Across 474 hospitals in 28 countries, 16.8% of 44,814 patients undergoing an elective inpatient procedure suffered an in-hospital complication (0.5% died). Almost a third (26.8%) of patients undergoing *major* procedures suffered a complication, versus 8% of those undergoing *minor* procedures (see Table 1.2). Note that when the outcome period is extended to the commonly used (and ESA-ESICM recommended) 30-days, the percentage of patients developing complications appears higher (e.g., Alibhai et al., 2005; Calland et al., 2002; Woodfield et al., 2016). Though, in contrast to inpatient surgeries, outpatient/day surgeries (i.e., ambulatory surgeries) - that is, procedures with no overnight hospital stay, may be relatively less risky[6]. Of course, all incidence rates are averaged across patients; individual risk may be greatly increased by certain patient factors (see section 1.5).

Table 1.2. In-Hospital Complications and Deaths by Surgical Complexity and Type (Within Categories) in Elective Admissions across 28 Countries.

	Complications (%)	Mortality (%)
Surgery complexity		
Minor	8.0	0.2
Intermediate	12.3	0.3
Major	26.8	0.9
Surgery type		
Orthopaedic	16.5	0.3
Breast	8.3	0.1
Obstetrics and gynaecology	9.8	0.1
Urology and kidney	14.8	0.2
Upper gastrointestinal	24.4	1.5
Lower gastrointestinal	24.3	1.0
Hepatobiliary	16.0	0.6
Vascular	25.6	0.9
Head and neck	10.4	0.2
Plastics and cutaneous	14.6	0.3
Cardiac	57.0	2.3
Thoracic	26.4	0.9
Other	10.0	0.2

Notes. Data were taken and adapted from ISOS (2016).

1.4.4 The Consequences of Surgical Complications

The effect of surgical complications can be considered from many angles: the physiological and psychological effect on patients, the psychological effect on clinical staff (particularly surgeons) and the cost on a micro level (e.g., to the hospital) and macro level (e.g., to the taxpayer).

Consequences to patients. Suffering a perioperative complication may have long-term effects on patients including prolonged or chronic pain and disability. Of course, this is highly heterogeneous and based on the specific nature of the complication (e.g., severity and area). On a more general level, suffering more severe versus less severe postoperative complications has shown to (as calculated by a standardised index based on Clavien-Dindo criteria) confer a 22% increased risk of 5-year mortality (Slankamenac et al., 2017), and significantly increase the risk of hospital readmission. In a large study of 105,951 patients undergoing eight types of surgeries, independent of preoperative risk factors (discussed later in section 1.5) patients suffering any complication up to 30 days post-surgery had a 69% reduced median survival time (versus those suffering zero complications) (Khuri et al., 2005). More specifically, the top three most risky complication types were: cardiac (reducing survival duration by 99%), pulmonary (87%) and neurologic (85%)[7].

It is highly likely that suffering the acute physiological consequences of complications (e.g., pain or discomfort) and being vulnerable to the chronic consequences (e.g., disability or death), would confer a great deal of mental distress. One systematic review found considerable support for this hypothesis (Pinto et al., 2016). Briefly, the review found statistically significant lower physical and mental quality of life scores in those suffering complications (versus those not so) with a majority of studies finding significantly worse postoperative psychosocial outcomes in those suffering complications, including in studies of minor as well as major surgeries (32 studies). Further, the effect often remained after controlling for confounding factors and persisted 12-months post-surgery or later. These negative findings are compounded by the fact that poor mental health and wellbeing have been observed to independently predict postoperative complications (after controlling for a host of confounding variables) in studies with samples including thousands of surgical patients (Britteon, Cullum & Sutton, 2017; Linnen et al., 2011). The effect may be a deleterious cycle: preoperative mental distress (which tends to be high in surgical patients *per se* e,g., Triffaux et al., 2001) increasing the risk of perioperative complications, and suffering complications increasing the risk of more mental distress. This cycle is discussed in greater detail in subsection 3.1.1.

Consequences to surgeons. There is a literature investigating the psychological impacts of medical errors on surgeons, where the direct consequences of adverse events can be relatively severe. For instance, in Shanafelt et al. (2010), 7199 surgeons who did not report making a major error in the previous 3-months were compared to 700 surgeons who did. The latter had twice the rate of clinical depression (27.5% versus 54.9%; $p < .001$) and scored significantly worse on features of burnout (i.e., emotional exhaustion; depersonalisation; and personal accomplishment), quality of life and career satisfaction (all with large effect sizes). Such findings have been replicated in other studies. For example, one UK study found that one-third of 47 surgeons suffered symptoms of traumatic stress one month after the event (while also finding that a specific coping style, self-distraction, was associated with worse outcomes) (Pinto et al., 2014). In a qualitative study involving 27 surgeons, it was found that: complications may make surgeons more risk-averse – possibly impacting on patient care; that surgeons felt that there needed to be more institutional support in place for them; and that many surgeons embraced coping styles that may not be conducive to maintaining mental health (Pinto, Faiz, Bicknell & Vincent, 2013)[8].

Consequences for the NHS. The financial burden of surgical complications on healthcare systems is considerable. Healy, Mullard, Campbell and Dimick (2016) managed to link datasets containing complications and internal costing data across Michigan based hospitals, where details of 5120 surgical procedures (across 24 types) were investigated. Almost 15% of all procedures involved a complication. It was found that surgical procedures involving a complication were 119% more expensive than those without (mean $36060 versus $16434). In support, Vonlanthen et al. (2011) managed to identify a form of dose-dependent relationship between complications and cost. Of 1200 surgeries (across four types), procedures without a complication cost an average of $27946, whereas those involving a Clavien-Dindo graded complication of I cost $30739. The cost dramatically increased each graded step, where procedures involving a grade IIIa, IIIb and IVa/b complication cost $53388, $97001 and $159345, respectively. Given that prolonged hospital stays may cost an excess of £2500 a week in the NHS (NHS, 2018) reducing the incidence of complications would save the NHS a significant degree of vital resources in this era of financial strain (see Robertson, Wenzel, Thompson & Charles, 2017).

1.5 High-Risk Patients and Preoperative Assessment

There are several ways the incidence of perioperative complications *may* be reduced, including the adoption of new surgical techniques. Perhaps one the most cost-effective, however, is to give patients about to undergo surgery the best chance of success. This success can be bolstered by preoperative screening and treating of conditions which may interfere with successful recovery. There is evidence to suggest that most of the cost of complications come from a group of patients who are at *high risk* (Pearse et al., 2006). There are numerous risk factors which may modify the outcomes of surgery.

1.5.1 Increasing Risk: Comorbidities

There are a number of conditions that are associated with an increase in perioperative complications, including: hypertension (Howell, 2018), anaemia (Musallam et al., 2011), arrhythmias, cerebrovascular and coronary artery disease (Fleisher et al., 2014), kidney disease (Ackland et al., 2011), pulmonary disease (Smetana, 1999), sleep apnoea (Casey & Teodorsescu, 2015), and endocrine disease (e.g., diabetes) (Buchleitner et al., 2012). Older patients have been observed to suffer a higher number of complications in many studies (e.g., Yu et al., 2013) – though a recent review found that this is best explained by a *geriatric syndrome* including increased levels of frailty and cognitive impairment (Watt et al., 2018a; 2018b). In a systematic review of predictors of complications, consistent predictors included: hyponatremia, preoperative sepsis and increased white blood cell count (Visser et al., 2015; see Table 1.3). Lastly, as above, there is a large amount of evidence to suggest that poor mental health and wellbeing is associated with poorer postoperative outcomes also (see subsection 3.1.1).

Table 1.3. Some Identified Predictors of Surgical Morbidity and Mortality.

Predictor	Mortality odds ratio ranges (*n* of studies)	Morbidity odds ratio ranges (*n* of studies)
Comorbidities		
ASA-PS classification	1.54–11.60 (4)	1.77–7.10 (8)
Dyspnoea	1.22–6.25 (5)	1.22–1.30 (3)
Previous cardiac intervention or failure	1.37–2.87 (3)	1.21–2.00 (5)
Preoperative sepsis	2.10–2.97 (3)	1.32–1.99 (3)
Chronic obstructive pulmonary disease	1.31–1.97 (4)	1.22–1.67 (3)
Ascites	1.80–3.54 (3)	1.47–1.77 (3)
Cerebrovascular disease	-	1.30–7.63 (3)
Diabetes	1.37–10.98 (3)	1.84–5.14 (2)
Dialysis	2.30–5.70 (3)	-
Hypertension	-	1.21–1.70 (3)
Laboratory values		
Increased creatinine	1.70–1.71 (3)	1.39–2.14 (5)
Preoperative albumin	1.33–2.20 (2)	1.13–1.67 (4)

Notes. Data taken and adapted from Visser et al. (2015). For ASA-PS definitions see Table 1.4.

1.5.2 Quantifying Risk

As there is a complex interaction between the risk of co-morbidities and the inherent risk of particular surgeries, a variety of tools exist to help guide clinical decisions based on observational data. Such calculators can quantify the individual risk of mortality or complications for specific patients. By outlining the *inputs* to these calculators (and thus the predictors the supporting models are based upon) factors considered most important in determining risk can be identified.

One calculator is the Surgical Outcome Risk Tool (SORT) (NCEPOD, n.d.)[9] which provides a percentage risk of 30-day postoperative mortality, after nine multiple choice entries are entered: four related to the surgery site and description, and one each related to the surgical complexity (in line with CCSD codes), the urgency (in line with NCEPOD guidelines), a diagnosis of cancer, and age. SORT also needs the clinician to enter an American Society of Anaesthesiologists Physical Status score (ASA-PS); a classification system widely used in routine practice to group patients according to the degree to which their co-morbidities may impact on surgical outcomes. ASA-PS classifications (see Table 1.3 for ASA-PS scores as predictors of complications; Table 1.4 for ASA-PS classification definitions alongside complication incidence data) have demonstrated considerable inter-clinician reliability (Sankar et al., 2014) and strongly predict the incidence of postoperative complications across procedures (Hackett et al., 2015). ASA-PS[10] scores are often used to partial out the confounding effect of co-morbidities when looking at factors which impact postoperative outcomes (as in Chapter 4, alongside other SORT inputs).

Table 1.4. ASA-PS Definitions and Complications.

ASA PS Classification	**Definition**	**% of patients with complications within classifications**
ASA I	A normal healthy patient	7.6
ASA II	A patient with mild systemic disease	13.5
ASA III	A patient with severe systemic disease	30.3
ASA IV	A patient with severe systemic disease that is a constant threat to life	53.4
ASA V	A moribund patient who is not expected to survive without the operation	-

Notes. Data were taken and adapted from ISOS (2016). ISOS (2016) did not use data from ASA V patients.

1.5.3 Detecting Risk

Nurse-led[11] preoperative assessment (as in subsection 1.3.1) is seen as an important feature of the perioperative pathway, where factors that may be to the detriment of a successful surgery are identified (and modifiable factors are targeted for intervention e.g., anaemia and iron injections). Preoperative assessments tend to follow the American Society of Anaesthesiologists' *Practice for Preanaesthesia Evaluation*: patient interview, an examination of the airway, lungs and heart; a review of relevant medical records; necessary preoperative tests; and consultations with specialists as appropriate (Apfelbaum et al., 2012).

Indeed, when conducting preoperative assessments, nurses generally interview patients in accordance with a standardized form with sections for detailing past medical history and screening for issues across bodily systems (e.g., gastrointestinal and endocrine systems) (see Appendix B). It is also common for one section to require assessors to ask the patient about lifestyle behaviours. As in Appendix C this section is often short, may neglect specific behaviours (e.g., physical activity) and often includes non-validated measures of behaviour. This is an important omission; lifestyle factors may have serious implications for surgical recovery (see subsection 1.6.1) - and, unlike comorbidities such as frailty, may be acutely modifiable. Lack of emphasis on lifestyle behaviours in routine practice is evidenced also i. in risk calculators as above (which often do not account for these behaviours), and ii. because patients are often not routinely exposed to preoperative interventions to alter behaviours e.g., alcohol use. This emphasis, however, may be changing.

1.6 Lifestyle Behaviours: Recent Interest

In recent years, there has been a boom in interest and discussion around lifestyle behaviour and surgery. This includes an editorial in the British Medical Journal stating that while there have been some fantastic efforts to improve surgical care (e.g., the Enhanced Recovery programme; Paton et al., 2014): "*the focus is largely on in-hospital care* [and that] *current approaches fail to acknowledge the role of the patient in optimising their eligibility for surgery and improving surgical outcomes"* (Wynther-Blyth & Moorthy, 2017, online). Similarly, the initiation of a new programme by the Royal College of Anaesthetists (with a "*vision document*") entitled *Perioperative Medicine: The Pathway to Better Surgical Care* (2014) calls for improved and evidence-based targeted care at all stages of the patient journey, including "*prehabilitation"*[12]*.* There has also been controversy in the UK press following decisions by two clinical commissioning groups to deny elective surgery to obese patients and patients who smoked ("*Decision to deny surgery to obese patients like 'racial discrimination'" -* Rawlinson & Johnston, 2016; "*NHS under fire after announcing obese patients will not get non-urgent surgery until they lose weight"* - Bulman, 2017) (but see a detailed response from medical professionals: Pillutla, Maslen & Savulescu, 2018). A 2015 piece by two prominent clinicians suggests that pre-surgery may be a *teachable moment* (see subsection 2.6.3 for more discussion of this concept) to modify lifestyle behaviours; that lifestyle behaviours' "*risk increase is not marginal, with reported increased complication rates up to five-fold for each individual unhealthy behaviour*."; and that "*The number of behaviours* [that can be targeted effectively] *appears to be two to three, with this creating an* *opportunity to address smoking, alcohol excess and inactivity as a minimum in the weeks available prior to surgery. Although a major challenge, the benefits accrued by achieving change would be substantial*." (Danjoux & Kothmann, 2015, p. 27). These calls, no doubt, are in response to an ever-growing literature base demonstrating a link between lifestyle behaviours and perioperative outcomes.

1.6.1 Increasing Risk: Lifestyle Behaviours

Aside from a variety of physical and mental health conditions, there is a great deal of evidence to suggest that specific lifestyle behaviours may impact on the success of surgery. Onerup et al. (2015) found that among 200 cholecystectomy patients, those engaging in regular versus zero physical activity where significantly more likely to return to work in three weeks (26% increased chance); and Nevo et al. (2016) who found that a lower postoperative step counts could significantly predict postoperative complications. This is mirrored in studies including breast cancer (Nilsson et al., 2016), and esophagectomy patients (Feeney, Reynolds & Hussey, 2011; Tatematsu et al., 2013). Systematic reviews of exercise therapy before and after surgery (Hoogeboom et al., 2014) seem to corroborate the above evidence, and a recent and in-depth report in the *British Journal of Anaesthesia* (Richardson et al., 2017) recommends more attention to, and research in, the area.

Associated with a lack of physical activity, but also eating behaviours, is obesity. While this may be not a behaviour *per se*, weight is eminently modifiable and may be considered an index of one's eating and exercise behaviour. There is an abundance of research outlining the specific issues of operating on obese patients (e.g., Pasulka et al., 1986; Motonari, Aikou & Seto, 2018). Of observational evidence, individual meta-analyses have found that obesity is associated with various complications related to breast reconstruction surgery (Lee & Mun, 2016; and mammaplasty specifically: Myung & Heo, 2017), transplant surgeries (Barone et al., 2017; Sood, Hakim & Hakim, 2016), and orthopaedic surgery (Yuan & Chen, 2013). Many clinicians may refuse to operate on non-urgent patients who are obese; it may be in the patient's best interest to avoid surgery - especially considering weight loss prior to surgery may reduce the incidence of postoperative complications (e.g., Anderin, Gusafsson, Heijbel & Thorell, 2015). Sleep hygiene behaviour, which may also greatly impact surgical recovery, has also been highlighted as an area for further research (Su & Wang, 2017).

Many of the co-morbidities outlined in subsection 1.5.1 may actually be a result of lifestyle behaviours, though unique variance in outcomes is often explained despite controlling for morbidities. One key difference between many of the above comorbidities and behaviours is the degree of modifiability; while certain conditions may be chronic and permanent, behaviour is always subject to change. Thus, deleterious lifestyle behaviours may be particularly useful intervention targets for reducing excess risk.

CHAPTER 2. PERIOPERATIVE SUBSTANCE USE: A LITERATURE REVIEW

2.1 Introduction

Behaviours may greatly impact recovery from, and success of, surgery. This chapter examines one such behaviour: recreational substance use. This chapter partly aimed to provide a rationale for the thesis aims and objectives introduced at the end, though also aimed to be a standalone and comprehensive literature review - providing directions for future research not addressed in this thesis. Discussed are topics that are essential to the formulation of a preoperative intervention, namely preoperative substance use: risk magnitude and mechanism(s), prevalence, identification and detection (modelled in *Figure 2.1*), and the current literature regarding possible intervention strategies.

Smoking was not a focus of this chapter or thesis for three reasons: i. there has been an abundance of research on smoking (e.g., subsection 2.3.2), ii. supervisors of the PhD candidate were concurrently engaged in a project on preoperative smoking cessation, and iii. contrary to alcohol use, smokers are often *routinely* advised to quit. Nevertheless, given evidence linking smoking and postoperative complications, it was deemed useful to briefly outline some below. Note also that this thesis has an emphasis on alcohol use over other substance use. This for two key reasons: i. as outlined below, hazardous preoperative alcohol use is more prevalent than other substance use, and ii. users of substances other than alcohol are largely represented by younger individuals, who may be less likely to suffer surgical complications due to age-related conditions (or have surgery *per se*)[13].

2.2 Recreational Substance Use in the UK

According to the Office for National Statistics (ONS, 2017), 8.5% of 16-59 year-olds used an illicit substance in England and Wales in 2016/17, and at the time of survey, 4% of all respondents had used an illicit substance in the previous month (though this figure was over double in 16-24 year-olds). Deaths attributed to illicit substances amounted to 2,593 in 2016 – the highest ever recorded, and from 2006/2007 to 2016/2017 hospitalisation due to illicit substance poisoning and substance influenced mental and behavioural disorders rose by 40% and 115%, respectively. Illicit substance use is a public health issue costing NHS England £488 million and UK society £15.4 billion (Public Health England, 2014). Though illicit substance use is significant, the prevalence of hazardous alcohol use is much greater, and the impact on society greater still.

Around 24% and 11% of British males and females drink at risky levels (approximately 5% and 2% drinking at high risk or dependent levels) (Public Health England, 2017). Alcohol Concern (2016) highlights that i. alcohol use is a causal factor in 60 physical/mental health conditions, ii. alcohol use was responsible for approximately 9000 UK deaths in 2016, and iii. in 2014/15 there were 1.1 million hospital admissions due to alcohol use. Further, just 15% of alcohol-dependent individuals in treatment were referred from healthcare professionals and that among 595,131 alcohol-dependent Britons just 108,696 are receiving help. Excessive alcohol use costs the NHS £2.7-3.5 billion yearly (HSCIC, 2015), though this figure is likely rising; admission rates to hospital due to mental and behavioural disorders associated with alcohol use has increased 94% from 2006-2016.

2.3 Perioperative Substance Use Risks

2.3.1 Alcohol

In a meta-analysis including over 1.2 million patients (Eliasen et al., 2013), hazardous preoperative alcohol use versus non-hazardous use or abstinence (i.e., highest alcohol use categories versus the lowest in each study) significantly and greatly increased the risk of 30-day postoperative complications across various outcomes (e.g. 73% increased risk of postoperative infection). In studies with *clearly defined* high alcohol use (e.g., Alcohol Use Disorder Identification Test-Consumption [AUDIT-C] score of >4), these differences were greater (e.g., 168% increased risk of death). There was no strong tendency for complications to be more prevalent between noted surgery types, though some surgery types were more conducive to particular types of complications. For a more in-depth overview of the results see Table 2.1.

There have however been several other studies not identified in this meta-analysis. In some, hazardous alcohol use may have increased the incidence of complications in samples lower than 200. Mulligan et al. (2018) (*n* = 132) found that those reporting more than 2 alcohol drinks per day versus those not so had significantly higher rates of minor complications (OR [odds ratio] = 4.71; 95% CI: 1.46-15.26) (elective ankle and hindfoot reconstruction surgeries); Harris et al. (2011) (*n* = 185) found that every additional point above 1 (out of 12) on a 3-item measure of alcohol use consumption (the AUDIT-C) conferred a 29% increase in the mean number of complications (OR = 1.29; 95% CI: 1.02–1.63) (total joint arthroplasty); and van Rooijen et al. (2016) (*n* = 139) found that those who drank more than 3 daily units of alcohol versus those not so had a 78% increased risk of *severe* complications (colorectal surgery). The largest recent study comes from Rotevatn et al. (2017) (*n* = 30,799). Here, it was found that mortality and morbidity were *reduced* in low to moderate alcohol drinkers versus abstinent individuals. This was not generally the case for those in the higher alcohol use categories thus supports the notion of a *J shaped curve*[14] in the perioperative context (which has long been a focus of research assessing the effects of alcohol use on health generally; e.g., Gmel, Gutjahr & Rehm, 2003). The implication, therefore, is that interventions and research should focus on *hazardous* preoperative alcohol consumption.

Gordon (2018) provides a concise but comprehensive overview of possible mechanisms for the impact of hazardous alcohol use on postoperative outcomes. First, excessive alcohol users may have lower T-cell counts (a white blood cell that destroys infected cells) and decreased delayed type hypersensitivity responses (a major physiological defensive against pathogens) – thus, in effect, alcohol use depresses the immune system, leading to increased infection susceptibility; second, they may have slower wound healing (a reduction in *protein accumulation*); third, they may have increased bleeding duration and frequency of bleeding episodes; fourth, they have a higher prevalence of cardiomyopathy (diseases of the heart muscle – more specifically, a *dilated left ventricle and reduced ejection fraction* i.e., a reduced ability to pump blood effectively) which, when combined with the increased cardiac exertion that accompanies surgery, may lead to postoperative arrhythmia (an irregular heart rhythm) and ischemia (an inadequate blood supply to the heart); fifth, alcohol dependent patients may suffer alcohol withdrawal syndrome; sixth, excessive alcohol users may require greater and unpredictable dose of anaesthetics making intraoperative management much more complicated (alcohol use acutely before surgery may *prolong* certain medications, though chronic use may reduce their effectiveness); seventh, surgery is known to activate the body's hypothalamic pituitary axis (HPA; the body's stress regulation system) greatly (termed the *surgical stress response*, leading to, for example, a greater production of immunosuppressive hormones) which excessive alcohol use has shown to increase; eighth, excessive alcohol use may affect intraoperative blood pressure homeostasis – which may exacerbate haemorrhage (an escape of blood from a blood vessel) or lead to postoperative delirium. (For more detail see Tønnesen et al., 1992; Spies et al., 1996; 2001; Tønnesen, Pedersen, Lavrsen, Tuxøe & Thomsen, 2012; Tønnesen, Nielsen, Lauritzen & Møller, 2009).

Aside from physical health, one potentially important and seemingly unexplored negative postoperative outcome of preoperative alcohol use is reduced mental health. For example, it is well established that both alcohol use and impending surgery (and having significant co-morbidities generally) are independently associated with an increase in psychiatric diagnoses (e.g., Conner, Pinquart & Gamble, 2009; Timberlake et al., 1997). It may be that the former may precipitate the latter and given evidence that certain individuals may increase substance use in times of mental stress (as a coping strategy e.g., Park, Armeli & Tennen, 2004), this may be a reciprocal relationship. Further, it has been repeatedly demonstrated that both alcohol use and low mental health may lead to an increased incidence of postoperative complications in very large studies – which in turn, may have long-lasting and large negative impacts on wellbeing and mental health outcomes (which may precipitate *further* complications) (Pinto et al., 2016).

There have been no studies to date looking at the relationship between preoperative alcohol use and postoperative mental health outcomes despite this plausible cycle. Chapter 3 explores this issue further.

Table 2.1. Preoperative Alcohol Use and Risk of 30-day Postoperative Complications.

	Risk ratio (95% CI) [*n* of studies]								
	Mortality	**Morbidity**	**Infection**	**Wound**	**Pulmonary**	**Cardio**	**Neuro**	**> LoS**	**ICU admis.**
All studies	1.36 (0.97–1.92) [14]	1.56 (1.31–1.87) [15]	1.73 (1.32–2.28) [12]	1.23 (1.09–1.40) [21]	1.80 (1.30–2.49) [12]	1.12 (0.78–1.61) [8]	1.11 (0.69–1.76) [8]	1.24 (1.18–1.31) [4]	1.29 (1.03–1.61) [3]
Clearly defined*	2.68 (1.50–4.78) [8]	1.84 (1.49–2.27) [8]	2.32 (1.54–3.48) [9]	1.58 (1.19–2.09) [11]	2.51 (1.29–4.90) [8]	1.28 (0.70–2.36) [6]	1.36 (0.64–2.90) [6]	-	-
Surgery type									
Abdominal	0.74 (0.34–1.63) [3]	1.28 (1.00–1.64) [4]	-	2.09 (0.73–6.02) [4]	-	2.16 (0.60–7.79) [1]	2.26 (0.15–33.71) [2]	-	-
Thoracic	2.51 (0.82–7.64) [6]	1.24 (0.91–1.70) [2]	2.70 (1.37–5.34) [5]	2.12 (0.72–6.18) [5]	2.11 (0.86–5.18) [5]	0.71 (0.46–1.08) [2]	0.97 (0.60–1.56) [2]	-	-
Head and neck	1.92 (1.04–3.53) [2]	2.31 (1.74–3.08) [6]	2.31 (1.17–4.56) [2]	1.15 (0.94–1.41) [6]	1.75 (0.50–6.04) [3]	1.23 (0.21–6.13) [3]	-	-	-
Other	1.18 (0.72–1.92) [3]	1.49 (1.09–2.03) [3]	1.22 (1.07–1.39) [5]	1.19 (1.15–2.44) [6]	1.98 (1.47–2.67) [4]	1.13 (0.92–1.39) [2]	1.17 (0.51–2.67) [4]	-	-

Notes. Data taken and adapted from Eliasen et al. (2013); * Clearly defined excessive alcohol use was defined as >24 grammes per day for women, > 36 for men, or AUDIT-C scores >4, or classification as having alcohol use related disorders; Cardiac: cardiovascular; neuro: neurological; > LoS: extended length of hospital stay; ICU admis: admission to an intensive care unit.

2.3.2 Smoking

As stated above, this thesis will not focus on smoking - though it is the second most used recreational substance in the UK, so a brief outline of the perioperative risks is outlined below.

In a meta-analysis of 107 studies, Grønkjær et al. (2014) demonstrated that smokers versus non-smokers were at higher risk of: mortality (in adjusted studies only; Risk ratio [RR]: 1.30; 95% CI: 1.08–1.56), general morbidity (RR: 1.52; 95% CI: 1.33–1.74), and wound (RR: 2.15; 95% CI: 1.87–2.49), infectious (RR: 1.54; 95% CI: 1.32–1.79), pulmonary (RR: 1.73; 95% CI: 1.35–2.23) and neurological complications (RR: 1.38; 95% CI: 1.01–1.88), to name a few. In another meta-analysis of randomized controlled trials of interventions to reduce preoperative smoking, it was found that intervention versus controls had significantly reduced postoperative morbidity (RR = 0.44; 95% CI: 0.27–0.65) and wound complications (RR = 0.31; 95% CI: 0.16–0.62) (Thomsen, Villebro & Møller, 2014). Given the above and given plausible physiological mechanisms (e.g., Tønnesen et al., 2009) a causal relationship appears likely. Due to the weight of evidence, and because cigarette smoking is *relatively* common (around one in six UK subjects; ASH, 2016) and easy to identify, patients are i. often advised to quit prior to their operation in routine practice and ii. often offered support to do so. It has been estimated that NHS London could save £2.6 million a year if 8-17% of smokers quit before having surgery (ASH, 2014). Note also that hazardous alcohol users/other substance users are more likely to smoke (e.g., see section 2.4 and Chapter 4).

2.3.3 Cannabis

Cannabis is the most commonly used illicit substance in the UK; 6.6% of all adults (16-59 years-old) used cannabis in the last year in 2016/2017 (9% of all males, and 4.2% of females) (ONS, 2017). England and Wales has the sixth highest lifetime cannabis use per capita in the European Union (ONS, 2017). Generally regarded as one of the least harmful illicit substances (e.g., Nutt, King & Phillips, 2010), there has been little observational research into its effects in the perioperative context. It is important to note that cannabis is commonly smoked (and often mixed with tobacco) when consumed, so many of the risks associated with perioperative smoking may be relevant here. A systematic review of the perioperative complications of cannabis use is currently in progress (see protocol: Tait, Aganesova, Sheridan, Møller & Imberger, 2016) – thus more robust conclusions may be drawn upon its completion. In the meantime, there have been many concerning case reports and several journal articles discussing the topic.

It has been suggested that cannabis has the potential to both antagonise and agonise anaesthetic drugs that affect blood pressure and respiratory and cardiovascular depression (n.b., Dickerson, 1980; see Kuczkowski, 2004) – making anaesthetic management difficult and unpredictable (such interaction effects have been observed in some case reports e.g., see Mills & Penfold, 2003; Kumar, Chambers & Pertwee, 2001). In one case report, cannabis was also implicated in one patient requiring double the average narcotic requirements for a patient of the same body weight and height (Karam, Abbasis & Khan, 2015), in others, preoperative cannabis use has purportedly been observed to induce postoperative airway obstruction (Mallat, Roberson & Brock-Utne, 1996), intraoperative convulsions (Symons, 2002), and lead to sustained and abnormal tachycardia (Gregg, Campbell, Levin, Ghia and Elliott, 1976). Indeed, aside from drug interactions, cannabis may induce respiratory and cardiovascular complications *per se* (Ashton, 1999). Importantly, due to its high fat solubility, cannabis may take up to 30 days to be eliminated from the body completely – thus, it may take a month of abstinence before these effects can be eradicated (Sharma, Murthy & Bharath, 2012; Kuczkowski, 2004). However, Dickerson (1980) recommended that anaesthesia i. be avoided within 72 hours of cannabis use, and ii. if unavoidable, regional anaesthesia should be used in place of general anaesthesia (as well as increased monitoring of respiratory and circulatory systems).

2.3.4 Cocaine

Cocaine is the second most commonly used illicit substance in the UK; from 2014-2015, cocaine was used by 2.4%% of all 16-59 year-olds (4.8% of 16-24 year-olds) (ONS, 2015). England/Wales has the highest lifetime cocaine use per capita in the European Union at one in ten adults (ONS, 2017). Cocaine use is considerably more concerning than cannabis use; even in casual users, the risk of myocardial infarction increases 24-fold, just one hour after taking cocaine (Mittleman et al., 1999). Again, however, there has been little observational evidence in the perioperative context.

There are numerous case reports of intraoperative and postoperative complications purportedly attributed to previous cocaine use (Inouye, Navin, Hardman, 2004; Vagts, Boklage & Galli, 2003; Elia, Gaeta, Licciardi & Boccalatte, 1996; see Skerman, 2005). The primary perioperative risks are related to the ability of cocaine to promote thrombosis – blood clots that can greatly increase cardiovascular and/or cerebrovascular morbidity (e.g., ischemia, arrhythmias or cerebral infarct) (Dwarakanath, Cook & Fahy, 2013). Cocaine may complicate anaesthetic care by inducing either hypo-, or hypertension; one study found that in cocaine-positive versus cocaine-negative patients, 62% of patients needing intraoperative vasopressors (i.e., anti-*hypo*tensives), and 76% anti-hypertensives, were from the former group – thus, the need for haemodynamic support is greatly increased in this population (Baxter & Alexandrov, 2012). Patients need not be cocaine-positive at the time of operation, as outlined with alcohol above, long-term use may induce a *sub-clinical cardiovascular risk* (Hernandez, Birnbach & Van Zundert, 2005). Cocaine use may also influence perioperative complications via pulmonary alterations; one review identified 20 different categories of such complications, including lung abscesses, infections and pneumonia (Terra Filho et al., 2004).

2.3.5 MDMA and Amphetamines

The third and fourth most used illicit substances are 3-4-Methylenedioxyamphetamine (MDMA, or ‘Ecstasy’) (an amphetamine-like stimulant) and amphetamines. The former may not pose considerable preoperative risks as MDMA use is often used irregularly (ONS, 2017) (and is considered not dependence forming e.g., Nutt, King & Phillips, 2012). There have, however, been concerns raised regarding emergency surgery performed on individuals with MDMA in their system. MDMA has been observed to induce hyperthermia (Dar & McBrien, 1996; Green, Cross & Goodwin, 1995; Henry, 2000) and through a mechanism which renders dantrolene, a common agent used to prevent this condition, ineffective (Steadman & Birnbach, 2003). Hyperthermia can cause rhabdomyolysis, among other maladies (Steadman & Birnbach, 2003; Moro, Ferraz & Módolo, 2006). The central *intraoperative* issues related to MDMA use are hypertension and tachycardia (Steadman & Birnbach, 2003; Moro, Ferraz & Módolo, 2006). Given these risks, there have been published guidelines for the intraoperative management of MDMA-positive patients (DeMaria, Bryson & Frost, 2009).

Pure amphetamines are widely prescribed for conditions such as narcolepsy. Unlike MDMA, amphetamines may be more conducive to habitual use. One prospective study found that legal preoperative use of amphetamines was not associated with any postoperative or intraoperative complications (Fischer, Schmiesing, Guta & Brock-Utne, 2006) though conflicting evidence exists **(**e.g., Perruchoud & Chollet-Rivier, 2008). However, amphetamines exert their action in a similar way to cocaine (Wise, 1984) so must share at least some of the perioperative risks. Additionally, those who use amphetamines are likely to take much higher doses for greater recreational effects, use adulterated batches, and use riskier routes of administration (e.g., intravenous or intranasal use). Indeed, one report outlined the intraoperative death of an amphetamine abusing patient due to *adverse cardiac decompensation* (Samuels, Maze, & Albright, 1979; see Vorrakitpokatorn & Limsakul, 2002). Other reports illustrate that amphetamines can interfere with anaesthetic requirements e.g., "*decrease the duration of thiopental* [and] *attenuate both the strength and length of succinylcholine muscle relaxation*" (Steadman & Birnbach, 2003, p. 149) and diminish the effects of Ephedrine (commonly used to mitigate hypotension) (Stibolt & Wachowiak-Anderson, 2002)**.** Lastly, a report of three cases of Khat (an African plant, often chewed, containing the amphetamine-related compound cathinone) users highlights that both the chronic (e.g., cardiomyopathy and arrthymia) and acute (e.g., analgesia and delayed gastrointestinal motility) have implications for anaesthesia (Bamgbade, 2008).

Importantly, MDMA and amphetamines are often adulterated with other potentially harmful substances (Green, King, Shortall & Fone, 2012) – and those admitting using in preoperative assessments may be unaware. This complicates matters further – the assessor and patients' medical team may have to be vigilant to this issue and consider the perioperative risks of compounds often mixed with these substances.

2.3.6 Opioids

Drugs within the opioids class of drugs (e.g., heroin) provide a particularly complicated situation for perioperative care. In the UK, seven in 1000 16-59 year-olds use opioids, with Yorkshire and the Humber having the highest prevalence (one in every 100 use crack-cocaine and/or opioids) (HSCIC, 2014). These drugs are particularly addictive, with an especially gruelling withdrawal syndrome. They are often used intravenously, adding a host of additional physiological risks (Mathers et al., 2013).

Comparing 15,901 dependent orthopaedic patients with millions of controls, Menendez, Ring and Bateman (2015) found that preoperative opioid users had 3.7 times the odds of dying in the perioperative period versus non-users (odds ratio [OR] 3.7; 95% CI: 2.7-5.1), 2.3 times the odds of suffering any morbidity (OR 2.3; 95% CI: 2.2-2.4) (including respiratory failure [OR 3.1; 95% CI: 2.7-3.6], and surgical infections [OR 2.5; 95% CI: 2.0-3.0]). In addition, these patients were more likely to have a prolonged hospital stay (OR 2.5; 95% CI: 2.4-2.5). The authors recommend preoperative screening for opioids, denying/delaying opioid users' surgery and closely monitoring users that do undergo surgery. Two other large studies have observed increased readmission (Ben-Ari et al., 2017) and length of hospital stay (Waljee et al., 2017). The second of these studies also found that opioid users versus non-users require more resource utilisation at 30 days ($5,405.40 vs. $3,681.70), 60 days ($10,148.20 vs. $6,469.80) and 90 days ($19,695.60 vs. $11,419.40) following surgery.

If surgery does indeed go ahead with opioid users, several points should be addressed. Firstly, patients requiring anaesthesia may be hypotensive and have haemodynamic instability (Hernandez, Birnbach & Van Zundert, 2005). Postoperative pain is likely to be more pronounced also (Huxtable, Roberts, Somogyi & MacIntyre, 2011). Intraoperative and postoperative opioid analgesia doses may need to be increased (Armaghani et al., 2014) – indeed, some 30-100% (Goyal, Khurana, Jindal & Sharma, 2013) and it should be noted that opioid use induces a cross-tolerance to many anaesthetics (Hernandez, Birnbach & Van Zundert, 2005). A carefully managed substitution therapy – primarily using methadone – has been recommended for dependent inpatients (see Goyal, Khurana, Jindal & Sharma, 2013). Indeed, there is nascent evidence to suggest that reduction prior to surgery can confer significant benefits (Nyugen, Sing & Bozic, 2016; McAnally, 2017). For ex-dependent patients, it has been recommended that opioids be used sparingly (alongside non-opioid alternatives) (see Hariharan & Garg, 2015). Practitioners should be vigilant to common comorbidities in these patients also (e.g., 57.7% of methadone users have shown to be in poor health [including 54.3% having arthritis [Rosen, Smith and Reynolds, 2008]). For a review of opioid use and surgery, see McAnally (2017).

2.3.7 Other Substances

Other substances that are often used recreationally have drawn little attention but should be considered. A review of 29 cohort studies found that benzodiazepine use was associated with a 110% (95% CI: 1.23–3.59) increased risk of postoperative delirium (Kassie et al., 2017). Highlighting the impact substances may have generally on postoperative outcomes, this review also found that preoperative psychoactive medicine users' *per se* had a two-to-seven-fold higher risk of delirium versus patients not taking these medicines prior to surgery. A review of preoperative inhalant (e.g., Butane) use provides some concerns; inhalants may induce intraoperative "*airway hyper-reactivity, cardiac dysrhythmias* [and] *alterations in* [anaesthetic] *drug metabolism*" (Kong & Schmiesing, 2005, p. 115). Intuitively, chronic recreational use of ketamine and other dissociative substances are likely to interfere with anaesthetic requirements though no study has systematically delineated the perioperative risks. Substances within the hallucinogenic class (e.g., LSD, psilocybin) may not pose much of problem, however, most – relative to substances such as alcohol – are physiologically harmless after both chronic and acute use (e.g., Taylor et al., 2012), and have a short half-life (Hernandez et al., 2005). Lastly, the concerning rise of *novel psychoactive substances* has flooded the UK market with a multitude of novel stimulants and depressants. For these substances, almost no research has been conducted addressing their chronic or acute risks; thus perioperative research here is, naturally, non-existent.

2.3.8 Polysubstance Use

Perhaps the most troubling aspect of all is that many of these substances are co-ingested, that is, many patients are poly-substance users.

For example, UK government statistics show that 58% of methadone users frequently co-ingest other illicit substances, as well as 49%, 48%, and 43% of ecstasy, ketamine and amphetamine users (ONS, 2015). This compounds the issue greatly. Not only are the perioperative risks of specific substances likely to cause complications, but the interaction effects between them may cause unpredictable and greater harms. Some combinations, such as cocaine and alcohol, produce a novel compound endogenously – in this case, cocaethylene (which may be more cardiotoxic than cocaine (Wilson, Jeromin, Garvey & Dorbandt, 2001). In the perioperative context, therefore, polysubstance use must be accounted for. Polysubstance use and perioperative outcomes are partially investigated in Chapter 4.

2.4 The Prevalence of Preoperative Substance Use

Without knowing the number of patients who may be undergoing elective surgical operations who may be a risk of substance use related complications, the *scale* of the issue cannot be delineated. Despite studies being relatively few in number and out-dated, research from other countries may provide some indication.

2.4.1 Alcohol

Harris et al. (2008) sought to systematically review the US literature on preoperative alcohol use prevalence. Here, 22 heterogeneous studies were found; studies used various self-report methods to assess alcohol use, most of which were non-validated. In studies assessing hazardous alcohol use *across* surgeries, the two largest studies (n = 83,958 and 160,805) found a prevalence rate of 15.2% and 11.2%, respectively (Khuri et al., 1995; Arozullah et al., 2001). In two studies of major cardiac surgeries only, the prevalence rate was 9.8% (n = 2108) and 9.5% (273) (Roach, 1996;

Wolman, 1999). In the only study to assess prevalence rates between surgery types, Moore et al. (1989) found that those undergoing ENT (ear, nose, throat) procedures had the highest prevalence (43%) followed by orthopaedic patients (28%) (the least was both obstetrics and gynaecology at 12.4%). At least, one in ten patients in the US appears to be at risk of postoperative complications due to alcohol use. However, the US may have very different alcohol use patterns when compared to the UK (and Europe generally) so may not be generalisable to these contexts.

Regarding the European literature on preoperative hazardous alcohol use prevalence, just three studies could be found for the present review – all of which were conducted in Germany, and the earliest of which published 6 years ago. Kip et al. (2008) surveyed 1921 preoperative patients undergoing a variety of surgeries using a validated measure of alcohol use (the Alcohol Use Disorder Identification Test, or AUDIT; Babor et al., 2001). It was found that nearly one in five patients were positive for an alcohol use disorder according to well-established cut-offs (18.1%; 95% CI: 16.3–20.1). Kleinwächter et al. (2010) surveyed 2938 patients, again using the AUDIT. Here, 14.4% (95% CI: 13.2–15.8) were positive for an alcohol use disorder. Lastly, Kork et al. (2012) found an AUDIT-positive rate of 15.1% (95% CI: 12.9–17.6).

2.4.2 Illicit Substance Use and Polysubstance Use

Just two previous studies could be found that have assessed the preoperative prevalence of illicit substance use. Both of which were one of the three aforementioned German studies. Kleinwächter et al. (2010) found a self-reported illicit substance use (per se) rate (in the last year) of 7.5% (95% CI: 6.6–8.5) (the most common substances included, in order: cannabis, cocaine, amphetamines and opioids) and around 1 in 50 patients used illicit substances 53 or more times within the previous 12 months. More importantly, over 40% acknowledged using more than one substance in the previous year, 38% of AUDIT-positive patients acknowledged illicit substance use versus 12.5% of AUDIT-negative patients and 70.6% of smokers versus 26.8% of non-smokers admitted likewise. Clearly, the rate of polysubstance use is high – compounding the perioperative risks. Among 939 patients, Kork et al. (2012) found a previous 12 months illicit substance use prevalence rate of 20.4% (95% CI: 17.9-23.2), and a previous 30-day prevalence rate of 12% (95% CI: 10–14.3). In the previous 30 days, patients most commonly used cannabis (8.2%), opioids (2%), amphetamines (1.9%), cocaine (1.8%) and benzodiazepines (1.6%) – all of which have been observed to have perioperative risks. Again, there was a high amount of polysubstance use e.g., 53.9% (95% CI: 44.4–63.1) of last 30-day users were AUDIT-positive and 41% (95% CI: 32–50.5) were smokers.

Regarding the above studies, it would be useful to gather further comparative data for the UK population. Not least because substance use patterns may greatly vary between countries. This is explored in further detail in Chapter 4.

2.5 Assessing and Detecting Preoperative Substance Use

For preoperative assessments (see section 1.5) to be useful for their intended purpose: identifying (and thus targeting) modifiable risk factors for complications, they must be able to accurately and readily detect issues which may affect patients' medical care. As briefly mentioned in subsection 1.5.3, in routine preoperative assessment, standardized forms typically guide the preoperative interview, and contain questions pertaining to certain lifestyle factors that may deleteriously affect surgery. For illicit substances, many routine preoperative assessment forms simply ask patients *do you use recreational drugs?*[15]. This ignores the multiple interpretations that one could have of this question, such that, i. an individual may state *no* if they only use them occasionally, ii. may have tried them in the recent past, or even, used them heavily in the past - but currently do not use them regularly, iii. misinterpret what defines a recreational drug or, iv. simply fail to reflect on the question given its terseness. Highlighting a similar issue, an Australian study found that pre-assessment forms aimed at detecting excessive alcohol use in eight preoperative assessment clinics were not established or validated measures (Shourie et al., 2007), in congruence with the UK example (see Appendix C[16]), which asks patients to report the amount of alcohol units consumed per day – ignoring features such as the pattern of use, and possibly adding cognitive demands on the assessor (i.e., having to calculate units as opposed to simple point scoring) (highlighted by findings in Chapter 4).

2.5.1 Measures

In an ideal world, all patients would be tested for illicit substance and hazardous alcohol use before surgery using well established objective methods (e.g., Neumann & Spies, 2015). This is unrealistic because doing so would be costly, impractical and for many patients, would be a waste of time. Most authors, therefore, recommend a system whereby validated questionnaires of substance use are used as first-line preoperative assessment (Gordon, 2018; Neumann & Spies, 2015; Kork et al., 2010; see Appendix D). Very brief questionnaires have shown to be useful for detecting hazardous alcohol use in patient populations (Fiellin, Reid & O’Connor, 2000), and could be implemented in routine preoperative assessment – with minimal impact on time demands and resources. One such measure, often cited as the gold standard, is the *Alcohol Use Disorders Identification Test* (AUDIT) (see Babor, Higgins-Biddle, Saunders & Monteiro, 2001). A shortened version known as the AUDIT-C (used in Study 2, 3 and 5) is just three items long and takes just two minutes to complete. The AUDIT-C has shown to be equally sensitive as the full AUDIT at detecting heavy drinking and active dependence (Bush et al., 1998) and has very strong predictive validity; for every additional point scored on the AUDIT-C, there was a 29% increase in the number of postoperative complications in Harris et al. (2011) (see also: Bradley et al., 2011). Similar measures could also be applied to routine pre-assessment for illicit substance use. Indeed, there is a multitude of screening instruments for both alcohol and other substances. For illicit substances specifically, one review found 26 such measures (Assanangkornchai & Edwards, 2015) (e.g., the DUDIT; Berman et al., 2005) – ranging from just four items to 28 items. The main problem with these, however, is that they are often not substance-specific. This can be overcome by using composite measures such as reliable and valid the WHO ASSIST (Numeniuk et al., 2008) which is scaled in length depending on the amount of substances the respondent uses (thus economical with regard to time) and can account for both individual and polysubstance use (see Chapter 4).

2.5.2 Support for Self-Report

There has been some evidence showing that the use of structured self-report questionnaires may be preferable to routine preoperative assessment without such measures. Again, there have been no UK studies (despite a preponderance of non-validated measures in routine use). In Kip et al. (2008) routine assessment detected 107 hazardous drinkers, whereas the researchers, using a validated measure (AUDIT), found 282 (6.9% versus 18.1%). Of patients identified as suffering from possible dependence with the AUDIT, just 25.2% were identified with routine assessment, and routine assessment detected just 36.7% of those using alcohol daily or almost daily on the AUDIT. In Kleinwächter et al. (2010) a structured questionnaire assessing illicit substance use (as opposed to *ad hoc* identification) identified 221 out of 2938 as previous 12-month illicit substance users of which routine assessment identified just 30.8%.

In further support of the utility of routine screening questionnaires, there is evidence to suggest that self-report measures may be superior to certain forms of objective measures in the preoperative context. A study by Kork et al. (2012) found that self-reported preoperative illicit substance use (last 30-days) was biologically confirmed 77% of the time when conferred with a gold standard blood test. Oral fluid substance use tests were biologically confirmed only 6% of the time. In the absence of resources or necessity for gold standard blood tests in routine practice, clearly self-report questionnaires are ideal; being cheap to implement, sensitive, specific and have (in the case of alcohol use measures) predictive validity for complications.

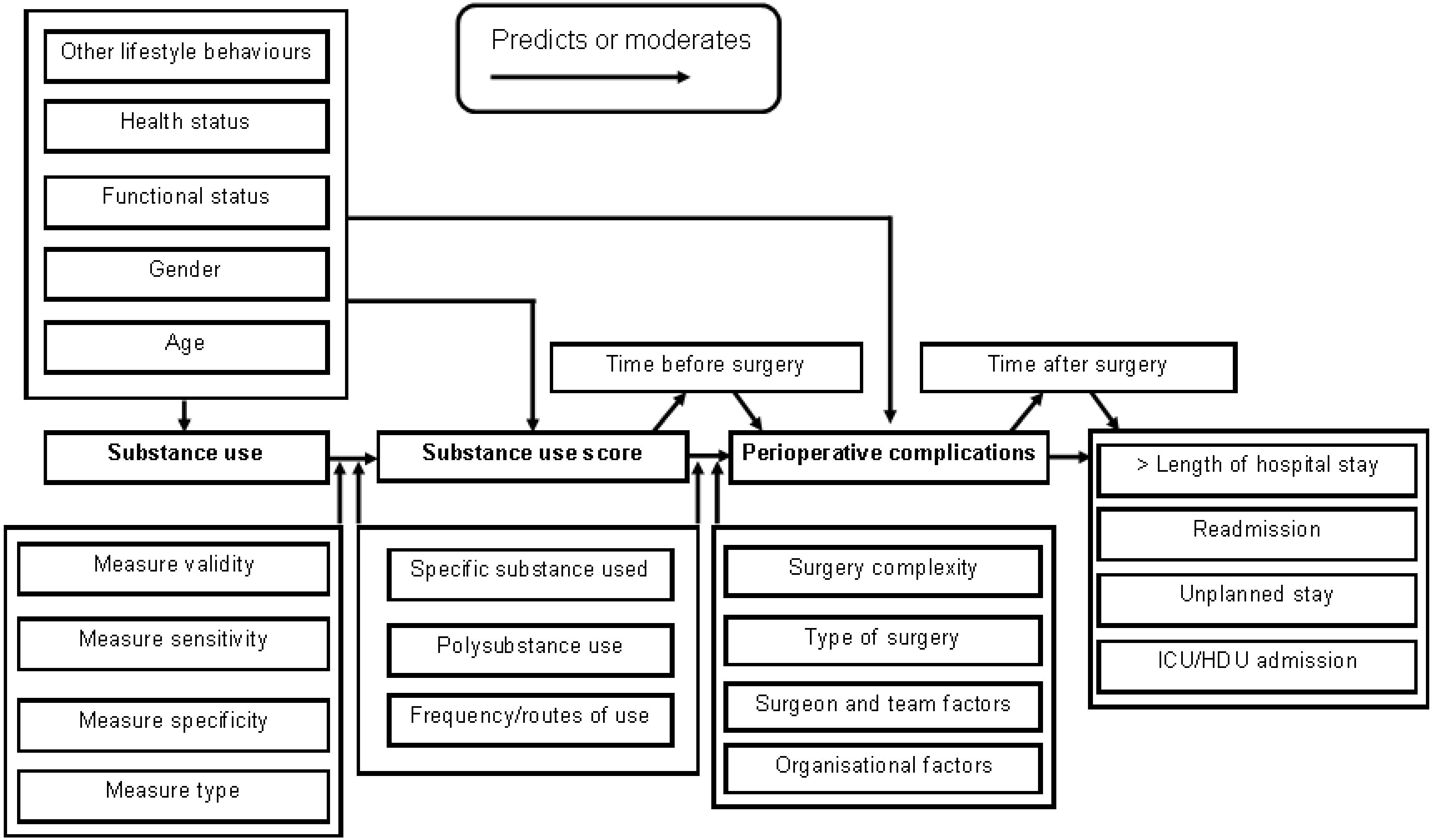

Figure 2.1. Substance Use *x* Perioperative Complications Conceptual Model.

2.6 Preoperative Interventions for Substance Use: Evidence and Issues

2.6.1 Background

Given the recent interest in lifestyle behaviour prior to surgery (see section 1.6) many clinicians realise the importance of lifestyle behaviours in this context, but there is uncertainty about how to address the issue. On the one hand is a *stick-based* approach: simply refusing patients unless they change their behaviour (which may be highly controversial to the public and clinicians alike). Another approach could be to utilize best-practice and cost-effective interventions to help patients modify their behaviour.

Given that the NHS provides a maximum preoperative period of 18-weeks for elective surgeries (see section 1.3), many of the perioperative risks of substance use may be mitigated; this preoperative period provides a useful window of time to intervene, allowing flexibility in the intensity of interventions which may be tailored to the amount of time abstinence is necessary (depending on the scheduled surgery date, or likelihood of the specific substance in question causing complications [e.g., intrinsically, or by half-life]). These interventions may also occur at a time where patients are sensitive to change (a *teachable moment*; see subsection 2.6.3). As such, insights and developments in the behaviour change literature would be highly useful to apply in this context (see subsections 2.6.5 and 6.1.1).

2.6.2 Preoperative Abstinence

Guidelines in practice. Many of the associated risks of preoperative substance use (see section 2.3) may be mitigated by preoperative abstinence. Worryingly, however, one study found that 70% of anaesthetists and 42% of surgeons do not routinely advise smokers to abstain before surgery (Khullar, Schroder & Maa, 2013). Given that alcohol and other substances are often relegated in importance to smoking, routine advice for these substances may be even lower. One reason for a lack of routine advice may be a lack of formalised guidelines. Granite, Farber and Adler (2007) found that 84% of 241 oral and maxillofacial surgery training programmes had no formalised policy for cocaine screening prior to surgery and that 60% of clinicians do not proceed with anaesthesia and surgery when patients are cocaine-positive. While Elkassabany et al. (2013) found that 66% of 172 US anaesthesia departments cancelled or delayed patients with a positive cocaine screen (regardless of clinical symptoms) and just 10.6% had a protocol in place to deal with this eventuality, even though 80% believed they should. A qualitative study with a sample of nurse anaesthetists highlighted that many of the participants felt like they offered worse care for substance-dependent patients due to lack of formal knowledge of their management, and no specific guidelines for their care (Forsberg et al., 2018). Whilst mostly non-standardised, several authors recommend specific preoperative abstinence time-periods for reducing the negative perioperative effects of substance use.

Guidelines from the literature. One review of preoperative smoking and alcohol abstinence provides useful guidelines (Tønnesen et al., 2009). The authors conclude that abstinence starting from eight (up to three) weeks before surgery may reverse some of the perioperative risks of these substances. The authors found that, after this abstinence period, negative immune and stress responses due to alcohol could be reversed, in addition to the prevalence of cardiomyopathy and hypoxia, and increased bleeding time and decreased wound healing.

In terms of illicit substances, recommendations are much more diverse; given the lack of current research addressing their relative perioperative risks. One author recommends a 72-hour preoperative abstinence from cannabis (Dickerson, 1980). Others are more lenient, one author recommending just 8-hours of cocaine abstinence before surgery (Granite, Farber & Adler, 2007) another recommending that non-symptomatic cocaine-positive patients can be operated on successfully (Hill, Ogunnaike & Johnson, 2006), whilst a contrasting study recommends a week of cocaine abstinence at minimum (Vagts, Boklage & Galli, 2003 [similarly Kong & Schmiesing, 2005 recommend a one week abstinence from inhalants]). A survey of anaesthetists found that just 30% believed surgery should be postponed by a week after a patient is found positive for substance use per se (Demaria & Weinkauf, 2011). Given the above, standardised protocols for dealing with hazardous substance using patients appear to be heterogeneous in perioperative care. Regardless of specific recommendations, all the above studies agree on one point: from a medical point of view[17], abstinence as early as possible is preferable; best practice must be to identify hazardous substance use as early as possible and to aid the patient in reducing use as long before surgery as possible.

2.6.3 The Preoperative Period: A Teachable Moment?

One study found that, in the preoperative period, up-to 80% of elective surgery patients become motivated to change their lifestyles regarding excessive alcohol use and smoking (Boel, Kannegaard, Goldstein & Andersen, 2004[18]). Similar studies have found likewise; some patients even naturally decrease these behaviours (Maina Carstensen & Tønnesen, 2002; Backer, Nelbom, Duus & Tønnesen, 2007). This speaks to what is often termed in the medical/psychological literature as a *teachable moment*; defined as an opportunity for behaviour change (e.g. a context which enables a higher than expected success of behaviour change) and a cueing event that prompts *specific cognitive and emotional responses* (Lawson & Flocke, 2009). There have been several studies that have shown that certain health-related or other life-changing events may provoke increased success at breaking deleterious, and well ingrained habitual behaviours (e.g., Pettersen et al., 2018). As such, the preoperative period may be a time of increased sensitivity to behaviour change acutely (i.e., preoperatively) and in the longer term (e.g., Lee et al., 2015). In this way, while a surgical operation may be considered a stressful and negative life event, it can be a time of positive change in a patient's life. To capitalise on this opportunity and to support those finding it difficult to abstain, further intervention may desirable.

2.6.4 Preoperative Intervention Trials

While there have been a multitude of intervention trials to support preoperative smoking cessation (e.g., Prestwich et al., 2017: 22 trials), the same is not true of alcohol use. For alcohol, one systematic review found just two preoperative interventions (including 69 patients) – though stringent selection criteria (e.g., including only alcohol dependent patients) may have reduced the number of eligible studies (Oppedal, Møller, Pedersen & Tønnsesen, 2012). When the results from both studies were pooled in a meta-analysis, the total number of postoperative complications was significantly fewer in the intervention groups (OR = 0.22; 95% CI: 0.08–0.61), though no effects were found on mortality, postoperative alcohol use and length of hospital stay. Another alcohol-focused review looked at behavioural strategies uniquely (Fernandez, Claborn & Borsari, 2015), finding four studies eligible for inclusion. Trials were generally small and had mixed results. These reviews, may however, be out of date; the first conducted their literature search in 2011, the second in 2013, thus there may have been more available evidence in the meantime. To the present author's knowledge, there appears to have been no previous review assessing the literature regarding preoperative substance use other than alcohol and smoking. Chapter 5 provides an updated alcohol review, as well as a review of illicit substance interventions.

2.6.5 Defining a Goal Standard for Intervention

Aside from a lack of research in the area, perhaps the biggest issue with the interventions included in previous alcohol intervention reviews is the lack of a theoretical basis (confirmed in Chapter 5), no standardization in reporting of intervention components and lack of any evidence of sufficient *elicitation research*; that is, the use of *off the shelf* intervention strategies not based on any evidence from research *within this context*. As per the UK Medical Research Council (MRC) guidelines (Craig et al., 2008), behaviour change interventions should be rigorously developed after, and informed by, a full examination of what has or has not worked in the previous literature (i.e., through systematic reviewing) and identification of an appropriate theoretical basis for the intervention: i. allowing for an identification of *mechanisms of action* of the intervention, and ii. allowing for intervention *targets* that are likely to modify the behaviour. The latter may be supplemented using interviews or questionnaires with relevant stakeholders (e.g., preoperative patients). There is some evidence showing that theory-based interventions are more successful than those not so (Webb et al., 2010; though conflicting evidence exists: Prestwich, Webb & Conner, 2015) and good evidence to suggest that certain theories of health behaviour, with testable and targetable constructs, can explain a significant degree of variance in certain behaviours (Conner & Norman, 2005) – including alcohol use (Cooke et al., 2016).

COM-B model and the behaviour change wheel approach. One problem with the use of behaviour change theories is that if one only targets or assesses constructs specified in one theory, they may ignore constructs that have been shown to be associated with behaviour specified in another. As such, many researchers have developed unified theories, alongside frameworks to ease the process of intervention design. Perhaps the framework receiving most attention in recent years has been the *behaviour change wheel* (BCW) approach (Michie, van Stralen & West, 2011) which introduces the COM-B (capability, opportunity, motivation - behaviour) model of behaviour change (*Figure 2.2*).

According to this model, the beginning of intervention development must be to identify factors which may determine an individual's capability, opportunity and motivation to enact a behaviour. Using three broad determinants, the COM-B allows intervention designers to target a swathe of proposed determinants of behaviour from a plethora of theories. In the BCW approach, after identifying what determinants are seen to be associated with behaviour, behaviour change techniques (BCTs) demonstrated to modify the behavioural determinants and/or behaviour may be chosen as components of an intervention (see the behaviour change taxonomy; Michie et al., 2013). These may be identified using past literature, or through primary research (e.g., asking stakeholder's what may or may not work; what is feasible; or what is unrealistic). Perhaps the main benefit of the use of BCTs is their replicability; if researchers document exactly what an intervention consisted of, those most effective may be utilised by future interventionists. For more elaboration see Chapter 6 (where COM-B constructs were applied to preoperative alcohol use to construct a questionnaire) and Chapter 7 (where they were used to inform an interview schedule).

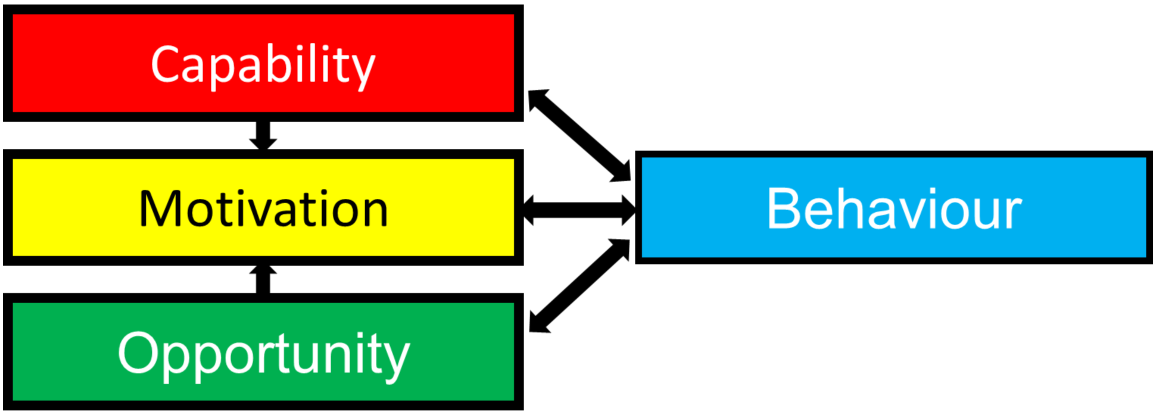

Figure 2.2. COM-B Model (Higher Order Domains)

2.7 Thesis Aims, Structure and Objectives

Figure 2.3 below provides a visual framework of the thesis aims, objectives and structure.

2.7.1 Aims

Given the wide scope of this literature review, only some of the above avenues could be explored in the present thesis. Those chosen were based on perceived importance, originality and feasibility. In line with the thesis title, there were two overarching aims, both of which may be considered elements necessary in conducting a *needs assessment* - that is assessing i. the nature and extent of the problem, ii. for whom and at what levels the problem exists, iii. potential causes of the problem (e.g., intervention targets) and iv. what has been effective in addressing the problem. Always mindful that the local context of the research may be important (e.g., determinants may be context specific, or substance use prevalence rates may differ between regions), broad thesis aims included:

1. **Risk analysis:** To assess the risk of preoperative substance use (POSU).
2. **Intervention development research:** To inform preoperative intervention development for POSU.

In relation to those above, more specific aims were to:

1.a. Explore uninvestigated routes through which POSU may have deleterious outcomes.

1.b. Assess the local extent (prevalence) of POSU.

1.c. Assess patient characteristics that may be associated with POSU.

1.d. Assess the local detectability of POSU.

2.a. Identify, assess and critically appraise current interventions to counteract POSU.

2.b. To build upon limitations of previous interventions by conducting research to inform future interventions to counteract POSU (e.g., assessing determinants of POSU reduction).

2.7.2 Thesis Structure and Study Objectives

Chapter 3. Study 1 focused on aim 1.a. Through analysis of two waves of a longitudinal dataset (n = 18508) the objective was to investigate a possible relationship between hazardous preoperative alcohol use and reduced postoperative wellbeing and increased depressive symptoms. The robustness of the results was also assessed by i. investigating whether any possible effects were stable between respondents having inpatient, outpatient or either surgery, ii. controlling for possible confounds and iii. reanalysis after accounting for missing data using multiple imputation.

Chapter 4. This chapter presents two studies. The first (Study 2) focused on aim 1.b and 1.c, while the second (Study 3) on 1.a, 1.b, 1.c and 1.d. The former was a cross-sectional study, the latter a hybrid cross-sectional/prospective study.

The objectives of Study 2 (*n* = 196) were to i. investigate the prevalence of POSU in a preoperative assessment clinic (St James' University Hospital, Leeds) and ii. to provide some insight into the characteristics of patients who may be at risk of complications due to substance use (which may be useful information to tailor future interventions to vulnerable demographics).

The objectives of Study 3 (*n* = 273) were to i. verify the prevalence rate in the previous sample in a second preoperative assessment clinic (Leeds General Infirmary), ii. to provide a more detailed look at patient characteristics associated with hazardous preoperative substance use, iii. to compare routine preoperative assessment *detections* with those of validated measures (to see whether vulnerable patients are missed in routine practice), iv. to assess whether: routine versus validated measures were inferior at predicting postoperative complications using data extracted from local clinical administration systems, and v. to assess the utility of an index of polysubstance use at predicting complications.

Chapter 5. Study 4, a systematic review and meta-analysis, addressed aim 2.a. Objectives were to i. update previous reviews of preoperative interventions for alcohol, ii. to identify interventions for preoperative illicit substance use reduction, iii. assess the efficacy of previous interventions at modifying substance use and *determinants* of preoperative substance use, iv. critically appraise the literature, and v. characterize successful intervention components (i.e., by coding BCTs.).

Chapter 6. Using a cross-sectional design**,** Study 5 (*n* = 102) addressed aim 2.b. Primary objectives were to i. develop a brief questionnaire for assessing COM-B related determinants of preoperative alcohol use and ii. to assess it's psychometric properties (e.g., predictive validity). Both to provide targets for future interventions *generally* and potentially provide a tool for rapidly identifying targetable determinants for brief *tailored* interventions.

Chapter 7. Study 6 (*n* = 36) also addressed aim 2.b. This was a qualitative study involving semi-structured interviews. Objectives were to identify i. perceived barriers and facilitators to POSU reduction in substance-dependent individuals, and ii. to identify their preferred preoperative intervention formats and strategies.

Chapter 8. The objective of this chapter was to provide a synthesis of all findings from the above chapters, the implications of the results and future directions for research and practice.

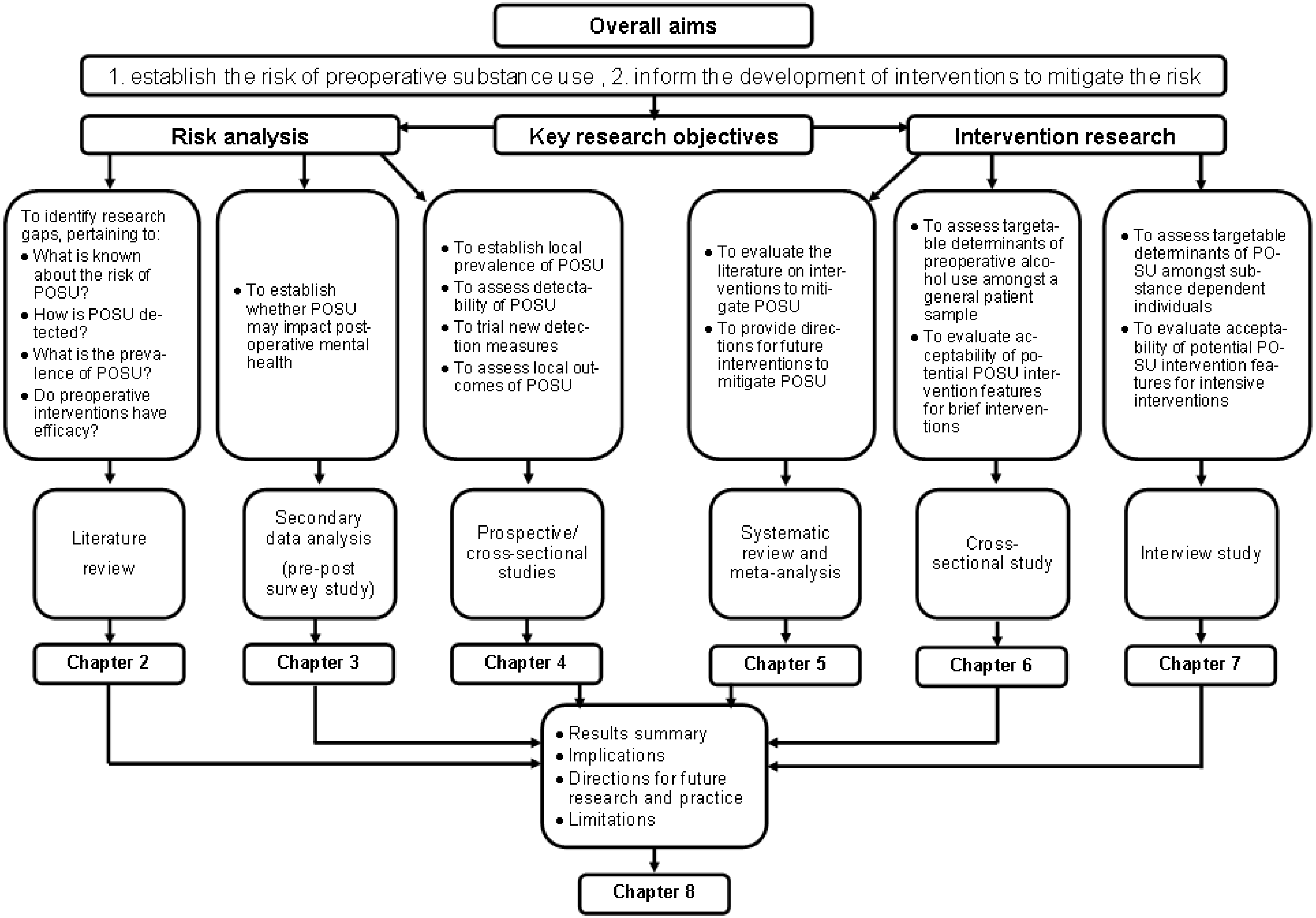

Figure 2.3. Thesis Framework.

CHAPTER 3. THE IMPACT OF HAZARDOUS PREOPERATIVE ALCOHOL USE ON POSTOPERATIVE WELLBEING AND DEPRESSIVE SYMPTOMS: A SECONDARY DATA ANALYSIS (STUDY 1)

3.1 Introduction

3.1.1 Background

It is well demonstrated that acute and chronic hazardous preoperative alcohol use may have a deleterious effect on the success of, and recovery from, various surgical procedures (see subsection 2.3.1). The prevalence of hazardous preoperative alcohol use has been shown to be high in European studies (see subsection 2.4.1) and in the first known UK study (see Chapter 4: e.g., 31.6% in Study 2). It is likely therefore that many patients undergoing surgery drink, in the preceding preoperative weeks or months, at levels which may be detrimental to the outcome of their surgical procedure.

Another important risk factor for perioperative complications is psychological morbidity; the presence of mental disorders or related symptoms, such as low mood and wellbeing, anxiety and stress. Linnen et al. (2011) screened 5708 preoperative patients for depressive symptoms (using the WHO-5 measure; Topp et al., 2015) of whom 29.7% were found to have clinical levels of depressive symptoms. After controlling for demographics, health behaviours, surgery type and comorbidity, these patients had increased odds of increased length of hospital stay versus patients with non-clinical symptoms (OR = 1.52; 95% CI: 1.32-1.75). Britteon et al. (2017) similarly found that among 176,827 preoperative patients depression and/or anxiety (measured in three different ways) was consistently associated with increased length of hospital stay, and increased odds of wound complications and readmission due to wounds (versus patients with no reported depression and/or anxiety, across each type of surgery)[19].

As well as cumulative measures of depression-related syndromes, a variety of individual psychological variables related to general wellbeing have been observed to uniquely associate with poorer surgical recovery such as trait and state anxiety, anger, avoidance coping, loneliness, worry about the surgery, and stress (Mavros et al., 2011). As a surgery is a potentially life-changing event associated with physical discomfort and uncertainty about the future, this may be no surprise. In outlining the interdependent relationship between various psychological and physiological mechanisms that influence surgical recovery, Kiecolt-Glaser et al. (1998) highlight the close relationship between psychological morbidity and health behaviour; indeed, suggesting that surgery associated anxiety and low mood may potentiate alcohol use, and that alcohol use may potentiate related symptoms. Although there are no direct studies of the reciprocal relationship between psychological morbidity and alcohol use in the preoperative setting, there is considerable evidence for this assertion in other contexts.

Many studies have observed a co-occurrence, and dose-dependent relationship between alcohol use and lower wellbeing and symptoms of mental distress (e.g., Burns & Teesson, 2002; Mäkelä, Raitasalo & Wahlbeck, 2015) and diagnosis of a range of psychiatric disorders such as major depressive disorder and anxiety disorders (e.g., Kessler et al., 1996a; 1996b; Regier et al., 1990). Prospective studies have shown that alcohol use can proceed psychological morbidity and vice-versa (Boden & Fergusson, 2011; Boschloo et al., 2012; Crum et al., 2013a; 2013b; Wang & Patten, 2001). Many researchers have proposed that alcohol use is often used as coping strategy for stressful life events (e.g., the Tension Reduction hypothesis; Conger, 1956; and the Affect Regulation Model; Wills & Shiffman, 1985), a view supported by several studies (e.g., Windle & Windle, 2015). As well as stress *per se*, alcohol use has been found to be a maladaptive coping strategy to deal with the distress associated with numerous psychiatric disorders (e.g., Carpenter & Hasin, 1999; Holahan et al., 2001; Holahan et al., 2003).

In this way, psychological distress related drinking may be a deleterious cycle whereby negative psychological affect may increase drinking (and vice-versa), increased drinking may increase negative psychological affect, and this increased negative psychological affect may lead to increased coping related drinking. Unfortunately, therefore, the relatively high prevalence of both low wellbeing and psychological distress in preoperative patients, along with the fact that the preoperative period may promote stress (through fear of surgery), may partially explain high prevalence rates of hazardous alcohol use and vice-versa. More worrying is the fact that both psychological distress and hazardous preoperative alcohol use have been demonstrated to be independently associated with an increase in the incidence of postoperative complications; the presence of both may compound the risk severity (e.g., magnitude), and mutually reinforce an increased likelihood of risk (e.g., frequency).

As above, it is well established that low psychological affect (e.g., depressive symptoms) and hazardous alcohol use can increase risk of postoperative complications, and it may also be the case that hazardous alcohol use and low affect may be mutually reinforcing (thus both may potentiate the risk of complications). However, in addition, recent research has demonstrated that affect may be severely reduced in patients suffering perioperative complications.

A systematic review of 50 studies by Pinto et al. (2016) found that perioperative complications were associated with reduced positive affect up to 12 months post-surgery or later. Thus, not only is low positive affect a risk factor for complications, but complications may also further decrease positive affect, perhaps leading to a dramatically increased period of time wherein, for example, the risk of an infection or delayed wound healing may be more likely. Further, low positive affect in individuals with a disposition to use alcohol as a coping strategy may again, compound the issue. A cohort study of 785 NHS patients indeed found that suffering a postoperative complication was associated with lower wellbeing at 1 month, 4 months and 12 months postoperatively, and that more complications were associated with a greater effect on wellbeing. There was, as above, some evidence also that those with avoidance (or maladaptive) related coping strategies were more prone to reduced positive affect (Archer et al., 2018). In another study, substance use as a coping strategy was specifically associated with increased perioperative anxiety (Pinto et al., 2013).

3.1.2 Study Overview and Aims

To ground the aims of the present study within a conceptual framework, *Figure 3.1* unites the literature outlined above into a conceptual model. The present study aimed to assess one part of the model; that is, to assess the relationship between alcohol use and affect in the perioperative context.

Given surgery is stressful (e.g., Wetsch et al., 2009), that stress may be associated with mental ill health (e.g., Hammen et al., 2009), that stress may be potentiated by alcohol use (e.g., Brady & Sonne, 1999), and that both preoperative alcohol use and mental ill health *may* cause postoperative complications (e.g., Eliasen et al., 2013; Ghoneim & O'Hara, 2016) (and postoperative complications may severely reduce wellbeing; Pinto et al., 2016; which may prolong and/or increase the risk of further complications, and/or increase alcohol use), it may be that hazardous preoperative alcohol use can impact on subsequent wellbeing/mental health outcomes after surgery. Assessing the latter was the purpose of the present study.

To obtain, what may be (given the time-constraints of a PhD, and in lieu of a very large budget) a prohibitively large sample size for a primary study, the present study adopted a secondary analysis approach. Several data repositories (e.g., the UK data service) were searched to find datasets which assessed the appropriate variables. Data from the Survey of Health, Ageing and Retirement in Europe (SHARE) project (Börsch-Supan et al., 2013) were obtained following application with a brief protocol of the proposed study aims and method. While this dataset did not provide perioperative complications data (meaning the full theoretical model outlined in *Figure 3.1* could not be investigated), it provided both pre and post- measures of wellbeing and depression, alongside measures of alcohol use and surgery - meaning the relationship between preoperative hazardous alcohol use and postoperative mental health could be assessed by modelling an interaction term between *hazardous alcohol use (yes/no)* and *surgery (yes/no)*. It was predicted that positive affect may be reduced in those having surgery *per se,* but in line with the above research, it was hypothesized here that hazardous alcohol use may *compound* this effect such that hazardous versus non-hazardous alcohol use prior to surgery would be associated with lower positive affect after surgery.

The present study aimed to assess the robustness and consistency of the results to bolster the potential reliability of the findings. This was done in three ways: i. by systematically controlling for possible confounding variables, ii. by assessing whether any effects were consistent between patients having more minor and major procedures (e.g., inpatient versus outpatient surgery) and iii. by assessing whether results were stable in complete case analyses versus analyses that accounted for missing data using multiple imputation.

3.1.3 Objectives

1. To assess whether hazardous preoperative alcohol use may be associated with reduced postoperative i. wellbeing and ii. symptoms of depression after inpatient surgery.
2. To assess results between i. participants having had outpatient surgery, or either inpatient or outpatient surgery, ii. after adjusting for potential confounds, and iii. after multiple imputation of missing data.

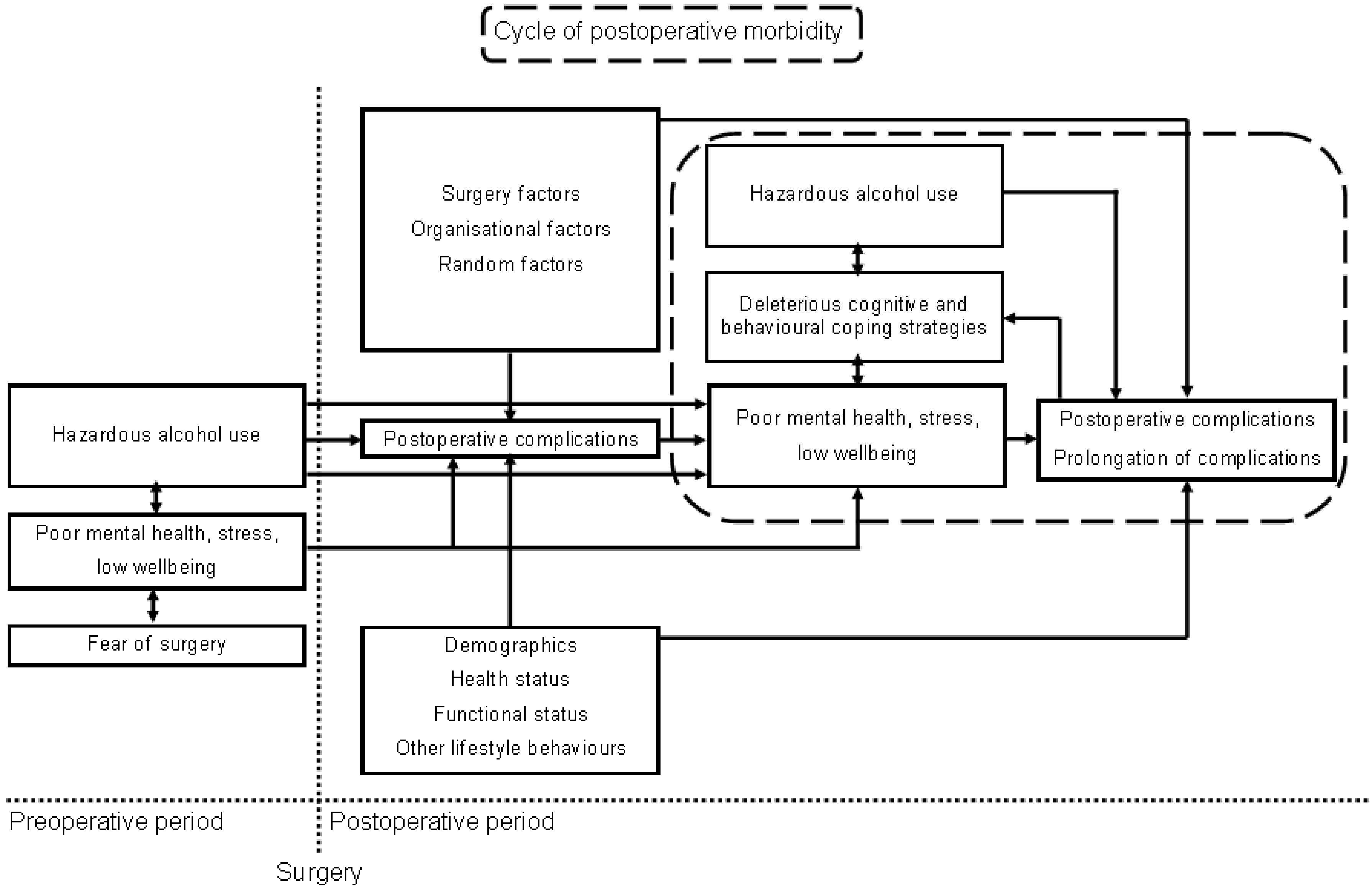

Figure 3.1. Study 1 Conceptual Model.

3.2 Method

3.2.1 Participants and Design

The SHARE project surveys health, health behaviour, social, as well as various other demographic variables in 50-year-olds or older across 27 European countries (and Israel). Ninety-minute interviews are conducted by researchers at the respondents' home. As of 2018, the SHARE project comprises six waves of longitudinal data. Wave 1 included anyone born in 1954 or earlier and their spouse (if applicable) of any age. Excluded from the survey were those i. unable to speak the native language of the country they inhabited, ii. incarcerated, iii. hospitalised, iv. out of the country during the survey, or those v. who moved to an unknown address.

The present study linked data from Wave 1 (2004-5) and 2 (2006-7) releases (versions 6.0.0, 31st March 2017; Börsch-Supan, 2017a; 2017b[20]) using cross-wave respondent IDs and one-to-one matching. Wave 1 had 30,434 respondents, Wave 2, including *refreshers* (non-Wave 1 participants), had 37,174. The present sample included 18,508 respondents across 11 different countries (though unfortunately not the UK). Analysis here was limited to those i. participating in both waves (*n* = 20,916), ii. individuals born in 1954 or before at Wave 1 (to ensure sample homogeneity, and because SHARE does not provide weights for those born after 1954), and iii. those recruited in all countries apart from Israel (which had a follow-up two years longer than any other country and was the only non-European country). The average percentage of participants retained between waves was 71.6% (see Table 3.1; Bergmann et al., 2017). Wave 1 measures included alcohol use, health, demographics and other health behaviours. Wave 2, which was on average 2.5 years post-baseline (slight variations across countries; see Börsch-Supan et al., 2013), included an item relating to inpatient (or outpatient) surgery in the previous 12 months. The impact of alcohol use could, therefore, be assessed (Wave 1; 0 years) on all follow-up outcome variables (Wave 2; 2.5 years) between those having, and not having, surgery approximately 1.5-2.5 years post-baseline (see *Figure 3.2*).

Table 3.1. Retention Between Waves by Country.

Country	**Retention (Wave 1 – 2)**
Austria	74.4%
Belgium	76.3%
Denmark	77.0%
France	67.0%
Germany	55.1%
Greece	86.3%
Italy	75.6%
Netherlands	62.3%
Spain	68.6%
Sweden	70.6%
Switzerland	74.6%

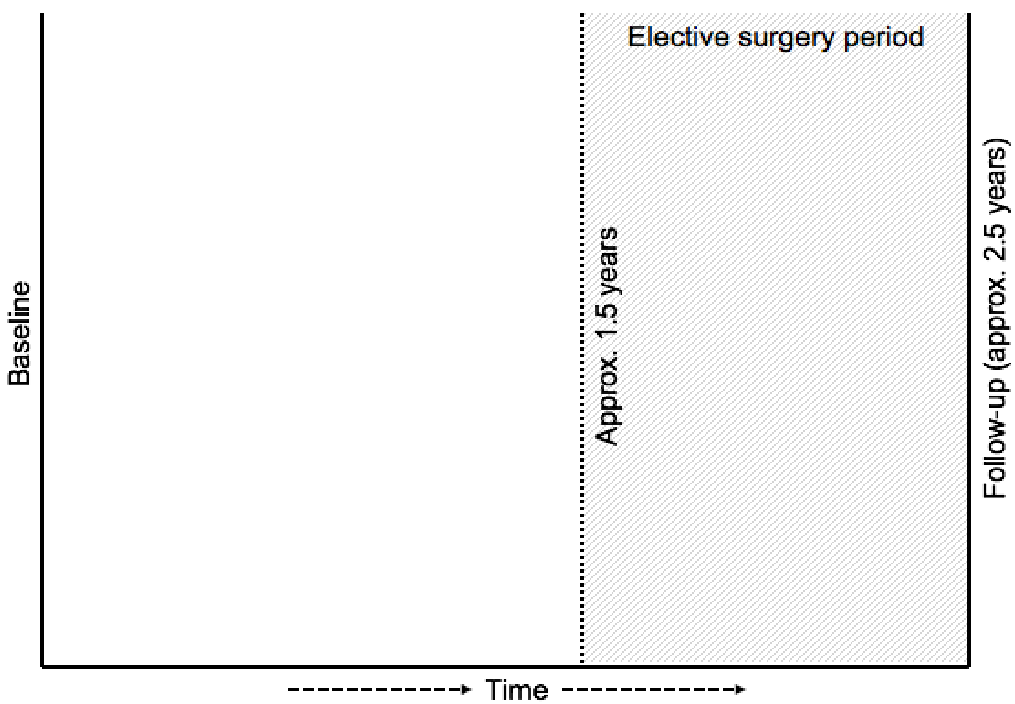

Figure 3.2. Survey Timepoints.

3.2.2 Measures

Outcomes.

Wellbeing. Wellbeing was assessed using the SHARE project's pre-generated 12-item, truncated version of the 19-item CASP-19 scale: the CASP-12 (Hyde et al., 2003). During CASP-19 development, items were chosen through expert consensus, focus groups and cognitive pretesting (indicating high face and content validity), before analyses indicated good psychometric properties (i.e., construct validity, concurrent validity with the Life Satisfaction Index [Adams, 1969], and internal consistency) (Hyde et al., 2003). Items are statements or questions which respondents are required to rate: *never*, *rarely*, *sometimes* or *often* (e.g., *I feel that the future looks good to me*). Higher scores on the CASP represent higher wellbeing, based on 3-item domains of self-perceived: *control, autonomy, pleasure* and *self-realisation* (e.g., life satisfaction, positive view of the future).

Depressive symptoms. Symptoms of depression were assessed using the EURO-D scale (Prince et al., 1999). The EURO-D was developed using items from similar valid and reliable instruments and expert consensus. The purpose of the EURO-D was to create an instrument that could reliably assess the co-occurrence of depression across European countries. In 21,724 65 years-old+ respondents, the scale showed good internal consistency, criterion validity and construct validity (Prince et al., 1999). EURO-D Items probe domains of depression, pessimism, suicidality, guilt, (increased or decreased) sleep, (loss of) interests, irritability, (increased or decreased) appetite, fatigue, concentration, enjoyment, and tearfulness. There are 16 items in total, though some items are contingent on responses to others. Example items include: *…have you felt sad or depressed?* and *…have you felt that you would rather be dead?* Each domain is rated 1 for present or 0 for absent. A score of four or above has been identified to be a good cut-off for clinical depression previously (Prince et al., 1999).

Predictors

Alcohol use. The present study used a pre-generated binary variable indicating hazardous drinking versus non-hazardous drinking at baseline (Wave 2 did not have a comparable measure). Hazardous drinking was defined as drinking more than two glasses of (any) alcohol *five to six days a week* or *almost every day*. Using a conservative estimate of one glass of alcohol for one unit of alcohol (equal to 87.5ml of 12% ABV [alcohol by volume] wine, 76ml of 13% wine, 250ml of 4% beer or 25ml of 40% liquor) - at minimum, this would represent 15 units (5 days *x* 3 units) of alcohol a week, which is one unit above the UK government guidelines (see Department of Health, 2016). This cut-off would also approximate an exact minimum Alcohol Use Disorder Identification Test-Consumption (AUDIT-C) score of 5 (albeit without assessing binge drinking, in addition to use *frequency* x *amount*) - which, in line with Chapters 4 and 6 (and previous studies e.g., Eliasen et al., 2013) would constitute hazardous drinking. Preoperative patients with AUDIT-C scores of 5 or above have been observed to have a significantly higher incidence of postoperative complications than those less than 5 (Eliasen et al., 2013).

Surgery. Respondents were asked whether they had stayed in hospital overnight in the previous 12 months, including stays in *medical, surgical,* *psychiatric or in any other specialised wards*. Those that stated yes were asked why. Included as a binary response was inpatient surgery. Respondents were also asked, simply: *during the last twelve months, have you had outpatient surgery?* (after interviewers reminded respondents that an outpatient surgery is a surgery that *does not* involve an overnight hospital stay). Data used were from the follow-up (Wave 2), thus respondents may have had surgery from 1.5 to 2.5 years post-baseline.

Covariates.

Categorical/binary variable categories can be seen in Table 3.2.

Demographics. Included here were baseline self-reports of age, gender, marital status, and current home country. Years in education was also used as a proxy measure for higher education attainment and socioeconomic status. The number of years was based on International Standard Classification of Education (ISCED; UNESCO Institute for Statistics, 2015) guidelines, such that an increased number represented higher educational attainment and not the possibility that someone with repeated educational failures may have had a relatively high number of years in education.

Health & health behaviour. Respondents were asked whether, at any point in the past, a doctor had told them they had previously had a heart attack (including myocardial infarction or coronary thrombosis or any other heart problems e.g., congestive heart failure) hypertension, high cholesterol, stroke or cerebral vascular disease, diabetes or pre-diabetes, chronic lung disease (e.g., chronic bronchitis or emphysema), asthma, arthritis (including rheumatism and osteoarthritis), osteoporosis and/or cancer or malignant tumour(s) (including leukaemia or lymphoma). A composite score from 0 (zero conditions) to 10 (all ten conditions) was used as an indication of co-morbidity. Additionally, functional physical limitations were assessed using the single item Global Activity Limitation Indicator (GALI) (see Robine et al., 2003) measure. The GALI has shown good concurrent validity with other, longer, instruments to assess multiple aspects of physical and mental health (van Oyen, van Der Heyden, Perenboom & Jagger, 2006).

Respondents' body mass indexes (BMI) were calculated from self-reported height and weight. In all analyses BMI was entered as a continuous variable, though participant BMI categories are noted below (Table 3.4) in line with WHO classifications of: underweight (<18.5 Kg/m^2), normal (18.5-24.9 Kg/m^2), overweight (25-29.9 Kg/m^2) and obese (≥30 Kg/m^2). A variable indicating current cigarette smoker, ex-smoker, or those who never smoked daily for one year, was used to determine smoking status. Lastly, SHARE's binary physical activity variable was used to determine whether respondents were sedentary; those endorsing *hardly ever, or never* as a frequency response to two questions asking whether respondents engage in vigorous (e.g., heavy housework, sport, a job that requires physical labour) and moderate (e.g., gardening, cleaning the car, walking) activity were classified as physically inactive

3.2.3 Data Analysis

STATA 13 (StataCorp, 2013) and R studio (RStudio, 2017) were used to conduct statistical analyses. Two third-party STATA packages were used: i. *coefplot* (Jann, 2014) to create forest plots of regression coefficients and ii.

mimrgns (Klein, 2014) to generate marginal means outputs following regression analyses of multiply imputed data. An R package named *esc* (Lüdecke, 2018) was used to calculate between-means effect sizes. Analyses were conducted accounting for complex design features of the survey using the STATA SVYSET function; data were weighted using the SHARE project's pre-generated calibrated (Wave 1 to Wave 2) longitudinal weights (for a detailed explanation of the methodology see Börsch-Supan et al., 2005; 2008). Weighting is necessary to conduct valid inferences when the presence of unit nonresponse could bias the demographic variability of the sample, such that certain groups are over or underrepresented. Longitudinal weighting was necessary here to account for attrition (by demographics) and to provide a nationally representative sample of those in each country surviving up to Wave 2. Analyses were conducted with robust standard errors using Taylor linearization. Alpha was set at .05 (two-tailed).

To investigate the effect of hazardous preoperative alcohol use on postoperative outcomes, a series of regression models were performed including an interaction term representing possible effects of hazardous alcohol use (yes/no) *x* inpatient surgery (yes/no) on each outcome variable. As continuous outcomes, wellbeing (CASP-12) and depressive symptoms (EURO-D) were included in separate linear regression analyses. For each analysis, a series of models were assessed (all controlled for baseline scores on each outcome variable). The first was a crude model including hazardous alcohol use, inpatient surgery and hazardous alcohol use *x* inpatient surgery. In the second model, demographic factors were controlled for (e.g., age, gender, country). Including country as a covariate allowed for a control of unmeasured differences between countries with regard to variables such as the quality of individual healthcare services, and as stated in Angelini, Klijs, Smidt and Mierau (2016, p. 6): "*with the inclusion of additional covariates, the country fixed effects also absorb systematic differences between countries so that the estimated impact of each covariate is the within-country effect of a variation in a specific covariate*". The third model included health and health behaviours (e.g., smoking, BMI, number of chronic illnesses). To investigate whether the results held or differed between those having outpatient, inpatient or either surgery type, an interaction term between alcohol use and outpatient or either surgery was entered in a fully controlled model (e.g., model 3) as with the main analysis.

Given that this was an analysis of secondary data, the sample size was not - and could not be modified. As such, the sample size was not oriented towards (i.e. purposefully powered for) detecting a specific effect size of interest. Nevertheless, given that there was a large number of respondents, and that there is a well-established relationship between alcohol use and low affect (as above), it was predicted that even trivial effects may have been detected. It was deemed particularly important therefore to not only investigate the statistical significance of the results, but to highlight effect size magnitude. Accordingly, after each analysis, significant interactions were explored further by inspecting marginal means (predicted mean scores of each outcome variable after controlling for all variables included in the model). Scale-free, standardized between-means effect sizes were then calculated using Hedges' *g* (based on means and standard errors), where 0.2 was considered small, and 0.5 and 0.8

medium and large effect sizes, respectively. The precision of the estimates was estimated and interpreted also through calculation of 95% confidence intervals (which is a feature of all studies within this thesis).

As in the SHARE project guidance - where the longitudinal weights were calculated based on the assumption that data were missing data random (MAR) – data here were analysed using complete case analysis (list wise deletion); under MAR conditions, inferences based on complete cases analyses are deemed valid (e.g., Mukaka et al., 2016). However, a significant degree of power may be lost using complete cases only. The robustness of the results using complete case analysis was therefore tested by also conducting analyses (exactly as above) using multiple imputation. Multiple imputation is a simulation-based approach for analysing incomplete data, where missing data for each variable with missing data are replaced with simulated data based on their predicted values from (in this case) all other variables in the respective analyses multiple times (such that multiple datasets are created). Data are then analysed as normal for each imputed dataset before the parameter estimates for each analysis are pooled, adjusting for uncertainty. In the present study, five iterations were used, thus pooled parameter estimates were based on analyses from five regression analyses. The specific procedure used was multivariate imputation using chained equations (MICE; van Buuren & Oudshoorn, 1999) which allows for various data formats (e.g., categorical, continuous).

3.3 Results

As well as providing missing data frequencies and percentages, Table 3.2 below provides an overview of sample characteristics and descriptive statistics for all variables i. in the total sample, ii. between those having inpatient surgery or not having inpatient surgery and iii. between hazardous drinkers and non-hazardous drinkers. Table B1 provides sample characteristics and descriptive statistics cross-tabulated between inpatient surgery status (yes or no) and hazardous drinker status (yes or no).

3.3.1 Wellbeing (Inpatient Surgery)

In multiple linear regression analyses (with robust standard errors using Taylor linearization) three models were computed to assess the relationship between alcohol use at time 1 (baseline) and time 2 (follow-up) wellbeing (CASP-12), between those having or not having surgery in the previous 12 months at time 2. A forest plot of the unstandardized regression coefficients with the key predictors (and interaction term) between models can be seen in *Figure 3.3*, where higher scores represent higher wellbeing.

In the first model just hazardous alcohol use (yes or no) at time 1, and inpatient surgery status (yes or no) in the previous 12 months at time 2 and the interaction between both variables were entered as predictors (time 1 wellbeing i.e., CASP-12 scores, was also entered as a covariate). Model 1 explained 35.1% of the variance in wellbeing scores, $F(4, 11226) = 462.07$, $p < .001$. Hazardous drinking ($b = -.35$, 95% CI: -.07-.76, $p = .26$) and inpatient surgery ($b = -.33$, 95% CI: -.94-.25, $p = .26$) were not significantly associated with wellbeing scores, though there was a significant interaction effect, such that the presence of both was associated with significantly lower wellbeing over and above each ($b = -1.64$, 95% CI: -3.12- -.17, $p = .03$).

The second model included all previous variables, but also included demographic variables (e.g., country, age, gender). Model 2 explained 41% of the variance in wellbeing scores, *F*(22, 10943) = 189.42, *p* <.001. Again, neither hazardous drinking (*b* = .38, 95% CI: -.03-.80, *p* = .07) nor having inpatient surgery in the previous 12 months (*b* = -.36, 95% CI: -.92-.21, *p* = .22) was significantly associated with reduced wellbeing. Again, however, the interaction effect was significant, albeit imprecise (*b* = -1.60, 95% CI: -3.01- -.18, *p* = .03).

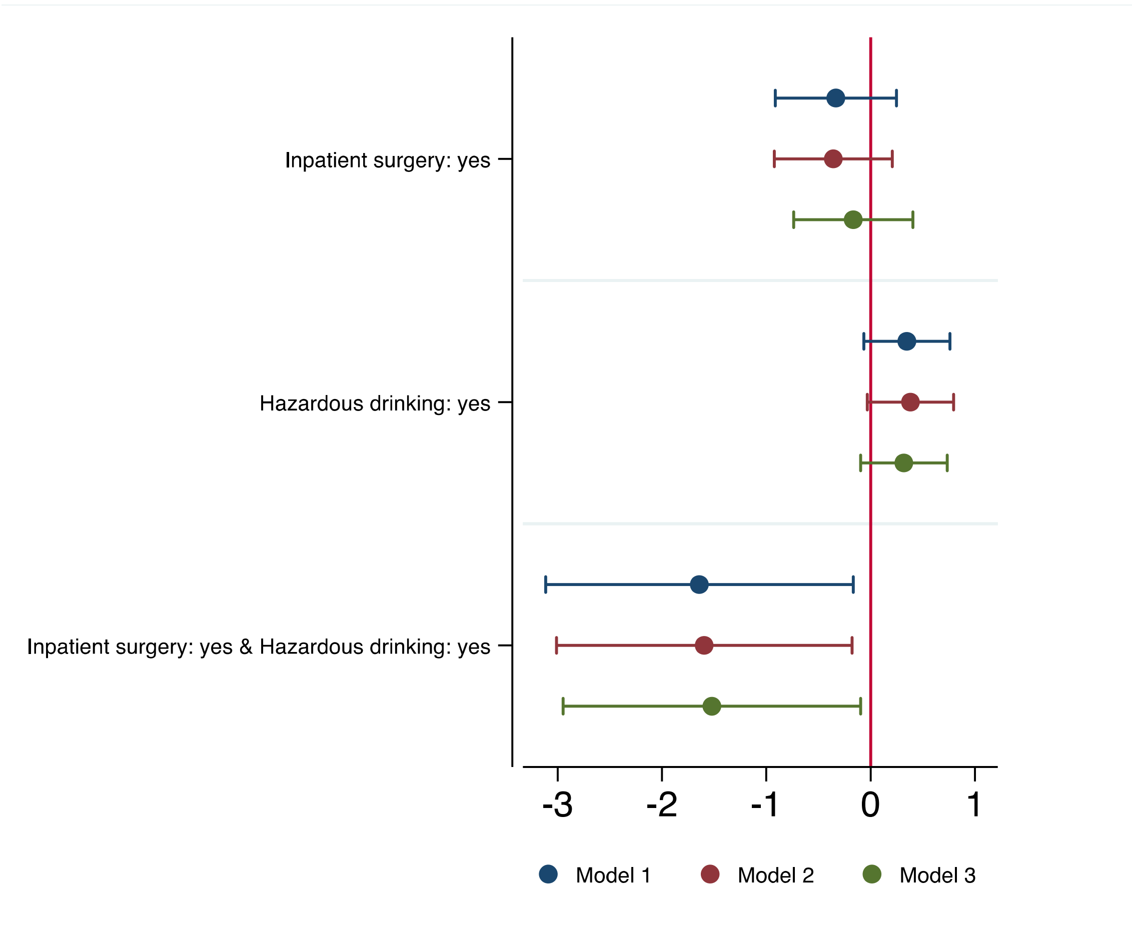

Figure 3.3. Unstandardized Regression Coefficients with the Key Variables. Higher Scores Represent Higher Wellbeing.

A third, fully-adjusted model included all aforementioned variables plus variables assessing health and health behaviours. Model 3 explained 43% of the variance in wellbeing scores, $F(28, 10808) = 161.76$, $p < .001$. As with previous models, only the interaction term was significant (interaction: $b = -1.52$, 95% CI: -2.95- -.10, $p = .04$; hazardous drinking: $b = .32$, 95% CI: -.10-.73, $p = .13$; inpatient surgery: $b = -.17$, 95% CI: -.74-.40, $p = .57$). A moderation plot (i.e., plot of the included interaction term) of the model 3 linear predictions of wellbeing (CASP-12 scores) can be seen in *Figure 3.4*.

After assessing model 3 marginal means, it was identified that within time 1 non-hazardous drinkers, having inpatient surgery (versus no surgery) in the previous 12 months at time 2 was associated with lower wellbeing (Hedges' g = -0.06, 95% CI: -13 0.01), though in time 1 hazardous drinkers this effect was much larger (Hedges' g = -0.35, 95% CI: -0.54- -0.15). Among all individuals having inpatient surgery in the previous 12 months at time 2, hazardous alcohol use versus no hazardous alcohol use at time 1 was associated with a lower wellbeing (Hedges' g = -.22, 95% CI: -.42- -.02). Lastly, having inpatient surgery and being a hazardous drinker at time 1 was associated with lower wellbeing than not having had inpatient surgery and not being a hazardous drinker at time 1 (Hedges' g = -0.28, 95% CI: -0.47- -0.09). For further results see Table 3.3 below. .

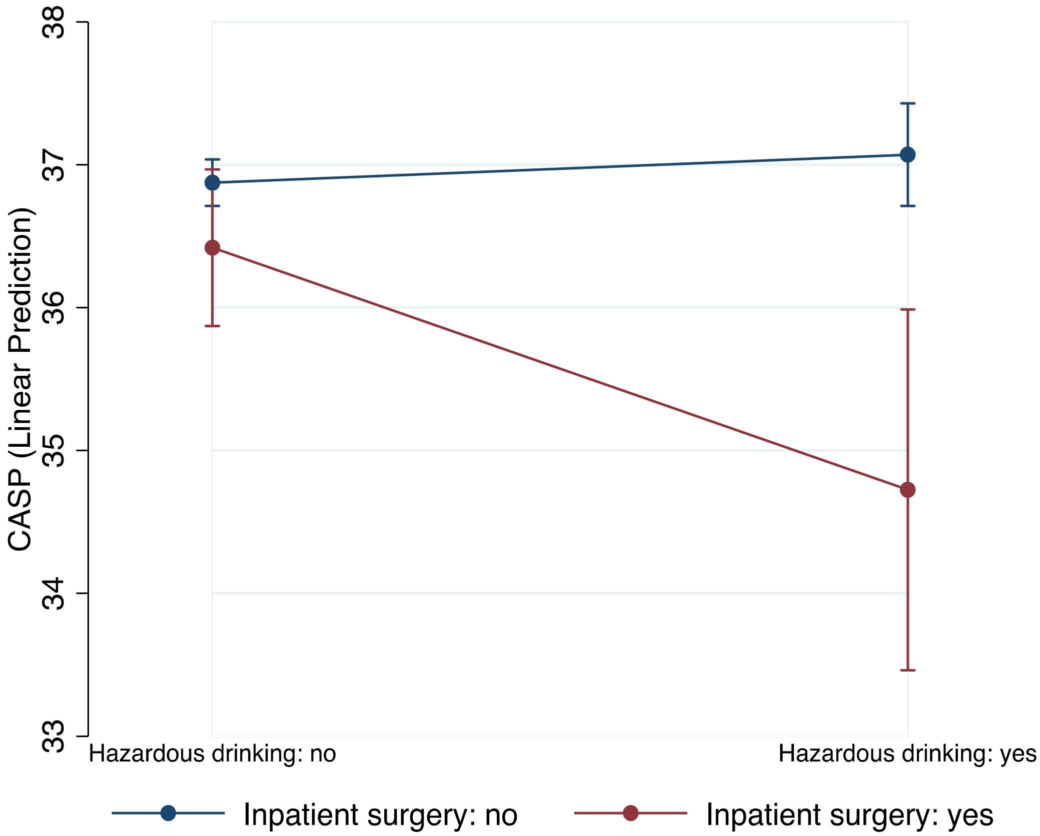

Figure 3.4. Moderation Plot of Mean Wellbeing Scores. Higher Scores Represent Higher Wellbeing.

Table 3.2. Sample Characteristics by Inpatient Surgery Status and Hazardous Alcohol Use.

Characteristic (95% CI)	**Total sample (18508)**	**Inpatient surgery: no (16928)**	**Inpatient surgery: yes (1523)**	**Hazardous alcohol use: yes (2567)**	**Hazardous alcohol use: no (15890)**
Mean age	67.47 (67.24-67.71)	67.33 (67.07-67.58)	68.91 (68.18-69.63)	66.49 (65.93-67.04)	67.68 (67.42-67.95)
Gender					
Male	8383 (45%, 44-46)	7618 (45%, 44-46)	731 (48%, 44-52)	1909 (77%, 75-79)	6446 (39%, 38-40)
Female	10125 (55%, 54-56)	9310 (55%, 54-56)	792 (52%, 48-56)	658 (23%, 21-25)	9444 (61%, 60-62)
Marital status					
Divorced	1176 (6%, 6-7)	1075 (6%, 6-7)	96 (6%, 4-8)	164 (7%, 5-8)	1010 (6%, 6-7)
Married (living together)	12980 (66%, 65-67)	11896 (66%, 65-67)	1047 (65%, 61-68)	1991 (74%, 71-76)	10968 (64%, 63-65)
Married (living separated)	211 (1%, 1-2)	192 (1%, 1-2)	18 (1%, 1-3)	21 (1%, 1-2)	188 (1%, 1-2)
Registered partnership	283 (1%, 1-1)	267 (1%, 1-1)	16 (0%, 0-1)	32 (1%, 0-1)	249 (1%, 1-1)
Never married	1023 (7%, 6-8)	939 (7%, 6-8)	78 (7%, 5-9)	140 (8%, 6-10)	881 (7%, 6-7)
Widowed	2816 (19%, 18-20)	2544 (19%, 18-20)	266 (21%, 17-24)	219 (10%, 8-12)	2593 (21%, 20-22)
Mean years of education (from ISCED)	10.05 (9.95-10.15)	10.06 (9.96-10.17)	9.96 (9.62-10.29)	10.41 (10.15-10.67)	9.98 (9.87-10.09)
Mean number health conditions	1.60 (1.57-1.63)	1.56 (1.53-1.60)	1.97 (1.85-2.09)	1.46 (1.39-1.53)	1.63 (1.59-1.67)
Mean BMI	26.62 (26.51-26.72)	26.59 (26.48-26.69)	26.97 (26.61-27.34)	26.65 (26.42-26.87)	26.61 (26.50-26.72)
Underweight	202 (1%, 1-1)	189 (1%, 1-1)	12 (1%, 0-2)	20 (1%, 0-2)	182 (1%, 1-1)
Normal weight	7027 (38%, 37-39)	6480 (38%, 37-39)	519 (34%, 31-89)	906 (34%, 32-37)	6113 (38%, 37-40)
Overweight	7761 (42%, 41-44)	7070 (42%, 41-43)	673 (44%, 40-48)	1212 (48%, 45-50)	6540 (41%, 40-43)
Obese	3246 (19%, 18-20)	2945 (19%, 18-20)	296 (20%, 18-24)	408 (17%, 15-19)	2836 (19%, 18-20)

Characteristic (95% CI)	Total sample (18508)	Inpatient surgery: no (16928)	Inpatient surgery: yes (1523)	Hazardous alcohol use: yes (2567)	Hazardous alcohol use: no (15890)
Physical activity					
Never vigorous nor moderate	1593 (11%, 11-12)	1404 (11%, 10-12)	179 (15%, 12-18)	159 (8%, 6-9)	1431 (12%, 11-13)
Other	16879 (89%, 88-89)	15496 (89%, 88-90)	1338 (85%, 82-88)	2407 (92%, 91-94)	14456 (88%, 87-89)
GALI					
Limited	7477 (44%, 43-45)	6628 (42%, 41-44)	817 (56%, 52-60)	886 (36%, 33-28)	6578 (45%, 44-46)
Not limited	11002 (56%, 55-57)	10276 (58%, 56-59)	703 (44%, 40-48)	1681 (64%, 62-67)	9311 (55%, 54-56)
Smoking					
Current	3485 (18%, 17-19)	3207 (18%, 17-19)	267 (17%, 14-20)	751 (29%, 27-32)	2732 (15%, 14-16)
Stopped	5249 (26%, 25-27)	4746 (25%, 24-26)	490 (29%, 26-32)	1031 (37%, 35-40)	4210 (23%, 22-24)
Never	9740 (57%, 56-58)	8948 (57%, 56-58)	761 (54%, 51-58)	785 (34%, 31-36)	8947 (61%, 60-62)
Hazardous alcohol use					
Yes	2567 (17%, 16-18)	2355 (17%, 16-18)	200 (14%, 12-17)	2567 (100%)	-
No	15890 (83%, 82-84)	14530 (83%, 82-84)	1317 (86%, 83-88)	-	15890 (100%)
Country					
Austria	1103 (2%, 2-3)	945 (2%, 2-3)	157 (4%, 3-5)	98 (1%, 1-2)	1004 (3%, 3-3)
Belgium	2735 (3%, 3-3)	2457 (3%, 3-3)	276 (4%, 3-4)	407 (3%, 3-3)	2322 (3%, 3-4)
Denmark	1197 (2%, 2-2)	1110 (2%, 2-2)	86 (1%, 1-2)	175 (1%, 1-2)	1016 (2%, 2-2)
France	1931 (19%, 18-20)	1705 (19%, 18-19)	191 (21%, 18-24)	458 (28%, 26-30)	1454 (17%, 16-18)
Germany	1569 (27%, 26-29)	1402 (27%, 26-28)	166 (32%, 28-36)	165 (17%, 14-19)	1403 (30%, 28-31)
Greece	2260 (3%, 3-4)	2193 (4%, 4-4)	67 (1%, 1-2)	181 (2%, 1-2)	2079 (4%, 4-4)
Italy	1733 (20%, 19-21)	1593 (20%, 19-21)	139 (17%, 15-20)	404 (28%, 26-31)	1328 (18%, 17-19)
Netherlands	1755 (5%, 5-5)	1621 (5%, 5-5)	130 (4%, 3-5)	316 (5%, 4-6)	1436 (5%, 4-5)
Spain	1467 (13%, 12-13)	1346 (13%, 12-14)	118 (12%, 10-14)	218 (13%, 11-15)	1242 (13%, 12-14)
Sweden	2054 (3%, 3-3)	1913 (3%, 3-3)	132 (2%, 2-3)	39 (0%, 0-0)	2009 (4%, 3-4)
Switzerland	704 (2%, 2-2)	643 (2%, 2-3)	61 (2%, 2-3)	106 (2%, 2-2)	597 (2%, 2-3)

Characteristic (95% CI)	**Total sample (18508)**	**Inpatient surgery: no (16928)**	**Inpatient surgery: yes (1523)**	**Hazardous alcohol use: yes (2567)**	**Hazardous alcohol use: no (15890)**
Mean CASP BL	36.78 (36.59-36.94)	36.94 (36.73-37.14)	36.82 (36.14-37.50)	36.76 (36.28-37.24)	36.96 (36.74-37.17)
Mean CASP FU	36.39 (36.24-36.55)	36.85 (36.65-37.05)	36.17 (35.45-36.89)	36.87 (36.42-37.32)	36.77 (36.56-36.99)
Mean EURO-D	2.49 (2.44-2.54)	2.31 (2.24-2.38)	2.56 (2.31-2.81)	2.16 (2-2.31)	2.37 (2.29, 2.44)
Mean EURO-D FU	2.42 (2.37-2.48)	2.24 (2.16-2.31)	2.96 (2.69-3.23)	2.06 (1.90-2.23)	2.35 (2.27-2.43)

Notes. Raw *n* figures are unweighted whereas confidence intervals (95% CI) were calculated accounting for sample weighting; BL: baseline; FU: follow-up; All percentages are rounded to the nearest integer; Missing data (% of total sample): inpatient surgery = 57 (0.3), marital status = 19 (0.1), years of education = 398 (2.2), BMI = 272 (0.5), physical activity = 36 (0.2), GALI = 29 (0.2), hazardous alcohol use = 51 (0.3), smoking = 34 (0.2), number of chronic conditions = 38 (0.2), CASP BL = 6681 (36), CASP FU = 1219 (6.6), EURO-D BL = 302 (1.6), EURO-D FU = 451 (2.4).

Table 3.3. Between Marginal-Mean Effect Sizes (Inpatient Surgery).

Outcome *x* variable		**Hedges' *g* (95% CI)**
Wellbeing (↑ = better)		
IP: yes	IP: no	-0.06 (-0.12-0.01)
HD: yes	HD: no	0.02 (-0.03-0.08)
IP: yes, HD: yes	IP: no, HD: yes	-0.35 (-0.54- -0.15)
	IP: yes, HD: no	-0.22 (-0.42- -0.02)
	IP: no, HD: no	-0.28 (-0.47- -0.09)
IP: no, HD: yes	IP: yes, HD: no	0.09 (0.00-0.18)
	IP: no, HD: no	0.03 (-0.03-0.08)
IP: yes, HD: no	IP: no, HD: no	-0.06 (-0.13-0.01)
Depressive symptoms (↓ = better)		
IP: yes	IP: no	0.13 (0.08-0.18)
HD: yes	HD: no	-0.01 (-0.05-0.03)
IP: yes, HD: yes	IP: no, HD: yes	0.35 (0.20-0.50)
	IP: yes, HD: no	0.11 (-0.04-0.26)
	IP: no, HD: no	0.29 (0.14-0.43)
IP: no, HD: yes	IP: yes, HD: no	0.00 (-0.07-0.07)
	IP: no, HD: no	-0.02 (-0.06-0.02)
IP: yes, HD: no	IP: no, HD: no	0.17 (0.12-0.23)

Notes. IP = inpatient surgery; HD = hazardous drinking.

Wellbeing (outpatient and either surgery). As in the fully adjusted model 3 above, two adjusted models were analysed including interaction terms, but this time including a variable indicating whether the respondent had had outpatient surgery in the 12 months in place of the inpatient surgery variable, likewise for a computed variable indicating whether the respondent had had either type of surgery.

Models including outpatient-only surgery and either surgery variables each explained less variance than the corresponding inpatient surgery model, and none of the key predictors (i.e., hazardous alcohol use, surgery, and the interaction between the two) was significant.

3.3.2 Depressive Symptoms (Inpatient Surgery)

As in the previous analysis, three increasingly adjusted regression models were computed. The outcome variable in this analysis was depressive symptoms (as assessed by the EURO-D), where higher scores indicated the presence of more depressive symptoms (as opposed to the previous analysis where higher scores indicated more positive wellbeing). A forest plot of the unstandardized regression coefficients with the key predictors (and interaction term) between models can be seen in *Figure 3.5*.

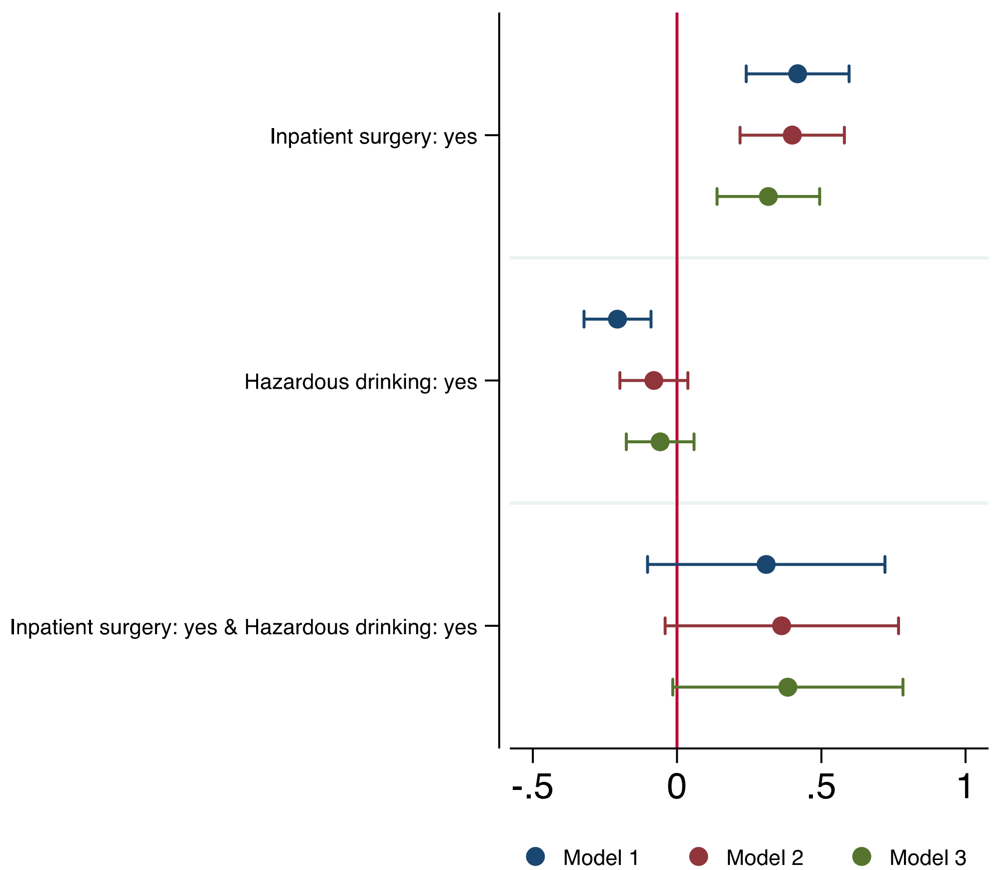

Figure 3.5. Unstandardized Regression Coefficients with the Key Variables. Higher Scores Represent More Depressive Symptoms.

Results indicated that model 1 explained 29.7% of the variance in depression scores, $F(4, 17828) = 537.12$, $p < .001$. Hazardous drinking at time 1 ($b = -.21$, 95% CI: -.32- -.09, $p = .001$) was significantly associated with fewer depressive symptoms at time 2, though having inpatient surgery in the last 12 months at time 2 was significantly associated with more depressive symptoms at time 2 ($b = .42$, 95% CI: .24-.60, $p < .001$). The interaction effect was not significant ($b = .31$, 95% CI: -.10-.72, $p = .14$), indicating no difference in depressive symptoms at time 2 in those having had surgery and being hazardous drinkers at time 1 than those not so.

Model 2 explained 32% of the variance, $F(22, 17462) = 129.51$, $p < .001$. While having inpatient surgery remained a significant predictor of higher depression scores ($b = .40$, 95% CI: .22-.58, $p < .001$), hazardous drinking at time 1 did not remain a significant predictor of reduced depression scores ($b = -.08$, 95% CI: -.20-.04, $p = .18$). The interaction effect in this model was marginally significant ($b = .36$, 95% CI: -.04-.077, $p = .08$).

Model 3 explained 34% of the variance, $F(28, 17245) = 109.17$, $p < .001$. As in model 2, inpatient surgery remained a significant predictor ($b = .32$, 95% CI: .14-.49, $p < .001$) while hazardous drinking did not ($b = -.06$, 95% CI: -.18-.06, $p = .33$). The interaction effect in this case was very close to significance ($b = .38$, 95% CI: -.01-.78, $p = .059$), and the parameter estimate indicated that having surgery and being a hazardous drinker at time 1 was associated with higher depression scores at time 2 than having surgery alone. See *Figure 3.6* below for a visual representation of this interaction.

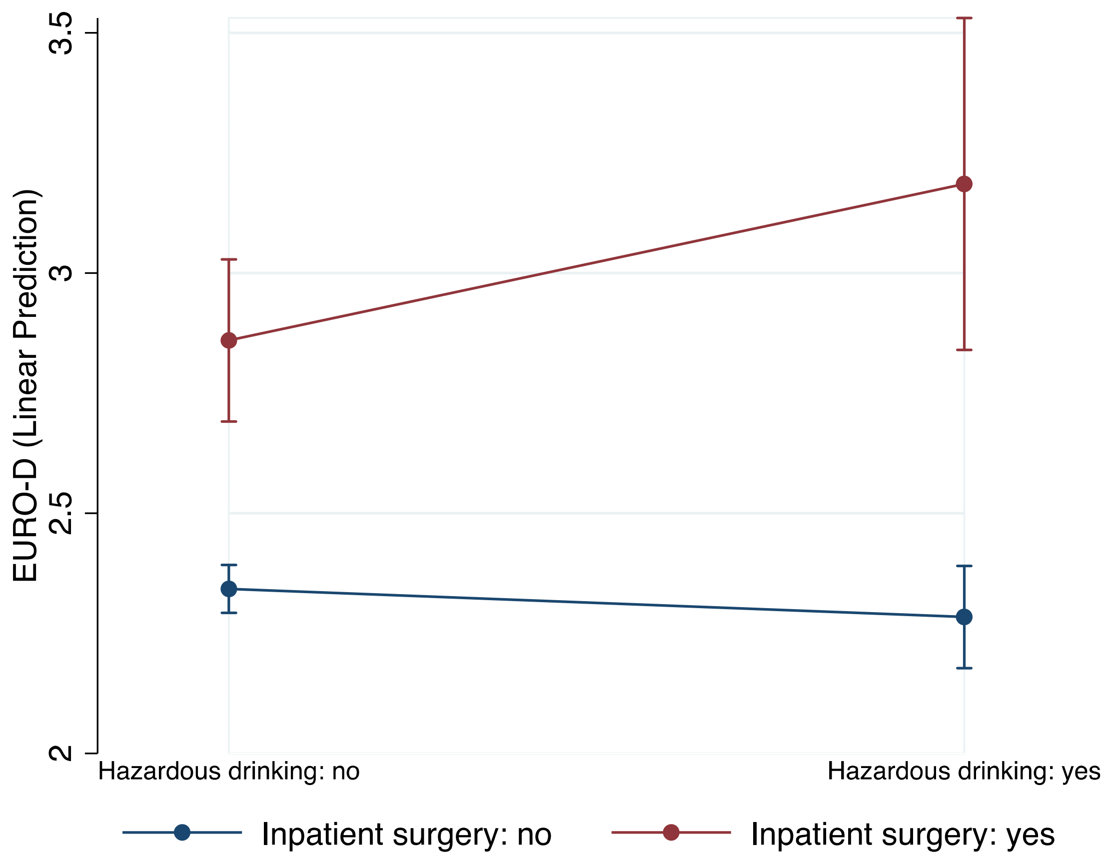

Figure 3.6. Moderation Plot of Mean Depression Scores. Higher Scores Represent Higher Depression Scores.

Inspection of model 3 marginal means indicated that, among all non-hazardous drinkers, having inpatient surgery versus no inpatient surgery in the last 12 months at time 2 was associated with higher time 2 depression scores (Hedges' *g* = 0.17, 95% CI: 0.11-0.23). Among hazardous drinkers, having inpatient surgery versus not having inpatient surgery was associated with even higher time 2 depression scores (Hedges' *g* = 0.35, 95% CI: 0.20-0.50). Of all respondents having had surgery, being a hazardous alcohol user versus not being a hazardous alcohol user at time 1 was associated with higher depression scores (Hedges' *g* = 0.11, 95% CI: -0.04–0.26). Lastly, both having inpatient surgery and being a hazardous drinker was associated with higher depression scores than those who had not had inpatient surgery and were not hazardous drinkers (Hedges' *g* = 0.29, 95% CI: 0.14–0.43). For further results see Table 3.3 above.

Depressive symptoms (outpatient and either surgery). In a full-adjusted model including outpatient surgery only, having outpatient surgery was significantly associated with higher depression scores though hazardous drinking and the interaction between the two were not. Whereas the interaction term in the inpatient surgery model was marginally significant, the model including an interaction term between hazardous alcohol use and either surgery met the threshold for significance (b = .34, 95% CI: -.02-.67, p = .04), which indicated higher scores above just having surgery alone (b = .33, 95% CI: .19-.47, p < .001). Marginal means were similar to the inpatient surgery analysis (see Table 3.4). See *Figure 3.7* below for a plot of the coefficients between models including the different surgery types.

Table 3.4. Between Marginal-Mean Effect Sizes (Either Surgery).

Outcome *x* variable		**Hedges' *g* (95% CI)**
Depressive symptoms (↓ = better)		
S: yes	S: no	0.13 (0.09-0.18)
HD: yes	HD: no	-0.01 (-0.05-0.04)
S: yes, HD: yes	S: no, HD: yes	0.32 (0.21-0.44)
	S: yes, HD: no	0.09 (-0.02-0.21)
	S: no, HD: no	0.26 (0.15-0.37)
S: no, HD: yes	S: yes, HD: no	-0.20 (-0.26- -0.14)
	S: no, HD: no	-0.02 (-0.07-0.02)
S: yes, HD: no	S: no, HD: no	0.16 (0.11-0.21)

Notes. S = either surgery; HD = hazardous drinking.

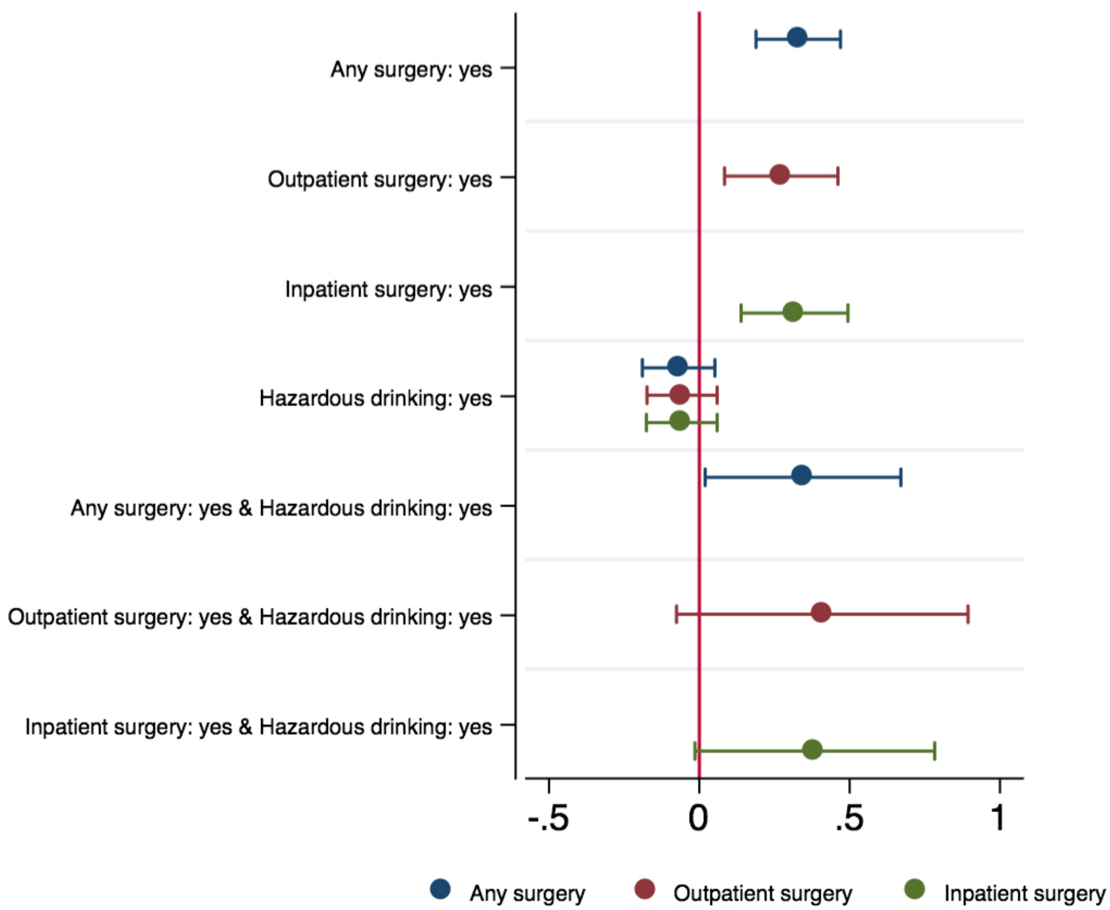

Figure 3.7. Fully Adjusted Unstandardized Regression Coefficients with Different Surgery Variables. Higher Scores Represent Higher Depression Scores.

3.3.3 Multiple Imputation Analyses

All the above analyses were repeated using multiple imputation to account for missing data. All results can be viewed in Appendix E. Discrepancies between findings following complete case analyses and multiple imputation analyses are described below.

Wellbeing. All CASP results remained similar to the complete case analyses. However, model 1 indicated that having inpatient surgery was associated with a marginally significant reduction in wellbeing, and hazardous drinking a marginally significant increased wellbeing score. In model 2, inpatient surgery remained a marginally significant predictor, hazardous alcohol use did not. In both models the interaction term was significant. In model 3 just the interaction term was significant. All regression co-efficient remained similar to the complete case analyses. All between-mean effect sizes were reduced in size but in the same direction. There remained no significant effects involving the key variables in models including outpatient or either surgery.

Depressive symptoms. EURO-D results were altered significantly in multiple-imputation analyses. In model 1 inpatient surgery was significantly associated with increased depression scores, and hazardous drinking was significantly associated with reduced depression scores (the interaction term was non-significant). In model 2 and 3 only inpatient surgery remained a significant predictor. All regression coefficients remained similar to the complete case analyses. While the interaction term was not significant in the inpatient model and outpatient model, it remained marginally significant in a model including a variable indicating having had either surgery. As above, all between-mean effect sizes were in the same direction and remained very similar in size to the complete case analyses.

3.4 Discussion

The present study has, for the first time, provided some evidence that hazardous alcohol use prior to having a surgical procedure may deleteriously impact on mental health and wellbeing outcomes up to one year postoperatively. In adjusted (e.g., for demographic variables and baseline outcome values) complete case analyses, inpatient surgery was observed to negatively affect wellbeing and depressive symptoms, though hazardous drinkers who underwent inpatient surgery were shown to have lower wellbeing (a drop as large again as having inpatient surgery *per se*) and higher levels of depressive symptoms postoperatively than those having surgery alone. This significant interaction effect (*surgery x hazardous drinking*) was present in those having inpatient, but not outpatient (or *either* inpatient or outpatient) surgery for wellbeing, and for those having *either* type of surgery for depressive symptoms (and marginally for those having inpatient surgery). Among all respondents having inpatient surgery, baseline hazardous drinking versus no hazardous drinking was associated with a lower score of postoperative wellbeing and more depressive symptoms (with small effect sizes). Interestingly, the impact of having inpatient surgery versus not having inpatient surgery on lower wellbeing and higher depressive symptoms was greater amongst baseline hazardous drinkers (with small-medium effect sizes); perhaps providing some indication of a greater sensitivity and a greater magnitude of a negative affective response to the psychological stress of having surgery. All the above results held in analyses accounting for missing data using multiple imputation, though the marginal significant *inpatient surgery x hazardous drinking* effect on depressive symptoms became non-significant (the *either surgery x hazardous drinking* effect did, however, remain significant). Results are discussed henceforth.

The present study may further emphasise the importance of routine promotion of alcohol use reduction for patients awaiting inpatient surgery, given that there is a robust body of evidence to suggest that psychological morbidity and hazardous alcohol use may be independently associated with an increase in perioperative physiological morbidity (Brittleon et al., 2017; Ghoneim & O'Hara, 2016; Linnen et al., 2011; Eliasen et al., 2013), and that the prevalence of preoperative hazardous alcohol use (see Chapter 4) may be as high as one in every three patients. The present results may also suggest that intervention as early as possible is necessary; significant effects were observed despite the alcohol measure in the present study reflecting respondents' alcohol use up to two and half years pre-surgery.

As with previous studies demonstrating that self-reported alcohol use one year prior to surgery could predict perioperative complications (Bradley et al., 2011; Rubinsky et al., 2012), the present study could not elucidate whether the chronic effects of alcohol use over a longer time period, or the acute effects of recent use (i.e., hazardous drinking maintained from baseline to follow-up) were responsible for the observed effects. If the latter was most responsible, it may be that the present effects may actually be an underestimate: some respondents may have reduced or even abstained from alcohol prior to their operation, reducing the observed effect sizes. The effect sizes may have also reduced given the long length of follow-up. Indeed, some respondents may have had surgery up to a year prior to the follow-up, at which point it would be expected that at least some of the initial stress of, and recovery from, surgery would have taken place. These facets and wide confidence intervals (given a relatively small proportion of the sample who had surgery and an even smaller proportion who were hazardous drinkers *and* had surgery) may be partially responsible for the lack of significant effect observed in the multiple imputation analysis of *surgery x hazardous drinking* on depressive symptoms.

While the present study could not: i. establish whether some of the effects of alcohol use on postoperative complications are explained by increases in decreases in positive affect (or whether alcohol use and low affect could independently predict complications); ii. assess whether stress or worry about surgery predisposed certain individuals to increased alcohol use and clinical levels of low affect; iii. confirm previous research observing a bi-directional negative relationship between increased alcohol use and decreased positive affect; and iv. observe differential effects on affect between preoperative and postoperative alcohol use - the results provide very initial evidence that having surgery may negatively impact on wellbeing and depressive symptoms, and that this *may* be compounded by hazardous alcohol consumption. There may be several mechanisms and explanations for these observations.

It may be no surprise that there was some evidence of significantly increased depressive symptoms in respondents having had inpatient surgery versus those not so. There is evidence to suggest that suffering perioperative complications can have a dramatic and negative impact on mental health (Pinto et al., 2016), an eventuality at least a subset in the present study are likely to have experienced (e.g., Abbot et al., 2017). Indeed, even without suffering a complication, having surgery is a potentially life-disrupting experience, accompanied by illness and a period of increased disability – both of which have both been observed to predict lowered mental health and wellbeing generally (e.g., Wetsch et al., 2009; Kang et al., 2015). In the present study, disability and comorbidity (among a variety of other factors) were controlled for, perhaps suggesting that, along with possible complications (which could not be captured with the current dataset), psychological determinants (e.g., stress, uncertainty, or stress *x* uncertainty) (and a possible mutually reinforcing effect of complications and psychological determinants) may partially explain the observed negative effect of surgery on mental health outcomes. Further, even after adjusting for a variety of potential confounds, patients with a recent stay in hospital seem to suffer more postoperative complications in subsequent surgical procedures than those having surgery without a recent hospital stay – meaning simple exposure to a stay in hospital may adversely impact on physical, and consequently mental health functioning, and vice-versa (Brownlee et al., 2017) (a phenomenon termed post-hospital syndrome, thought to be explained by in-hospital sleep deprivation, reduced nourishment, pain and deconditioning due to physical inactivity; Krumholz, 2013).

There may be a multitude of explanations for the observed, compounding effect of hazardous alcohol use and inpatient surgery on mental health outcomes. Firstly, as above, patients with a recent stay in hospital may be susceptible to post-hospital syndrome. As in Goldwater et al. (2018), post-hospital syndrome has been explained by dysregulation of normal allostasis; that is, a disruption of the evolutionary adaptive, physiological mechanisms though which stress responses (e.g., fight or flight, adrenaline production and so on) are rapidly activated and suitably deactivated in response to legitimate threats. A rapid succession of, or prolonged stressors (e.g., in-hospital fear of illness, reduced autonomy and so on; see Douglas & Douglas, 2004) impairs the mechanism responsible for the deactivation of stress, and the hormone most associated with physiological stress, cortisol, increases. This state, known as allostatic overload, is associated with increased susceptibility to illness through downward pressure on the immune system (McEwen, 2005). It may be that this state of vulnerability to illness is adversely affected further by alcohol use.

Alcohol use can have depressant effects on the immune system (Sarkar, Jung & Wang, 2015) and has been observed to increase objective physiological indicators of (e.g., increased cortisol; Badrick et al., 2008), and self-perceived, stress (Brady & Sonne, 1999). As mentioned previously, both illness and stress are predictive of worsened mental health. The effect of alcohol on the immune system also partially explains how hazardous alcohol use can negatively affect physiological perioperative outcomes such as delayed wound healing (see Gordon, 2018). Such negative perioperative outcomes have in turn been shown to be associated with worsened mental health up to a year postoperatively (Pinto et al., 2016), another route through which the present results may be explained. Lastly, given that alcohol use has also been observed to increase in both amount and frequency during times of stress in individuals with particular coping styles (e.g., San Jose et al., 2000), there may be a mutually reinforcing two-way relationship between hazardous alcohol use and states such as post-hospital syndrome; the more stress experienced, the more alcohol use, which may lead to more stress, and so on, finally cumulating in worsened mental health. Hazardous alcohol users, who may be likely to use alcohol as a coping strategy more often (e.g., Cooper, Frone, Russell & Mudar, 1995), may, therefore, be more susceptible to the stress of surgery; individuals with more adaptive coping styles may be able to buffer against some of the stress, and heavier alcohol users may have a lower stress threshold.

As above, the present study could not directly address several interesting research questions that, for example, may have shed some light on the mechanisms of the present findings. This limitation was, as with many of the following limitations, borne out of constraints posed by the dataset (i.e., the SHARE project) itself.

Indeed, several data repositories were searched for surveys on health and behaviour, though just one dataset was found appropriate to assess the objectives of this study. This meant that additional variables that would be useful to control for (e.g., surgery types), or include as dependent variables (e.g., perioperative complications) were not assessed, and this study had no control over the timepoints at which measures were taken – meaning, for example, it could not be determined when exactly respondents had surgery, and whether they engaged in hazardous behaviours up to the point of surgery. Due to alcohol use data being provided in a single *frequency x amount* binary format, this also meant that a dose-response assessment of alcohol use could not be performed (i.e., with different cut-offs) - which would allow some indication of causality, and that the (non-validated) measure of alcohol use only approximately corresponds to hazardous alcohol use as defined in previous perioperative studies. Nevertheless, the definition of hazardous alcohol use here can be interpreted as an exact *minimum* of an AUDIT-C score of 5, which has been recommended as a useful cut-off previously and has been associated with adverse perioperative outcomes (e.g., Bradley et al., 2011).

Conducting primary studies (thus having greater control over the study design) in this area would be preferable to the present secondary analysis approach - indeed here, with a total sample size of over 18,000, just 200 respondents were hazardous alcohol users and had had inpatient surgery in the previous year. This low rate meant that there was some degree of uncertainty in some of the observed effect sizes and coefficients (i.e., wide confidence intervals), though this was no doubt also a result of the previously mentioned very long follow-up and measure of alcohol use taken a long time before the follow-up period. If surgeries were subdivided, for example, by speciality (e.g., neurology, general) and/or complexity (e.g., minor, complex major) the sample size would be further reduced such that no inferential analyses could have been conducted. This is an important limitation; different types of surgery, especially those more conducive to disability and complications may have had differential effects on mental health than those less so, it would be important to identify these to take preventive measures. Regardless, the present dataset did not allow us to separate surgeries in this manner – future studies, or indeed surveys on health, may note and assess this. Additionally, as with most large-scale surveys, objective measures of behaviour and other variables susceptible to social desirability biases were often not taken in the SHARE project, meaning there may have been some degree of self-report bias. Lastly, the present results may not generalise to the UK population (who may have very differing drinking patterns to the participating countries) and those under the age of 50 years-old (who may be at reduced risk of perioperative complications).

In sum, the present study found some initial evidence that surgery may negatively impact on wellbeing and depressive symptoms, and that hazardous preoperative alcohol use may further compound this effect. This is particularly important as low positive affect has been observed to predict perioperative complications. While the present study could not shed light on the exact mechanisms for the findings, there may be several explanations including i. deleterious effects on already weakened immune systems leading to increased susceptibility of complications, in turn worsening mental health, and ii. alcohol compounding the already stressful experience of having surgery (e.g., through increasing cortisol production). As the study was a secondary analysis of an existing dataset, many variables useful for the present study were neglected and taken at inopportune times meaning there were several limitations and caveats. Primary studies with more control over study designs would be very useful to investigate related hypotheses further.

3.5 Key Findings: Study 1

- Drinking more than two glasses of alcohol five or six days a week (~15 units a week) before surgery had a small to medium negative effect on postoperative wellbeing and depression scores (which may predict complications).
- Having inpatient surgery *and* being a hazardous alcohol user was associated with a synergistic negative effect on wellbeing and depression (i.e. there was a residual effect over and above the individual effects of having surgery and alcohol overuse).
- The above results held in models adjusted for a variety of potential confounds (e.g. comorbidities, age, gender, country).
- The results mostly held in analyses accounting for missing data using multiple imputation.
- Effects on wellbeing and depression scores was less prominent in those having lower risk (outpatient) surgeries.

CHAPTER 4. THE PREVALENCE, DETECTION AND OUTCOMES OF HAZARDOUS PREOPERATIVE ALCOHOL AND OTHER RECREATIONAL SUBSTANCE USE IN LEEDS: A CROSS-SECTIONAL AND PROSPECTIVE ANALYSIS (STUDY 2 AND 3)

4.1 Introduction

4.1.1 Background

Preoperative substance use may be modifiable - particularly through behaviour change interventions (section 1.6). However, given that the NHS is under considerable financial and time pressures (Robertson et al., 2017), it is imperative that the integration of new interventions into routine practice is warranted; there must be sufficient evidence to suggest that there are a specific need and justification for additional use of staff time and increased resources. To improve efficiency, it may be beneficial also to identify ways of improving the potential efficacy of future interventions, such as i. improving methods of identifying suitable intervention recipients (are current screening methods able to predict which patients are at risk of complications?) and ii. identifying patients who may be at most risk of hazardous substance use (can research identify patient characteristics often associated with substance use?). The present studies sought to address all these factors within the context of Leeds, UK.

While there is robust evidence to suggest that hazardous preoperative alcohol use may be a potential risk factor for perioperative complications *per se* (see section 2.3) (as well as some evidence that preoperative alcohol use may be associated with increased psychiatric comorbidities that may precipitate complications; see subsection 3.1.1 and section 3.3), and some evidence to suggest (with plausible mechanisms) that illicit substance use may also be deleterious to postoperative outcomes (see section 2.3), without knowing the *prevalence* of these behaviours one cannot establish whether these behaviours are cost-effective to target (as few patients may be engaging in hazardous use). As outlined in section 2.4, there have been a limited number of studies addressing this issue, and to the author's knowledge, there have also been no published UK studies assessing the prevalence of preoperative substance use

Across three studies conducted in Germany, hazardous preoperative alcohol use (assessed with a validated measure of alcohol use; the Alcohol Use Disorder Identification Test [AUDIT]) was identified in around 1 in 6 patients (Kip et al., 2008; Kleinwächter et al., 2010; Kork et al., 2012). Two of these studies also identified a previous month illicit substance use prevalence rate of around 1 in 10 patients (Kleinwächter et al., 2010; Kork et al., 2012). More worrying rates of polysubstance use were high; in Kork et al. (2012) for instance, 53.9% (95% CI: 44.4–63.1) of last 30-day users were AUDIT-positive. While these data may be used to approximate UK prevalence, this may be unwise; base population prevalence rates of substance use *per se,* as well as specific substances vary greatly between countries - meaning preoperative rates may vary likewise. For instance, the UK has more than double the rates of heavy episodic drinking (bingeing) and alcohol dependence, as well as much higher rates of illicit substance use than Germany (WHO, 2014; ONS, 2015; EMCDDA, 2014; Global Drug Survey, 2015). UK rates of *hazardous* preoperative substance use may, therefore, be much higher meaning more patients may be suffering substance-associated perioperative complications - especially in UK regions with inflated hazardous drinking and other substance use prevalence (e.g., Yorkshire and the Humber; ONS, 2017). In such regions, and in the UK versus Germany more generally, interventions may, therefore, be more necessary and - with resource use in mind, justifiable.

Aside from assessing the general prevalence, it is useful to see whether prevalence rates are associated with particular demographic or other characteristics; that is, to understand *who* may be most likely to be an intervention recipient, and thus *who* may be best to target for behavioural intervention. Previous authors have emphasized that when it comes to intervention: *one size does not fit all*. Interventions designed with the recipients in mind may be tailored (e.g., choosing particular intervention modalities/formats, location and so on) towards unique factors that may be particularly relevant for certain populations (Kreuter, Strecher & Glassman, 1999). Interventions tailored to specific demographics (e.g., age or socioeconomic status) in many cases have been observed to better change behaviour above non-tailored interventions (Noar, Benac & Harris, 2007; Beck et al., 2011; though see Conn et al., 2008), and thus may be more efficient in any potential preoperative intervention.

Aside from demographic-type characteristics, it may be useful also to assess the extent to which preoperative hazardous substance use prevalence is related to the prevalence of other behaviours associated with poor perioperative outcomes (e.g., low physical activity; see subsection 1.6.1). This may allow some indication of, for example, the degree to which patients may require increasingly multi-faceted or more complex interventions. While previous studies, in general, have observed a high degree of clustering of deleterious lifestyle behaviours (e.g., Poortinga, 2007; Schuit, van Loon, Tijhuis & Ocke, 2002) to the author's knowledge, there have been no such published studies in the perioperative context assessing the co-prevalence of such behaviours.

In medical practice, efficient risk screening tools are vital for providing evidence-based care; allowing clinicians to identify, prepare for and intervene on factors which may be detrimental to a patient's prospects regarding health and wellbeing in a time-limited manner. The process of preoperative assessment is essentially a series of such screening measures, however, as mentioned previously in subsection 1.5.3, it is often the case that measures used are non-validated. This is particularly the case for assessment of lifestyle behaviours, including substance use.

Measures of substance use need to be demonstrably sensitive enough to detect patients at risk, and specific enough to predict postoperative complications; for an intervention to be useful for its intended purpose, patients who may benefit from intervention must be identified efficiently and accurately - such that potential recipients do not slip through the net. It has been demonstrated that very short self-report measures (time and financially efficient) of substance use can predict postoperative complications (e.g., the 3-item AUDIT-C; Bradley et al., 2011) and that routine preoperative assessment using non-validated measures may underestimate the degree to which patients use substances versus validated measures (see subsection 2.4.1). To the author's knowledge, however, there have been no previous UK studies assessing the degree to which preoperative assessment underestimates substance use (versus validated measures) and no studies - UK or otherwise - comparing routine versus validated measures at predicting perioperative complications. If validated measures were better predictors, it may justify their inclusion into routine practice and for potential intervention eligibility screening.

The integration of validated measures of substance use into preoperative assessment is complicated by the fact that there is a multitude of different substances - making it potentially infeasible to have a validated measure for each. A solution comes in the form of *index* measures. The World Health Organisation's (WHO) Alcohol, Smoking and Substance Involvement Screening Test (ASSIST; Humeniuk et al., 2008) - which, through extensive assessment has been demonstrated as "*feasible, reliable, valid, flexible, comprehensive and cross-culturally relevant, and able to be linked to brief interventions*" (WHO, n.d., online), has many desirable properties. First, the measure assesses what substances (e.g., cigarettes, steroids) an individual has used in their lifetime, before probing the current use frequency of each, and indicators of dependency per substance. As such, the measure is scaled in length depending on the number of substances the individual uses; meaning the assessment may take under a minute for patients for which it is not relevant, and increasingly longer (but still less than 20 minutes) for patients for which more detail is needed. Risk scores per substance may be calculated using ASSIST algorithms, meaning (for research purposes) a continuous score may be used to see whether increasingly hazardous substance use scores can predict complications, and thus clinically relevant cut-offs, per substance, may be identified for routine practice. This potentially also allows for an analysis of the relative contribution of different substances in models predicting complications (e.g., explanation of variance) and potential compounding polysubstance interactions, all with one measure.

The most useful element for routine practice, however, may be the

ASSIST measure's *global continuum of risk* algorithm; that is, the sum of all the specific substance risk scores, which is in effect a continuous polysubstance use score. In preoperative assessment, instead of disparate non-validated measures of drug and alcohol use, and instead of having measures which may detect risk - but which do not account for potential multiplicative effects of the use of multiple substances, patients' overall perioperative substance use risk may be encapsulated in this one global risk score from this single measure. This may provide better quantifiability for research, predictability/detection for practice (with hazardous score cut-offs), and more efficiency - thus clinical utility. No previous study has assessed the ability of the ASSIST in predicting complications.

4.1.2 Study Overview and Aims.

The present chapter consists of two studies. Given the important gaps in the (particularly UK) literature identified above, the present analyses sought to address these gaps with the aim of informing any future interventions based in the local context (Leeds, UK).

Data for Study 2 (previously unpublished) were obtained from a physician who undertook a service evaluation at St James's University Hospital preoperative assessment clinic (Leeds). Relevant raw data were analysed by the present author to assess i. the prevalence of hazardous alcohol and illicit substance use (and polysubstance use), and ii. whether the prevalence was associated with certain patient characteristics (e.g., age, surgery type). Given that the aforementioned physician also asked and documented whether patients would be interested in a programme to help them reduce their substance use, available response data are reported here also (as this was deemed highly relevant to the present thesis).

Study 3 was designed and conducted by the present author and took place at a different preoperative assessment clinic in Leeds General Infirmary. Broad aims were to i. assess the prevalence of hazardous alcohol and illicit substance use (and polysubstance use), ii. to assess whether this prevalence was associated with certain patient characteristics (e.g., age, health status, surgery type), and behaviour-related risk factors (i.e., low physical activity, high BMI and smoking status), iii. to compare prevalence rates of hazardous substance use between routine assessment and validated measures, iv. to assess and compare the ability of routine and validated measures at predicting perioperative complications, and v. to assess the utility of the ASSIST measure's *global continuum of risk* (an index of polysubstance use) at predicting perioperative complications.

4.2 Study 2

4.2.1 Objectives

1. To assess the prevalence of preoperative patients who may be at high-risk of complications arising from preoperative substance use.
2. To assess whether alcohol and illicit substance use prevalence were associated with other substance use, age, surgery type, and gender.
3. To assess whether patients would be willing to engage with a service aiming to help them reduce alcohol and illicit substance use.

4.3 Method

4.3.1 Participants

Patients were recruited via opportunity sampling. Patients had to be undergoing an elective surgery and speak sufficient English to participate (or have a translator present).

4.3.2 Design and Procedure

This was a cross-sectional study. All patients meeting the inclusion criteria were approached in the dedicated preoperative assessment clinic at St James's University Hospital, Leeds (UK) prior to, or after, their routine preoperative assessment appointment before being given a brief outline of the study and the participant requirements. After consenting into the study, patients completed the study measures via a structured interview after being informed that the interview was confidential and that their responses would not be shared with NHS staff. This was a service evaluation and thus required site, but not formal, ethical approval.

4.3.3 Materials

Study Questionnaire.

Demographic and other patient characteristics. Patients reported their gender and age. Details regarding patients' surgical procedures were taken from completed preoperative assessment forms. In this secondary analysis, these documented surgeries were categorised as per their speciality by two experienced surgical research nurses.

Alcohol use. The first three items of the alcohol use disorder identification test (AUDIT) form a truncated measure of alcohol use disorders: the AUDIT-Consumption (AUDIT-C). The 3-item AUDIT-C, with a maximum score of 12, has been found to be almost as effective as the AUDIT as a routine screening instrument and has shown to be a valid and reliable standalone measure (Bush et al., 1998; Bradley et al., 2003; 2007; Rubinsky et al., 2010). Item one probes frequency of alcohol use (from *never* = 0, to *4+ times per week* = 4), item two probes typical amounts drunk when drinking (from *1-2 drinks* = 0, to *10+ drinks* = 4) and item three assesses heavy episodic (*binge*) drinking (frequency of 6 or more drinks on one occasion from *never* = 0, to *4+ times per week* = 4).

Patients scoring AUDIT-C ≥5 were considered positive for an alcohol use disorder, in line with previous studies demonstrating that this cut-off is a good discriminator of at-risk perioperative patients (e.g., Bradley et al., 2011). The current study also employed cut-offs of 0 for non-drinkers, 1-4 for *low-risk* drinkers, 5-8 for *at-risk* drinkers and 9-12 for *high-risk* drinkers, in line with previous studies investigating the relationship between AUDIT-C scores and postoperative complications (e.g., Rubinsky et al., 2012).

Illicit substance use. Patients reported whether they currently used illicit substances (*yes* or *no*), what particular substances they used, and the frequency of use (*monthly or less*, *2-4 times per month*, *2-3 times per week* and *more than 4 times per week*).

Smoking. Patients were also required to report whether they were a current or former smoker (*yes* or *no* to either) and, if a current or former smoker, how many cigarettes they smoke(d) daily.

Acceptability of an intervention programme. A subset of patients identified as at-risk drinkers, and all current smokers/illicit substance users were asked whether they would consider accepting help from the hospital to aid them in cessation (*yes* or *no*) for each substance. Reasons for declining help are reported (if a reason was given).

4.3.4 Data Analysis

STATA was used to conduct all analyses. As a secondary data analysis, the sample size was not pre-planned by the present author and all analyses were considered exploratory. Though the set alpha level was at the conventional .05, all prevalence and effect sizes estimates were presented with 95% confidence intervals (95% CI). The potential stability and precision of the estimates could therefore be judged by the wideness of the intervals.

Prevalence *x* patient characteristics. To assess whether demographic characteristics were associated with substance use, as well as polysubstance use, logistic regression models were planned with outcomes of i. AUDIT-C positive (5) or negative (<5), and ii. self-reported current illicit substance user (yes or no). Planned multinomial regression models with an outcome of the AUDIT-C cut-off categories (0 = non-drinkers [reference category], 1-4 = low-risk drinkers, 5-8 = at-risk drinkers and 9-12 = high-risk drinkers) can be seen in Appendix F.

Logistic, rather than linear, models were chosen as this study was fundamentally interested in whether particular groups of patients met thresholds shown to predict complications previously, as opposed to having higher AUDIT-C scores *per se*. Analyses were conducted in two ways. In the first analysis, univariate associations between variables and AUDIT-C cut-offs/illicit substance use binary responses were assessed using *t*-tests and ANOVAs for continuous variables involving two, and more than two groups respectively, while Chi-squared (χ^2) tests were used for categorical variables. All variables with univariate associations at the p <.20 level (Costanza & Afifi, 1979; see similar approaches: Harris et al., 2011; Ranganathan, Pramesh & Aggarwal, 2017; Ricco et al., 2016; Schurks et al., 2006) were forced into multivariate logistic/multinomial regression models. Given controversy about such approaches (e.g., Heinze & Dunkler, 2016) the second analysis strategy was to add all variables into multivariate models.

Odds ratios (OR; with 95% CIs) were used as the effect size metric for

χ^2 and regression analyses (Hedges' *g* and eta-squared for univariate *t*-tests and ANOVAs, respectively). Note that for variables with two categories, odds ratios are appropriate to interpret predictor effect size in multinomial models, while those with more than two should be interpreted as relative risk ratios. Note also that for the continuous variables in the regression models, odds ratios here represented change in odds per one unit increase in the variable of interest, and that increases were multiplicative; two unit increases would be the change in odds squared, three unit increases would be the change in odds cubed, and so on.

4.4 Results

For this dataset, 200 patients were recruited. The original data collector stated that all who were approached participated and remained in the study. In the present analysis, a total of 196 adult patients were included; four were excluded for being under 18 years old. Patients were a mean age of 55.3 years (95% CI: 52.8-57.8) and 58.2% (51.1-64.8) were female. Further patient characteristics can be viewed in Table 4.1.

4.4.1 Prevalence

Alcohol use. The AUDIT-C identified 62 hazardous drinkers (31.6%; 95% CI: 25.1%-38%) (AUDIT-C ≥5) and 134 non-hazardous drinkers. A total of 46 (23.5%; 17.7%-30%) were non-drinkers, 88 (44.9%; 37.8%-52.1%) low risk (AUDIT-C 1-4), 55 (28.1%; 21.9%-34.9%) at risk (AUDIT-C 5-8), and 7 (3.6%; 1.4%-7.2%) high risk drinkers (AUDIT-C 9-12).

Illicit substance use. Just three patients (1.5%; 0.3%-4.4%) were identified as illicit substance users. One patient used cocaine and heroin 2-4 times a month, a second cannabis 2-3 times a week and a third cannabis monthly or less.

4.4.2 Patient Characteristics *x* Substance Use Prevalence

See Tables 4.2 (AUDIT-C hazardous versus non-hazardous), C1 (AUDIT-C cut-offs; and Appendix F for elaboration) and C2 (current illicit substance user: yes versus no) for prevalence statistics by patient characteristics as well as effect size estimates for inferential analyses.

AUDIT-C: hazardous versus non-hazardous. In univariate analyses, AUDIT-C positive (hazardous) patients were significantly more likely to be male versus female, current smokers versus non-smokers, and current illicit substance users. There was also some indication of a between-group difference on surgery type (where the surgery with the lowest hazardous prevalence rate, uro-gynaecology, was the reference category), but no significant age differences (and all $p > .20$).

In a logistic regression including all predictors apart from age, ($\chi^2(10) = 28.74$, $p < .001$, Nagelkerke's $R^2 = 0.21$), males versus females and current versus non-smokers were marginally ($p = .06$) significantly more likely to be AUDIT-C positive versus negative. In a model including all variables, ($\chi^2(11) = 31.79$, $p < .001$, Nagelkerke's $R^2 = 0.23$), males versus females were significantly more likely to be AUDIT-C positive, and there was some evidence (marginally significant) that AUDIT-C positive patients were younger and current versus non-smokers.

Illicit substance use. Given the low prevalence of illicit substance users (three patients), inferential analyses were not performed. Descriptively, illicit substance users versus non-users seemed to be younger (35.7 versus 55.7 years old) and more likely to be male. As above, all illicit substance users were smokers and AUDIT-C positive (100% being the high-risk category).

4.4.3 Acceptability of an Intervention Programme

Alcohol Use. Twenty-two at-risk drinkers were asked whether they would consider accepting help from the hospital in stopping drinking before surgery. Seven (32%) said *yes*. Of the 68% declining, reasons included: i. they did not need to cut down, ii. they did not want to cut down and iii. they believed that they could cut down by themselves if they wanted.

Illicit Substance Use. Just one of three illicit substance users stated they would accept help in quitting. This patient (a current cocaine/heroin user) was already receiving substance use treatment. The two (both cannabis users) declining help stated that i. they could give up by themselves and ii. they did not want to stop.

Table 4.1. Patient Characteristics (Study 1).

	Total	**95% CI**
Total (*n*)	196 (100%)	-
Age (mean, SD)	55.3 (17.51)	52.8-57.8
Sex (*n*)		
Male	82 (41.8%)	35.1%-48.8%
Female	114 (58.2%)	51.1%-64.8%
AUDIT-C (increasing risk)	***n* (%)**	
No risk (0)	46 (23.5%)	18.0%-29.9%
Low risk (1-4)	88 (44.9%)	38.1%-51.9%
At risk (5-8)	55 (28.1%)	22.2%-34.7%
High risk (9-12)	7 (3.6%)	1.7%-7.2%
AUDIT-C (positive/negative)		
Non-hazardous (0-4)	134 (68%)*	61.6%-74.5%
Hazardous (≥5)	62 (32%)*	25.5%-38.4%
AUDIT-C (total score)	**Mean (SD)**	
All patients	3.27 (2.75)	2.88-3.66
Just drinkers (>0)	4.27 (2.37)	3.94-4.60
AUDIT-C (frequency score)**	1.76 (1.34)	1.57-1.95
AUDIT-C (amount score)	0.80 (1.02)	0.66-0.94
AUDIT-C (binge score)	0.70 (0.99)	0.56-0.84
Smoker (*n*)		
Current	42 (21.4%)	15.9%-27.8%
Former	54 (27.6%)	21.4%-34.4%
Never	100 (51%)	43.8%-58.2%
	Mean (SD)	
Daily cigarettes (current)	16.84 (11.90)	13.2-20.5
Illicit substance user (*n*)		
Yes	3 (1.5%)	0.5%-4.4%
No	193 (98.5%)	95.6%-99.5%
Type of surgery (*n*)* **		
Bariatric	3 (1.5%)	0.5%-4.4%
Colorectal	2 (1%)	0.3%-3.6%
General	40 (20.4%)	15.4%-26.6%
Hepatobiliary	7 (3.6%)	1.7%-7.2%
Thoracic	17 (8.7%)	5.5%-13.5%
Gynaecology	40 (20.4%)	15.4%-26.6%
Urology	60 (30.6%)	24.6%-37.4%
Uro-Gynae.	13 (6.6%)	3.9%-11.0%

Notes. *Excluding non-drinkers, non-hazardous: 88 (59%; 50.7% - 66.2%), hazardous: 62 (41%; 33.8% - 49.3%); **item 1= frequency score, 2 = amount score, and 3 = binge score, ***missing data for 14 surgeries because of inaccurate or uninterpretable documentation on medical notes.

Table 4.2. AUDIT-C Hazardous versus Non-Hazardous x Other Patient Characteristics.

	Non-hazardous (0-4)	**Hazardous (>4)**	**Uni OR**	**Multi OR 1**	**Multi OR 2**
Total	134 (68.4%; 61.4-74.8)	62 (31.6%; 25.2-38.6)			
Mean age	53 (47.9-58.1)	57.6 (53.9-61.3)	ns (p > .20), g = .13 (-.18-.42)	-	ns (p = .09), OR: 0.98 (0.96-1)
Gender			***	ns (p = .06)	*
Male	45 (54.9%; 43.5-65.8)	37 (45.1%; 34.2-56.5)	2.93 (1.57-5.45)	2.15 (0.97-4.73)	2.60 (1.13-5.96)
Female	89 (78.1%; 69.2-85.1)	25 (21.9%; 15-30.9)	*Ref*		
Smoker			*	ns (p = .09)	ns (p = .11)
Current	23 (54.8%; 38.8-69.8)	19 (45.2%; 30.2-61.2)	2.13 (1.06-4.30)	2.02 (0.90-4.54)	1.93 (0.86-4.34)
Former	34 (63%; 48.7-75.4)	20 (37%; 24.6-51.3)	*Ref (former + never)*		
Never	77 (77%; 67.3-84.6)	23 (23%; 15.4-32.7)			
Illicit substance user			*	ns	ns
Yes	-	3 (100%; 31-100)	15.82 (0.80-311.18)	-	-
No	134 (69.4%; 62.3-75.7)	59 (30.6%; 24.3-37.7)	*Ref*		
Type of surgery			*	ns	ns
Bariatric	1 (33.3%; 1.8-87.5)	2 (66.7%; 12.5-98.2)	11 (0.65-187.18)	-	-
Colorectal	2 (100%; 19.8-100)	-	-	-	-
General	31 (77.5%; 61.1-88.6)	9 (22.5%; 11.4-38.9)	1.60 (0.30-8.56)	-	-
Hepatobiliary	4 (57.1%; 20.2-88.2)	3 (42.9 %; 11.8-79.8)	4.13 (0.49-34.5)	-	-
Thoracic	9 (52.9%; 28.5-76.1)	8 (47.1%; 23.9-71.5)	4.89 (0.82-29.06)	-	-
Gynaecology	33 (82.5%; 66.6-92.1)	7 (17.5%; 7.9-33.4)	1.17 (0.21-6.47)	-	-
Urology	35 (58.3%; 44.9-70.7)	25 (41.7%; 29.3-55.1)	3.93 (0.80-19.30)	-	-
Uro-Gynae.	11 (84.6%; 53.7-97.3)	2 (15.4%; 2.7-46.3)	*Ref*		

Notes. * p < .05. ** p < .01, *** p < .001; ns = non-significant; OR = odds ratio; 95% confidence intervals in parentheses; Ref = reference category/level; Uni ES = univariate effect size (OR unless otherwise specified); Multi OR 1 = multivariate effect size for univariate predictors p < .20; Multi OR 2 = multivariate effect size for model including all variables.

4.5 Study 3

4.5.1 Objectives

1. To assess the prevalence of preoperative patients who may be at high-risk of complications arising from alcohol and illicit substance use.
2. To assess whether alcohol and illicit substance use prevalence were associated with patient demographics (e.g., age, comorbidities), and ii. other substance use, smoking, body-mass index and physical activity.
3. To compare i. rates of hazardous alcohol use detection between established cut-offs on a validated measure with demonstrated predictive validity (AUDIT-C) and routine preoperative assessment, and ii. to compare routine assessment illicit substance user detections versus a more structured assessment (ASSIST).
4. To compare the AUDIT-C versus routine preoperative assessment at predicting indicators of perioperative complications.
5. To assess whether the ASSIST ‘global continuum of risk’ score (a measure of polysubstance use) could predict indicators of perioperative complications.

4.6 Method

4.6.1 Participants

Patients were recruited via opportunity sampling. Patients had to i. have a scheduled elective surgery, ii. be over 18 years old, iii. have the capacity to give consent (judged by staff on site), and iv. speak sufficient English (or have a translator present) to answer the relevant questions and to understand the nature, aims and requirements of the study.

4.6.2 Design and Procedure

This was both a cross-sectional and prospective cohort study. The former approach was used to assess the prevalence, detection and characteristics of patients with hazardous levels of substance use, the latter to assess objectives 4 and 5. The recruitment aim was 300 patients; this was deemed sufficient to detect between AUDIT-C cut-off differences in perioperative complications and approximated previous prospective studies (e.g., van Rooijen et al., 2016; Harris et al., 2011; Mulligan et al., 2018).

All patients meeting the above criteria were approached in a preoperative assessment clinic (Leeds General Infirmary, Leeds, UK) before their routine preoperative assessment appointment. After reading an outline of the study, participant requirements and rights and being encouraged to ask questions, patients consented into the study. In a private room used for routine preoperative assessments, each patient completed study measures in a structured interview format with the lead researcher (much like a routine appointment) after being informed that their responses were confidential. After each patient had had their routine preoperative assessment, their nurse-completed routine preoperative assessment documents were taken, and relevant details extracted (e.g., nurse documented comorbidities, body mass index [BMI], lifestyle behaviours data) - this allowed for an efficient way of obtaining relevant patient characteristics (and thus covariates) and a way of comparing nurse documented (or *detected*) alcohol and other substance use with that of the study measures. After patients completed the structured interview, they were not contacted again; all perioperative follow up data were obtained from the local clinical systems (PPM+ and PAS). Ethical approval was obtained by the NHS health research authority East Midlands

(Derby) research ethics committee (REC reference: 17/em/0007).

4.6.3 Measures, Covariates and Outcomes

Demographic and other patient characteristics. Patients' age, gender, NHS number (to link to their computerized medical records), nurse documented comorbidities (after detailed examination) and a description of each patient's surgery were taken from their respective preoperative assessment forms.

Comorbidities. Using nurse documented comorbidities, patients were coded according to the American Society of Anesthesiologists physical status score (ASA-PS) criteria (see Table 1.4) (which accounted for BMI but not substance use behaviours) by an experienced surgical research nurse and a consultant anaesthetist (in that order). In an analysis of 2.3 million patients, an ASA-PS score of 1 (a healthy patient) versus scores of 2, 3, 4, 5 were associated with 2x, 5x, 17x, and 63x increased odds of perioperative morbidity, and 6x, 47x, 293x, 2011x perioperative mortality, respectively (independent of specific procedures; Hackett, DeOliveira, Jain & Kim, 2015). As such, ASA-PS scores were deemed to serve as an appropriate measure of comorbidity in the present study.

Body-mass index (BMI) was used also. BMI was extracted from patients' medical records after objective measurement and documentation by the clinical support worker staff on site. As in subsection 1.6.1, obesity (and high BMI specifically) has been associated with considerable perioperative morbidity.

Surgical classification. Using patients' surgery descriptions documented on their preoperative assessment forms, surgeries were categorized according to the AXA schedule of procedures (see subsection

1.2.2). Again, this was conducted by a surgical research nurse and a consultant anaesthetist. As in previous studies (e.g., Abbot et al., 2017), the potential complication risk of a particular surgery in this study was determined using two variables: i. surgical descriptions at the broad level (e.g., vascular system or ear, nose and throat) and ii. by surgical complexity/severity (minor, intermediate, major and extra major/complex). Surgeries categorized in these ways have been shown to parse out differing complication incidence rates with sufficient granularity (e.g., Abbot et al., 2017).

Substance use.

Routine preoperative assessment. Routine assessment forms at the clinic require the assessor to document patients' responses to three substance-related items: i. *do you smoke?* (number per day), ii. *do you drink alcohol?* (number of units per day) and iii. *do you use non-prescription drugs or recreational drugs?* [blank space for details]. For each recruited patient, these response data were transcribed from their preoperative assessment form, serving as a measure of nurse assessed substance use. A scan of this form can be seen in Appendix C.

Study measures: alcohol use. As in Study 2, this study used the AUDIT-C.

Study measures: polysubstance use & individual substances. The World Health Organization's Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) was used as a standalone measure to screen for hazardous substance use. The ASSIST has been demonstrated to be reliable, valid (e.g., predictive, concurrent), generalizable across cultures and acceptable/feasible (WHO, n.d.). The ASSIST takes approximately 10 minutes to complete but is scaled in length (i.e., some items are not asked) depending on the amount of substance use risk a patient may have. This makes it a good candidate for inclusion in the time-limited context of preoperative assessment, especially considering it could replace single measures (as above) which are not validated, not able to produce quantifiable risk scores, do not probe for many substances and are less structured - thus, possibly, more prone to incomplete or improper completion.

The ASSIST consists of eight items, after probing lifetime substances used (3 points for each substance), patients are asked four *how often*? questions for each substance with responses: *never* (0), *once or twice* (3), *monthly* (4), *weekly* (5) or *daily/almost daily* (6). These are, how often: i. each substance has been used (in the previous three months), ii. the respondent experienced social/legal/health/financial problems due to each substance (previous three months), iii. the respondent experienced failure to fulfil obligations due to each substance (previous three months), and iv. the respondent craved or strongly desired each substance (previous three months). Two further items, with responses: never (0), *yes, but not in the past three months* (3) and *yes, in the past three months* (6), ask i. *has a friend or relative ever expressed concern about use of each substance?* and ii. *have you ever tried but failed to control, cut down or stop using each substance*? Lastly, one item asks *have you ever used any drug by injection?* (*never* = 0, *yes, not in the previous three months* = 1 and *yes, in the previous three months* = 2).

For each substance, a substance-specific risk score can be derived from summing the scores from questions 2 to 7. A polysubstance or *global continuum of risk* score can be derived from summing scores on all items.

Both are reported in this chapter.

Other behaviours. For the purposes of assessing co-prevalence of alcohol and illicit substance use with other perioperative risk behaviours, measures of physical activity and smoking were taken.

Low physical activity, which is associated with perioperative morbidity (subsection 1.6.1), was assessed using the self-report Total Activity Measure 2 (TAM-2) (Orrell et al., 2007). This measure was chosen due to its brevity, which is necessary for the preoperative assessment context. The TAM-2 consists of 6 items. For strenuous, moderate and mild activities (with provided examples), participants are asked how many times *per se* and for how long in total (minutes), on average, they engage in each type a week. Total minutes per week is multiplied by 9 (strenuous), 5 (moderate) and 3 (mild) (in line with metabolic equivalent table values; METs) and summed for a total activity score (higher = more active). The TAM-2 has demonstrated good test-retest reliability and acceptable agreement with objective measures of physical activity (Orrell et al., 2007).

As a supplement to the ASSIST measure, patients were asked whether they were current, former or never cigarette smokers. Current smokers were asked how many cigarettes they smoke per day. Patients were also asked whether they currently used electronic cigarettes (*yes* or *no*).

Perioperative health outcomes. As there was no patient reported follow-up in this study, all indications of *deviations from the ideal perioperative course* (see subsection 1.4.1) - that is, events suggestive of perioperative complications, were extracted from the relevant clinical systems.

Perioperative complications. Inspired by expert-consensus recommendations (Jammer et al., 2015), one-hundred and fifty-eight conditions were specified according to routine, on-site clinical codes (e.g., *I21.9: Acute myocardial infarction, unspecified*). These could be categorized as complications related to delirium, as well as cardiovascular, pulmonary, wound-related, and infection-related complications (approximating approaches in previous studies; e.g., Bradley et al., 2011). All codes and descriptions can be seen in Table C3.

Unfortunately, only *in-hospital* events were assessed by the clinical codes. This meant that any complications that occurred (e.g., 30 days) post-discharge could not be detected. This was not true of mortality, for which 365-day post-discharge data could be retrieved from administrative data. A follow-up of 365 days for mortality has been recommended previously (Jammer et al., 2015). For the present study, a binary indicator of any in-hospital complication, total number of complications, total *x* type and a binary indicator of mortality are reported.

Length of hospital stay derivatives. Length of hospital stay is a common proxy measure of perioperative complications; as in Jammer et al. (2015), any severe complication is likely to significantly prolong hospital stay. In the present study, binary extended hospital stay is reported - that is, a longer elective stay than was intended from the preoperative management plan of the patient (which is documented in routine data). Lastly, a binary proxy of unplanned admission for day case patients was derived by identifying patients with intended management = day case with >0 length of hospital stay in days.

Hospital readmission. As with length of hospital stay, all-cause readmission rates are a typically used proxy for deviations from ideal postoperative recovery (e.g., Lucas & Pawlik, 2014). Here, all-cause readmission at 30-days and 90-days is reported.

Composite measure. To bolster statistical power, a composite measure of *deviations from the ideal perioperative course* was derived from the above indicators. This was a binary indicator of any complication, death, extended length of stay, ‘unplanned admission’ or 90-day readmission.

4.6.4 Data analysis

STATA was used to conduct all statistical analyses. The set alpha level was .05. As in Study 2, all estimates were presented with 95% confidence intervals. The Study 3 target sample size was oriented to power the detection of differences in postoperative complications between hazardous versus non-hazardous alcohol users. Three-hundred patients was deemed appropriate assuming an α of .05, a β of .20, a baseline adverse event (i.e. composite outcome of readmission, in-hospital complications, mortality, extended length of stay and unplanned admission) risk of 25% (perhaps a conservative estimate given the chosen clinic predominantly consisted of *major* or above surgeries; ISOS, 2016), a hazardous alcohol use prevalence of 15% (e.g., Kip et al., 2008) and an effect size of RR = 1.84 (Eliasen et al., 2013).

Prevalence. Prevalence-related analyses were conducted as per Study 2. Again, multinomial analysis results involving AUDIT-C risk categories can be seen in Appendix F. Given the low prevalence (relative to sample size) of illicit substance users identified, current illicit substance users were defined as those who reported *any* use of *any* illicit substance in the previous three months (item 2 of the ASSIST). Note that because the comorbidity indicator (ASA-PS score) was dependent on BMI scores, potential multivariate models including either variable did not include both. Thus, separate analyses were planned with one variable in place of the other. Odds ratios (OR; with 95% CIs) were used as the effect size metric for Chi-squared and regression analyses (Hedges' *g* and *eta*^{2} for univariate *t*-tests and ANOVAs).

Detection. Current UK government guidelines dictate that 14 units of alcohol per week is the maximum one should consume (both males and females). This is thus the recommended cut-off for detection of hazardous drinking in routine preoperative assessment. The original planned analysis strategy was to compare rates of hazardous alcohol detection between routine assessment (>14 units versus <15 units) and AUDIT-C cut-offs (score of 5 versus <5) but this soon proved unfeasible; it was identified that, in many instances, preoperative assessors did not document units on the routine measure, favouring written idiosyncratic terms in the space allocated to units (e.g., "*occasional drinker"*). A detection of hazardous alcohol use in routine assessment was therefore coded as present if anything written on each patient's preoperative assessment form indicating risky or hazardous drinking (e.g., "*binge drinker*", or "*heavy drinker*"). As this was deemed a subjective judgment to make, the reliability of this coding was tested; two independent raters (blind to each other's decisions) coded whether routine assessment detected hazardous alcohol use (transcribed exactly as written on the preoperative assessment forms). Agreement on the codes between raters was assessed using Cohen's Kappa (where >.70 was deemed good agreement), and any disagreements were resolved through discussion.

After coding, potential differences between routine detection rates and hazardous AUDIT-C scores were outlined. This included calculating sensitivity (a/[a + c]), specificity (d/[b + d]), and positive (a/[a + b]) and negative (d/[c + d]) predictive values of the routine assessment versus AUDIT-C hazardous cut-off, where a = n of positive agreement on both tests (i.e., both hazardous), b = AUDIT-C negative/routine positive, c = AUDIT-C positive/routine negative and d = negative agreement on both tests (i.e., both non-hazardous) (all were multiplied by 100 to estimate percentages).

Given that there has been no established cut-off for ASSIST substance-specific use scores that predict complications, and that the routine illicit substance use measure was essentially a freehand description, comparing detection rates was not straightforward. A detection on both the ASSIST and routine measure was considered i. data indicating illicit substance use *per se* in the previous three months, and ii. data indicating use of cannabis or cocaine in the previous three months (just cannabis and cocaine users were identified across both measures within the detection analysis subsample). Again, subjective judgments were made whether whatever was written on preoperative assessment forms met the detection thresholds. Assessment of the reliability of coding and analysis of difference was as written above.

Outcomes. First, patients with follow-up data were compared to those for which the data was not available on key variables, namely AUDIT-C scores, age, gender, ASA-PS scores, surgical classification and ASSIST global continuum of risk scores. Any differences, and thus potential biases, were described.

To compare AUDIT-C versus routine alcohol assessment as predictors of complications, binary routine detections (as categorized above) were used as the routine assessment predictor variable versus binary AUDIT-C hazardous cut-offs. The planned outcome was the binary composite *deviations from the ideal perioperative course* measure. Similar to Harris et al. (2011) to maximize power, associations between all potential covariates (e.g., age, ASA-PS scores) and outcome measures were first assessed using *t*-tests, ANOVAs or Chi-squared analyses as appropriate. Covariates with a $p < .20$ association with the outcome variables were entered into a model with *either* hazardous versus non-hazardous AUDIT-C scores, or hazardous versus non-hazardous routine assessment scores. From there, for model comparison, i. the statistical significance and effect size (odds ratios) of the alcohol use predictors were compared narratively, ii. the overall fit of each model was assessed using χ^2 goodness of fit tests and iii. various model fit measures were compared between models narratively (Nagelkerke's R^2; Area under the curve [AUC]; Bayesian Information Criterion [BIC] and Akaike Information Criterion [AIC]). Higher R^2 and AUC values and lower AIC and BIC values indicated better overall fit. Fully adjusted analyses were also planned.

To assess whether the ASSIST global continuum of risk scores could predict complications, analyses were conducted as above (i.e., partially-adjusted and fully-adjusted models) where, again, planned outcomes were composite *deviations* (logistic regression).

4.7 Results

Participant flow can be seen in *Figure 4.1.* A total of 305 patients were approached of which 273 (89.5%) were recruited. No patients withdrew from the study. Perioperative outcomes data could be retrieved for 206 (75.5%) patients. Substance use data for comparison between nurse and study measures could be obtained for 255 (93.4%) patients. All patient characteristics can be seen in Table C4 (general) and C5 (substance use prevalence), and perioperative health outcomes data can be seen in Table 4.3.

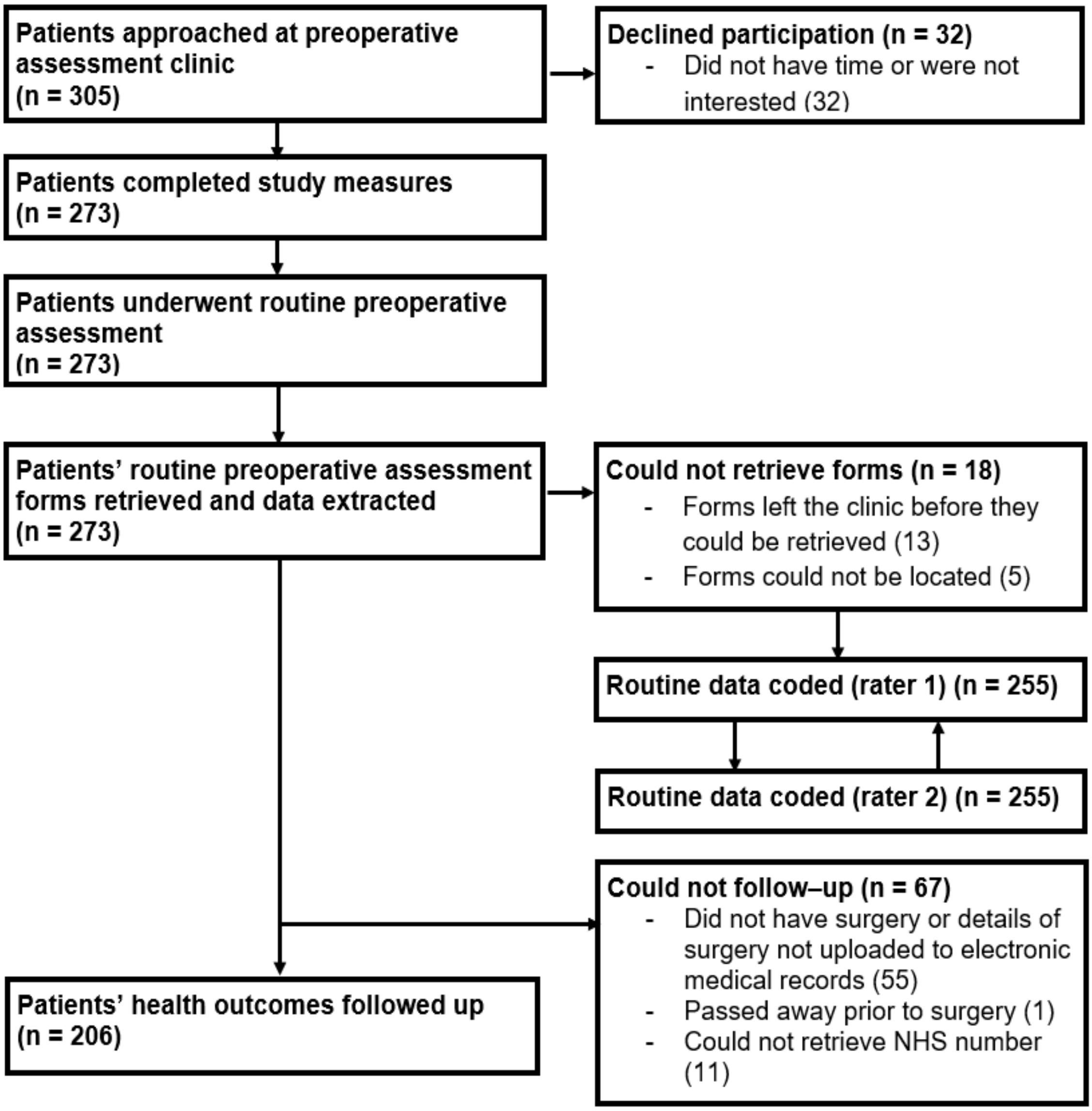

Figure 4.1. Participant Flow Diagram (Study 3).

Table 4.3. Adverse Perioperative Events.

Outcome	**Outcome subtype**	**Follow-up sample (*n* = 206)**
Extended length of stay (*n*, %)	-	4 (2%)
Unplanned admission (*n*, %)	-	22 (10.7%)
In-hospital complications	Total (*n*, %) suffering suspected complication	6 (2.9%)
	1 complication	5 (1.8%)
	3 complications	1 (0.4%)
	Total by type (across and within patients)	Cardiovascular: 2 Delirium: 1 Infectious: 1 Pulmonary: 1 Wound-related: 3
Readmission	30-day (*n*, %)	7 (3.4%)
	90-day (*n*, %)	9 (4.3%)
Mortality	365-day (*n*, %)	1 (0.5%)
Adverse events	Total (*n*, %) with a complication, death, extended length of stay, unplanned admission or 90-day readmission	33 (16%)
Adverse events (excluding unplanned admissions) *	Total (*n*, %)	14 (6.8%)

Notes. * as noted in the results section, this variable was used in outcome analyses due to suspected unreliability of the unplanned admission variable.

4.7.1 Prevalence

Alcohol use. The AUDIT-C identified 121 hazardous drinkers (44.3%; 95% CI 38.4-50.2) (AUDIT-C ≥5) and 152 (55.7%; 49.8-61.6) non-hazardous drinkers. A total of 54 (19.8%; 15.5-24.9) were non-drinkers, 98 (35.9%; 30.4-41.8) low risk (AUDIT-C 1-4), 103 (37.7%; 32.2-43.6) at risk (AUDIT-C 5-8), and 18 (6.6%; 3.7-10) high risk drinkers (AUDIT-C 9-12).

Illicit substance use. Nineteen (7%; 4.5%-10.7%) patients were identified as previous three-month illicit substance users; substances used were cannabis, cocaine and sedatives (zolpidem). Five patients each were daily/almost daily and weekly cannabis users (both 1.8%; 0.8-4.3), one (0.3%; 0.05-3.9) patient was a monthly user, and four (1.5%; 0.5-3.9) patients reported that they had used cannabis once or twice. One (0.3%; 0.05-3.9) patient reported using cocaine weekly, four (1.5%; 0.5-3.9) once or twice. One (0.3%; 0.05-3.9) patient reported weekly illicit sedative use. Two patients had used both cocaine and cannabis, the single sedatives user used no other illicit substances.

4.7.2 Patient Characteristics *x* Substance Use Prevalence

See Tables 4.4 (AUDIT-C hazardous versus non-hazardous), 4.5 (previous three months illicit substance user: yes versus no) and C6 (AUDIT-C cut-offs; and elaboration in Appendix F) for prevalence statistics by patient characteristics as well as effect size estimates for inferential analyses.

AUDIT-C: hazardous versus non-hazardous. In univariate analyses, AUDIT-C positive (hazardous) versus negative (non-hazardous) patients were significantly more likely to be i. much younger, ii, past three-month illicit substance users, iii. have fewer comorbidities (ASA-PS of 1 = reference), and iv. have a lower BMI. There were also some differences between the surgery complexity patients were undergoing; a larger proportion of non-hazardous AUDIT-C patients were undergoing minor, intermediate, extra-major and complex procedures (a larger proportion of AUDIT-C positive patients were undergoing major surgeries). While only marginally significant, males were more likely to be AUDIT-C positive. There were no between-group differences on physical activity, surgery type or smoking status - though surgery type (p = .14) met the threshold (p < .20) for inclusion in the proceeding multivariate models (i.e., mutually exclusive models including

BMI and ASA-PS scores separately).

In a logistic regression model including all predictors apart from BMI, smoking status and physical activity, ($\chi^2(21) = 54.45$, $p < .001$, Nagelkerke's $R^2 = 0.26$), AUDIT-C hazardous patients were more likely to be younger, male, and have fewer comorbidities. In a logistic regression including all predictors excluding BMI only, ($\chi^2(23) = 53.31$, $p < .001$, Nagelkerke's $R^2 = 0.27$), all effects remained in the same direction. Age remained significant and gender and comorbidities became marginally significant. In repeated analyses replacing the ASA-PS variable with the BMI variable, models were less explanatory and fewer predictors were significant (just age in model 1 and 2).

Illicit substance use. Given the low number of illicit substance users (19 patients), analyses tended to produce imprecise effect size estimates, meaning results should be interpreted with caution. In univariate analyses, illicit substance users versus non-users were significantly younger, more likely AUDIT-C positive, lower in BMI, lower regarding comorbidity scores and more likely to be smokers and (marginally) male versus female. All variables met the threshold for inclusion in the proceeding multivariate model apart from surgery complexity. Perhaps due to low power, just smoking status remained significant in both multivariate models. The same was true of models including BMI.

Table 4.4. AUDIT-C Hazardous versus Non-Hazardous x Other Patient Characteristics (Study 3).

	Non-hazardous (0-4)	**Hazardous** (>4)	**Uni OR**	**Multi OR 1**	**Multi OR 2**
Total	152 (55.7; 49.8-61.6)	121 (44.3; 38.4-50.2)			
Mean age	54.9 (52.5-57.4)	45.2 (42.1-48.3)	******* *g* = 0.60 (0.36-0.85)	***** 0.98 (0.96-0.99)	** 0.97 (0.95-0.99)
Gender			ns (p = .07)	*****	ns (p = .07)
Male	65 (50%; 41.4-58.6)	65 (50%; 41.4-58.6)	1.56 (0.97-2.53)	1.82 (1.01-3.28)	1.78 (0.96-3.29)
Female	86 (61%; 52.6-68.8)	55 (39%; 31.2-47.4)	*Ref*		
Smoker			ns (p > .20)	-	ns
Current	38 (50.7%; 39.3 - 62)	37 (49.3%; 38-60.7)	1.32 (0.78-2.25)	-	-
Former	51 (60%; 49.1 - 70)	34 (40%; 30-50.9)	*Ref (former + never)*	-	-
Never	38 (55.8%; 46.4 - 64.7)	37 (44.2%; 35.3-53.6)			
Illicit substance user			******	ns (p = .12)	ns
Yes	5 (26.3%; 10.4-52.4)	14 (73.7%; 47.6-89.6)	3.85 (1.34-11)	2.93 (0.73-11.78)	-
No	147 (57.9%; 51.2-63.8)	107 (42.1%; 36.2-48.3)	*Ref*	-	-
Mean $\log_{10}$ TAM-2	3.4 (3.4-3.5)	3.5 (3.4-3.6)	ns (p > .20) *g* = -0.09 (-0.34-0.16)	**-**	ns
ASA-PS			*******	*****	ns (p = .09)
I	21 (32.8%; 22.2-45.5)	43 (67.2%; 54.5-77.8)	*Ref*		
II	64 (58.7%; 49.1-67.7)	45 (41.3%; 32.3-50.9)	0.34 (0.18-0.66)	0.39 (0.18-0.83)	0.46 (0.20-1.03)
III	55 (71.4%; 60.1-80.6)	22 (28.6%; 19.4-39.9)	0.20 (0.10-0.40)	0.29 (0.12-0.68)	0.32 (0.13-0.79)
IV	6 (66.6%; 26.2-91.9)	3 (33.3%; 8.1-73.8)	0.24 (0.06-1.07)	0.37 (0.06-2.16)	0.29 (0.04-2.24)

Non-hazardous (0-4)	**Hazardous** (>4)	**Uni OR**	**Multi OR 1**	**Multi OR 2**	
Mean BMI	29.7 (28.7-30.8)	27.9 (26.9-28.9)	* *g* = 0.30 (0.05-0.55)	See *notes*	See *notes*
Surgery complexity			*	ns	ns
Minor	11 (55%; 31.8-76.2)	9 (45%; 23.8-68.2)	*Ref*		
Intermediate	40 (51.3%; 40.1-62.4)	38 (48.7%; 37.6-60)	1.16 (0.43-3.11)	-	-
Major	26 (43.3%; 31.1-56.4)	34 (56.7%; 43.6-68.9)	1.60 (0.58-4.42)	-	-
Extra major	32 (66.6%; 51.8-78.8)	16 (33.3%; 21.2-48.2)	0.61 (0.21-1.77)	-	-
Complex	40 (66.6%; 53.5-77.7)	20 (33.3%; 22.3-46.5)	0.61 (0.22-1.71)	-	-
Type of surgery			ns (*p* = .14)	ns	ns
Abdomen	5 (50%; 18.1-81.9)	5 (50%; 18.1-81.9)	2.38 (0.54-10.53)	-	-
Bones, joints and connective tissues/tendon muscle	13 (43.3%; 26.2-62.2)	17 (56.7%; 37.8-73.8)	3.11 (1.04-9.30)	-	-
Brain, cranium and intracranial organs	9 (50%; 26.4-73.6)	9 (50%; 26.4-73.6)	2.38 (0.69-8.20)	-	-
Ear, nose and throat	13 (44.8%; 27.2-63.9)	16 (55.2%; 36.1-72.8)	2.92 (0.97-8.81)	-	-
Endoscopic gastrointestinal procedures	3 (42.9%; 9.1-85)	4 (57.1%; 15-90.9)	3.17 (0.57-17.50)	-	-
Face, mouth, salivary and thyroid	19 (55.9%; 38.3-72.1)	15 (44.1%; 27.9-61.7)	1.88 (0.64-5.46)	-	-
Female reproductive organs	2 (28.6%; 4.2-78.5)	5 (71.4%; 21.5-95.8)	5.94 (0.95-37.24)	-	-
Skin and subcutaneous tissue	4 (36.4%; 11.7-71.2)	7 (63.6%; 28.8-88.3)	4.16 (0.95-18.27)	-	-

	Non-hazardous (0-4)	**Hazardous (>4)**	**Uni OR**	**Multi OR 1**	**Multi OR 2**
Spine, spinal cord and peripheral nerves	57 (67.9%; 56.9-77.1)	27 (32.1%; 22.9-43.1)	1.13 (0.44-2.89)	-	-
Thorax and intra-thoracic organs	4 (66.6%; 14.9-95.8)	2 (33.3%; 4.2-85.1)	1.19 (0.18-7.84)	-	-
Urinary system and male reproductive organs	1 (33.3%; 0.08-99.7)	2 (66.6%; 0.3-99.9)	4.75 (0.38-60.15)	-	-
Vascular system	19 (70.4%; 49.6-85.2)	8 (29.6%; 14.8-50.4)	*Ref*		

Notes. * p < .05, ** p < .01, *** p < .001; ns = non-significant; OR = odds ratio; 95% confidence intervals in parentheses; Ref = reference category/level; Uni ES = univariate effect size (OR unless otherwise specified); Multi OR 1 = multivariate effect size for univariate predictors p < .20; Multi OR 2 = multivariate effect size for model including all variables; TAM-2: total (physical) activity measure (higher = more activity) - note log transformation to mitigate skew; ASA-PS: American Society of Anaesthesiologists physical status score; BMI: body-mass index; note that multivariate analyses were conducted without covarying both BMI and ASA-PS scores, results here are those including ASA-PS scores.

Table 4.5. Previous Three-Month Illicit Substance Users: Yes versus No x Other Patient Characteristics (Study 3).

	No	Yes	Uni OR	Multi OR 1	Multi OR 2
Total	254 (93%; 89.3-95.5)	19 (7%; 4.5-10.7)			
Mean age	51.6 (49.6-53.7|	37.1 (30-44.1)	*** *g* = 0.89 (0.40-1.37)	ns	ns
Gender			ns (*p* = .06)	ns (*p* = .10)	ns
Male	117 (90%; 83.4-94.1)	13 (10%; 5.9-16.6)	2.50 (0.92-6.79)	3.31 (0.75-14.61)	-
Female	135 (95.7%; 90.8-98.1)	6 (4.3%; 1.9-9.2)	*Ref*		
Smoker			***	*	*
Current	61 81.3%; 70.6-88.8)	14 (18.7%; 11.2-29.4)	8.86 (3.07-25.59)	5.01 (1.27-19.72)	4.99 (1.20-70.73)
Former	84 (98.8%; 91.8-99.8)	1 (1.2%; 0.2%-8.2)	*Ref (former + never)*	-	-
Never	109 (96.5%; 90.8-98.7)	4 (3.5%; 1.3-9.2)			
AUDIT-C			**	ns	ns
Hazardous	107 (88.4%; 81.3-93.1)	14 (11.6%; 6.9-18.7)	3.85 (1.34-11.00)	-	-
Non-hazardous	147 (96.7%; 92.3-98.6)	5 (3.3%; 1.4-7.7)	*Ref*	-	-
Mean $\log_{10}$ TAM-2	3.5 (3.4-3.5)	3.7 (3.5-3.9)	ns (*p* = .11), *g* = -0.40 (-0.89-0.09)	ns	ns
ASA-PS			*	ns	ns
I	55 (85.9%; 74.8-92.7)	9 (14.1%; 7.3-25.2)	*Ref*	-	-
II	105 (96.3%; 09.5-98.6)	4 (3.7%; 1.4-9.5)	0.23 (0.07-0.79)	-	-
III	74 (96.1%; 88.3-98.8)	3 (3.9%; 1.2-11.7)	0.25 (0.06-0.96)	-	-
IV	8 (88.9%; 37.4-99.1)	1 (11.1%; 0.9-62.6)	0.76 (0.09-6.86)	-	-
Mean BMI	29.2 (28.4-29.9)	26 (22.8-29.3)	* *g* = 0.52 (0.02-1.01)	See *notes*	See *notes*

	No	Yes	Uni OR	Multi OR 1	Multi OR 2
Surgery complexity			ns ($p > .20$)	ns	ns
Minor	18 (90%; 64.5-97.8)	2 (10%; 2.2-35.5)	*Ref*	-	-
Intermediate	69 (88.5%; 79-94)	9 (11.5%; 6-21)	1.17 (0.23-5.92)	-	-
Major	58 (96.7%; 87.2-99.2)	2 (3.3%; 0.8-12.8)	0.31 (0.04-2.36)	-	-
Extra major	46 (95.8%; 84.1-99)	2 (4.2%; 1-15.9)	0.39 (0.05-2.99)	-	-
Complex	57 (95%; 85.2-98.4)	3 (5%; 1.6-14.8)	0.47 (0.07-3.06)	-	-
Type of surgery			ns ($p = .15$)	ns	ns
Abdomen	8 (80%; 37.8-96.3)	2 (20%; 3.7-62.2)	7.25 (0.58-90.54)	-	-
Bones, joints and connective tissues/tendon muscle	29 (96.7%; 77.8-99.6)	1 (3.3%; 0.4-22.2)	*Ref*	-	-
Brain, cranium and intracranial organs	17 (94.4%; 64.5-99.4)	1 (5.6%; 0.6-35.5)	1.51 (0.10-29.07)	-	-
Ear, nose and throat	24 (82.8%; 63.3-93)	5 (17.2%; 7-36.7)	6.04 (0.66-55.30)	-	-
Endoscopic gastrointestinal procedures	6 (85.7%; 25.7-99)	1 (14.3%; 1-74.3)	4.83 (0.26-88.54)	-	-
Face, mouth, salivary and thyroid	30 (88.2%; 71.4-95.7)	4 (11.8%; 4.3-28.6)	3.87 (0.41-36.69)	-	-
Female reproductive organs	7 (100%)	-	-	-	-
Skin and subcutaneous tissue	10 (90.9%; 46.3-99.1)	1 (9.1%; 0.9-53.7)	2.90 (0.17-50.82)	-	-
Spine, spinal cord and peripheral nerves	83 (98.8%; 91.7-99.8)	1 (1.2%; 0.2-8.3)	0.35 (0.02-5.77)	-	-
Thorax and intra-thoracic organs	6 (100%)	-	-	-	-

	No	Yes	Uni OR	Multi OR 1	Multi OR 2
Urinary system and male reproductive organs	3 (100%)	-	-	-	-
Vascular system	25 (92.6%; 72.8-98.3)	2 (7.4%; 1.7-27.2)	2.32 (0.20-27.14)	-	-

Notes. * $p < .05$, ** $p < .01$, *** $p < .001$; ns = non-significant; OR = odds ratio; 95% confidence intervals in parentheses; Ref = reference category/level; Uni ES = univariate effect size (OR unless otherwise specified); Multi OR 1 = multivariate effect size for univariate predictors $p < .20$; Multi OR 2 = multivariate effect size for model including all variables; TAM-2: total (physical) activity measure (higher = more activity) - note log transformation to mitigate skew; ASA-PS: American Society of Anaesthesiologists physical status score; BMI: body-mass index; note that multivariate analyses were conducted without covarying both BMI and ASA-PS scores, results here are those including ASA-PS scores.

4.7.3 Detection

Alcohol use. Of those identified as alcohol users *per se* in routine assessment (165 out of 255 [64.7%] of patients), alcohol units per week were documented for just 75 patients (75 out of 165 [45.5%]). In 20 additional cases, however, units could be approximated from the description provided (e.g., "*one bottle of wine a day*") thus judging hazardous alcohol use was quite straightforward for 58.1% of alcohol using patients. The remaining patients' alcohol use was typically described using terms such as "*occasionally*", or "*weekly*" which presented more difficulty (e.g., how occasionally? How much or often weekly?).

As described above, judging whether what was written on routine forms constituted hazardous alcohol use was undertaken by two independent raters and agreement assessed statistically. There were good levels of agreement (κ = 0.90) between raters; there were just seven instances of disagreement (from 254 judgments; one patient was excluded as they refused to disclose their alcohol use amount during routine preoperative assessment). These disagreements were resolved through correspondence.

In total, 36 patients (14.2%) were identified as potentially hazardous alcohol users using routine measures, versus 111 (43.7%) patients meeting the AUDIT-C hazardous cut-off. The proportion of AUDIT-C *positive* patients identified positive by routine measures was 30.9% (95% CI: 22.5-40.4) (sensitivity), while 98.6% (96.2-100) of AUDIT-C *negative* patients were identified as negative by routine measures (specificity). The likelihood of a positive AUDIT-C score given a positive detection on routine measures was 97.1% (82.5-99.6) (positive predictive value [PPV]) and the converse - the likelihood of a negative AUDIT-C score given a negative routine detection, was 65.3% (63.6-75.3) (negative predictive value [NPV]).

Illicit substance use. Given a relatively small number of illicit substance-using patients identified, there was complete agreement between raters regarding coding of routine assessment detections. Routine assessment noted just five (2%) illicit substance users (all cannabis users only) with use frequencies within the previous three months (three daily users, one weekly and one bi-weekly user). The ASSIST measure identified 18 (7.1%) illicit substance-using patients in total; two of whom had used *both* cannabis and cocaine in the previous three-months, three just cocaine and 12 just cannabis.

Of 15 (5.9%) previous three-month cannabis users detected by the ASSIST measure, 10 (66.7%) were therefore missed by routine preoperative assessment (including two daily users and four weekly users). Routine assessment had a sensitivity of: 33.3% (11.8-61.6), specificity: 100% (98.47-100), PPV: 100% and NPV: 96% (94.4-97.2) for cannabis detection versus the ASSIST. All five (100%) cocaine users identified by the ASSIST were missed by routine assessment, though the use frequency was low in all cases (4 = once or twice in the previous three months, 1 = monthly). For illicit substance use *per se*, routine assessment missed 13 (72.2%) patients identified by the ASSIST, giving an overall sensitivity of: 27.8% (9.7-53.5), specificity: 100% (98.5-100), PPV: 100% and NPV: 94.8 (93.2-96%).

4.7.4 Outcomes

The 206 (75.5%) patients with available follow-up data were compared with those for which data were not available. There were no significant differences between groups with regard to: gender, AUDIT-C cut-offs, smoking status, ASA-PS scores, illicit substance use (yes/no), ASSIST global continuum of risk scores, age, TAM-2 scores, or BMI. There was a significant difference with regard to surgery complexity classifications; in those who could not be followed up versus those who could, a higher proportion was undergoing complex or extra major surgeries, and a smaller proportion was undergoing major, intermediate and minor surgeries.

Upon examination of univariate associations between patient characteristics variables and the binary composite *deviations* (adverse events) outcome, it was identified that zero variables had an association at the $p < .20$ level. Further inspection revealed that a composite measure *excluding* the unplanned admission events was much more sensitive (i.e., ASA-PS scores and surgery complexity were significantly associated with the outcome) indicating that the routine management intention coding may have been inaccurate. For example, some patients may have been coded as day cases when they were in fact inpatients, or their intended management statuses, if altered at some point in the perioperative pathway, were not updated on the electronic medical records. Correspondence with NHS coding staff revealed that this was common and that intended management codes were often unreliable. A composite measure excluding this outcome was used for all further analyses. This outcome had just 14 adverse events versus the previous 33, meaning power was greatly reduced. As a result, only partially adjusted models were fitted (to prevent overfitting).

Routine assessment versus AUDIT-C. Patients with higher ASA-PS scores had a significantly higher likelihood of an adverse event ($p = .01$), as did those undergoing more complex surgeries ($p = .006$). These estimates were however imprecise (wide confidence intervals) and no other variable was significant (including all alcohol/illicit substance use measures - though smoking status met the threshold for inclusion in partially adjusted models). As shown in Table 4.6, individual models including these variables plus binary AUDIT-C or routine assessment variables were both significant. Both alcohol measures were non-significant in both models, though both effects sizes (odds ratios) were in the predicted direction (i.e., hazardous drinkers were at increased odds of complications versus non-hazardous drinkers). The routine measure had a higher odds ratio - though both estimates were highly imprecise with wide confidence intervals. The model fit statistics were almost identical between models, thus there was zero to little evidence of superiority of either measure in this sample.

ASSIST global continuum of risk *x* complications. A logistic regression model including ASA-PS scores, surgical complexity and ASSIST global scores was fitted (smoking status was omitted as this confounded with the ASSIST measure). As shown in Table 4.7, while non-significant, the ASSIST measure was in the predicted direction.

Table 4.6. Logistic Models: AUDIT-C versus Routine Measure Predicting Adverse Perioperative Events.

	AUDIT-C	**Routine measure**
Model fit	$\chi^2(9) = 23.45$**	$\chi^2(9) = 24.37$**
	$R^2_N = 0.29$; BIC = 124.42; AIC = 91.79; AUC = 0.85	$R^2_N = 30$; BIC = 123.50; AIC = 90.87; AUC = 0.85
AUDIT-C	ns	-
Hazardous	1.20 (0.29-5.06)	-
Non-hazardous	*Ref*	-
Routine measure	-	ns
Hazardous	-	2.25 (0.48-10.66)
Non-hazardous	*Ref*	-
ASA-PS	ns	ns (p = .08)
I	(0 events)	-
II	*Ref*	-
III	1.65 (0.41-6.59)	1.86 (0.46-7.53)
IV	3.99 (0.50-31.90)	5.02 (0.64-39.42)
Surgical complexity	*	*
Minor	*Ref*	-
Intermediate	0.54 (0.04-7.29)	0.47 (0.03-6.59)
Major	(0 events)	-
Extra major	1.86 (0.16-21.22)	1.70 (0.15-19.67)
Complex	2.67 (0.27-26.25)	2.25 (0.22-22.89)
Smoking status	ns	ns
Current	0.39 (0.04-3.34)	0.39 (0.04-3.35)
Never/former	*Ref*	-

Notes. * = $p < .05$, ** $p < .01$, *** $p < .001$; ns = non-significant; *Ref* = reference level/category; χ^2 = chi-squared (degrees of freedom) test of model fit; ASA-PS: American Society of Anaesthesiologists physical status score; R^2_N = Nagelkerke's R^2; AUC = Area under the curve; BIC = Bayesian Information Criterion; AIC = Akaike Information Criterion.

Table 4.7. Logistic Model: ASSIST Global Continuum of Risk Scores Predicting Adverse Perioperative Events.

Model fit	$\chi^2(8) = 23.94$** $R^2_N = 0.30$ BIC = 118.67 AIC = 89.31 AUC = 0.87
ASSIST	1.03 (0.98-1.08)
ASA-PS	*
I	(0 events)
II	*Ref*
III	1.87 (0.47-7.35)
IV	5.16 (0.68-38.93)
Surgical complexity	*
Minor	*Ref*
Intermediate	0.39 (0.03-5.36)
Major	(0 events)
Extra major	1.90 (0.17-21.46)
Complex	2.31 (0.24-22.06)

Notes. * = $p < .05$, ** $p < .01$, *** $p < .001$; ns = non-significant; Ref = reference level/category; χ^2= chi-squared (degrees of freedom) test of model fit; ASA-PS: American Society of Anaesthesiologists physical status score; R^2_N = Nagelkerke's R^2; AUC = Area under the curve; BIC = Bayesian Information Criterion; AIC = Akaike Information Criterion.

4.8 Discussion

In the first known studies of UK preoperative substance use prevalence, and across two separate UK-based (Leeds) preoperative assessment clinics, a sizeable proportion (31.6% and 44.3%) of preoperative patients scored AUDIT-C ≥ 5 - a score associated with alcohol-related perioperative complications previously (e.g., Bradley et al., 2011; Eliasen et al., 2013). Further, nearly one in fourteen and one in twenty-five patients met the threshold for high-risk drinking (Rubinsky et al., 2012). Illicit substance use prevalence was low in Study 2 (1.5%), though Study 3 (which unlike Study 2 used a more standardised measure) identified a 7% prevalence rate. In both cases, cannabis was the most used substance. Polysubstance use was high; 100% and 73.7% of illicit substance users were hazardous alcohol users in Study 2 and 3 respectively, and both studies found a higher proportion of smokers among hazardous alcohol users (Study 2: 31% versus 17%; Study 3: 31% versus 25%) and illicit substance users (Study 2: 100% versus 0%; Study 3: 12% versus 3%). Across all analyses, males, younger patients and those with lower ASA-PS scores were at most risk of hazardous substance use. In Study 2 it was identified that few hazardous alcohol users and illicit substance users would be receptive to intervention, suggesting that such patients may be lacking sufficient motivation for behaviour change. In Study 3 routine preoperative assessment versus validated measures was much less sensitive at detecting hazardous drinkers and illicit substance users, suggesting that some potentially high-risk patients may be unidentified in routine practice. There was, however, no evidence here that the AUDIT-C was superior to routine measures at predicting indicators of complications. Lastly, the utility of a polysubstance measure at predicting complications was not established.

Hazardous alcohol use prevalence rates identified in the present studies were high. Previous German studies have identified hazardous alcohol use prevalence rates of around 1 in 6 patients (Kip et al., 2008; Kleinwächter et al., 2010; Kork et al., 2012), American studies 1 in 10 patients (Harris et al., 2008). While it could be argued (and is likely true to *some* extent) that the present chapter rates reflect less specificity and more sensitivity in the chosen measure (AUDIT-C) versus measures used in previous studies - the AUDIT-C has demonstrated good concordance with other, longer and more in-depth measures in previous research. For example, the chosen hazardous cut-off used in the present studies has an approximate 80% level of specificity/sensitivity with DSM III-R, DSM-IV and

DSM-5 diagnosed alcohol use disorders (Dawson et al., 2012; Rumpf et al., 2002). The AUDIT-C has also been demonstrated to be as - and in some cases, more effective than the full 10-item AUDIT at detecting hazardous alcohol use (Bush et al., 1998; Bradley et al., 2003; 2007; Rubinsky et al., 2010) (the measure used in the German prevalence studies) - while maintaining the desired brevity necessary for inclusion in the time-limited context of preoperative assessment.

One explanation of the above results may be that because the UK has higher base rates of population *hazardous* drinking than the countries in which previous prevalence data has been collected (see section 2.4) (and because Yorkshire and the Humber, and Northern England more generally have above average UK rates; ONS, 2017), the prevalence was higher in preoperative assessment. This is worrying; by estimating complication rates using data from a previous large study (Bradley et al., 2011) it can be approximated that (allowing for differences in patient characteristics) 6.2 (Study 3) and 5.5 (Study 2) of AUDIT-C non-hazardous, versus 13.8 and 15.3 AUDIT-C hazardous patients in the present studies would suffer a *30-day* postoperative complication - over twice the incidence rate. It may be, therefore, at least in the context of Leeds, perioperative interventions for alcohol use may be justified on grounds of health - and, given the high cost of complications (see subsection 1.4.4), on the grounds of possible financial savings (though, to the author's knowledge, the cost-effectiveness of preoperative substance use interventions has never been examined; see Chapter 5).

In contrast to the identified hazardous alcohol use prevalence rate, a much smaller proportion of patients were illicit substance users, though this was to be expected from base UK rates (ONS, 2017). The Study 3 *last three months* prevalence rate (7%) was similar to a previous German study with a 7.5% *last year* rate (Kleinwächter et al., 2010). Across both present studies, cannabis was the most used substance, followed by cocaine and one patient in each study for zolpidem (a sedative drug) and heroin.

While it could be argued that a low prevalence may preclude concerted effort to develop and implement counteractive interventions (likely with time and financial costs), given that each of these substances has at least some evidence of perioperative use risk (see section 2.3) 7%, or one in fourteen patients, may be a non-trivial number. Very brief (and thus cheap and readily translatable) interventions for illicit substance use have been effective in similar contexts (Harland, Gowing & Ali, 2014) and may be useful here (though there has been no formal review of previous intervention studies in the perioperative context; see Chapter 5). Further, despite a low illicit substance use prevalence, rates of *polysubstance* use were very high. This mirrors previous research in the perioperative context (e.g., Kleinwächter et al., 2010) and population statistics generally (ONS, 2017). In both studies a 31% smoking prevalence rate was observed amongst AUDIT-C hazardous patients (though the rate was only *significantly* higher in this group in Study 2); meaning a third of already at-risk patients (or in Study 2 and 3, 1 in 10 and 1 in 7 of total patients, respectively) may be compounding their perioperative risk. Among illicit substance users, the present data indicated that if detected in routine practice, assuming that such patients were also smokers (Study 2: 100%; Study 3: 74%), hazardous drinkers (Study 2: 100% [all within the highest risk category]; Study 3: 74% [32% = highest risk]) or both (Study 3: 100%; Study 3: 53%) would not be an inaccurate supposition.

It is thus important to emphasize that targeting groups of patients that constitute a *minority* of patients, may reduce the *majority* of the complication incidence. This may be particularly true for patients who meet the highest alcohol risk categories (e.g., probable dependence) or use illicit substances particularly conducive to dependency (e.g., heroin and cocaine); i. the substances themselves may have a large impact on perioperative outcomes (e.g., Eliasen et al., 2013; Menendez et al., 2015), ii. common polysubstance use may increase the risk and iii. substance-dependent individuals tend to have risk-increasing poor physical and mental health (e.g., Regier et al., 1990). Higher comorbidity amongst hazardous substance users was however not demonstrated in the present studies - perhaps through a failure to identify a significant number of substance-dependent patients. Indeed, apart from polysubstance use, the co-occurrence of substance use and other perioperative risk factors was generally low. For instance, patients with lower ASA-PS (co-morbidity) scores were less likely to have hazardous AUDIT-C scores (though there was some indication of an exception in the highest risk category), there was no consistent association between high BMI or low physical activity levels with substance use, and illicit substance/hazardous alcohol users were generally younger. While this is positive, it is still the case that a sizeable proportion of patients were exposing themselves to *modifiable* perioperative harms that may offset, to some degree, the benefits conferred by their favourable characteristics.

Based on the present studies, routine preoperative interventions for substance use may be best placed to tailor development towards males, as well as younger and more healthy patients. They may wish also to target the use of multiple substances. Methods used to do this may vary, though future studies may choose to purposively sample such individuals for primary behavioural determinant identification research (e.g., males may be sampled for their attitudes to preoperative alcohol use reduction), learn from previous research (e.g., a lower age may signal that patients may be more receptive to internet or app-based interventions; Granger et al., 2016) or use intuition (e.g., healthier patients may be more able to travel to multiple intervention appointments). Intervention designers may also note that among a subset of Study 2 patients asked whether they would be receptive to intervention, most declined. With the caveat of a small sample, these patients appeared to lack sufficient motivation to change, perhaps indicating that they were not aware of the perioperative risks of substance use. Future studies would be useful to explore this further.

One unexpected, but interesting finding was the lack of adherence by nursing staff to the routine measure of alcohol use in Study 3. Despite explicitly asking for alcohol units, just 46% of alcohol users' units were documented. Nurses often favoured freehand descriptions. As an example of the poor utility of such terms, the phrase "*on special occasions*" - when cross-tabulated with AUDIT-C scores, was used for one patient with a high-risk AUDIT-C score, three patients with at-risk scores, and six patients with low-risk scores (a range of 1-9 on a measure with a scale of 0-12). More quantifiable unit approximations (e.g., "*one bottle of wine a night*") were often used also, however.

One explanation for this non-adherence is that calculating units - for staff and patients alike - may be a non-trivial task (i.e., the sum of total millilitres *x* ABV/1000 per drink, on an average day) requiring cognitive (memory and arithmetic) and material effort (determining the ABV of different drinks, or the millilitres in a pint, and so on) to complete accurately[21]. This is in stark contrast to a structured measure such as the AUDIT-C which utilizes checkboxes and a simple total score system (while at the same time capturing more useful information i.e., alcohol use frequency *x* amount, and bingeing *x* frequency). The utility of an AUDIT-C type over the routine measure, at least in regard to adherence, may, therefore, be considerable.

Versus the AUDIT-C, routine assessment (after coding for indicators of *detections*) had a high specificity; that is, patients who were AUDIT-C non-hazardous were nearly all identified as negative on routine measures, but a low sensitivity; the proportion of AUDIT-C hazardous patients identified positive by routine measures was 30.9%. There were, however, no notable differences between measures at predicting (indicators of) complications in Study 3. Indeed, while the odds of a complication were in the predicted direction on both measures, neither was significantly associated with complications in univariate analyses nor after controlling for factors that would be expected to - and indeed were, most highly associated with complication rates (ASA-PS scores and surgical complexity). It is true to say, however, that routine assessment appeared to be missing a number of patients that have AUDIT-C scores observed to predict complications in previous large studies (e.g., Eliasen et al., 2013).

There may be several reasons for the lack of significant effects between alcohol measures. The most prominent being sample size *x* event rate. Study 3 had an aim of 300 patients, which was deemed sufficient to predict complications based on previous studies (e.g., van Rooijen et al., 2016; Harris et al., 2011; Mulligan et al., 2018) (not least because most of the surgeries in the chosen clinic were *major* or above i.e., 76% in this sample). Despite this target almost being achieved (273), the effective sample size was greatly reduced due to a large proportion of patients not having had surgery during the study period (e.g., surgeries being delayed[22] or cancelled) or details of surgery not being uploaded to the electronic medical records during the study period. The in-hospital complication event rate was also very low versus previous studies (e.g., see Table 1.2) suggesting that the 158 chosen routine codes were not sensitive enough to detect sufficient events. By default, *in-hospital* complications are less sensitive than 30-day complications; 33% of all complications have been observed to occur in the post-discharge period (Woodfield et al., 2016). However, having 90-day readmission data was believed to offset this somewhat (34% of post-discharge complications have been observed to cause a readmission; Woodfield et al., 2016) alongside other indicators (e.g., extended length of stay) in a composite measure. This was to no avail. In sum, future studies may want to learn from the present findings; for instance, perioperative outcome data for an intervention trial may be best retrieved using patient-contact follow-up or by integrating standardized complication measures into participants' perioperative pathway. It would also be highly useful to confirm whether difference in detection rates in other preoperative assessment clinics predict complications using more sensitive measures (to assess whether routine practice can be improved).

As with alcohol *detections*, nurse-led preassessment versus the ASSIST measure failed to detect the majority of previous three months illicit substance users (sensitivity = 28%). Given that the routine measure was essentially a freehand description, this may not be surprising; the structured nature of the ASSIST may be, by default, more probing (e.g., asking about use of, potentially, all substances as opposed to any *per se*). Again, however, there was no evidence in this study that the sum of ASSIST scores could predict complications. Despite no significant effect here, i. this was likely due to sample size *x* event rate (the effect was in the predicted direction), and ii. replacing disparate measures with one standardized index may still have benefits (e.g., time, familiarity and standardization). Given that the ASSIST has many desirable properties (described in section 2.5 and subsection 4.1.1), it may be useful to integrate this measure into routine practice, though particularly so if future studies demonstrate the predictive utility of the ASSIST with larger samples and more sensitive outcomes (e.g., to assess clinically relevant cut-offs, interactions between *specific* substance use scores and so on).

The present studies both had limitations. First, the present samples may have been insufficiently large to detect significant trends between certain variables and substance use prevalence (especially illicit substance use) and, of course, may only generalize to the local area (Leeds) and specific clinics. This latter point was highlighted by the noticeable difference between clinics with regard to hazardous alcohol use prevalence (likely partially explained by differences in surgery types, as well as more female and older patients in Study 2). Study 2 also did not use an established illicit substance use measure, favouring a method very similar to routine assessment. This may have reduced sensitivity, and certainly reduced comparability between studies. Study 2 (which the present author had no control over) also did not record other useful information that Study 3 had (that would have also eased comparability between studies) such as documenting surgeries in manner that would have facilitated categorization using a standardized system (e.g., AXA categories) or patient co-morbidities, BMI, and physical activity. Neither Study 2 *nor* 3, however, assessed other useful variables that may have shed some light on who may be potential intervention recipients (e.g., socio-economic status) - at least in the case of Study 3, this was due to time limitations (i.e., reducing patient and staff time burden). If more time was available, it may have been useful to document co-prevalence of substance use with other potential risk factors for perioperative complications also such as sleep and psychiatric co-morbidity (the latter for reasons outlined in subsections 1.6 and 3.4).

Of course, the use of self-report measures, in general, may always invite some degree of social desirability bias; especially when discussing sensitive topics such as (particularly *illicit*) substance use, and especially when, despite the reassurance of confidentiality, patients may feel their surgery is contingent on a successful preoperative assessment. Relatedly, it could be that some of the observed difference between prevalence in routine assessment and validated (study) measures was due to a perception that answers on the latter were deemed to have no impact on their medical care. A true comparison would have a randomized selection of preoperative assessors using both methods, which future studies may wish to do. Next, while measures were compared for their predictive utility regarding complications, another useful strategy (that would have provided more insight into their respective psychometric properties) would have been to compare *detections* to a third, more gold-standard method (e.g., objective indicators, or a DSM interview). This was not done due to feasibility concerns (i.e., patient burden, time, costs) but would be useful for future studies to address. Lastly, a key limitation was the use of insufficiently sensitive perioperative outcomes data, or a failure to recruit (and/or retain) a sample large enough to detect significant effects using the available data. This, unfortunately, led to a failure to meet two of the main objectives of Study 3.

In sum, the present studies identified that over a third of patients in two Leeds (UK) based preoperative assessment clinics were *hazardous* alcohol users; achieving a score on a validated measure shown to predict postoperative complications previously. Fewer patients were illicit substance users, but polysubstance use was high. Routine measures were i. less sensitive than validated measures at detecting substance use and ii. were often incomplete (reflecting a possible lack of acceptability for staff and patients). Neither routine or validated (study) measures showed superiority at predicting complications. This was most likely explained by failure to detect a large enough complication event rate using routine data. Nevertheless, UK intervention studies may be necessary due to the observed prevalence, especially given low identified motivation for behaviour change, and especially for male, younger and less ill patients. Future studies may wish to address many of the identified limitations, which may be primarily addressed using a larger sample size.

4.9 Key Findings: Study 2 & 3

- The prevalence of hazardous preoperative alcohol use (AUDIT-C >4) was high in both studies (31.6% and 44.3%), though the use of illicit substances was much lower (1.5% and 7%).
- Hazardous alcohol use was highly associated with use of other substances such as tobacco and cannabis.
- Hazardous preoperative alcohol use and illicit substance use tended to occur most prominently amongst males, younger patients and those with fewer comorbidities
- Routine preoperative assessment was highly specific at detecting hazardous alcohol use and illicit substance use (versus validated measures) but very insensitive - meaning patients at risk of complications may be routinely missed.
- No substance use measure predicted postoperative complications, though effects were in the predicted direction (suggesting a lack of power - or insensitivity in the outcome measure).
- There was no evidence of superiority of validated alcohol measures versus routine practice at predicting alcohol-related postoperative complications. Again, this may be explained by the outcome measure.

CHAPTER 5.THE EFFICACY AND CHARACTERISTICS OF PREVIOUS PREOPERATIVE INTERVENTIONS FOR ALCOHOL AND OTHER RECREATIONAL SUBSTANCE USE: A SYSTEMATIC REVIEW AND META-ANALYSIS (STUDY 4)

5.1 Introduction

5.1.1 Background and Rationale

Despite evidence that preoperative substance use may increase perioperative complications (and initial evidence that use may affect mental health outcomes; Chapter 3), two studies in Chapter 4 demonstrated for the first time that hazardous alcohol use and illicit substance use were common amongst UK preoperative patients also (albeit limited to data in one city). Indeed, over a third of patients had AUDIT-C scores predictive of complications (e.g., Bradley et al., 2011; Eliasen et al., 2013) and one in fourteen (7%) patients were previous three-month illicit substance users. Polysubstance use was also very high, for instance, 74% of Study 3 patients were both illicit substance users and hazardous alcohol users.

For tobacco smoking, it has been demonstrated that interventions to support patients in quitting are effective at modifying surgical outcomes (Theadom & Cropley, 2006; Thomsen, Villebro & Møller, 2014). Intervention components, delivery, modes and contexts have also been studied, showing that intervention efficacy may be optimised using specific behaviour change techniques and other intervention characteristics (Prestwich et al., 2017). Reducing alcohol use from four to two standard drinks a day may reduce the incidence of perioperative complications by up-to 50% (Tønnesen et al., 2009).

Prolonged bleeding time and surgical stress responses may be reversed by an abstinence period of four weeks (Tønnesen et al., 2009). Preoperative abstinence or reduction in illicit substance use could incur similar benefits (see subsection 2.6.2). Both alcohol and illicit substance use may thus be modifiable risk factors for poor surgical outcomes. Consequently, interventions aimed at supporting surgical patients to modify their use are warranted, to protect patients and reduce healthcare costs (Scott, Seifert, Grimson & Glass, 2005).

Two previous reviews of preoperative interventions addressing alcohol use have shown that interventions may be effective at reducing drinking in surgical patients (Oppedal, Møller, Pedersen & Tønnesen, 2012; Fernandez, Claborn & Borsari, 2015) (see subsection 2.6.4). However, Oppedal et al. (2012) had very strict inclusion criteria (e.g., including only randomised controlled trials), limiting the scope of the review, and undertook their literature search in 2011, while Fernandez et al. (2015) included only behavioural interventions (excluding pharmaceutical support), undertook their literature search in 2013, and did not calculate pooled effects.

To the author's knowledge, there have been no previous reviews assessing the efficacy of preoperative interventions for illicit substance use. Additionally, psychological determinants (e.g., motivation to abstain) of alcohol and/or illicit substance use in the surgical context, and intervention components that may be predictors of behaviour change (i.e., successful behaviour change techniques, intervention formats and modalities), have not been investigated in previous reviews. Identifying salient determinants may provide useful intervention targets for the future, while identifying successful intervention components may provide useful methods of modifying these targets.

5.1.2 Objectives

1. To update previous alcohol intervention reviews and identify characteristics of effective (or ineffective) interventions.
2. Systematically review the literature on illicit substance use interventions, assessing quantitative evidence of their efficacy or otherwise at reducing substance use, and/or perioperative complications.
3. Assess whether interventions could modify psychological determinants which may predict preoperative substance use cessation and/or reduction.
4. To characterise intervention components of any behavioural interventions using a behaviour change taxonomy (Michie et al., 2013), so future researchers can more precisely replicate successful interventions.

5.2 Method

5.2.1 Search Strategy

An initial search of The Cochrane Library, PsycINFO, EMBASE, MEDLINE and CINAHL was conducted in November 2015 (see example search strategy in Appendix G). Further searches were carried out approximately bi-monthly up-to August 2018. These follow-up searches were conducted using Epistemonikos.org and Google Scholar (limiting search to articles published after 2014). Terms for these follow-up searches were simply "*alcohol",* and/or *"drugs"* and "*preoperative"* – meaning the searches were highly sensitive.

Additional studies were located via hand searching reference lists of included studies and relevant narrative reviews. Titles and abstracts were screened for eligibility by one reviewer before a random sample (*n* = 200) were screened by two others side-by-side with open discussion (almost perfect levels of agreement: κ = .87; Landis & Koch, 1977). Any disagreements were resolved through in open discussion between the three reviewers. Full-texts of potential studies were inspected by two reviewers, with full agreement regarding their eligibility.

5.2.2 Eligibility and Inclusion

Interventions targeting i. alcohol and/or illicit substance use in the preoperative period (with or without postoperative maintenance sessions), and/or ii. cognitive/behavioural determinants of alcohol and/or illicit substance use in iii. elective patients only, were included. Any designs, surgical populations, and comparator groups (or lack thereof) were eligible.

5.2.3 Primary Outcomes

1. Level (e.g., amount, frequency) and/or severity (e.g., dependence scores) of alcohol and/or illicit substance use at any time point (pre-surgery and/or post-surgery)
2. Perioperative: mortality (at any postoperative time-point), total complications (as defined by individual studies; at any postoperative time-point), and length of hospital stay (days);
3. Measures of psychological determinants of perioperative substance use (e.g., self-efficacy at reducing preoperative substance use).

5.2.4 Secondary Outcomes

1. Other outcomes idiosyncratic to each study deemed clinically relevant (e.g., patient satisfaction, and quality of life).

5.2.5 Risk-of-Bias and Data Extraction

Risk-of-bias was assessed using the Cochrane Collaboration risk-of-bias assessment tool (Higgins et al., 2011). While it is acknowledged that other tools are often used to assess non-RCT designs, we felt it appropriate to appraise all studies against desired gold standard research methods. For all studies, risk-of-bias and data for primary and secondary outcomes, patient demographics, retention rates and study design features were single coded before being checked by a member of the review team. There was full agreement.

Behaviour change techniques (BCTs) (Michie et al., 2013) targeted at alcohol or illicit substance use were coded by two authors to determine intervention components. Disagreements were resolved via discussion. Many interventions were poorly described. Studies with ambiguous descriptions of intervention components were coded *social support (unspecified)* (BCT 3.1) while BCTs for one intervention (Weinrieb et al., 2011) and all control groups were not coded due to insufficient reporting (the author, upon contact, could not elaborate on the intervention strategies). BCTs outlined in this report, therefore, should be considered approximate.

5.2.6 Data Analysis

Comprehensive Meta-Analysis (CMA; Borenstein, Hedges, Higgins & Rothstein, 2009) was used to compute, and where possible, pool effect sizes. Unadjusted data were used where possible. Cohen's *d* was used as the effect size metric and was calculated based on studies' reported means and standard deviations, events in each group, other effect size measures (e.g., odds ratios) or other statistical information such as *t* or *p* values (CMA allows the user to readily convert any of this information into a chosen metric). For some outcomes, it was not possible to calculate pre- to post-intervention between-subjects effect sizes. In these cases, post-intervention data were used. For within-subjects outcomes, $d > 0$ favoured post-intervention, $d < 0$ vice-versa. For between-subjects outcomes, $d > 0$ favoured intervention patients versus controls, $d < 0$ vice-versa. If outcomes were assessed at various time points, *d* for each was calculated – in addition to the average *d* across time points (pooling all in a within-study random effects meta-analysis). For studies using various measures for a related outcome, *d* for these measures were calculated individually – as well as the pooled *d* across them (pooled in a within-study random effects meta-analysis) – providing measure-specific *d*, and overall outcome-specific *d*.

Random effects meta-analyses were used to pool data for the primary outcomes (where possible). For each primary outcome with at least two studies, all studies were first meta-analysed, before a series of sensitivity analyses investigated the results further - accounting for unique trial features. Only between-subjects data were used. The average *d* across within-study time points and measures assessing a related outcome were entered for each study (as detailed above). Homogeneity *Q* and I^2 statistics assessed heterogeneity.

Though planned, the number of studies and degree of heterogeneity across them precluded planned meta-regressions assessing whether between-study intervention efficacy could be predicted from the use of different BCTs and certain design features (see Hempel et al., 2013; i.e., there would be insufficient power to detect even large effects).

5.3 Results

5.3.1 Characteristics of the Included Studies

From 8688 studies identified in the original search, nine were eligible (see *Figure 5.1*): five randomised controlled trials (Weinrieb et al., 2011; Tønnesen et al., 1999; 2002; McHugh et al., 2001; Kummel et al., 2008) two non-randomised controlled trials (Shourie et al., 2006; Hansen, Bredtoft & Larsen, 2012) one pre- post-intervention study (Ashton et al., 2013) and one mixed design study (Wyman et al., 2014) (which compared some outcomes between a control group [CG] and an intervention group [IG] and some within the IG only). Two studies targeted the use of alcohol and illicit substances (Ashton et al., 2013; Wyman et al., 2014), the rest alcohol use only. Three studies aimed to modify other behaviours in conjunction with alcohol use such as exercise and smoking (McHugh et al., 2001; Kummel et al., 2008; Hansen et al., 2012). Five studies aimed to assess whether interventions could alter perioperative health outcomes (Tønnesen et al., 1999; 2002; Shourie et al., 2006; Hansen et al., 2012; Wyman et al., 2014). See Table 5.1 for study characteristics, Table 5.2 for outcomes measures/results.

Across the studies, patients were awaiting various surgical procedures (e.g., liver transplant, colorectal and coronary bypass surgeries). Sample sizes ranged from 28 to 174 (total: 903), with a large gender bias (approximately 72% male). Six studies did not report patients’ ethnicity; of three that did (Weinrieb et al., 2011; Ashton et al., 2013; Wyman et al., 2014) the majority were white (69%). All patients were adults.

Five studies delivered multi-session interventions (Tønnesen et al., 1999; 2002; McHugh et al., 2001; Kummel et al., 2008) (the rest one session only) and three (Kummel et al., 2008; Ashton et al., 2013; Wyman et al., 2014) involved group (as opposed to one-on-one) interventions. In three studies (McHugh et al., 2001; Kummel et al., 2008; Hansen et al., 2012) the intervention was delivered by nurses, in four (Weinrieb et al., 2011; Tønnesen et al., 1999; 2002; Shourie et al., 2006) by a member of the research group**,** one (Wyman et al., 2012) with multiple interventionists (psychologist, social worker or nurse), and one (Ashton et al., 2013) a psychologist. All studies described a motivational (e.g., motivational interviewing or motivational enhancement therapy) or general psychosocial behavioural intervention of some sort, but none described their intervention in terms of a behaviour change technique taxonomy. In addition to *motivational counselling*, Tønnesen et al. (2002) prescribed 800mg of disulfiram a week (400mg taken under supervision, 400mg unsupervised), B vitamins and offered chlordiazepoxide for withdrawal symptoms. Tønnesen et al. (1999) had patients receive 800mg of disulfiram weekly (other support unspecified).

Six studies (Tønnesen et al., 1999; 2002; McHugh et al., 2001; Kummel et al., 2008; Shourie et al., 2006; Hansen et al., 2012) reported that controls received treatment as usual or routine care. Weinrieb et al. (2011) reported that controls received treatment as usual plus a referral to community Alcoholics Anonymous and *standard intensive outpatient therapy*; Wyman et al. (2012) that controls were informed that they were at high-risk due to their substance use and were advised to reduce or cease alcohol use. Ashton et al. (2013) did not have a control group

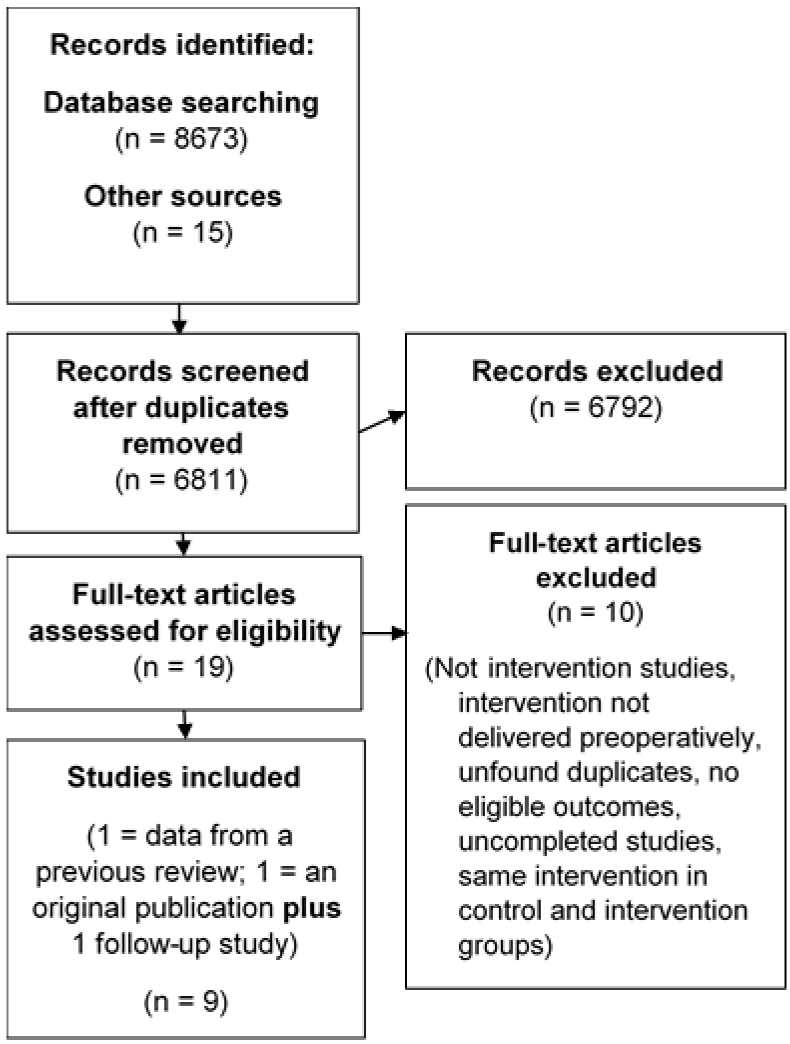

Figure 5.1. Flow Diagram of the Screening Process.

Table 5.1. Design, Participant Demographics and Intervention Details.

Study	Study design & sample size	Patient characteristics	Substance-related inclusion criteria	Patient substance use characteristics (baseline)	Targets	Intervention description	Deliverer	BCTs*	Timing
Ashton and others (2013) (USA)	Pre- post-intervention study ('pilot study') Total: 86	**Mean age** 46 **Gender** 32.6% male **Ethnicity** *White* 65.1% *Black* 29.5% *Other* 5.4% **Surgery** Bariatric	Patients with a history of substance misuse or at-risk substance use	22% positive for AUD (AUDIT-C). 43% abstinent from alcohol. 1 patient current cannabis user	**Determinants of substance use**	A brief group-based psychosocial intervention consisting of '*psychoeducation and discussion about the effects of substances and addictions after surgery*'	Psychologist, or postdoctoral psychology fellow	1.2; 3.1; 5.1; 11.2 (no specific protocol cited)	1 session 90 minutes long Time before surgery unknown
Hansen and others (2012) (Denmark)	Controlled trial Total: 132 IG: 78 CG: 54	**Mean age** IG: 68 CG: 69 **Gender** IG: 43.6% male CG: 61% male **Ethnicity** Not reported **Surgery** Hip and knee arthroplasty	Males drinking >21 units, female drinking >14 units of alcohol per week	**IG:** 4 patients identified as risky drinkers **CG:** not stated	**Alcohol use** Healthy eating Exercise Smoking Medication use	**IG:** A brief one-to-one preoperative '*motivational conversation'* intervention with tailored information, recommendations and referral to specialists **CG:** Treatment as usual (no further elaboration)	Nurse	5.1; 9.1 (no specific protocol cited)	1 session Unknown duration 31 days before surgery

Kummel and others (2008) (Finland)	Randomised controlled trial Total: 117 IG: 49 CG: 68	**Mean age** IG: 72 CG: 72 **Gender** IG: 69% male CG: 75% male **Ethnicity** Not reported **Surgery** Coronary artery bypass	None	**IG:** 40% alcohol use > once weekly, 47% 1-2 times a month **CG:** 44% > once weekly, 31% 1-2 times a month	**Alcohol use** Self-care Exercise Healthy eating	**IG:** A multi-session group counselling and guidance intervention, with ‘*adjustment education*’ **CG:** Treatment as usual (no further elaboration)	Nurse	3.1 (no specific protocol cited)	5 sessions, 1 before surgery, 4 after Time before surgery unknown Duration unknown Unclear when or how many times alcohol use addressed
McHugh and others (2001)** (UK)	Randomised controlled trial Total: 98 IG: 49 CG: 49	**Median age** IG: 61 CG: 63 **Gender** IG: 71.4% male CG: 79.6% male **Ethnicity** Not reported **Surgery** Coronary artery bypass	None	**IG:** mean (SD) = 6.9 (10.5) drinks weekly (8g pure alcohol) **CG:** 6.6 (8.5) drinks weekly	**Alcohol use** Exercise Healthy eating	**IG:** A multi-session one-to-one health education intervention, with general advice/information, motivational enhancement techniques, and telephone support **CG:** Treatment as usual (no further elaboration)	Nurse	1.1; 2.3; 3.1; 9.1; 9.2 (no specific protocol cited)	Monthly sessions up-to the month of surgery (average 8 months) Flexible in length Unclear when or how many times alcohol use addressed

Shourie and others (2006) (Australia)	Controlled trial Total: 136 IG: 91 CG: 45	**Mean age** IG: 55 CG: 52 **Gender** IG: 91.1% male CG: 74.4% male **Ethnicity** Not reported **Surgery** Mixed	Males drinking >60g, females drinking >40g alcohol daily	**IG:** mean (SD) = 8.2 (1.9) AUDIT-C score, 66.8 (43.9) grams of alcohol per day. 13.3% alcohol dependent (DSM interview diagnosed) **CG:** 8.3 (1.7) AUDIT-C score, 73.7 (50.1) grams per day	**Alcohol use**	**IG:** A brief one-to-one motivational enhancement-based intervention named the 'Drink Less' programme Dependent users referred to alcohol specialists for withdrawal management **CG:** Treatment as usual ('*a description of process of admission, preparation for, and recovery from surgery and written material as routinely provided by each surgeon and/or hospital*')	Member of research team	1.1; 1.2; 2.3; 3.1; 3.3; 5.3; 5.6; 8.1; 12.2; 12.3; 15.1 (protocol cited)	1 session Unknown duration At minimum, more than 7 days before surgery

Tønnesen and others. (1999) (Denmark)	Randomised controlled trial Total: 41 IG: 20 CG: 21	**Median age** IG: 58 CG: 61 **Gender** IG: 100% male CG: 84% male **Ethnicity** Not reported **Surgery** Colorectal surgery	Patients drinking >60g alcohol daily	**IG:** median (range) = 84 (60-480) grammes of alcohol per day **CG:** 72 (60-480) grammes per day	**Alcohol use**	**IG:** 800mg Disulfiram taken under supervision twice weekly **CG:** Treatment as usual (no further elaboration)	Member of research team	11.1	Weekly up-to the week before surgery
Tønnesen and others (2002) (Denmark)	Randomised controlled trial Total: 28 IG: 15 CG: 13	**Age range** Entire sample: 39-75 **Gender** IG: 100% male CG: 100% male **Ethnicity** Not reported **Surgery** Hip arthroplasty	Patients drinking >60g alcohol daily, or 420g weekly	**IG:** median (range) = 72 (60-156) grammes of alcohol per day **CG:** 72 (60-96) grammes per day	**Alcohol use**	**IG:** 400mg Disulfiram taken under supervision, and 400mg taken without supervision per week Brief weekly motivational counselling sessions Use of B vitamins Telephone support **CG:** Treatment as usual (no further elaboration)	Member of research team	3.1; 11.1 (no protocol for counselling intervention cited)	Weekly up-to the week before intervention

Weinrieb and others (2011) (USA)	Randomised controlled trial Total: 91 IG: 46 CG: 45	**Median age** IG: 51 CG: 48 **Gender** IG: 85% male CG: 82% male **Ethnicity** *White* IG: 85%; CG: 78% *Other* IG: 15%; CG: 22% **Surgery** Liver transplant	Patients who had drank at least 1 alcoholic drink within 2 years preceding a liver transplant evaluation (who were previously alcohol dependent)	**IG:** median (range) = 20.5 (10-28) years of past alcohol misuse, 9 (6-15) months since last drink, 17.4% received illicit substance use treatment in the past **CG:** 15 (10-20) years of past misuse, 9 (4-18) months since last drink, 22% past illicit substance use treatment	**Alcohol use** (possibly **illicit substance use**)	**IG:** A multi-session intervention consisting of '*motivational enhancement therapy*', '*case management*' and '*encouragement to attend AA meetings*' **CG:** Treatment as usual consisting of referral to community AA and '*standard outpatient therapy*'	Member of research team	Uninterpretable (no specific protocol cited)	7 sessions 50 minutes long Time to surgery unknown

Wyman and others (2014) (USA)	Controlled trial/pre-post ('pilot study') Total: 174 IG: 107 CG: 67	**Mean age:** IG: 57 CG: 51 **Gender:** IG: 95.3% male CG: 91% male **Ethnicity:** *White* IG: 58.9%; CG: 73.1% *Black* IG: 35.5%; CG: 23.9% *Other* IG: 5.6%; CG: 3% **Surgery** Mixed	Patients scoring 6 or above on the AUDIT-C Patients who reported any illicit substance use in the previous 6 months	**IG:** mean (SD) = 5.4 (3.4) AUDIT-C score, 39% used illicit substances in the previous 6 months, 43.4% previously treatment for substance use disorder **CG:** 4.7 (3.4) AUDIT-C score, 60.6% illicit substance use, 42.4% past illicit substance use treatment	**Alcohol use** **Illicit substance use** (*per se*)	**IG:** A brief group-based psychosocial intervention based on motivational interviewing techniques, with referral to substance abuse treatment specialists if requested **CG:** Results of preassessment screening, and brief education on perioperative substance abuse, and advice to quit	Psychologist, social worker or nurse	1.1; 1.2; 1.3; 1.5; 2.2; 3.1; 9.1 (no specific protocol cited)	1 session 2 hours long 59 days before surgery on average

Notes. IG, intervention group; CG, control group; SD, standard deviation; AA. Alcoholics anonymous; AUDIT-C, alcohol use disorder identification test – consumption; DSM, diagnostic and statistical manual of mental disorders; BCT, behaviour change technique(s); 1.1 Goal Setting (behaviour); 1.2 Problem Solving; 1.3 Goal Setting (outcome); 1.5 Review behaviour goal(s); 2.2 Feedback on behaviour; 2.3 Self-monitoring of behaviour; 3.1 Social support (unspecified); 3.3 Social support (emotional); 5.1 Information about health consequences; 5.3 Information about social and environmental consequences; 5.6 Information about emotional consequences; 8.1 Behavioural practice/rehearsal; 9.1 Credible source; 9.2 Pros and cons; 11.1 Pharmacological support; 11.2 Reduce negative emotions; 12.1 Restructuring the physical environment; 12.3 Avoidance/reducing exposure to cues for the behaviour; 15.1 Verbal persuasion about capability.* Behaviour change techniques (BCTs) were reported for no study. ** Note. In the secondary follow-up analysis of this study (Rideout, Lindsay & Godwin, 2011) 110 patients were included.

Table 5.2. Assessment Timing, Recruitment, Retention, Outcome Measure and Results.

Study	Assessment time points	Substance use & determinants	Perioperative complications	Secondary outcomes	Recruitment & retention	Summary of results: Substance use & determinants	Summary of results: Perioperative complications	Summary of results: Secondary outcomes
Ashton and others (2013)	**Baseline:** Immediately pre-intervention (after being referred from preassessm ent) **Follow-up:** Immediately post-intervention	**Baseline and follow-up:** Intentions to use substances after surgery ('not likely') Knowledge of the negative effects of postoperativ e substance use (quiz format, score/10) Coping strategies to aid postoperativ e substance use reduction (number noted)	-	**Follow-up:** Patient satisfaction (questionnaire)	**Recruitment:** Duration of recruitment not specified **Retention:** No dropouts	**Intentions:** *d: 0.97; 95% CI: 0.49-1.45* **Knowledge:** *d: 4.57; 95% CI: 3.85-5.28* **Coping:** *d: 2.05; 95% CI: 1.67-2.42*	-	**Patient satisfaction:** *High*

Hansen and others (2012)	**Baseline** (at surgical preassessment) **Follow-up:** 3 months (via patient chart review)	-	**Follow-up:** Length of hospital stay Mortality Total complications '*Unintentional patients paths'*** Readmissions Number of patients meeting discharge criteria late	**Baseline and follow-up:** Health-related quality of life (EuroQuol 5d) Disease-specific outcome score (DSOS)	**Recruitment:** Over 2 months for each group. 5.7% of eligible patients declined participation **Retention:** No dropouts	-	**Length of hospital stay:** *d: 0.51; 95% CI: 0.15-0.86* **Mortality:** *Zero deaths* **Total complications:** *d: 0.39; 95% CI: -0.19-0.97* **Unintentional patient paths:** *d: 0.37; 95% CI: -0.06-0.80* **Readmissions:** *d: 0.21; 95% CI: -1.33-1.75* **Late discharge:** *d: 0.72; 95% CI: -0.20-1.24*	**EuroQUOL 5d:** *d: 0.13; 95% CI: -0.22-0.48* **DSOS:** *d: 0.32; 95% CI: -0.03-0.67*
Kummel and others (2008)	(via survey questionnaires sent to participants) **Baseline** **Follow-up:** 3, 6 & 12 months	**Baseline and follow-up:** Use of alcohol (none versus ≥ once a week calculated)	-	**Baseline and follow-up:** Symptoms of angina pectoris (not at all versus ≥ at least once a day) Functional abilities (questionnaire probing stair climbing ability)	**Recruitment:** Over 3.5 years. 38% approached met the inclusion criteria **Retention:** 68% completed all follow-ups	**Alcohol use (3 months):** *d: 0.09; 95% CI: -0.59-0.77* **Alcohol use (6 months):** *d: -0.22; 95% CI: -0.63-0.20* **Alcohol use (12 months):** *d: -0.18; 95% CI: -1.83-0.82*	-	**Angina symptoms:** *d: -0.05; 95% CI: -0.31-0.22* **Functional abilities:** *d: 0.29; 95% CI: 0.07-0.52* (pooled across time points)

McHugh and others (2001) **& Rideout, Lindsay & Godwin** (2011)	(via visitation by liaison nurse at home, or at a general practice clinic) **Baseline Follow-up:** 15 months **Secondary follow-up**: 12 years post-randomisation	**Baseline and follow-up:** Grammes per week of alcohol	**Secondary follow-up:** Mortality (not strictly 'perioperative')	**Follow-up:** Patient satisfaction (questionnaire) **Baseline and follow-up;** Health status (e.g., pain, general health; SF-36) Depression and anxiety (HADS) Physical health (objective measures e.g., BMI, blood pressure etc.)	**Recruitment:** Over 15 months. 85% of patients approached participated **Retention:** 79% of the IG, 83% of CG retained in the primary study. All but 12 retained for long-term follow-up	**Alcohol use:** *d: 0.28; 95% CI: -0.12-0.68*	**Mortality:** *d: 0.32; 95% CI: -0.12-0.76*	**Patient satisfaction:** *High* **SF-36 (pooled across domains):** *d: 0.73; 95% CI: 0.55-0.90* **Depression & Anxiety:** *d: 0.73; 95% CI: 0.32-1.14* **Physical health:** *d* range = *0.34-0.85;* all *p* < *.05*
Shourie and others (2006)	**Baseline** (at surgical preassessment) **Up to 5 days post-surgery** (via patient chart review) **Follow-up:** 6 months (via interview)	**Baseline and follow-up:** AUDIT-C score Grams per day of alcohol Number of DSM diagnosed alcohol-dependent patients (only follow-up data used to calculate effect size)	**Up to 5 days post-surgery:** Length of hospital stay Total complications Mortality **Follow-up:** Hospital admissions	**Follow-up:** Number of GP visits (past 6 months) Number of days off work sick (past 6 months)	**Recruitment:** Over 2 years, 10 months. 2889 patients ineligible, 114 refused participation. 4.3% of those approached recruited **Retention:** 4 of the IG, 13 of the CG dropped out	**AUDIT-C:** *d: 0.27; 95% CI: -0.11-0.65* **Grams per day of alcohol:** *d: -0.03; 95% CI: -0.41-0.35* **Number of alcohol-dependent patients:** *d: -0.11; 95% CI: -0.76-0.55*	**Length of hospital stay:** *d: 0.19; 95% CI -0.17-0.55* **Total complications:** *d: -0.48; 95% CI: -0.89 - -0.06* **Mortality:** *d: -0.40; 95% CI: -1.94-1.15* **Hospital readmissions:** *d: 0.27; 95% CI: -0.11-0.65*	**GP visits:** *d: 0.11; 95% CI: -0.27-0.49* **Days off work:** *d: 0.17; 95% CI: -0.21-0.55*

Tønnesen and others (1999)	**Baseline** **Follow-up:** 1 month post-surgery	**Baseline and follow-up:** Number of non-hazardous drinkers Number of drinks consumed a week	**Follow-up:** Length of hospital stay Mortality Total complications	-	**Recruitment:** Over 2.5 years **Retention:** 2 IG, 4 CG patients dropped out	**Number of non-hazardous drinkers:** *d: 0.38; 95% CI: -0.31-1.08* **Drinks consumed:** *d: 0.88; 95% CI: 0.18-1.57*	**Length of hospital stay:** *d: 0; 95% CI: -0.61-0.61* **Mortality:** *d: 0.38; 95% CI: -0.99-1.75* **Total complications:** *d: 0.99; 95% CI: 0.24-1.74*	-
Tønnesen and others (2002)	**Baseline** **Follow-up:** 1 and 3 months post-surgery	**Baseline and 1-month post-surgery:** Number of non-hazardous drinkers Number of alcoholic drinks consumed a week **Baseline and 3 months post-surgery:** Number of alcoholic drinks consumed a week	**1-month post-surgery:** Length of hospital stay Mortality Total complications	-	**Recruitment:** Duration of recruitment unspecified. 1.5% of those approached were included **Retention:** 4 of the CG, 5 of the IG dropped out	**Number of non-hazardous drinkers:** *d: 1.61; 95% CI: -0.04-3.26* **Drinks consumed (1 month):** *d: 0.78; 95% CI: 0.01-1.55* **Drinks consumed (3 months):** *d: 0.65; 95% CI: -0.11-1.41*	**Length of hospital stay:** *d: 0; -0.74-0.74* **Mortality:** *d: 0.72; 95% CI: -1.09-2.54* **Total complications:** *d: 0.64; 95% CI: -0.23-1.51*	-

Weinrieb and others (2011)	**Baseline Follow-up:** 12, 24, 48, 72, 96 weeks pre-surgery (maximum 108 weeks). Alcohol outcomes reported across all time points (up-to 108 weeks post-randomisation, pre-surgery)	**All time points:** Number of drinks consumed Number of drinking days Number of drinks per drinking day Number of patients who drank before surgery Number of illicit substance users (data between groups reported at follow-up only)	**All time points:** Stages of change scores (SOCRATES), domains of: '*ambivalence*', '*recognition*', and '*regarding taking steps'*	**All time points:** Health-related quality of life (MOS-SF 12) Depression and anxiety (BDI/BAI)	**Recruitment:** Duration of recruitment unspecified. All potential liver transplant candidates screened **Retention:** 66/91 dropped out up to the final follow-up (comparable drop out between groups at each time point)	**Total drinks consumed:** *d: 1.81; 95% CI: 0.64-2.98* **Number of drinking days:** *d: 1.73; 95% CI: 0.58-2.89* **Drinks per drinking day:** *d: 1.17; 95% CI: 0.10-2.24* **Number who drank before surgery:** *d: -0.05; 95% CI: -0.57-0.47* **Number of illicit substance users:** *d: -0.16; 95% CI: -1.02-0.7* **SOCRATES**:** IG had a significant decrease in *ambivalence* and *recognition* scores across time, versus CG. *Regarding taking steps* did not change over time	-	**MOS-SF 12**:** *No significant differences* **BDI/BAI**:** *Very little between-group differences*

Wyman and others (2014)	**Baseline** (at surgical preassessment) **Follow-up:** approximately 3 months post-surgery (82.75 days on average [range 14-308 days] via telephone) (Post-discharge (via patient chart review)	**Baseline:** Questionnaire items (i. illicit substance use in the past 6 months, ii. the past year) AUDIT-C Follow-up (IG only): Items: use of illicit substances/ non-prescribed pharmaceuticals in the past 6 months AUDIT-C Post-discharge: Number of patients screened positive for illicit substances (day of surgery)	**Post-discharge:** Postponement/ cancellation of surgery ICU admissions Total complications	**Follow-up:** Patient satisfaction (questionnaire)	**Recruitment:** Over 2.5 years. 56 of the CG, 105 of IG underwent surgery – thus were eligible for analysis **Retention:** Only IG followed up (18.1% dropped out)	**Illicit substance use:** *d: 1.43; 95% CI: 0.95-1.91* **AUDIT-C:** *d: 1.14; 95% CI: 0.87-1.41* **Positive for illicit substances:** *d: 0.17; 95% CI:0.21-0.55 -*	**Postponement/cancellation of surgery:** *d: 0.22; 95% CI: -0.08-0.52* **ICU admissions:** *d: -0.04; 95% CI: -1.37-1.30* **Total complications:** *d: 0.01; 95% CI: -0.41-0.42*	**Patient satisfaction:** *High*

Notes. AUDIT-C, Alcohol use disorder identification test (consumption); BAI, Beck's anxiety inventory; BDI, Beck's depression inventory; BMI, Body mass index; CG, Control group; DSM, Diagnostic and statistical manual of mental disorders; DSOS, disease-specific outcome score (functional ability questions relating to issues such as walking distance and ability); EUROQUOL 5D (a measure of quality of life); GP, General practitioner; HADS, Hospital anxiety and depression scale; ICU, Intensive care unit; IG, Intervention group; MOS-SF 12, Medical outcome study short form (12 items; a measure of health-related quality of life); SF-36, Short form health survey (a measure of health status); SOCRATES, Stages of change readiness and treatment eagerness scale (a measure of motivation to receive alcohol treatment).* Unintentional patient pathways defined as: '*a path by which the patient did not reach the discharge criteria within five days (minor complications), or had any postoperative complication within three months (major complications) leading to a non-planned inpatient visit, was readmitted within three months irrespective of cause, or died within three months postoperatively irrespective of cause*.'** Effect size could not be calculated.

5.3.2 Risk-of-Bias

Judgments can be seen in *Figure 5.2*.

Random sequence generation. Four studies (Ashton et al., 2013; Hansen et al., 2012; Shourie et al., 2006; Wyman et al., 2014) were deemed at high risk of bias as they did not use randomised designs. Three randomised studies (Kummel et al., 2008; McHugh et al., 2001; Weinrieb et al., 2011) were at an unclear risk as they did not report how the randomisation sequence was generated.

Allocation concealment (selection bias). All apart from two studies (Tønnesen et al., 1999; 2002) were deemed at high risk as they did not conceal allocations.

Blinding of patients and personnel (performance bias). All studies were deemed at high risk of bias. Given the nature of the interventions (all requiring some degree of face-to-face contact), blinding was not achievable.

Blinding of outcome assessment (detection bias). All did not report whether they (at minimum) blinded data analysts, all were deemed high risk.

Incomplete outcome data (attrition bias). One study (Kummel et al., 2008) was deemed as high risk because no reasons for drop-outs were reported, the authors did not mention how many dropped out between groups, and when the authors compared drop-outs and non-drop-outs there were significant differences in certain variables (e.g., females' ages).

Selective reporting (reporting bias). All studies were stringently judged to be at high risk for selective reporting. We made this decision on the basis that no pre-registered protocol for any of the included studies could be found, thus there was a chance that authors could have consciously or unconsciously omitted any results inconsistent with their hypotheses. To locate pre-registered studies, each study article was checked for a passing reference or citation to a protocol, and the reviewers also noted any protocols found in the database and hand searches

Other bias. Six studies (Wyman et al., 2014; Weinrieb et al., 2011; Kummel et al., 2008; Tønnesen et al., 1999; 2002; Shourie et al., 2006) were deemed at an unclear risk of bias due to recruited patient demographics. The decision of unclear was made on the basis that it was unclear whether or how the particular variables could bias the results. Five studies (Wyman et al., 2014; Weinrieb et al., 2011; Tønnesen et al., 1999; 2002; Shourie et al., 2006) had a large gender bias towards males, and one study (Kummel et al., 2008) only recruited patients above 65 years-old.

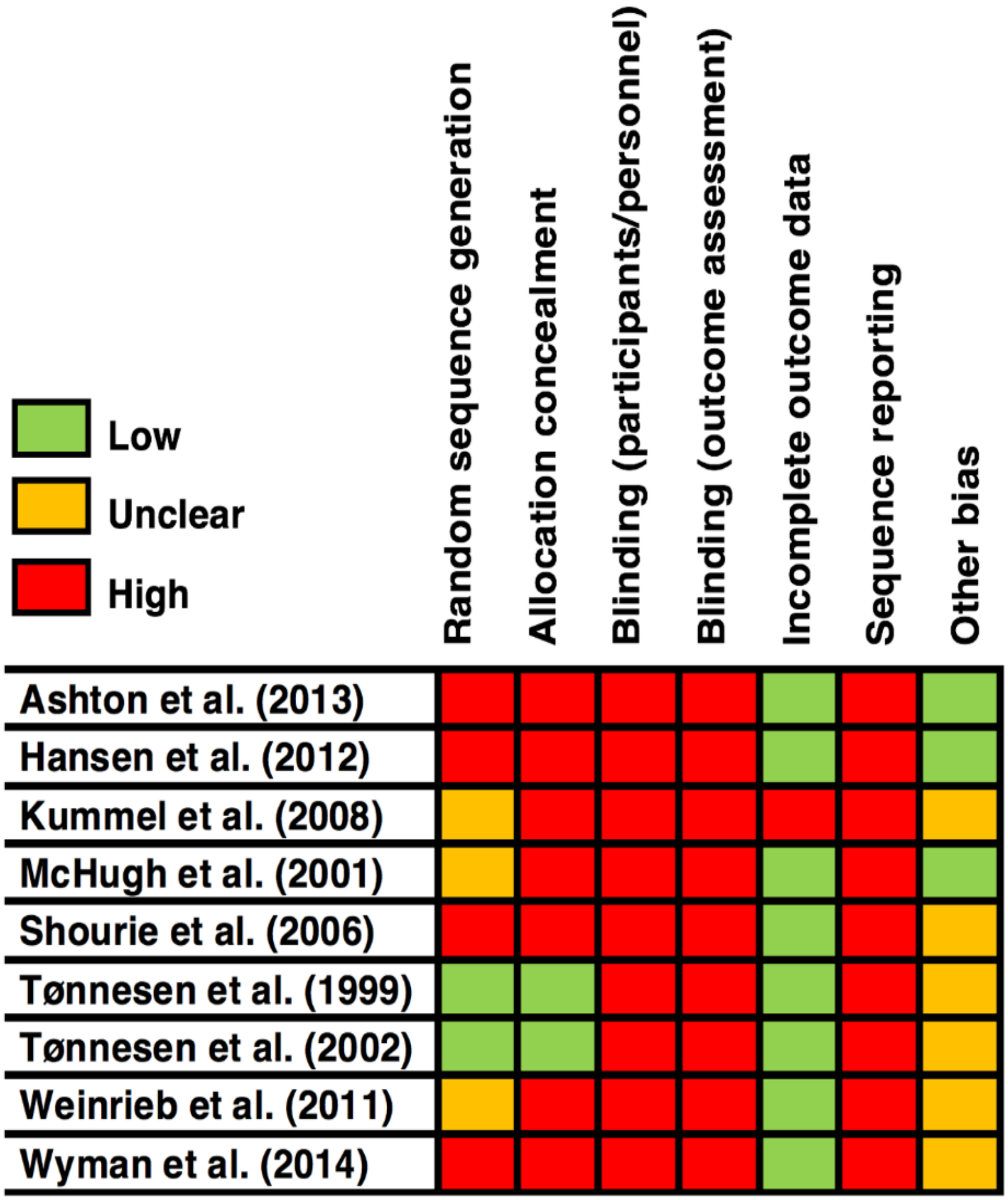

Figure 5.2. Risk-of-Bias Judgments.

5.3.3 Primary and Secondary Outcomes

Effect sizes across individual study outcomes are reported in Table 5.2.

Alcohol Use.

Individual study results (seven studies).

1. Wyman et al. (2014): Large and significant reduction in alcohol use disorder scores pre- to post-intervention (in the IG only). In addition, 73.8% of the IG stated that they reduced or stopped alcohol use before surgery and 64.8% up-to follow-up. Though 9.1% and 17% reported no change in their alcohol use before surgery and up-to follow-up. Zero percent of participants said they would stop using alcohol in the next six months, but 18.8% said they would reduce their use. In contrast, 5.9% said they would increase use, and 24% continue to use the same amount. Many participants reported that the questions were not applicable to them.
2. Kummel et al. (2008): Small beneficial effect for the IG over CG at three months, but benefits for the CG over IG at six, and 12 months, with an overall small and non-significant effect size favouring controls – in relation to the between groups proportion of patients reporting zero alcohol use, versus use more than once a week.
3. McHugh et al. (2001): Non-significant, but medium-sized reduction in grammes per week of alcohol consumed in the IG versus CG from baseline to 15-month follow-up.
4. Shourie et al. (2006): Medium-sized but non-significant reduction in alcohol use disorder scores in the IG over CG from baseline to six-

month follow-up. Small and non-significant reduction in grammes of alcohol consumed per day in the CG over IG from baseline to follow-up. Non-significantly fewer alcohol-dependent diagnosed CG patients between groups at follow-up, with a small effect.

5. Tønnesen et al. (1999): Non-significantly more non-hazardous alcohol users in the IG versus CG at one-month follow-up (medium effect). Significantly fewer alcohol drinks consumed weekly in the IG versus CG at follow-up, with a large effect.
6. Tønnesen et al. (2002): Very large and marginally significant benefit for the IG over CG in regard to non-hazardous drinking at one-month follow-up. Significantly fewer grammes per week of alcohol consumed in the IG versus CG at follow-up, with a large effect - but not at three-month follow-up, though the effect was moderately large.
7. Weinrieb et al. (2011): Up-to 108 weeks post-randomisation the IG consumed significantly fewer drinks, had significantly fewer drinking days and consumed significantly fewer drinks per drinking day versus the CG, all with very large effect sizes (but with wide confidence intervals). Fewer patients in the CG drank before surgery versus the IG, though the effect was small and non-significant.

Meta-analysis. A pooled analysis including all six studies (Weinrieb et al., 2011; Tønnesen et al., 1999; 2002; Shourie et al., 2006; McHugh et al., 2001; Kummel et al., 2008) with between-groups alcohol outcomes significantly favoured IGs, with a small to medium effect size (d: 0.34; 95% CI: 0.05-0.64; p = .02). There was significant heterogeneity (I^2 = 66%; Q(5) = 14.7, p = .01).

Separate pooled analyses were conducted for four trials using behavioural interventions (Weinrieb et al., 2011; Shourie et al., 2006; McHugh et al., 2001; Kummel et al., 2008), and the two trials (Tønnesen et al., 1999; 2002) using disulfiram (as reported previously in Oppedal et al., 2012). Because two (McHugh et al., 2001; Kummel et al., 2008) of the behavioural-interventions did not have alcohol use related inclusion criteria and targeted multiple health behaviours, it was decided to conduct a pooled analysis without these studies also.

Across behavioural intervention trials there was a very small, non-significant effect on alcohol consumption (*d*: 0.14; 95% CI: -0.13-0.41; $p = .30$; $I^2 = 45\%$; $Q(3) = 5.5$, $p = .14$). In the two behavioural trials with alcohol-related inclusion criteria there was a medium-sized, but again, non-significant effect (*d*: 0.45; 95% CI: -0.49-1.39; $p = .94$; $I^2 = 70\%$; $Q(1) = 3.3$, $p = .07$). In the two disulfiram trials there was a large significant effect (*d*: 0.71; 95% CI: 0.36-1.07; $p < .001$) with little heterogeneity ($I^2 = 0\%$; $Q(1) = 0.22$, $p = .64$).

Illicit Substance Use (ISU).

Individual study results (two studies). Only two studies considered ISU. One study (Wyman et al., 2014) explicitly aimed the intervention at illicit substance as well as alcohol use, another study (Weinrieb et al., 2011) assessed ISU in addition to alcohol use, but it was unclear whether this was an intervention target.

1. Wyman et al. (2014): Large and significant reduction in the number of patients reporting ISU in the last six months at follow-up (three-months post-surgery) versus baseline (IG only). Laboratory screening

on the day of surgery found fewer patients in the IG positive for ISU versus the CG (11 of the IG [105 patients], 5 controls [56 patients]), though the effect was small and non-significant.

2. Weinrieb et al. (2011): No significant difference between groups in regard to the number of patients using illicit substances post-baseline (four of the IG [46 patients] and three of the CG [45 patients]). There was a small effect favouring the CG.

Meta-analysis. After combining data from between-subjects outcomes in these two studies, the pooled effect size was small, non-significant and favoured the IG (d: 0.12; 95% CI: -0.24-0.47; p = .52; I^2 = 0%; $Q(1)$ = 0.47, p = .49).

Determinants of behaviour.

Individual study results (two studies). Two studies assessed determinants of perioperative substance use (see Table 5.2).

1. Ashton et al. (2013): Large pre-post intervention increases in patients' knowledge of the deleterious effects of substance use *per se*; the number of patients reporting that they were *not likely* to return to drinking post-surgery; the number of coping strategies patients could list to enable continuing abstinence; the number of patients citing health reasons as their primary motivation for abstinence.
2. Weinrieb et al. (2011): IG significantly decreased in *ambivalence* and *recognition* scores across time versus the CG – though, scores *regarding taking steps* did not show a change across time. All three determinants relate to the likelihood of engaging in and seeking out alcohol use treatment.

Perioperative complications.

Individual study results (five studies).

1. Tønnesen et al. (1999): Significantly more CG patients suffered any complication versus those in the IG up-to one month postoperatively, with a very large effect.
2. Tønnesen et al. (2002): Medium to large positive effect for the IG over CG in relation to total complications up-to one month postoperatively, but no significant difference between groups.
3. Wyman et al. (2014): No significant difference in total complications between-groups during their hospital stay. Non-significantly fewer cancellations or postponements in surgery in the IG versus CG (small effect). Non-significantly more perioperative ICU admissions in the IG versus CG (very small effect).
4. Hansen et al. (2012): No significant difference, but medium effect favouring the IG in total complications between-groups up-to three-month follow-up. Non-significantly fewer hospital readmissions in the IG versus CG up-to three-month follow-up with a small effect. Significantly more patients in the CG versus IG met hospital discharge criteria late (medium to large effect). Non-significantly more *unintended patient pathways* (see Table 5.2) in the CG versus IG, with a medium effect.
5. Shourie et al. (2006): Significantly higher total number of complications in the IG versus CG up-to five days postoperatively, with a medium effect. Non-significantly more hospital admissions in

the CG versus IG in the previous six months with a small to moderate effect (at six-month follow-up).

Meta-analysis. In a pooled analysis of all five studies assessing perioperative complications, there was a non-significant effect favouring IGs, with a small effect (*d*: 0.24; 95% CI: -0.26-0.73; $p = .35$). There was significant heterogeneity ($I^2 = 74\%$; $Q(4) = 12.3$, $p = .004$). In total there were sixty-two complications in the IGs (253 patients) and sixty-seven in the CGs (235 patients).

A pooled analysis excluding Hansen et al. (2012) was conducted for two reasons: i. the authors aimed to target several health behaviours as well as alcohol (confounding the potential beneficial effect of preoperative alcohol reduction), and ii. because the authors only recruited four participants they deemed hazardous alcohol users. The effect remained non-significant and small (*d*: 0.21; 95% CI: -0.40-0.82; $p=.50$; $I^2 = 78\%$; $Q(3) = 13.8$, $p = .003$).

Lastly, analyses were conducted separately (without Hansen et al., 2012) for the two behavioural-intervention controlled trials (Wyman et al., 2014; Shourie et al., 2006) and the two disulfiram-based randomised controlled trials (Tønnesen et al., 1999; 2002) (as reported previously in Oppedal et al., 2012). The latter found a large significant effect (*d*: 0.71; 95% CI: 0.36-1.07; $p < .001$; $I^2 = 0\%$; $Q(1) = 0.2$, $p = .64$), the former a small non-significant effect (*d*: -0.23; 95% CI: -0.71-0.24; $p=.33$; $I^2 = 61\%$; $Q(1) = 2.6$, $p = .11$).

Length of Hospital Stay.

Individual study results (four studies).

1. Tønnesen et al. (1999) and (2002): Zero difference in length of stay in

both studies.

2. Shourie et al. (2006): Non-significantly fewer days in the IG versus CG with a small effect (a mean reduction of one day).
3. Hansen et al. (2012): Significantly fewer days in the IG versus CG with a medium effect (a median reduction of one day).

Meta-Analysis. A pooled analysis of all four studies significantly favoured IGs, with a small effect size (d: 0.27; 95% CI: 0.04-0.5; p = .02). There was low heterogeneity (I^2 = 5%; $Q(3)$ = 3.2, p = .37).

Again, a pooled analysis was conducted without Hansen et al. (2012), this resulted in a small and non-significant effect (d: 0.12; 95% CI: -0.16-0.41; p = .41; I^2 = 0%; $Q(2)$ = 0.4, p = .82).

Mortality.

Individual study results (five studies).

1. Tønnesen et al. (1999): One death occurred in the IG, and two in the CG up-to one-month follow-up – a non-significant, medium effect favouring the IG.
2. Tønnesen et al. (2002): One death occurred in the total sample (CG) up-to one-month follow-up – a non-significant, medium to large effect favouring the IG.
3. Shourie et al. (2006): One death occurred in each group up-to five days post-surgery – a non-significant, small to medium effect favouring the CG.
4. Hansen et al. (2012): Zero deaths per group up-to three-month follow-up.

5. Rideout, Lindsay & Godwin (2011): Up-to 12 years post-randomisation in McHugh et al. (2001), there were 15 (50 patients) and 26 (60 patients) deaths in the IG and CG respectively – a non-significant, small effect favouring the IG (likely due to general, not perioperative benefits of alcohol use reduction).

Meta-Analysis. When considering perioperative mortality post-surgery (three studies targeting alcohol use only: Tønnesen et al., 1999; 2002; Shourie et al., 2006) the effect size was small and non-significant (*d*: 0.21; 95% CI: -0.69-1.10; $p = .65$) with little heterogeneity ($I^2 = 0\%$; $Q(2) = 0.96$, $p = .62$). Across the three studies, there were two deaths in the IGs (126 patients), and in the CGs four (79 patients). An additional study was not included in this analysis as zero deaths were reported in either group up to three months post-surgery (Hansen et al., 2012).

The two disulfiram trials were pooled in a separate analysis. Again, as reported previously in Oppedal et al. (2012), there was a non-significant, moderately large benefit for IG patients with low heterogeneity (*d*: 0.51; 95% CI: -0.59-1.60; $p = .36$; $I^2 = 0\%$; $Q(1) = 0.1$, $p = .77$). There were three deaths in the CGs (34 patients) and one death in the IGs (35 patients) up to one-month post-surgery.

Health Status/Health-Related Quality of Life.

Individual study results (five studies). Five studies (Weinrieb et al., 2011; McHugh et al., 2001; Kummel et al., 2008; Shourie et al., 2006; Hansen et al., 2012) assessed general health-related outcomes.

1. Hansen et al. (2012): Small non-significant improvement in health-

related quality of life in the IG versus CG from baseline to three-month follow-up. Likewise for disease-specific outcome scores.

2. McHugh et al. (2001): Average effect size across health-related domains significantly much improved in the IG over CG from baseline to 15-month follow-up. Large and significant benefit for the IG in terms of both depression and anxiety scores from baseline to follow-up. A range of physical outcomes was improved in the IG versus CG, including BMI, and blood pressure from baseline to follow-up.
3. Shourie et al. (2006): Small, non-significant benefits for the IG in regard to the number of GP visits, and number of days off work sick in the last six months, at six-month follow-up.
4. Weinrieb et al. (2011): The authors report that there were no significant differences across all time points for both groups in relation to health-related quality of life and very little difference in regard to depression and anxiety. Effect sizes could not be calculated.
5. Kummel et al. (2008): Average effect size for symptoms of angina pectoris (not at all versus at least once daily) across all time points was very small and non-significantly favoured the CG. Across all time points, the IG reported significantly, but moderately, better functional abilities versus controls.

Patient Satisfaction.

Individual study results (three studies). Of three studies (McHugh et al., 2001; Ashton et al., 2012; Wyman et al., 2014) assessing patient satisfaction, all reported high satisfaction with the respective interventions.

5.4 Discussion

The present review identified a small number of low-powered, high risk of bias and demographically and methodologically heterogeneous studies. Based on current evidence it cannot be concluded that interventions may be delivered prior to patients' surgery to reduce illicit substance use, and certainly no one intervention strategy can be recommended. Across individual studies, there was some evidence that interventions can be delivered from pre- to post-surgery to reduce alcohol consumption, though two very small trials using disulfiram (Tønnesen et al., 1999; 2002) were far superior to trials of behavioural strategies alone. While meta-analyses revealed small effects on alcohol consumption, there was no evidence that preoperative interventions for alcohol or ISU could reduce the incidence of perioperative complications overall, though again, Tønnesen et al. (1999; 2002) bucked this trend. Lastly, there were no clear effects of interventions on mortality and length of hospital stay in studies solely targeting alcohol use.

A major finding of this review was the lack of studies investigating interventions for preoperative ISU, despite evidence that ISU can impact on surgical outcomes. Wyman et al. (2014) targeted ISU (in addition to alcohol use), and Weinrieb et al. (2011) assessed ISU, but it was unclear whether ISU was targeted. While the former found that IG patients were less likely to report using an illicit substance at follow-up versus baseline (with a very large effect), the absence of controls obfuscates any causal relation the intervention may have had on ISU. Furthermore, responses were susceptible to social desirability biases given that a non-validated, non-blinded self-report measure was used –

clearly evidenced by the fact that whilst the study did find that more controls were positive for ISU via objective screening on the day of surgery, the effect was very small. In this study, over 40% of patients had previously entered substance use treatment, suggesting that patients were either current or previously dependent illicit substance users. ISU dependency is notoriously difficult to treat, especially in the case of opiates – speculatively, this short, one session intervention may have been more effective with more casual users. More intensive strategies may be necessary for those with dependency. Again, while Weinrieb et al. (2011) found that controls were less likely than intervention patients to be positive for ISU, baseline ISU data was absent from the final publication and could not be retrieved after correspondence with the authors. Given that the study primarily aimed to reduce alcohol use this is unsurprising. Pooling both studies' between-group outcomes found a small and non-significant benefit for the IGs, but more evidence is needed to form substantial conclusions regarding the efficacy of ISU targeted interventions.

While there is more evidence to suggest interventions can be delivered to reduce preoperative alcohol versus ISU, the evidence is still not strong. A pooled analysis of all six studies investigating this outcome has a small and significant effect, though the confidence intervals were wide and studies heterogeneous. Behavioural interventions showed to be largely ineffective on the whole. Two behavioural intervention trials (Shourie et al., 2006; Weinrieb et al., 2011) which included risky alcohol users fared better, but this was to be expected given that these interventions had primary a focus on alcohol use as opposed to multiple behaviours (indicating that more intervention components and time were focused on one behaviour). Disulfiram trials (Tønnesen et al., 1999; 2002) were by far the most effective – both achieving complete abstinence prior to surgery and benefits up to one-month post-surgery. However, these trials were both small, and given dangerous side effects (e.g., neurotoxicity) and generally low compliance (e.g., Fuller et al., 1986; Kalra, De Sousa & Shrivastava, 2014; Pettinati et al., 2008), disulfiram is a medication to be used with caution and only in a small population of highly motivated, alcohol-dependent patients.

As there were no significant overall effects on perioperative complications, mortality and length of hospital stay, this may be explained by intervention timing. Some studies neglected to report the time from intervention to surgery, thus interventions may have been delivered so close to surgery that any beneficial effects could not have time to materialise. Furthermore, acute cessation in risky alcohol users may incur withdrawal symptoms, leading to counterproductive effects. In support, Shourie et al. (2006), who did report time to surgery, and included risky alcohol users only, found significantly more complications in the IG but had only a minimum of one week from intervention to surgery. While two trials of disulfiram (Tønnesen et al., 1999; 2002) appeared superior to two behavioural trials for perioperative complications, this may be explained by the length of follow-up. While Tønnesen et al. (1999; 2002) assessed between group complications up to one-month post-surgery, Wyman et al. (2014) and Shourie et al. (2006) only assessed intraoperative and immediate post-surgical complications. It is well known that many complications may only emerge in the postoperative recovery period (e.g., Woodfield et al., 2016), thus these studies may have missed any between-group differences in recovery. Lack of complications in the immediate postoperative period may also explain the lack of differences in length of hospital stay across all studies – and as is likely in the case of mortality, may be a result of small sample sizes, and thus lack of power. Lastly, the fact that the disulfiram trials both achieved complete preoperative abstinence (as opposed to moderate reductions in alcohol use in both behavioural trials) more than likely had beneficial implications for surgical complications.

One study (Ashton et al., 2013) showed that an intervention could boost patients' intentions to reduce alcohol-use post-surgery, increase their knowledge of the harms of perioperative substance use, and increase the number of coping strategies – to aid perioperative cessation - patients could list. Though it is unclear whether this influenced their actual behaviour, medium to large effects on intentions may lead to small to medium effects on behaviour (Gollwitzer & Sheeran, 2006). Increased knowledge of harm *may* be associated with lower alcohol consumption also (e.g., Thadani, Huchting & LaBrie, 2009). Another study showed some beneficial intervention effects on stages of change scores. This is a positive finding as motivation to reduce alcohol use is a predictor of an actual reduction in alcohol use (e.g., Kohler & Hofmann, 2015). There were several methodological issues with these studies, however, as both studies were generally at high risk-of-bias.

There were some positive intervention effects regarding other outcomes, for instance, McHugh et al. (2001) found intervention benefits for BMI/cholesterol and general health. Though all positive results outlined in subsection 5.2.3: *Health Status/Health-Related Quality of Life* may be confounded by targeting of multiple health behaviours, another, exclusively alcohol-focussed study (Weinrieb et al., 2011), found intervention benefits for outcomes relating to general health.

All interventions that assessed patient satisfaction reported high levels. Patients, therefore, may be receptive to behaviour change in the perioperative period. This may have positive implications for patient retention within trials and may foster patient acceptability and motivation. However, almost uniformly high patient satisfaction may highlight another issue; those recruited may represent only those most motivated, and thus intervention efficacy may be artificially inflated (a small indicator of this may be low motivation observed in Study 2 subsection 4.4.3). Indeed, it took many studies over a year to recruit their participants, and those agreeing may have been only those most receptive to intervention. This is highlighted by an incredibly small proportion (1.5%) of those approached being recruited in Tønnesen et al. (2002). Recruitment is clearly a challenge in this area, with a relatively small total *n* of 903 across nine trials.

The relative efficacy of interventions on preoperative versus postoperative alcohol use (or ISU) use could not be established - an important distinction, as complications such as prolonged bleeding time, may be reversed by a preoperative alcohol abstinence period of four weeks. Just one study (Weinrieb et al., 2011) assessed preoperative alcohol use (apart from the two studies achieving complete abstinence: Tønnesen et al., 1999; 2002) but did not assess complications – so the causal relation between preoperative reduction or abstinence and complications could not be delineated. As few studies were identified, meta-regression analyses aiming to assess whether retrospectively identified BCTs could predict intervention efficacy could not be performed.

Across studies, no pre-published study protocols were found, thus there was a risk of selective reporting; just five studies were randomised, though just two (Tønnesen et al., 1999; 2002) reported the method of sequence generation; no studies were blinded in any way; and just two studies (again, Tønnesen et al., 1999; 2002) concealed allocations. Many studies had a large bias towards male patients (though this may reflect a higher hazardous use prevalence amongst males; e.g., Chapter 4), and one study (Kummel et al., 2008) included patients over 65 only. Such biases may have influenced the effect sizes across studies, so must be considered when interpreting the results. Additionally, different surgical populations have different prevalence rates of substance use and different underlying conditions and procedures naturally lead to different complication rates. Readers should be mindful that the type of surgery may have impacted on both substance use cessation rates and the number of complications suffered.

There were a number of other potential moderators such as length of follow-up, and patient demographic variables (e.g., comorbidities). If more studies were available, subgroup analyses would have been useful to investigate these. Publication bias might account for some of the observed effects also. The number of studies located was not sufficient to conduct a formal analysis of this phenomenon.

For behavioural interventions, just one study (Shourie et al., 2006) cited a replicable intervention protocol. For most studies, it was not explicit what intervention techniques were used. Therefore, accurately replicating successful interventions is difficult for future researchers. In this review, behaviour change techniques (BCTs) were retrospectively identified – providing a non-comprehensive indication of the techniques used, but the above issues made the process difficult. Future studies should aim to characterise BCTs, or at minimum, cite - or describe in sufficient detail - intervention protocols. Further, it is not clear whether any studies undertook appropriate elicitation research – that is, systematically identified salient, population-specific behavioural determinants. This is a vital component of intervention development, ensuring that intervention techniques are aimed at appropriate targets and allowing researchers to link interventions with behaviour change theory (identifying interventions' *mechanisms of action*). Numerous guidelines exist (e.g., Michie et al., 2011) for this process and researchers should be mindful of these conventions.

Future studies should consider solely targeting alcohol or illicit substance use, so that any confounding influence of changing other behaviours on perioperative outcomes is minimised. Researchers should also consider intervening on *specific* illicit substances (an intervention may be useful at reducing cannabis, but not heroin use). Researchers should aim to measure behaviour both preoperatively and postoperatively, to i. assess whether interventions can have differential effects between time periods, and ii. assess the causal relation between a preoperative reduction in substance use and perioperative outcomes. The number and length of intervention sessions, and the time from intervention to surgery should be reported also, as these may be key moderators of intervention efficacy. Researchers may also explore whether intervention efficacy is moderated by patients' surgical procedure, and the frequency and/or extent of patients' alcohol or ISU. This may be achieved by having inclusion criteria that limits the sample to those undergoing specific surgeries, and those having varying levels of substance use.

The choice of outcome measures across studies was heterogeneous. It would be useful for researchers to standardise measures, easing comparisons between studies. Standardisation may be achieved by developing a substance-use specific core outcome set (see the COMET initiative; Prinsen et al., 2014), alongside the current set for postoperative complications generally (Jammer et al., 2015). It would also be beneficial to include more patient-centered outcomes such as return to work, functioning and quality of life. Similarly, objective measures for substance use are needed (e.g., urine and breath tests) to reduce recall and social desirability biases.

Future studies should aim to minimise risk-of-bias and improve on their designs. Though blinding is difficult with behavioural interventions, blinding of assessors could be achieved. Additionally, future studies should use randomised designs with appropriate controls, report their random sequence-generation method and pre-publish their protocols. Future studies should provide formal power calculations to estimate required sample sizes before recruitment, and therefore employ larger sample sizes to identify between-group differences in somewhat rare surgical complications. Studies should recruit more representative samples, including a wider range of patient ages, ethnicities and an equal distribution of both sexes.

Despite limitations, we have identified important gaps in the evidence base such as the small number of trials attempting to reduce ISU. Given the efficacy of the two small disulfiram trials, prescribing this pharmaceutical may be useful for a small subset of patients with alcohol dependency, though it may only be appropriate for patients most at risk (e.g., Kalra et al., 2014). For non-dependent heavy alcohol users, the best strategy has yet to be identified – though motivational strategies, and strategies targeted specifically at alcohol use, show mixed efficacy. Future studies would benefit from higher quality designs and more standardisation in measures and inclusion criteria across the field. In the case of behavioural interventions, more intervention development work may be necessary. As more robust evidence accumulates more evidence-based conclusions and implications for practice may be made.

5.5 Key Findings: Study 4

- Only nine trials were identified, where only three targeted preoperative alcohol use specifically and zero targeted illicit substance use specifically.
- There was some weak evidence that interventions could be delivered to reduce postoperative alcohol use, though only three studies assessed *preoperative* alcohol use.
- There was no robust evidence that illicit substance use could be modified.
- Two trials using disulfiram had a large effect on alcohol use; both achieving complete preoperative abstinence in two (very small) samples of alcohol-dependent patients.
- While behavioural trials were largely ineffective, no study aimed to target identified determinants of substance use specific to the perioperative context.
- Studies were generally heterogeneous with small samples and a high risk of bias. Studies did not report intervention behaviour change techniques.

CHAPTER 6. ASSESSING A BRIEF COM-B BASED INSTRUMENT FOR IDENTIFYING AND TARGETING DETERMINANTS OF PREOPERATIVE ALCOHOL USE: A CROSS-SECTIONAL ANALYSIS (STUDY 5)

6.1 Introduction

6.1.1 Background

In Chapter 5, a systematic review found that behavioural-only interventions (i.e., those not using disulfiram) were ineffective at reducing preoperative alcohol use and just one trial explicitly *targeted* illicit substance use. Given the relatively low prevalence rate of illicit substance users in the preoperative patient population (Chapter 4), a lack of trials is understandable; recruiting a sufficient number of patients may be an arduous and protracted process. For alcohol interventions, however, there may be several explanations for their lack of efficacy (e.g., intervention timing, frequency, modality), though one – the basis for the selected intervention strategies, may be central.

In Chapter 5, it was identified that no trial had conducted (or referred to) research aiming to assess determinants of *preoperative* alcohol use. Studies largely picked generalised motivational interviewing type interventions *off the shelf* or chose intervention targets - and techniques to modify them - using intuition not evidence. Even then, only one study (Shourie et al., 2006) cited an intervention protocol that could be readily and accurately translated into routine practice (should the intervention be successful). A less scattergun and more precision-based approach would be to determine exactly what barriers prevent a patient from reducing their preoperative alcohol use, and what facilitators best promote cessation and/or reduction. In short, studies need to identify relevant behavioural determinants, and the techniques that best alter them, as well as to carefully document the intervention development process so future researchers can *stand on the shoulders of* successful interventions and modify or indeed avoid those with lesser efficacy.

Health behaviour change theories provide a systematic way of understanding changes in behaviours. The absence of theory in the development of previous interventions for preoperative alcohol use is unsurprising, given that "*formal tests* [aiming to determine the prevalence of theory use] *suggest that between 36-89% of all health interventions are not explicitly based on theory*" (see Prestwich, Webb & Conner, 2015, p. 1; Mama et al., 2015; Quirk, Blake, Tennyson & Randell, 2014). These theories (of which there are a multitude; Michie, West, Campbell, Brown & Gainforth, 2014) each suggest a finite number of non-contextual, cross-behavioural determinants and explain testable, hypothesized relationship between them. For example, the Theory of Planned Behaviour (Azjen, 1991) suggests that intentions to perform a behaviour are the most proximal determinant of that behaviour, which is in turn shaped by an individual's attitude to the behaviour, perceived control over the behaviour and perception regarding the normative pressures of enacting or reducing a behaviour.

It is easy therefore to see the utility of such theories as a basis for intervention development; researchers could determine which model-specific constructs a behaviour is most associated with (e.g., experimentally, observationally or through qualitative research) and target them as appropriate (e.g., using behaviour change techniques identified as successful at modifying the construct previously). Further, just as a biochemist could explain the molecular structure and biological mechanism of a particular pharmaceutical intervention, using behaviour change theories allows behavioural researchers to structure, identify and measure (e.g., through questionnaires and mediation analyses) the mechanism of their interventions too – providing a window into the black box of behavioural intervention appraisal; indeed, understanding mechanisms may help researchers understand why some interventions are superior, and others less so (Michie & Johnston, 2012). Given the above, using theories in the design of behavioural interventions has been recommended by the UK Medical Research Council (Moore et al., 2015).

Evidence from reviews of interventions has suggested a positive effect of utilising theory in their development. Webb et al. (2010) for example showed that, across 85 internet-based trials, interventions utilising theories were significantly more efficacious than those not-so. While conflicting evidence exists (see Prestwich et al., 2015[23]) it is undeniable that theories are powerful tools for guiding intervention development, and likely that (on balance) theory-based interventions may be more efficacious while also having other desirable properties (e.g., identification of intervention mechanisms).

Intervention design can be streamlined using intervention development frameworks. That is, systematic guidelines outlining a process and intermediaries between specifying a targeted behaviour to designing an intervention to target the behaviour. As Michie et al. (2011) suggest, however, many frameworks generally have a *lack of coherence*. For example, MINDSPACE (a governmental framework for the development of policies to change behaviour) conceives influences on behaviour as a jumble of modes of intervention delivery, mechanisms of action, psychological constructs and others. They also suggest that many frameworks lack *comprehensiveness* (i.e., they fail to be applicable to *every intervention that has or could be developed*) and a clear link to theory; with a conception of, and starting point focused on, the *nature of the behaviour*.

Regarding theory, it is important to note that an additional hurdle for their use in intervention development, is a reluctance to adapt theories to recent developments in the literature. If one rigidly adheres, for example, to the use of constructs suggested by the Theory of Planned Behaviour outlined above, then several other empirically demonstrated and potential determinants of behaviour may be ignored (for alcohol use e.g., associative learning and cue reactivity; Carter & Tiffany, 1999). A resolution to this issue comes in the form of integrative theories; syntheses of behaviour change theories aimed at uniting overlapping between-theory constructs and categorising different conceptions of essentially the same determinants into aggregate, internally consistent, and targetable constructs.

With all the above in mind, Michie et al. (2011) developed the Behaviour Change Wheel framework for intervention development. On the outer ring of this wheel lies seven *policy categories* – things that enable an intervention occurring, and the inner ring nine *intervention functions* - methods of addressing three essential and inter-dependent behavioural determinants residing at the hub of the wheel - *capability, opportunity* and *motivation* (the COM-B model; *Figure 2.2*). Within the behaviour change wheel framework, the COM-B model is the initial stage towards, and essential component to, understanding the nature of the behaviour to be changed.

The COM-B model has many advantages from a theoretical and pragmatic point of view. Capability can be further subdivided into psychological (uniting a swathe of interlinked determinants from a range of theories e.g., knowledge, cognitive skills, memory and decision processes) and physical capabilities (such as skills); opportunity can be divided into physical and social opportunities (covering determinants such as myriad forms of social influence, and deleterious or adaptive environmental conditions, on behaviour); and reflective and automatic motivation (covering everything from volitional determinants such as intentions and goals, to autonomic or unconscious determinants such as emotions and reinforcement). The model, therefore, provides an inclusive starting point for intervention development; allowing interventionists to determine *what* interventions may work in a highly flexible manner and a platform to investigate *how* they may work. It is important to note that while five subdomains of the COM-B are necessary for a behaviour to occur, Michie et al. (2011) suggest that reflective motivation may be relevant, but not essential. This makes sense conceptually; if someone has no means or capability to inhibit or enact a behaviour, it, by definition, cannot occur – though it could occur, theoretically, in the absence of planning or forethought.

Attesting to its utility, the COM-B model has been used to assess determinants of a variety of behaviours across a variety of contexts such as physical activity in schoolchildren (Taylor et al., 2016), physical activity in adults *per se* (Howlett et al., 2017), physical activity for sedentary black women with asthma (Nyenhuis & Sharp, 2017), implementation of health assessment for preschool children (Alexander, Brijnath & Mazza, 2014), promoting gas stove use in rural Guatemala (Thompson, Diaz-Atriga, Weinstein & Handley, 2018) , improving hearing-aid use in adult auditory rehabilitation (Barker, Akins & de Lusignan, 2016), and tailoring an IT-based health communication programme for postpartum Latina women with gestational diabetes (Handley et al., 2015).

While the COM-B has primarily been used to guide interview schedules and understand behaviours in a qualitative manner – questionnaires present a more efficient method of assessing determinants with larger samples. Two studies using the COM-B to develop questionnaires to assess physical activity have shown that COM-B questionnaires can be designed with high predictive validity (Howlett et al., 2017; Taylor et al., 2015) and other desirable psychometric properties. To date only one study has developed an alcohol-related COM-B questionnaire; used to assess the impact of the revised UK drinking guidelines on determinants of behaviour (Stevely et al., 2018). This study did not, however, conduct any formal psychometric analysis of their questionnaire or assess whether the questionnaire could predict alcohol use. It is therefore unclear whether changes in capability, opportunity and motivation led to any changes in alcohol use behaviour, and unclear whether the items represented, or consistently assessed, the constructs they were assumed to represent.

6.1.2 Study Overview and Aims

The present study had several aims. The first was to develop a COM-B based questionnaire to assess determinants of preoperative alcohol use in a sample of preoperative patients. Given that the prevalence of illicit substance users in the preoperative population is low (Chapter 4) it was deemed unfeasible to recruit sufficient participants, and more important to evaluate an alcohol-focused questionnaire (especially considering determinants may be substance-specific). The utility of a questionnaire to predict preoperative alcohol use is manifest; determinants most predictive of the behaviour may be used as targets in future interventions and given the atheoretical basis and poor efficacy of previous trials (Chapter 5), may improve their outcomes.

As well as being used to target the *population* of preoperative alcohol over-users, the questionnaire could also be used to tailor interventions to *individuals*. One example of this includes patients completing the questionnaire (self-administered, or interviewed) in a GP appointment, after which a GP may be able to identify determinants most salient for that individual – and deliver brief intervention based on them. Such a tailoring strategy may be more efficient and is by nature more structured (thus freeing up cognitive resources for staff, increasing intervention standardisation, and saving valuable time) than *ad-hoc* alcohol use-related questioning (which may miss many important determinants). Tailored interventions have been shown to be beneficial previously (e.g., Baker et al., 2015; Schulz et al., 2013).

Other aims of the study were to determine the internal consistency and facets of the validity of the questionnaire; for the questionnaire to be useful for its intended purpose, it must be measuring what it intends and do so in a consistent manner. A suitable measure should predict or at least be associated with, the behaviour it is aiming to assess (criterion validity). Similarly, to reduce redundancy and increase precision, it is useful to determine whether different facets of a questionnaire are uniquely associated with the behaviour; for example, it would be vital to assess psychological capability in future if it highly and significantly predicted behaviour after controlling for all other COM-B subdomains; if it did not, it may be less necessary (incremental validity). It is also important to establish whether items assessing a construct (e.g., capability) share variance, and thus assess the same *latent* variable (convergent validity) and whether constructs are distinct enough to tap into unique phenomena (discriminant validity).

Lastly, to provide insight into patient preferences regarding potential interventions (and thus providing some useful information for future trials) patients were asked to rate potential intervention modalities and deliverers used in previous behavioural interventions (e.g., Wyman et al., 2014; Ashton et al., 2013; Shourie et al., 2006).

The study was conducted mindful that a much larger confirmatory sample would be necessary in the future. An initial piloting of the questionnaire has the benefit of identifying any potential problems that may arise should a larger study be conducted in the future. Halting a large study due to unforeseen issues (e.g., patients not understanding a particular item) would be expensive, a waste of time and thus has the potential to be unethical (e.g., wasting taxpayers' money).

6.1.3 Objectives

1. To develop a short COM-B model-based questionnaire to assess determinants of preoperative alcohol use reduction.
2. To administer the questionnaire to a sample of preoperative patients,

before conducting preliminary construct validity and internal consistency analyses.

3. To assess whether scores on the questionnaire show concurrent validity (correlate with measures of preoperative alcohol use) and incremental validity (whether each COM-B domain explains unique variance in measures of preoperative alcohol use when controlling for the others).
4. To assess whether a COM-B questionnaire can differentiate preoperative AUDIT-C (Alcohol Use Disorder Identification Test-Consumption [AUDIT-C]) hazardous versus non-hazardous scorers (assessing its utility in relation to an established cut-off).
5. Explore patient preferences regarding intervention characteristics in terms of the deliverer and the format.

6.2 Method

6.2.1 Study Design

The study was cross-sectional. The study took place from July 2017 to December 2018. Original ethical approval was obtained by the NHS health research authority East Midlands (Derby) research ethics committee (REC reference: 17/em/0007).

6.2.2 Questionnaire Design

COM-B items. Mindful that any questionnaire used in a healthcare context (e.g., preoperative assessment, during a GP appointment) would have to be quick to complete, questionnaire design was a balance between having sufficient items to represent multiple elements of the COM-B subdomains and keeping the questionnaire short. An initial 28 items were created by the author of this thesis; 10 each for capability and opportunity, and eight for motivation (fewer items here in line with the idea that capability and opportunity may be more important initially; Michie et al., 2011). Items used in other studies (e.g., Huijg et al., 2014) and recommendations found in the Behaviour Change Wheel manual (Michie, Atkins & West, 2014) were adapted for use here. The items were categorised via constructs on the Theoretical Domains Framework (TDF; Cane, O'Connor & Michie, 2012), mapped onto COM-B domains (which is consistent with the general COM-B, or behaviour change wheel framework of intervention design). The benefit of this was being able to identify several ways in which the subdomains of the COM-B could be represented (e.g., specifying items reflecting behavioural regulation and cognitive/interpersonal skills when determining constituent items of psychological capability). From here, the number of items was reduced to a select few felt to best encompass the subdomains of the COM-B. This was achieved through numerous debates and correspondence within the research team (consisting of experts in behaviour change). At the end of this process, a total of three items per COM-B subdomain was chosen, thus the total number of items was 18 (Appendix H).

After initial development, and after many rephrasing of items (to ease legibility), the questionnaire was tested on a set of patients for feedback (e.g., on readability, time to complete etc.). Eleven pilot patients were recruited from a preoperative assessment clinic in the same manner as the main sample (see below). In line with the principles of cognitive pretesting (see Lenzner, Neuert & Otto, 2016), these patients were asked to complete the questionnaire and 'think aloud’, before the questionnaire items were discussed in detail. Relevant feedback was noted by the researcher. Patients were positive with their feedback, though, following their advice, the font was made larger and sections were restricted from overlapping between pages. Patients made no comments that suggested the items needed to be altered and they all understood the nature of each item.

The research team agreed that the questionnaire had high face validity. Items asked about drinking alcohol between questionnaire completion and the day of their operation and closely reflected the underlying component of COM-B and its sub-domains (e.g., *people I spend time with drink often [social opportunity]; I plan to drink less [reflective motivation]*). Participants were required to note their agreement with the statements on Likert-type scales from 1 (strongly disagree) to 7 (strongly agree). A total COM-B score could be derived by adding all item scores together (with higher scores representing a lower number of barriers), though summing the three items per subdomain allowed for subscales representing each specific subdomain, but also total capability (psychological + physical capability scores), opportunity (physical + social opportunity scores) and motivation (reflective and automatic motivation scores) scores. There was also an additional free text box where patients were prompted to write any comments about any other related thoughts and feelings. Items were presented in a truly random order (generated using random.org), and six items were reverse scored (to mitigate acquiescence bias).

Assessing patient preferences. To provide some insight into patients preferred preoperative intervention deliverers and formats, patients rated five potential formats and six potential delivers from 1 (wouldn't be at all helpful) to 7 (would be very helpful). The choice of which was based on deliverers and formats used previously for preoperative interventions in Chapter 5, as well as others common in the behavioural intervention literature. Format options included: one-to-one sessions, group sessions, a guided workbook, computer-based and a phone helpline. Deliverer options included: anyone trained in alcohol use counselling, surgery team members (e.g., an anaesthetist or surgeon), nurses, general practitioners, or self-guided (with materials e.g., online/a workbook). For both formats and deliverers, participants had a free text section where they could note any others that they thought may be useful and/or add further detail.

6.2.3 Alcohol Measures

As in Study 4, the 3-item Alcohol Use Disorder Identification Test (consumption; AUDIT-C) was used to assess preoperative alcohol consumption. In this study, the AUDIT-C was used both as a continuous (up to a total score of 12) and a categorical measure (scores five or above indicating hazardous alcohol use).

The alcohol subscale of the WHO ASSIST used in Study 4 was used as a second measure of alcohol use. Instead of solely focusing on current consumption patterns like the AUDIT-C, the ASSIST probes the respondent's self-perceived social, legal and health impacts of alcohol use on their life, as well as features of dependency such failing to control use.

6.2.4 Participants and Procedure

Inclusion/exclusion criteria. Patients were included if they were above the age of 18, had the capacity to consent and were scheduled to have any type of elective surgery (day case or inpatient). Patients were excluded if they could not speak English, did not drink any alcohol and if they did not consent to all elements of the study (e.g., researchers viewing their medical records).

Recruitment and procedure. A convenience sample of patients was recruited from a preoperative assessment clinic in a large inner-city hospital in Leeds, UK (Leeds General Infirmary). Patients were approached as they waited for their preoperative assessment and asked whether they would be interested in answering questions related to lifestyle factors prior to surgery. Interested patients were given a participant information sheet with the study information and were encouraged to ask questions. If patients wished to proceed with participation, they were then taken to an empty, distraction-free room within the clinic, where they signed consent and completed the above questionnaire and measures of alcohol use. Patients' age, gender and surgery details were extracted from their medical records. Patients' surgeries were categorised into specialities by two surgical research nurses.

6.2.5 Data Analysis

Confirmatory factor analysis (CFA) was used to assess the factor structure of the COM-B questionnaire. Main analyses were performed using R Studio (RStudio, 2017) and Jamovi (Jamovi Project, 2017). The third-party STATA package *coefplot* (StataCorp, 2013; Jann, 2014) was used to generate forest plots of regression coefficients. CFA was conducted using the *cfa* function within the Lavaan R package (Rosseel, 2012). Reliability analyses were performed using the reliability function within the *semTools* R package

(Jorgensen et al., 2018). CFA is a special case of structural equation modelling (SEM) and has several desirable properties (Joreskog, 1993; Mulaik, 1989), including the ability to test theoretical relations between hypothesized latent factors. Maximum likelihood estimators were used with inter-factor correlations allowed (factors fixed at 1 for identification[24]). Two models were assessed to determine whether constituent items of the questionnaire accurately represented COM-B domains (see *Figures 6.1* and *A1*). The first was a three-factor solution representing higher order domains: motivation (automatic + reflective motivation scores), capability (physical + psychological capability scores) and opportunity (social + physical opportunity scores) as latent constructs. The second investigated the six COM-B subdomains as latent constructs (physical and psychological capability, social and physical opportunity and reflective and automatic motivation).

Goodness of model fit was assessed using Root Mean Square Error of Approximation (RMSEA with 90% CIs; .08 or under was deemed acceptable [Hair et al., 2010; Awang, 2012]), the Tucker-Lewis Index (TLI; .90 or above was deemed acceptable [Forza & Filippini, 1998; Awang, 2012]), the Comparative Fit Index (CFI; 0.90 or above deemed acceptable [Hair, 2010; Awang, 2012) and chi-squared model fit statistics divided by *df* (<3 good fit; Kline, 1998). Model 1 and 2 fit were compared using these indices, and via a chi-squared difference test (using the *anova* function of the lavaan package). Items of the better fitting model were inspected for their squared multiple correlation statistics (R^2). If items had R^2 = <.40 they were deemed potentially problematic (in line with guidelines; e.g., Moss, 2016; HCC Systems, n.d.). Similarly, modification indices (estimates of improved model fit following adjustments) were inspected. Items with high cross-loadings or residual correlations (representing the difference between observed and expected residual correlations) were candidates for exclusion. The process of removing items was iterative; after items were removed, overall model fit was inspected again. A final model was decided upon when all model fit indices were satisfactory and standardised residual scores did not exceed -4 or +4 (Hair et al., 2010).

Convergent validity was assessed by examining whether average variance extracted (AVE) per factor exceeded 0.50 (a measure of factor fit; Bagozzi & Yi, 1988) and by assessing whether factor loadings were sufficiently large (a measure of item fit; loadings above >0.40 were deemed acceptable; Stevens, 2002) and statistically significant. Discriminant validity was assessed by i. identifying any high correlations between factors, values above 0.85-0.90 suggest that factors may be better modelled as one construct (Kline, 2011; Teo et al., 2008) and ii. by taking the square root of the AVE and comparing that value to the highest correlation of that factor with the other factors (i.e., the Fornell–Larcker criterion; Fornell & Larcker, 1981). Though Cronbach's α has long been the standard index of internal consistency used in the psychological literature, several authors have raised concerns regarding its utility (e.g., Crutzen & Peters, 2015) and recommend alternatives such as McDonald's ω. Both α and ω are reported here to determine the internal consistency of the COM-B domains (pre and post-CFA), with values of .60-.70 indicating questionable, .70-.80 acceptable, .80-.90 good and >.90 excellent consistencies, respectively.

To assess criterion and incremental validities, relationships between COM-B scores with total scores on the 3-item Alcohol Use Disorders Identification Test (Consumption; AUDIT-C) and the alcohol subscale of the WHO ASSIST (a measure of hazardous alcohol use) were assessed using simple correlations and two separate multiple linear regression analyses (for each outcome). Multiple regression analyses were conducted using the forced entry method in lieu of any proposed hierarchal structure of the COM-B domains. Higher scores on both alcohol measures suggest increasingly hazardous alcohol preoperative use. Higher COM-B scores indicate fewer barriers in the way of preoperative alcohol use reduction. In addition, those scoring five or above versus 4 or below on the AUDIT-C were compared on COM-B scores (using one-way MANOVA).

As this was an initial psychometric testing of the questionnaire, the target sample size (100 patients) was based on pragmatic grounds (recruiting as many patients as possible over a limited time period) and not an *apriori* power calculation. Nevertheless, maximum likelihood estimators for confirmatory factor analysis are considered reliable with sample sizes ~ 100 (Hair, Black, Babin & Anderson, 2010) though 5 participants per item has been recommended also (which was met here) (HCC Systems, n.d.). Similarly, 100 participants for multiple regression analyses may have sufficient power when small-medium effects are predicted, and the number of predictors is kept to the minimum (e.g. 1 for every 10 participants) (Green, 1991). Regardless, as in all previous studies, 95% confidence intervals are presented alongside effect sizes meaning the direction and precision of all estimates could be judged.

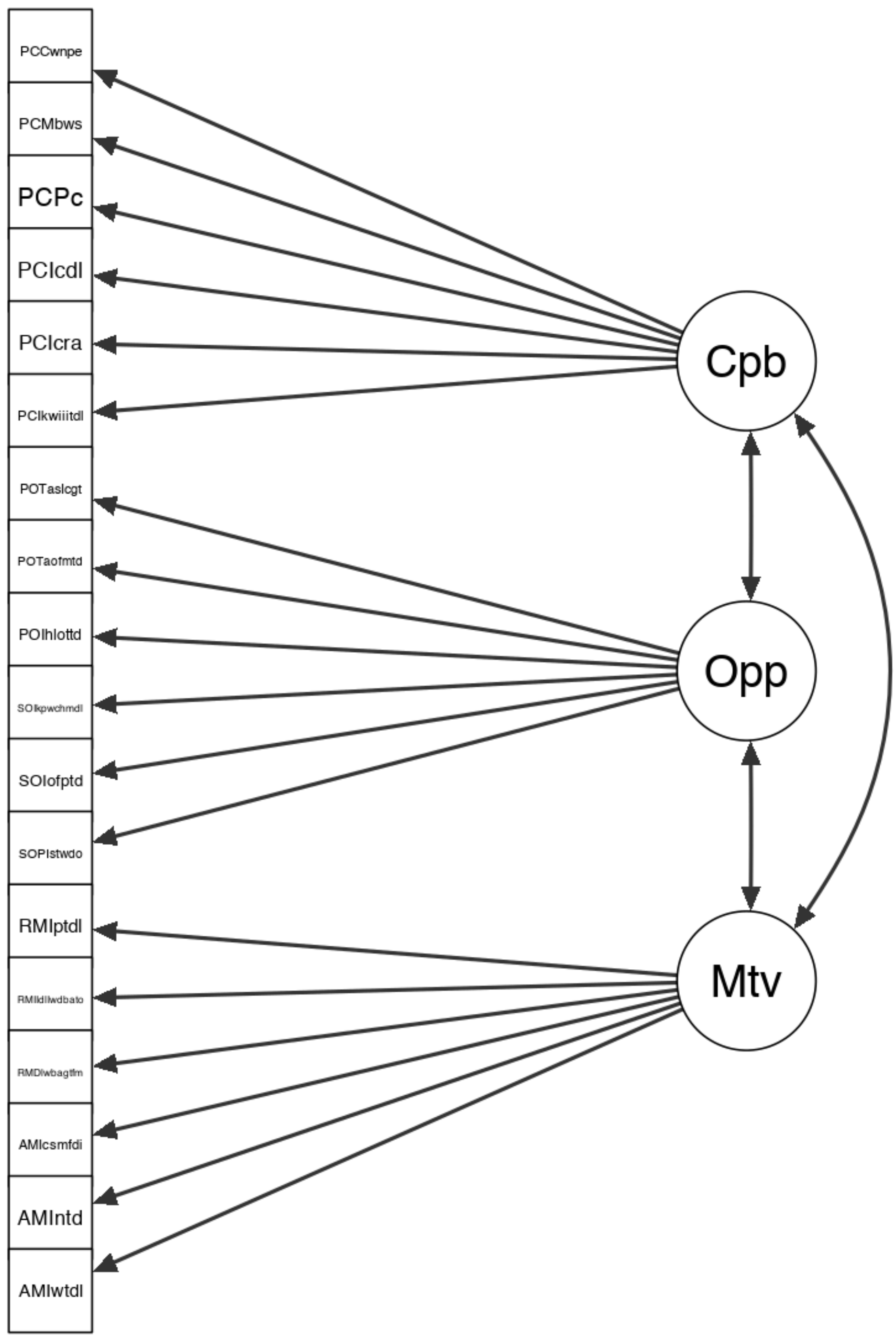

Figure 6.1. Model 1: COM-B Higher-Order Domains as Latent Constructs.

Patient preferences. AUDIT-C negative versus positive patients' mean format/deliverer scores were compared using two MANOVAs: one including all deliverer ratings as DVs, the other all format ratings as DVs. AUDIT-C positive patients' scores were explored further by comparing mean ratings between format/deliverer items. Lastly, qualitative comments were described narratively.

6.3 Results

A total of 102 patients were recruited (of 113 approached; 90.3%). A sample size of 102 provided 80% power ($\beta = 0.2$) to detect a moderate correlation of 0.28 at a two-tailed α of .05, or stronger correlations of 0.33 and 0.39 at a two tailed α of .01 and .001 respectively.

6.3.1 Sample Characteristics

The sample included 54 (54%) females and 46 (46%) males with an average age of 49.74 years (SD = 17.15 years; range = 19 - 84 years). Patients were undergoing surgery across a range of specialities (Table 6.1). The mean AUDIT-C and ASSIST scores were 4.74 (SD = 2.48) and 4.75 (SD = 3.47) respectively. By AUDIT-C cut-offs, the majority of the sample (54%) were hazardous drinkers (score >4) (7% were in the high-risk category [score = 9-12] as defined in Chapter 4). While there was no difference between genders in regard to those AUDIT-C *positive* or *negative*, AUDIT-C *positive* individuals were much younger (t[98] = 3.48; p <.001; mean difference 11.33 years [95% CI: 4.86-17.80 years; d = .70).

Table 6.1. Participant Surgery Types.

Levels	**Counts**	**% of Total**
Plastic	1	1 %
Urology	2	2 %
Gynaecology	3	3 %
General	3	3 %
Orthopaedic	4	4 %
Cardiac	4	4 %
Neurological	5	5 %
Pain management	7	8 %
Vascular	11	12 %
Ear, nose, throat	13	14 %
Maxillofacial	13	14 %
Spinal	24	27 %

Note. Missing data for 11 patients.

6.3.2 COM-B Questionnaire Analyses

Pre-CFA Internal consistency. The composite motivation subscale had acceptable consistency (α = 0.75, ω = 0.75), and both composite capability and opportunity subscales had very good to excellent consistency (α = 0.84, ω = 0.86 and α = 0.83, ω = 0.83, respectively). Internal consistency was excellent for *physical capability* (α = 0.82, ω = 0.85), and *psychological capability* (α = 0.80, ω = 0.83) subscales. Consistency on the *physical opportunity* (α = 0.67, ω = 0.71), *reflective motivation* (α = 0.69, ω = 0.70) and *automatic motivation* (α = 0.67, ω = 0.72) subscales were borderline acceptable. Lastly, the *social opportunity* subscale had acceptable consistency (α = 0.72, ω = 0.75).

Construct validity. Confirmatory factor analysis indicated that model 1 (a three factor solution representing higher-order COM-B domains) was a very poor fit (CFI = 0.74; TLI = 0.70; RMSEA = 0.13 [90% CI: 0.11 – 0.15]; χ^2/df = 2.71) though model 2 (a six factor solution representing COM-B subdomains) had a close to acceptable RMSEA value (0.10; 90% CI: 0.08-0.12), a chi-squared test statistic/*df* <3 (2) and better CFI (0.86) and TLI values (0.82). A chi-squared difference test indicated that model 2 was indeed superior, $\chi^2(12)$ = 114.53, p <.001.

Model 2 items were assessed for their communality (R^2) and modification indices were inspected. A total of five items were dropped (Table 6.2) from the model, cumulating in a very good fit (CFI = 0.95; TLI = 0.92; RMSEA = 0.08 [90% CI: 0.05 – 0.11]; χ^2/df = 1.70). The remaining 13 items shared at least 45% of their variance with their associated construct and all standardised residuals were > -4, or < 4. Convergent validity was excellent; all model 2 unstandardized and standardised factor loading estimates (reflecting the degree to which changes in item scores reflect changes in the underlying construct of interest) were significant, and standardised values were all > 0.67 (unstandardised values were all > 0.62; Table D1). In addition, average variance extracted for each factor were all > 0.56.

Factor covariance statistics (Table D2) indicated statistically significant, mostly small to moderate positive relationships between all subdomains, suggesting each were related, though tap unique phenomena. This was confirmed using the Fornell–Larcker criterion (accepting discriminant validity if the √(AVE) for each factor was greater than the largest correlation between that factor and another); all but one relationship indicated discriminant validity. The only area of concern was between the two *opportunity* subdomains, which showed very high covariance (0.91). Adjusting model 2 to absorb the *opportunity* subscales into one factor did not improve model fit on any goodness of fit index. Indeed, the original model remained a significantly better fit ($X^2(5)$ = 12.805, p = 0.02). Nevertheless, results here suggest a large overlap between these proposed constructs.

Items within subscales appeared to be adequately homogeneous post-CFA. Consistency for each factor was acceptable to excellent: *physical capability* (α = 0.89, ω = 0.90; two items), *psychological capability* (α = 0.80, ω = 0.83; three items) *physical opportunity* (α = 0.82, ω = 0.82; two items), *social opportunity* (α = 0.74, ω = 0.76; two items) *reflective motivation* (α = 0.69, ω = 0.70; two items) and *automatic motivation* (α = 0.76, ω = 0.76; two items).

COM-B questionnaire and preoperative alcohol use consumption scores[25]. There was evidence of criterion validity with significant (albeit imprecise) small to medium negative relationships between AUDIT-C scores and all COM-B subscale scores (Table D3); as alcohol use scores increased (indicating higher hazardous preoperative alcohol use), COM-B scores decreased (indicating more barriers). A similar result was found for the relationship between COM-B subscale scores and the WHO ASSIST, though the relationship between *psychological capability* and the ASSIST was small and non-significant (Table D3).

To assess incremental validity, patient age, gender and type of patient surgery were first assessed to see whether they had any association with AUDIT-C and ASSIST scores in separate regression models. It was found that gender and age predicted AUDIT-C scores, but not ASSIST scores. Age and gender were therefore controlled for in further analyses with AUDIT-C as an outcome variable, but not in analyses predicting ASSIST scores. A model including all COM-B subscales and age and gender regressed on AUDIT-C scores was significant, $F(8, 92) = 10.04$, $p < .001$, $R^2 = .47$. After controlling for the effects of all other subscales, *physical opportunity* ($\beta = -0.31$, 95% CI: -0.57- -0.04, $p = .02$), *physical capability* ($\beta = -0.25$, 95% CI: -0.44- -0.06, $p = .01$) and *reflective motivation* ($\beta = -0.23$, 95% CI: -0.43- -0.06, $p = .01$) remained significant (Table 6.3; Figure 6.2). When not controlling for age and gender, these results were largely the same[26]. A second model predicting ASSIST scores (not controlling for age and gender) was significant, $F(6, 95) = 4.33$, $p < .001$, $R^2 = .21$, though no individual predictors were significant after controlling for the effects of each other (Table D4). Perhaps due to lack of power, most parameter estimates were highly imprecise (particularly for ASSIST analyses) (*Figure 6.2*) so while significant results should be considered notable, non-significant results should be regarded with caution.

Inspection of means showed that AUDIT-C *positive* versus *negative* patients had lower COM-B scores on all subscales. Pretesting showed that there was a significant between gender (but not age and type of surgery) effect on COM-B subscales, thus gender was controlled for in the following analysis. A one-way MANOVA omnibus test indicated that these between groups differences were significant, $F(8, 92) = 4.07$, Wilk's $\Lambda = .79$, $p = .002$, and univariate tests indicated significant differences on each subscale (all $p < .04$).

Table 6.2. Model Iterations and Fit.

Model	**Items**	**CFI**	**TLI**	**RMSEA (90% CI)**	**χ^2/df**	**Reason(s) for exclusion**
1	All items	0.74	0.70	0.13 (0.11-0.15)	2.71	-
2	All items	0.86	0.82	0.10 (0.08-0.12)	2	-
2.1	Minus AUTMOT3	0.88	0.84	0.10 (0.08-0.12)	2	Very low R^2 (.29); high cross loadings; high residual correlations
2.2	Minus PHYSCAP2	0.89	0.86	0.10 (0.07-0.12)	1.93	Low R^2 (.35); very high cross loadings; high residual correlations
2.3	Minus SOCIALOP1	0.93	0.90	0.08 (0.05-0.10)	1.66	Very low R^2 (.26); high residual correlations
2.4	Minus PHYSOP1 and REFMOT3	0.95	0.92	0.08 (0.05-0.11)	1.70	Very low R^2 (.12); Very low R^2 (.25)

Notes. AUTMOT3 = “*I want to drink less*”; PHYSCAP2 = “*my body would suffer if drank less*”; SOCIALOP1 = “*I know people who can help me drink less*”; PHYSOP1 = “*there are services I can get to that can help me drink less*”; REFMOT3 = “*drinking less would be a good thing for me”*.

Table 6.3. AUDIT-C Regression Statistics.

Predictor	***B* (95% CI)**	***β* (95% CI)**
Gender (male – female)	0.42 (0.39–1.24)	0.09 (-0.08–0.25)
Age	-0.04** (-0.06– -0.01)	-0.25 (-0.41– -0.10)
Physical capability	-0.41** (-0.72– -0.10)	-0.25) (-0.44– -0.06)
Psychological capability	0.07 (-0.13–0.26)	0.07 (-0.13–0.26)
Physical. opportunity	-0.24* (-0.45– -0.03)	-0.31 (-0.57– -0.04)
Social. opportunity	0.00 (-0.23–0.24)	0.00 (-0.24–0.24)
Reflective motivation	-0.23** (-0.41– -0.05)	-0.24 (-0.43– -0.06)
Automatic motivation	-0.03 (-0.23– -0.17)	-0.03 (-0.23–0.17)

Notes. B = unstandardized estimate, *β* = standardised; * $p < .05$, ** $p < .01$, *** $p < .001$.

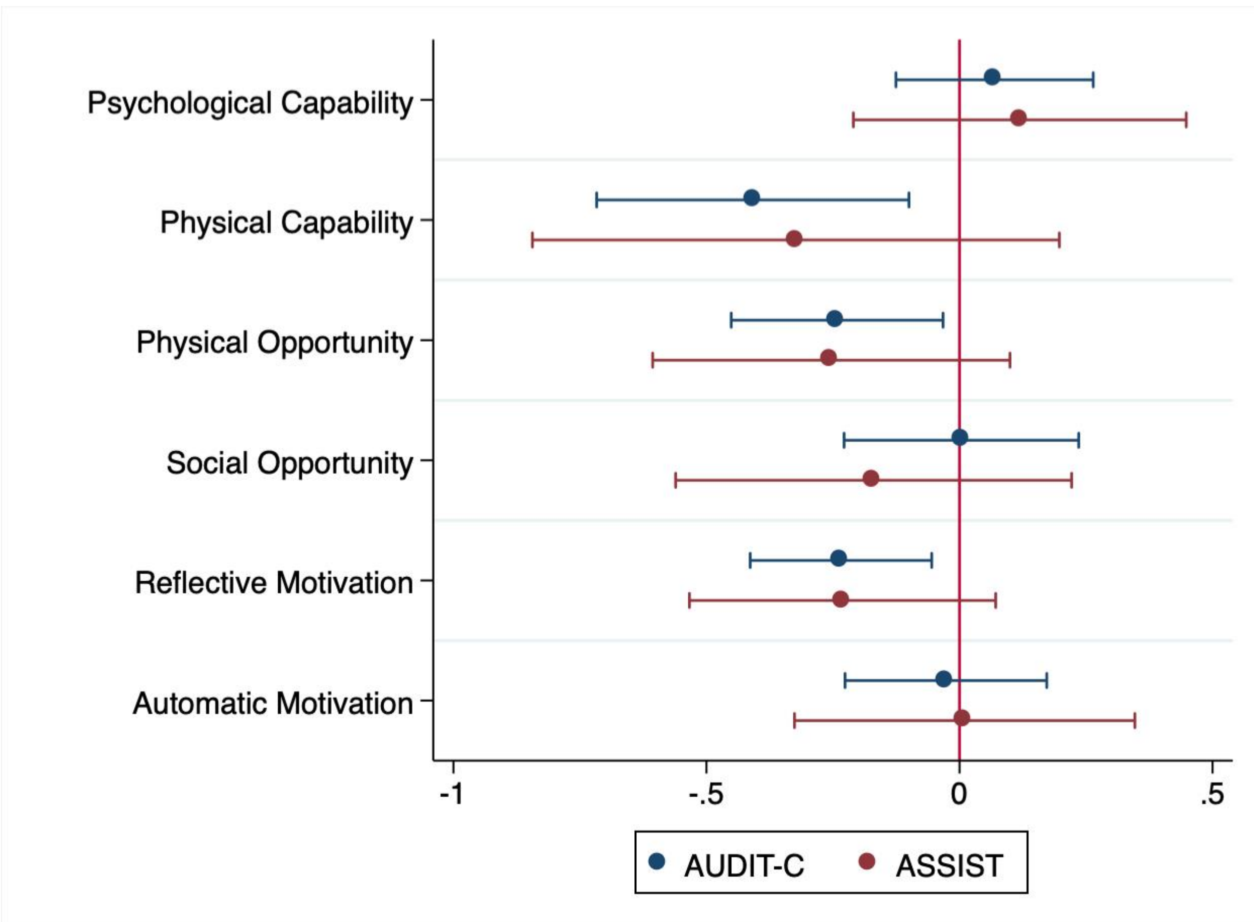

Figure 6.2. Regression Coefficients: COM-B on AUDIT-C and ASSIST Scores.

6.3.3 Patient Preferences

Format. Average format scores, across each item, did not differ greatly between those AUDIT-C positive and negative (MANOVA omnibus test: p = 0.68), though AUDIT-C negative patients rated all items *lower* than AUDIT-C positive patients (with the exception of *computer-based* interventions) (Table D5). This, speculatively, because they felt that any form of intervention was less applicable to them. Among AUDIT-C positive patients, all items were rated similarly. *One-to-one* interventions were the most favoured, and *computer-based* interventions were by far the least favoured (Table D5). Between format comparisons can be seen in Table 6.4.

Deliverers. As above, item scores did not differ greatly between AUDIT-C positive and negative patients (MANOVA omnibus: p = 0.13), and again, AUDIT-C negative patients rated each item lower on average (Table D5). Among AUDIT-C positive patients all item scores were similar (Table D5); nurses were rated the highest (closely followed by GPs) and alcohol counsellors were rated the lowest. Between deliverer comparisons can be in Table 6.4.

Free text suggestions. Six patients (5.9%) offered suggestions on the perceived usefulness of different intervention formats in the free text section. Three (AUDIT-C positive, all female) patients suggested that they would prefer app-based interventions (e.g., "*I use apps* [for calorie counting/weight monitoring] *so something like that to keep an eye on my alcohol use preop might be useful*"). Two (one AUDIT-C negative female, one positive male) suggested that they would need a combination of distance and one-to-one formats (e.g., "*I'd really really need it drilling home, probably GP appointments* *and some weekly reminders. Maybe phone-calls or text messages"*). Lastly, one participant (AUDIT-C positive male) stated that they would just like a leaflet with some risk information.

Eleven patients (10.8%) added suggestions related to intervention deliverers. A total of six patients (three each AUDIT-C positive [two males, one female] and negative [three females]) wrote comments suggesting that they wished to have more support from their GP (e.g., "*Not told anything about alcohol use before having my operation by my GP, would have been happy to get some information"; "my GP because I have been seeing her for years"*). Two patients (both AUDIT-C negative females) suggested that family could help them (e.g., *"my husband would be the best person to support me as he has through my illness").* Another two patients (one AUDIT-C positive male, one negative male) suggested that only if they themselves wanted to could they reduce, regardless of a deliverer ("*None of these matter. If I want to stop drinking I will do. They're all the same", "I have stopped drinking previously because of my health and willpower"*). Lastly, one (AUDIT-C negative female) patient suggested that positive past experiences with nurses led them to trust and respect their advice, so they would be the best to help them.

Table 6.4. Between-Item Comparisons for AUDIT-C Positive Patients' Format/Deliverer Scores.

Item 1	**Item 2**	**Mean difference (95% CI)**	**Cohen's *d***
	Format		
Computer based	Group-based	-1.38 (-1.99- -0.78)	-0.62
	Guided workbook	-1.02 (-1.68- -0.36)	-0.42
	One-to-one	-1.45 (-2.04- -0.87)	-0.67
	Phone helpline	-1.27 (-1.88- -0.66)	-0.56
Group-based	Guided workbook	0.36 (0.05-0.68)	0.31
	One-to-one	-0.07 (-0.19-0.04)	-0.17
	Phone helpline	0.11 (0.02-0.19)	0.35
Guided workbook	One-to-one	-0.44 (-0.72- -0.15)	-0.41
	Phone helpline	-0.25 (-0.60-0.09)	-0.20
One-to-one	Phone helpline	0.18 (0.03-0.33)	0.33
	Deliverer		
Alcohol counsellor	GPs	-0.51 (-0.90- -0.11)	-0.35
	Nurses	-0.55 (-0.93- -0.16)	-0.38
	Self-guided	-0.15 (-0.62-0.33)	-0.08
	Surgery team member	-0.31 (-0.76-0.14)	-0.18
GPs	Nurses	-0.04 (-0.09-0.01)	-0.19
	Self-guided	0.36 (0.01-0.72)	0.27
	Surgery team member	0.20 (-0.10-0.50)	0.18
Nurses	Self-guided	0.40 (0.05-0.75)	0.31
	Surgery team member	0.24 (-0.05-0.53)	0.22
Self-guided	Surgery team member	-0.16 (-0.37-0.04)	-0.21

6.4 Discussion

The present study iteratively developed a brief questionnaire assessing COM-B determinants of preoperative alcohol use to provide suitable intervention targets for future interventions, and provide a valid and reliable instrument to personalise and tailor brief preoperative interventions. The study also attempted to gain some insight into patients' preferred intervention modes of delivery and preferred deliverers. The results indicated that, after removing five items (a welcome reduction considering brevity was desired), a 13-item questionnaire probing the subdomains of the COM-B had a high degree of convergent validity and internal consistency; that is, the items assessed what they intended *per se* and measured what they intended in a consistent manner. Each subdomain was found to be significantly (and mostly moderately) associated with a validated and reliable measure of hazardous alcohol consumption (AUDIT-C), with *reflective motivation, physical capability* and *physical opportunity* predicting consumption even after controlling for all other subdomains plus age and gender. A between-groups comparison of patients scoring above and below a commonly used cut-off for hazardous alcohol use (AUDIT-C ≥5) was also shown to significantly differentiate COM-B subdomain scores. Subdomains were also mostly significantly, but all round less strongly, associated with an alcohol use measure (ASSIST) probing more distal features of alcohol overuse such as the legal and social impacts (though no subdomains were predictive after controlling for all). Discriminant validity, the degree to which subdomains tapped into unique phenomena was mostly demonstrated, though the *opportunity* subscales were highly intercorrelated – suggesting a large overlap and possible redundancy. Lastly, most deliverers and formats were rated similarly, though *computer-based* interventions were, by far, the least favoured intervention format amongst AUDIT-C positive patients.

The finding that COM-B higher order domains (e.g., *capability*, *opportunity* and *motivation*) did not form a well-fitting model, suggests, in this case, that factors associated with alcohol use in the preoperative context (or perhaps more generally) may be more nuanced – requiring measures of determinants with increased granularity. It is to the credit of the COM-B model that further subdivisions are specified; the findings of the present study indicated that the six subdomains suggested by Michie et al. (2011) were indeed associated with behaviour (albeit with some evidence of a unified *opportunity* subscale). Of course, an almost infinite number of item combinations may be used to represent the COM-B model, covering an incredibly wide swathe of hypothesized behavioural determinants, specified by a multitude of health behaviour theories. Thus, including different items to represent the COM-B may have supported a higher-order factor structure. Nevertheless, that is in an empirical question and, using expert agreement, the present study generated a set of purposefully broad items aiming to capture the essence of the COM-B domains, which (after reducing to those with most precision and consistency) performed well for their intended purpose: identifying potential intervention targets (in a time-limited manner).

As stated previously, a systematic review and meta-analysis of studies found a small and poor-quality literature base for behavioural interventions targeting preoperative alcohol use, with small and heterogeneous effects (Chapter 5). Intervention components were largely uninterpretable, as while *some* authors stated that (in a limited number of cases) they used interventions with an established theoretical base (e.g., Shourie et al., 2006), with established techniques they cited no specific protocol (meaning particular techniques or elements of an established intervention used in one study may have been disregarded in others). Many authors also described their intervention in very general terms (e.g., *psychoeducation*). An alternative approach is to disregard generalised top-down approaches and develop interventions from the ground up. This may be achieved by identifying and targeting determinants of behaviour in the specific target population. In the present study, we provide one small step towards this goal.

With the caveat of a small sample size and other limitations listed below, future researchers may wish to target resources/interventions at addressing patients' *reflective motivation* (evaluations and plans), *physical capability* (ability to cope with the physical effects of not drinking) and *physical opportunity* (time and exposure to opportunities to drink) (which even based on evidence from a limited sample, may be preferable to *not* targeting determinants associated with preoperative alcohol use). Future researchers may also note that *all* the subdomains seemed to be relevant in those scoring as hazardous drinkers (on the AUDIT-C), so a selection may be targeted. The behaviour change techniques (BCTs; Michie et al., 2013) used to target these determinants, ideally, would be based on evidence. Evidence may be obtained by conducting meta-analyses of techniques used to successfully modify related constructs previously or by reviewing the literature. For example, in the case of *reflective motivation*, which consists of evaluations and plans, one could make sure to prompt: 1.1 *Goal setting (behaviour)* (e.g., Epton, Currie & Armitage, 2017) while making sure to increase self-efficacy (which may bolster the success of goal setting e.g., Iwasaki et al., 2017) through prompting 2.3 *Self-monitoring of behaviour* (e.g., French, Olander, Chisholm & McSharry, 2014). One could then identify whether i. the techniques modified the particular determinant (e.g., through questionnaires), ii. whether the determinant predicted the behaviour, and iii. whether the intervention (consisting of individual BCTs) led to a desired behavioural outcome *through* modifying the determinant (e.g., using structural equation modelling).

Such an approach allows for i. identification of intervention mechanisms, ii. precise identification of techniques that are responsible for the intervention effects *on the mechanisms* (which *may* generalise to other behaviours) and specific behaviour, iii. precise replication of successful interventions, iv. the ability of researchers to add or subtract components to assess whether different techniques modify intervention effects (for example, in a differing contexts/populations) and v. to provide researchers with precise information on what components to avoid (in the case that the intervention was a failure). A preoperative intervention literature with this level of specificity may lead to more cost-effective approaches – a vital component of any intervention in a healthcare context. As in the present study, identifying determinants must begin this sequence; one must know what to target before choosing strategies aimed at such targets.

The above approach describes, what may be considered, a generalised strategy; that is, identification and targeting of determinants based on their salience averaged across all patients. An alternative approach is through individualisation. In this scenario, interventionists may deliver the COM-B questionnaire to a potential intervention recipient (perhaps, for example, if they scored above a certain threshold on an alcohol measure). Determinants most salient *in that individual* may then be addressed, using a set of BCTs, with proven efficacy. Such an approach may be integrated into the practice of brief interventions, for which there is a healthy literature. One meta-analysis of brief interventions in emergency care settings, found evidence, across 28 trials, that brief interventions were significantly better than controls (Schmidt et al., 2015) though the pooled intervention effect was small (d = 0.19) – perhaps, again, due to a lack of precision, which instruments such as the COM-B measure (and pre-specification of BCTs to modify constructs) may address. In a review of brief interventions, McCambridge and Saitz (2017) highlight that two key issues with the brief intervention approach are i. generalisability: strategies may not work across particular demographics, and ii. a previous lack of focus on the identification of intervention content and/or mechanism. An approach as described above would nullify, to some degree, issues regarding generalisability and would provide a window into mechanisms. An added potential benefit to the *screen-COM-B-intervene* approach may be to provide a less cognitively demanding (interventionists do not have to probe and question in detail), and thus more standardised approach to intervention; meaning the potential modifying effect of the skill or status of the interventionist may be lessened, cost and time reduced, and potential replication and translation bolstered.

One take-home message from this study must be that there was no strong preference for any particular intervention modalities within hazardous alcohol users, and that, across the entire sample - all intervention features were rated highly. Nevertheless, some potential intervention features may be *less* acceptable to patients with hazardous alcohol use scores; *computer-based* interventions, *self-guided* interventions, and those delivered by *alcohol counsellors.* For the latter, this contradicts previous evidence suggesting that a high perceived level of interventionist credibility – which is listed as an intervention technique in the BCT taxonomy – may be associated with successful alcohol reduction interventions (e.g., Hummer & Davison, 2016). This is perhaps best explained by many patients considering their alcohol use behaviours not serious enough to be addressed by a specialist. With regard to *self-guided/guided workbook* and *computer-based* interventions, these ratings may represent a general rejection of low-intensity or self-motivated intervention strategies. Individuals with higher alcohol use may be, by default, less motivated to engage with self-guided strategies (of which computer-based interventions may be one). Nevertheless, online/computer-based based interventions may be highly useful for intervening on populations who may not wish to attend alcohol services (White et al., 2010) and have shown to be efficacious in related contexts (Walton et al., 2016). An intervention may comprise many different delivery methods; an online component could still be one.

The present study had several limitations. First, all but one COM-B domain was represented by two items in the final CFA model. As outlined in Worthington and Whitaker (2006) while two item factors can be useful when it is demonstrated that the within-factor covariance is high and between-factor covariance is low (mostly demonstrated here), the more items, the more one can be confident that the factor will be reliable (in replication studies, for example). As suggested in other published research aiming to design very brief screening questionnaires, fewer items are sometimes a necessary trade-off between psychometric properties and the required brevity (e.g., Muck, Hell & Gosling, 2007; Rammstedt & John, 2007; Yoo & Donthu, 2001) - and, even when retaining *all* items, model fit indices (see iterations in Table 6.1) met thresholds deemed acceptable in previous studies (e.g., Dyson et al., 2013). Nevertheless, it remains the case that future studies, ideally with larger sample sizes may be necessary to replicate and confirm the factor analysis findings. Second, the limited sample size led to many imprecise parameter estimates. This is problematic because while it is important to identify significant predictors, it is equally important to establish the precise size of their effect. It may also be the case that non-significant results (e.g. predictors of ASSIST scores) were due to lack of power. Third, the initial items chosen for the questionnaire were chosen by a select few researchers, and not through comprehensive Delphi procedures with, for example, many experts or patients. Such strategies may have been incredibly difficult and time-consuming to adopt, within a very idiosyncratic and unique context, and in a very brief window of time (for patients, at the time of preoperative assessment). To reduce patient burden, and for purposes of expediency, items were designed from scratch with influence from previous studies. Fourth, a cross-sectional approach was adopted – though a prospective sample would have allowed for a temporal relation between determinants and alcohol use and an assessment of test-retest reliability. Again, this may have been unfeasible; patients typically only visit the preoperative assessment clinic once, patients' surgeries can be cancelled, delayed for considerable periods, and can be conducted in different hospitals. Patients would, therefore, be easily lost to follow-up, not to mention, asking patients to complete questionnaires when recovering from, or immediately before, surgery may have added a significant degree of patient burden (reducing recruitment figures and retention). Fifth, only self-report measures of alcohol use were used. It is acknowledged that social desirability effects may have altered patient responses, though all patients were reminded that everything was anonymous (including to medical staff) and that they were protected by strict NHS ethics. Sixth, in the context of the present thesis, illicit substance use was neglected. It was felt more appropriate to focus on the substance most used, and thus most likely to cause harm: alcohol.

In sum, the present study provides initial evidence that a 13-item COM-B based questionnaire assessing determinants of preoperative alcohol use can be designed with adequate construct, convergent and concurrent validity and reliability. The present study also suggests that patients may have no *strong* preferences regarding a number of potential intervention deliverers and modalities. The results of the study also provide evidence that future interventions may be best placed to target *reflective motivation, physical capability,* and *physical opportunity*, though all conclusions must be tempered in light of a number of limitations, including a relatively small sample size, cross-sectional design and self-report of alcohol use.

6.5 Key Findings: Study 5

- A COM-B based questionnaire for assessing targetable psychosocial determinants of preoperative alcohol use was created by a team of researchers before being completed by a general sample of preoperative patients.
- A 13-item version of the questionnaire (representing COM-B subdomains) performed well in factor analysis, with good model fit, high convergent validity and high internal consistency (though questionable discriminant validity).
- All COM-B sub-domains were significantly associated with AUDIT-C scores, though not ASSIST scores. In both sets of analyses, confidence intervals were wide suggesting lack of precision.
- *Reflective motivation, physical capability* and *physical opportunity* scores predicted AUDIT-C scores even after controlling for all other subdomains.
- Patients had no strong preferences for specific preoperative intervention formats, though hazardous alcohol users generally favoured computer-based interventions the least and one-to-one interventions the highest.

CHAPTER 7. POTENTIAL PREOPERATIVE INTERVENTION TARGETS AND FEATURES FOR SUBSTANCE-DEPENDENT ADDICTION SERVICE USERS: A QUALITATIVE THEMATIC ANALYSIS (STUDY 6)

7.1 Introduction

7.1.1 Background

In Chapter 6 (Study 5), a general patient sample was recruited to assess generalised determinants of hazardous preoperative alcohol use. Part of the rationale for this focus on determinants of *hazardous* alcohol use versus illicit substance use and *dependent* alcohol use, was a focus on a risk factor that may affect a larger number of patients (and thus increased recruitment feasibility). Indeed, as in Chapter 4, hazardous alcohol users may comprise a large proportion of patients, whereas dependent alcohol users and illicit substance users may be less prominent. While this focus on a larger number of patients may be useful, a second, but equally useful strategy, may be to focus only on patients at *most* risk. This thesis not only aimed to provide targets for brief and low-cost preoperative interventions suitable for the majority of at-risk patients (Study 5), but for more intensive interventions aimed at a high-risk minority. Thus, in Study 6, substance use determinants were assessed in a *purposive* sample of substance dependent individuals.

The relationship between preoperative substance use and negative health outcomes seems to be dose-dependent; complications appear more prevalent in the heaviest users (Eliasen et al., 2013; Menendez, Ring & Bateman, 2015[27]). Substance-dependent individuals may, therefore, be at most risk of complications, while also facing unique risks such as withdrawal (a physiological state independently associated with complications; Gordon, 2018) and relapse following analgesic exposure (Wesson, Ling & Smith, 1993). Polysubstance use is also common in individuals with substance dependency[28] this may have the potential to increase risks exponentially.

While the percentage of preoperative patients who are alcohol or illicit substance-dependent is likely small (see Chapter 4) - they may be overrepresented regarding suffering complications. Amongst substance-dependent individuals, perioperative substance use risk may be compounded, and partially explained by, a myriad of social factors and other comorbidities[29] that catalyse increased rates of poor health versus the general public (e.g., Schulte & Hser, 2014). Further, while illicit substance users *per se* tend to be younger (e.g., Chapter 4), and thus potentially less likely to have surgical operations in the first instance, and suffer complication promoting age-related comorbidities - this is not the case with substance-dependent individuals. While the prevalence of substance dependence amongst 16-34-year olds appears to be falling, rates remain stable among those older than 35 (a *generational effect*) (Roberts, Lepps, Strang & Singleton, 2014). As such, modifying substance use among these individuals may (if effective) have a disproportionally large impact on the overall complication incidence rate.

For those suffering substance-dependency, complex preoperative interventions may be necessary. While it has been demonstrated that a preoperative intervention can reduce alcohol intake in alcohol-dependent patients (and in turn reduce the incidence of perioperative complications) just two randomized controlled trials, both with small sample sizes, have shown this (see Chapter 5). The intervention in these studies also involved the use of disulfiram, a pharmaceutical drug which has many serious side effects (Kalra et al., 2014). In terms of trials of behavioural interventions, Chapter 5 found just two studies that targeted an intervention specifically at current hazardous (but not necessarily dependent) alcohol users. The first found no significant effects on both alcohol use or complications (Shourie et al., 2006), the latter did not report between-groups outcomes (Wyman et al., 2014). Wyman et al. (2014) was also the only identified study that trialled a behavioural intervention aiming to reduce patients' preoperative illicit substance use (again, not necessarily dependent patients), where objective substance testing on the day of surgery showed no significant intervention and control group differences.

One explanation for the failure of behavioural trials in this area may be the failure to adapt their intervention strategies and focus to determinants unique to the population of interest. Previous quantitative research has highlighted several issues that substance-dependent individuals *may* face in the perioperative period. Psychological determinants of substance dependency treatment failure includes increased psychiatric comorbidity (e.g., Choi et al., 2013; Mertens & Weisner, 2000), maladaptive coping styles (e.g., Kohn, Mertens & Weisner, 2002), low motivation or no goals to reduce or abstain from substances (e.g., Mertens & Weisner, 2000; Simpson, Dwayne & George, 1993), and low self-efficacy regarding cessation (e.g., Norozi et al., 2016). Environmental barriers include exposure and maintaining relationships with social circles involved with substance use (e.g., Shanmugam, 2017; Dingle, Stark, Cruwys & Best, 2014), reduced family support (e.g., Daley, 2013), and exposure to substance-related cues (see Mellentin et al., 2017). In addition, many determinants of substance use may be highly context specific. For example, the preoperative period may be a *teachable moment* wherein motivation to abstain is inherently boosted through, for example, fear for health (O'Toole et al., 2006; Shi & Warner, 2010). Motivation may, in turn, promote increased treatment seeking, compliance and self-efficacy (Kadden & Litt, 2011; DiClemente, 1999).

Unfortunately, it appears that no previous intervention trial in this area has aimed to develop an intervention from the *bottom up*, that is, conducted research to identify salient intervention targets tailored to the perioperative period (as in Chapter 6). Stakeholder input in the design of an intervention may increase the acceptability, efficacy and offer insights into the feasibility of that intervention (Moore et al., 2015). Prospective identification of techniques that may succeed, or obstacles to overcome, are clearly preferable to a retrospective (thus post-expenditure) identification of obstacles, and evaluations of why an intervention did or did not succeed.

Qualitative methods of data collection (such as interviews and focus groups), and analysis (such as thematic and interpretative phenomenological analyses) allow for a *rich* (Alshenqeeti, 2014) understanding of stakeholders' thoughts, feelings and beliefs, and are often recommended in the preliminary development of behavioural interventions (e.g., by the UK medical council's [MRC] guidance; Moore et al., 2015). This is especially the case where stakeholders, such as substance-dependent individuals, may present a particularly complex challenge for intervention designers. There is qualitative literature involving substance-dependent individuals that *may* be applicable to the present context. For example, Pettersen et al's (2018) found that one primary reason for spontaneous substance use cessation was having experienced significant adverse health events (e.g., surgery); perceived stigma around substance use may reduce intervention acceptability and disclosure to potential interventionists (Hines, 2013; McNeely et al., 2018); and local service variation (e.g., boundaries between healthcare and substance use treatment centres) may moderate perceived substance cessation outcomes (Gilburt, Drummond & Sinclair, 2015). However, there has been, to the author's knowledge, no previous qualitative research investigating substance-dependent patients' thoughts and feelings around substance use reduction (and/or cessation) prior to elective surgery. As above, this may be problematic; determinants of behaviour may be grounded in context. Understanding individuals' perceived barriers and facilitators within this context may provide more precise, relevant and acceptable intervention targets.

7.1.2 Study Overview and Aims

Given that i. substance-dependent individuals may be at increased risk of complications, ii. previous behavioural preoperative interventions for substance dependency have failed to improve outcomes, and iii. there has been, to the author's knowledge, no previous research aiming to explore the experiences, thoughts and feelings of substance-dependent individuals regarding elective surgery specifically, the present study aimed to purposefully sample this hard-to-reach population to inform future intervention development. More specifically, through face-to-face interviews and thematic analysis, this study aimed to investigate and identify potential barriers and facilitators to substance use reduction, as well as preferred intervention strategies and formats.

As highlighted by Chapter 4 (and highlighted by the protracted recruitment in Tonnesen et al., 1999; 2002 [Study 5]), recruiting a sample of *preoperative* substance-dependent patients may be incredibly time consuming and difficult. As such, it was determined that a non-patient sample would be approached, with the rationale that these individuals were key stakeholders in the research objectives. Given the inflated prevalence of comorbidities in this population, it was also predicted that many participants would have either had surgery or similar healthcare experiences (i.e. they may have been exposed to potential *teachable moments* for reducing substance use) or knew friends or family that had.

Instead of a more cursory and generalised approach to assessing determinants (as in Study 5) it was deemed more appropriate here to adopt a more exhaustive qualitative approach, given the complex nature of substance dependency. Indeed, this approach may encourage nuance, deviation and exposition about determinants in context (Atieno, 2009); allowing participants to tell and reflect upon anecdotes (importantly, those related to their own or members of their social circles' experiences with the NHS), discuss in detail what intervention strategies have been/would likely to be effective - and *why*, for themselves and their peers. This approach may allow for a more in-depth understanding of likely highly complex personal barriers and facilitators faced by substance-dependent individuals such that they may be understood in the wider context of the participant's internal (e.g., emotional) and external (e.g., environmental) situation.

Since i. polysubstance use is ubiquitous amongst substance-dependent individuals (e.g., Darke & Hall, 1995) (and hazardous users in general e.g., Chapter 4) and ii. dependency to substances may be partially explained by factors irrelevant to the particular substances used (e.g., coping with low affect, see Chapter 3), substance dependency was treated as a homogeneous entity - though substance-specific insights were outlined as appropriate.

7.1.3 Objectives

1. Understand perceived barriers and facilitators to preoperative alcohol and/or illicit substance reduction for individuals with substance dependency (thus identifying intervention targets).
2. Identify stakeholder issues around, and preference for, various interventions formats (e.g., group sessions) and strategies (e.g., giving risk information).

7.2 Method[30]

7.2.1 Design

This was a qualitative study consisting of a series of one-to-one, face-to-face semi-structured interviews. As opposed to remote contact (e.g., telephone calls) face-to-face methods have several desirable properties (Oltmann, 2016) such as allowing the researcher to discern participants' emotions and social cues more readily. For the present study, body language was deemed particularly important to monitor; allowing for a detection of emphasis, sarcasm, mood and other features that may significantly alter the interpretation of the interview transcripts. A semi-structured approach allows for a more open-ended conversation which leads to useful topics and themes that often were not, or could not be, predicted in advance. This is very useful in areas in which there are few if any, previous studies. In general, one-to-one interviews have several advantages over other methods of qualitative data collection. As compared to focus groups, for example, each individual participant is likely to offer more information and detail (as 100% of the allotted interview time is dedicated to them). Focus groups also have the drawback of group-think; may lead some participants to feel embarrassed to discuss certain topics in the presence of others and thus encourage reticence; and/or magnify the inherent social desirability effects which are likely present, to some degree, in all methods of psychological research but especially so when discussing potentially sensitive topics such as substance use.

Interviews and recruitment took place within a substance use treatment centre (Forward) in Leeds, UK. Forward, which has three Leeds--based centres, may be regarded as a *one-stop shop* for substance-dependent individuals. Each centre provides free harm reduction services (e.g., needle exchange, methadone prescriptions), as well as intervention services (with on-site substance-use counsellors [recovery coordinators], psychiatrists and mental health specialists, GPs and housing advisors). Forward centres are also part of the service user pathway for accessing free Leeds-based detoxification services. The present author was a long-term volunteer at one Forward centre based in North Leeds.

This study received approval from the University of Leeds School of Psychology Ethics committee (ethics reference number: 16-0189). The study also received approval from the manager of the recruitment centre (Irford House, Forward Leeds).

7.2.2 Participants

Eligibility. Purposive sampling was used to recruit potential participants. Included participants had to be current or ex-substance users with dependency issues. There were no exclusion criteria based on the particular substance(s) used by the potential participants. Potential participants under the age of 18 were excluded, as were those deemed to be particularly vulnerable, intoxicated, violent or disruptive by their recovery coordinator prior to, or at the time of approach.

Sample size. Potential participants were approached until it was felt that i. enough data were collected to answer the study objectives, and ii. novel insights and themes of discussion were felt to be waning (i.e., data saturation).

7.2.3 Procedure

Several recovery coordinators (RCs) at the centre were informed about the study and were asked to identify potential clients who met the pre-specified eligibility criteria. The RCs then introduced said clients to the researcher who gave them a participant information sheet (explaining study aims, topics, their rights, the method, dissemination strategy and contact details for withdrawal or further questions). They were then asked whether they would be interested in participating in the study and were encouraged to ask any questions. Interested participants then either organised a time and date to meet right away or approached the researcher on a future visit to the centre. Before each interview, participants were encouraged to ask any questions again before signing consent. Interviews were conducted and audio-recorded with permission of the interviewee in private, quiet and nondescript rooms used by recovery coordinators at the centre, before being transcribed verbatim.

In the pilot phase of the interviews, the semi-structured interview schedule was based upon each item within the Theoretical Domains Framework (see Cane et al., 2012) this proved to be inflexible and too time-consuming; participants seemed much more comfortable and open with a more conversational approach. The schedule was thus shortened to favour elaboration and discussion over questioning and answering (Appendix I). The shortened schedule aimed to probe participants' hypothetical or real capability, opportunity and motivation (as per the COM-B model [see Chapter 6]) to reduce or abstain from their substance use prior to an elective procedure (strategies to modify these constructs were discussed in an unstructured fashion). The schedule also aimed to probe possible past experiences with healthcare with general prompts. Interview techniques included clarification (e.g., asking participants to repeat something, sometimes by rephrasing a question) and elaboration probes (e.g., by prompting participants to provide more depth, through direct questions or by briefly staying silent). Participant statements were also often repeated back to them, so they could reflect and confirm agreement; a check for consistency.

The interviews were conducted by LB (MSc) who undertook the research as part of this PhD thesis and had no prior relationship with any of the participants. LB had previous experience conducting qualitative research in his undergraduate and postgraduate studies. Participants knew the nature and goals of the study and knew that the project was intended to form part of the interviewer's PhD thesis. Participants were made aware that their interviews were entirely confidential and that recovery coordinators or other employees at the recruitment centre had no access to the transcripts. As such, participants were encouraged to be as truthful as possible and were informed that they should not fear, for example, a discontinuation of their methadone prescription as a result of substance use disclosure.

7.2.4 Data Analysis

Aided by NVIVO, data were analysed according to principles of thematic analysis in line with guidelines outlined by Braun and Clarke (2006). Analysis was conducted from a critical realist position, which may be considered a middle ground between radical positivism and constructionism (Fletcher, 2017). That is, it was acknowledged that through analysis, a single truth or reality could only be approximated (as moderated by the analysts' subjective interpretation and mediated through a limited sample of sense data).

Notes on immediate reflections and emerging themes/ideas were kept throughout the interview process and were often used to generate *ad hoc* questions. After recruitment, the interviews were listened back to twice, during which more notes were made. Notes were illustrated into rough model diagrams, which gradually became more developed over time; familiarising the researcher with the data.

Interviews were transcribed verbatim and were initially coded by (LB). During analysis, discrepant evidence was noted, and deviant cases were given full attention. A hybrid inductive and deductive approach was used when coding interview transcripts (i.e., both hypothesis-driven [e.g., coding for barriers] and data-driven [e.g., coding for anything notable]). A separate set of themes were developed relating to each of the study aims: i. barriers/facilitators, ii. intervention strategies, and iii. intervention formats.

To assess the reliability of the thematic codes, a second, highly experienced qualitative researcher (RL) coded two random transcripts. When these coded transcripts were compared to the first researcher's, a good level of consistency was observed (e.g., similar code labels). Once an initial set of themes were created, both researchers then discussed, debated and edited them as appropriate. After refinement, the second researcher was given two random transcripts for a second time. The researcher then coded the transcripts and categorised codes under the generated themes. Again, through review and debate, both researchers agreed they had a good level of consistency.

7.3 Results

Forty-eight individuals were approached, ten refused participation (reasons primarily included lack of time, and lack of interest), and two did not meet the eligibility criteria (due to issues around vulnerability). No participants requested a withdrawal of their data or dropped out of the study for any reason. A total of 36 participants were interviewed. Interviews were a mean = 20:31 minutes with a range of 10:41- 42:12 minutes

7.3.1 Sample Characteristics

Table 7.1 provides a demographic overview of the sample. The 36 participants were mostly male (77.7%) and were an average age of 42.3 (SD = 11.1; range 24 - 72) years old. All but two participants were White British; one was Black British the other White Eastern European. *Including* polysubstance users, 19 (53%) participants were in treatment for heroin, 12 (33.3%) for alcohol, 10 (27.8%) for crack cocaine, three (8.3%) for cannabis, two each (5.6%) for diazepam and amphetamines, and one participant each for ketamine, powder cocaine and codeine. The total number of participants in treatment for more than one substance was 14 (38.8%; 10 of whom were heroin and crack cocaine users). Fifteen participants (41.6%) were currently abstinent. All but one heroin user was on a methadone or buprenorphine opioid maintenance prescription. Forty-seven percent, or 17 participants, stated that they had some degree of outpatient/inpatient experience with the NHS while actively using substances; (e.g., blood transfusions, and hernia, anterior cruciate ligament, gastric band surgeries).

Table 7.1. Sample Characteristics (Study 6).

Pseudo name	Gender	Age	Ethnicity	Currently in treatment for	Claimed abstainer?	Prescribed an opioid substitute?	Experience with healthcare (while using)?
Liam	Male	35	White (British)	Heroin	Yes	Yes	No
Noah	Male	41	White (British)	Heroin	Yes	Yes	Yes
Elen	Female	61	White (British)	Alcohol	Yes	-	No
Will	Male	36	White (British)	Heroin and crack cocaine	No	Yes	No
James	Male	55	White (British)	Heroin	No	Yes	No
Logan	Male	24	White (British)	Heroin and diazepam	No	Yes	No
Ben	Male	27	White (British)	Cannabis	No	-	No
Mason	Male	32	White (British)	Heroin and crack cocaine	Yes	Yes	Yes
Elijah	Male	57	Black (British)	Heroin and crack cocaine	No	Yes	Yes
Oliver	Male	46	White (British)	Amphetamine	No	-	No
Jacob	Male	33	White (British)	Codeine	No	No	Yes
Lucas	Male	62	White (British)	Heroin and crack cocaine	No	Yes	No

Pseudo name	Gender	Age	Ethnicity	Currently in treatment for	Claimed abstainer?	Prescribed an opioid substitute?	Experience with healthcare (while using)?
Hazel	Female	45	White (British)	Heroin and crack cocaine	No	Yes	Yes
Mike	Male	45	White (British)	Alcohol	Yes	-	No
Rachel	Female	26	White (British)	Cannabis	No	-	Yes
Alex	Male	34	White (British)	Alcohol	No	-	Yes
Ethan	Male	55	White (British)	Alcohol	No	-	Yes
Dan	Male	26	White (British)	Cannabis	No	-	Yes
Matt	Male	46	White (British)	Heroin and crack cocaine	No	Yes	No
Chloe	Female	39	White (British)	Alcohol and cocaine	Yes	-	No
Aiden	Male	52	White (British)	Heroin and crack cocaine	Yes	Yes	Yes
Henry	Male	50	White (British)	Alcohol	Yes	-	No
Joe	Male	38	White (British)	Heroin and crack cocaine	Yes	Yes	Yes
Jack	Male	57	White (British)	Alcohol	No	-	Yes
Sam	Male	39	White (British)	Alcohol	Yes	Yes	No

Pseudo name	Gender	Age	Ethnicity	Currently in treatment for	Claimed abstainer?	Prescribed an opioid substitute?	Experience with healthcare (while using)?
Dave	Male	39	White (British)	Alcohol	Yes	-	Yes
Owen	Male	30	White (British)	Heroin and amphetamine	No	Yes	No
Susan	Female	37	White (British)	Heroin, alcohol and crack cocaine	No	Yes	No
Rosie	Female	42	White (British)	Alcohol	Yes	-	Yes
Chris	Male	42	White (British)	Heroin	Yes	Yes	Yes
Ryan	Male	36	White (British)	Heroin	No	Yes	Yes
Jenny	Female	35	White (British)	Alcohol, ketamine and diazepam	Yes	-	Yes
Niamh	Female	32	White (Other)	Heroin	No	No	No
Charles	Male	46	White (British)	Heroin and crack cocaine	No	Yes	No
Leo	Male	72	White (British)	Alcohol	No	-	No
Rob	Male	45	White (British)	Heroin	Yes	Yes	No

7.3.2 Interview Reflections

It is acknowledged that certain participants may be overrepresented in the development of themes (and thus in the provided quotations). This reflects both a high degree of reticence in a small minority of participants and the varying length of the interviews. Some participants were resistant to elaboration probes and were, perhaps through disinterest or mistrust, unforthcoming. The exact converse was true of some participants; indeed, interviews were, at some points, prone to deviation from the subject matter at hand. As such, interviewing using a semi-structured approach was sometimes a difficult task - a balance between having specific research questions to answer and allowing for a conversational and candid discussion. The interviewer also quickly learned that participants had to be repeatedly reminded of the preoperative *context* of the discussion. Though participants seemed comfortable with hypothesising about their predicted behaviour/cognitions, in many cases, participants seemed to see no distinction between substance use in the preoperative period and in general life. This may reflect a failure to see how context *may* influence behaviour, or a genuine belief (perhaps through experience) that particular determinants, strategies and formats are highly generalisable across contexts, or non-context specific.

7.3.3 Thematic Analysis

Analysis led to i. eight data-driven themes related to potential barriers and facilitators, ii. ten for interventions strategies and iii. five for intervention formats. Theme titles may not refer to barrier or facilitators specifically, rather, reflect emergent topics of discussion across interviews – such that a theme (e.g., habit & automaticity) may encompass both barriers (e.g., low craving control) and facilitators (e.g., high craving control). Subthemes represent nuances within themes where appropriate; subthemes were only generated where a theme contained sufficient constituent codes that clear and consistent points of elucidation, elaboration, conflicting consensus or other objective-specific issues could be identified and made sense of as distinct, but thematically-related, constructs. Some subthemes contained further subthemes, generated based on the same criteria as above.

A brief outline of each theme is provided in the sub-sections below. These outlines provide a distillation of the essence of each theme in a concise manner - allowing for a general overview (at the expense of nuance). In contrast, and if preferred by the reader, Appendix J provides a more detailed account of each (including elaboration of subthemes and nuances related to participant characteristics), where each theme title is presented alongside the sum of codes that form them (and the number of times each code was referenced within and across interviews); providing a sense of the saliency of each theme. While each theme below is presented with a single supporting quotation, more detail can be found in Tables E1, E2 and E3. For further context, quotes in these tables can be cross-referenced with Table 7.1. The hierarchal structure of the themes can be seen in *Figure B1* (barriers and facilitators), *Figure B2* (intervention formats) and *Figure B3* (intervention strategies).

7.3.4 Themes: Barriers and Facilitators

Theme A1: Motivation & willpower. Participants emphasised that low motivation for preoperative substance use reduction/abstinence may be a barrier. Regardless of resources or strategies available to them, motivation was seen as the key determinant of change. Motivation was considered modifiable; fear for health was felt to enhance motivation (to protect health) but also reduce motivation (substance use may be attractive as a stress-related coping strategy). Participants also felt that many individuals have a disregard for health and that their behaviour would not be affected by an upcoming surgery. Other motivation moderators included: social influence and withdrawal symptoms. The former in a direct (e.g., friends/family may help engage in treatment) and indirect (e.g., fear of upsetting family by continuing substance use with risk of perioperative complications) sense. Withdrawal symptoms were felt to severely inhibit motivation as the negative psychological and physiological sequelae could be eliminated rapidly using substances - disincentivising long-term gains.

> **Aiden:** "*With surgery cos it's, surgery's irrelevant, innit, they do what they've got to do, you do what you've got to do. So, if your minds set for, if you're in heroin, amphetamine or whatever, you'll go and do it. It dun't matter what a doctor says*"

Theme A2: Interaction with healthcare. Many participants had the perception that they would receive i. inferior healthcare treatment compared to non-substance users and ii. may face discrimination due to stigma around substance use. Stigma was felt as a barrier to intervention/treatment engagement/compliance. Participants felt also that healthcare services had a lack of emphasis on substance use (e.g., some previous patients stated that preoperative assessment did not ask them about substance use). *Partly* as result of these factors, participants suggested they may not disclose substance use to healthcare staff (which removes the opportunity to intervene). This was compounded by a fear that surgery could be delayed/cancelled (if participants believed disclosure may lead to delayed treatment, they may keep it to themselves).

Rosie: *"…they do see addicts as a drain on the system, especially in Accident and Emergency, or when you're having a thousand pound operation because your habit has caused your health problem…"*

Theme A3: Substance use as a coping strategy. Substance use was seen as a method of coping with low affect arising from loneliness, boredom, distress/stress and, naturally, the negative psychological/physiological effects of withdrawal. As such, participants felt that reducing use of/abstaining from preoperative substance use would be unmanageable. This, especially considering the stress of surgery may precipitate feelings of distress.

Ryan: "[it's a] *vicious cycle where, you know, someone's got mental health problems and they feel a lot of anxiety from that so they take drugs to reduce the anxiety and the drugs they become tolerant so they use more drugs, they use more drugs, they use more money, so they've got more money problems and they've got more anxiety coming off the money problems…"*

Theme A4: Hopelessness and cynicism. Consistent across participants was a large degree of low self- and other-belief (low self-efficacy).

Many participants suggested that they, but particularly others, would be incapable of changing their behaviour. This hopelessness was associated with a degree of cynicism; health was disregarded, and interventions were considered futile.

> **Jenny**: *"Some people that I know probably wouldn't like doing anything. Even if you locked them up they would still try and get it in there or whatever, you know, to try and do it, and they wouldn't be bothered* [about their health]*."*

Theme A5: Triggers. Participants suggested that preoperative reduction/abstinence would be severely hindered by both internal and external triggers for substance craving, seeking and use. Internal triggers included boredom and low affect (e.g., mental ill health). External triggers included exposure to certain people and places (e.g., being around people who use or being in areas where it is easy to obtain substances). These two external triggers were considered most important. The idiosyncratic nature of triggers was repeatedly raised also; triggers were considered highly heterogeneous.

> **Hazel:** *"I've been using drugs since I were 11, at the moment it's a bit of erratic, it comes with me depression, and goes"*

Theme A6: Social influences. Social influences from friends and/or or family were considered both as facilitators and barriers to preoperative substance use reduction/abstinence. As in *theme A1* above, family/friends could facilitate in both a direct and indirect manner. It follows that the absence of a supportive network of family/friends was seen as a barrier for many participants. However, as in *theme A5* above, certain friends/family members were seen as external triggers for substance craving, seeking and use (but also internal triggers; having influence over the individual's internal mental state e.g., home life stress). **Susan:** "*I need to stop doing what I'm doing to get this surgery […] I've got two children to think about...*"

Theme A7: Habit and automaticity. Many participants felt that preoperative substance use may not be a choice available to them; they were too ingrained in their habit. Many participants framed their use as a loss of autonomy and constraint on free will. This was emphasized by many participants stating that they derived little pleasure from substance use in spite of repeated use.

> **Elen:** *"…it's like built into you, you know and you're telling yourself all the way there you don't want to go* [and buy heroin] *but you're still going and getting* [it]*."*

Theme A8: Preoperative reduction easier than postoperative maintenance. A common theme across participants was that particular periods in the perioperative pathway would be in of themselves barriers and facilitators. As the title of this theme suggests, patients deemed i. preoperative substance use more risky than postoperative use and ii. saw the preoperative period as more finite and manageable.

> **Rob:** *"…I'd stop taking methadone, I would, I'd want to live that much that it would, overnight it would change me, I can't guarantee that I'd stay off it once I'd come through the thing, but I would stop for the f*cking operation."*

7.3.5 Themes: Intervention Strategies

Theme B1: Setting goals. Highly endorsed strategies included specific goal setting, pre-emptive planning and substance use tapering. Most, if not all, participants favoured gradual substance use cessation over abrupt abstinence (which may be dangerous and unsustainable e.g., Monte et al., 2010; Sarkar & Mattoo, 2012) with small and manageable reduction goals, over a longer period of time. Big unmanageable goals were seen as destined to fail. To aid goal achievement, participants endorsed individualised, pre-emptive planning of strategies to avoid, or avoid the effects of, specific triggers for their substance use craving, seeking and use. Participants suggested that planning could be facilitated by having a concrete surgery date to aim for. Despite a preference for planning and goal setting related strategies, most participants were highly critical of substance use self-monitoring strategies (e.g., time-consuming, pointless, boring).

> **Ryan:** *"…small, manageable goals rather than saying, 'you know what, tomorrow I'm going to be clean, off everything, never going to touch it again'* […] *you're setting yourself to be disappointed* […] *you're setting up expectations which will, they're going to be violated and then it's going to make you feel worse, you know."*

Theme B2: Providing risk information. A majority of participants understood that preoperative substance use would confer additional risk above substance use generally. They were, however, less sure about the specific risks. While the most endorsed intervention strategy was the provision of risk information, there were several caveats. Risk information was considered less useful when not coupled with motivation to reduce, and many participants suggested that risk information would not affect motivation. As risk information may, by default, scare or cause stress/distress to participants, some participants said that exposure to risk information may *increase* their substance use. Endorsed methods of bolstering the impact of risk information included i. delivery from individuals/sources with a high degree of specialist substance use knowledge (this extended in some cases to NHS staff, but in others, participants considered staff not well trained in substance use issues), ii. repeated delivery of the information and iii. monitoring and managing participants' fear-related stress, anxiety and perceived control over their substance use.

> **Logan:** *"…if they said you'd die if you didn't have this surgery* […] *it depends, if they said it now, I might because I'm wanting to stop, I'm wanting to change it,* […] *but the majority of my life I'd just say, 'F*ck it, I'll take me chances', kind of thing."*

Theme B3: Heavy-handed approaches. There was a divide between a minority of participants favouring authoritarian, versus a majority of participants favouring a liberal approach to intervention. The former suggested surgery should be withheld for substance users (e.g., refuse to operate following a positive drug test) and were typically in favour of scare-tactics based strategies. The latter suggested that forced treatment/intervention may be useless (e.g., drawing on examples of poor adherence to court-mandated treatment) and that a warm or strong working relationship between the interventionist and intervention-receiver would improve the outcomes. The authoritarian view was in stark contrast to a common view across interviews that harm reduction should be the focus of any preoperative intervention, above complete abstinence.

> **Dave:** “[if surgery was withheld] *all they're going to do is just go out and drink even more.”*

Theme B4: Addressing stress, distress and mental health. Given the impact low affect and stress was deemed to have on substance use, it follows that participants endorsed strategies relating to supporting mental health. As such, many participants frequently suggested that mental health intervention would be a vital adjunct component for any intervention targeting substance use dependency. Accordingly, the ability of a preoperative intervention to identify, if not actively address, mental ill health and refer (and if necessary fast track) to services was considered highly desirable.

> **Logan:** *“I suppose, seeing a psychologist first might help, or something else rather than just, straight away, like asking them, ‘Oh, do you want to stop completely?”*

Theme B5: Avoiding and removing triggers. As in *theme B1* above, participants highly favoured plans to avoid or avoid/counteract the effects of, triggers on behaviour. It was suggested that this process i. could be aided and enhanced via structured guidance with an interventionist and ii. be bolstered learned coping strategies aimed at tempering craving in the presence of triggering situations.

> **Charles:** *“…when I've, I have stopped using a couple of times before, and, yeah, it's definitely, definitely worked, like sitting down and working out what those triggers are and trying to keep yourself away from them…”*

Theme B6: Flexibility and individualisation. A large majority of participants emphasized that i. preoperative interventions would have to be highly individualised, and ii. the efficacy of certain strategies depends on the individual's personal circumstances and substance use history.

> **James:** *"I think* [all strategies are] *worth* […] *a go and things are going to be different for different people, you know, everybody's going to react in different ways to different things."*

Theme B7: Harm reduction strategies more realistic than complete abstinence. Participants stressed that both intervention deliverers/receivers should manage their expectations. As in theme B1, aiming for complete preoperative abstinence was thought to be unrealistic and that any steps to a reduction in use and/or a reduction of harm (e.g., through less risky routes of administration) should be strived for. Endorsed methods of harm reduction included the avoidance of superfluous substance use (e.g., the use of substances other than the individual's dependency) and maintenance therapy for opioids (not without caveats, see *theme C5*).

> **Ryan:** *"But, you know, if you could say to people, I think if you gave across the idea, look, eighteen weeks, you know, you could stop completely but even if you reduce a bit, that'd be great, that would get rid of that tension I think, that's one avenue for getting rid of that tension, you know."*

Theme B8: Pre-surgery an opportune time to motivate detoxification and/or rehabilitation attendance. As a strategy to capitalise on the fact that preoperative reduction was considered easier than postoperative maintenance (*theme A8*), many participants suggested that the preoperative period would be an ideal time to enter into inpatient detox and/or a rehab community. Participants endorsed a fast track system, which they felt may be highly motivating. Participants typically held detox and rehab as the gold standard intervention strategy but warned that relapse was common without a strong commitment to abstain - and thus recommended additional support.

> **Chris:** *"…maybe after the assessment, I think the time in between surgery it would have been helpful for me to be detoxed, it would have been because I still, you know, I still came out after the surgery and spending time in hospital, I still came out with 60ml Methadone problem and I were using on top as well so..."*

Theme B9: Aiding memory. Some participants suggested that having reminders of a surgery date/appointments would help keep substance use reduction at the forefront of their mind. Memory aid suggestions included text messages/phone calls with a substance use counsellor. Two participants also suggested that having family or friends remind them of their goals, and/or organize appointments may be beneficial also.

> **Chloe:** *"Constant reminder, yeah I think that would be good."*

Theme B10: Just talking to someone. Some participants simply endorsed having someone to talk to about their substance use and life circumstances. More specifically, talking to someone who could provide unemotionally invested objective guidance (e.g., a substance use counsellor).

> **Rachel:** *"that's all a lot of people need, just people to listen and follow up on stuff I think…"*

7.3.6 Themes: Intervention Formats

Theme C1: Interventionists. The most discussed element relating to intervention formats was the interventionist. Many participants saw the interventionist as integral to the interventions success; often more so than the particular choice of intervention strategies. Moderators of successful interventionists included a warm relationship, particularly one built over a long time - though this latter point may be unrealistic in the preoperative period (though not having to see multiple interventionists prior to surgery and thus allowing a more personal relationship to develop may be a useful strategy). There were mixed opinions on NHS staff as interventionists; some suggested that clinicians may have more impact given their authority, while many felt that NHS staff were i. undertrained regarding substance use (underscored by a perception of stigmatisation) and ii. unable to relate to substance-dependent individuals. Participants generally favoured previous substance users or substance use specialists as interventionists. As such, referral to specialist services may be a vital component or adjunct to any preoperative intervention.

> **Mason:** *"…but a doctor or a nurse, yeah, I'd definitely take it on board because they're in that for a reason, aren't they, that's their job and they know what they're doing, so..."*

Theme C2: Timing. Patients generally favoured more intensive interventions; regular sessions (e.g., weekly) over a long period of time. Patients suggested that intervention as early before surgery was necessary, particularly so if the participant's goal was to taper down (e.g., through opioid maintenance therapy).

Joe: *"Well someone who's been doing it for 20 years isn't going to sort it out in 13 weeks, you know."*

Theme C3: Group sessions. The perceived value of preoperative *group-based* intervention had a mixed to negative reception among many participants; participants stressed that such groups often expose them to external triggers for substance craving, seeking and use (e.g., exposure to other substance users). Some participants suggested that groups may set off internal triggers too; some participants outlined their struggles with social anxiety, which group sessions – through the pressure to be open, may increase.

Noah*:* *"Just like people coming in and they're on heroin anyway, some people can come in and then they're showing their phone numbers and stuff…"*

Theme C4: One-to-one sessions. By far the most endorsed intervention format was one-to-one sessions, primarily because conversations could be more in-depth and confidential, and strategies could be more flexible and individualised. All participants, when asked to outline their ideal preoperative intervention, favoured weekly one-to-one intervention sessions, mostly composed of considered risk information and practical support (e.g., motivational interviewing, mental health support).

Mason: *"Yeah, I don't like groups, me, you get all kind of riff-raff in there, but yeah, one-on-one, because if there's loads of people in there you think they all judge you and stuff, yeah, I find it difficult…"*

Theme C5: Other modes of delivery. The relative pros and cons of formats other than group-based/one-to-one sessions were discussed also. For opioid users, many participants held opioid maintenance therapy in high regard and considered it very useful for goal setting/planning strategies. By removing the physiological/psychological effects of withdrawal, maintenance therapy was considered a useful facilitator for the targeting of other behavioural determinants. However, participants also highlighted that tapering is incredibly difficult, with many users having multiple cycles of tapering and relapsing over years. In a time-limited period, a significant degree of motivation on the part of the user would be required to reduce. One participant suggested that themselves, and most people they knew, would not stick to any taper schedule. Because tapering off the prescription would be necessary in the preoperative period, all the above issues present significant difficulties. In this way, opioid substitution may be counterproductive to preoperative reduction. Lastly, i. most participants considered remote interventions (e.g., phone calls) to be potentially ineffective, ii. some participants information stated that risk information leaflets could be useful if supplemented with more intensive strategies, and iii. two participants who previously tried disulfiram for alcohol were enthusiastic about its use (one of which was frustrated about not being to have it prescribed).

> **Joe:** *"You know, not just leaflets, talking information, that sort of thing. If you give people leaflets then they just tend to take them and not read them don't they? That sort of thing."*

7.4 Discussion

The present study aimed to involve potential intervention recipients in the design of a novel intervention for reducing preoperative substance use, for those with substance use dependency. The study involved 36 current or previous users of a variety of substances, of various ages; though participants, overall, were surprisingly homogeneous regarding their beliefs and opinions. As would be expected, this population presents a complex challenge for intervention designers – with a host of environmental, cognitive, social, and other variables at play. Through semi-structured interviews and qualitative analysis, several potentially modifiable determinants of behaviour change were identified (including low motivation, perception of stigma, hopelessness and habits), as well as several intervention strategies and formats deemed useful to address them (including pragmatism, individualisation, understanding, face-to-face interaction, strategic planning and more). Centred around key themes that emerged across interviews, theoretical and practical considerations are discussed henceforth.

Despite widespread belief (e.g., Ten Hoor et al., 2012) that inducing fear for health through emphasizing risk or threat may be useful tactics in stemming substance use[31], the consensus among participants in this study was that while risk information was perceived to be useful, it was considered ineffective alone, or even counterproductive; participants suggested that fear would be associated with an increase in substance use as a coping strategy. This is consistent with research demonstrating that inducing fear is counterproductive *without* a high degree of behaviour change self-efficacy, such that self-efficacy is a moderator of success: low self-efficacy and high perceived threat may lead to the opposite effect as desired, high self-efficacy and high perceived threat may lead to the desired behaviour change (Kok et al., 2018[32]). This may have important implications here; in addition to a rejection of fear appeals, participants often verbalized low self-efficacy at reducing substance use, high disregard for health, and low motivation to reduce. A high disregard for health and low motivation to reduce substance use in this study may be considered a by-product of high knowledge of risks (which, in the preoperative context, many participants assumed – despite not knowing specifics) coupled with low self-efficacy to reduce – a product of multiple past cessation failure attempts (which all participants had experienced).

It may be imperative, therefore, that any attempts at providing preoperative risk information need to be supplemented by tools and techniques to bolster self-efficacy (e.g., Kadden & Litt, 2011; Prestwich et al., 2014). As well as *targeting* perceived self-efficacy, the use of intervention techniques which an intervention recipient favours or is comfortable with, may, by definition, incur higher self-efficacy in that individual. In this way, endorsed preoperative intervention strategies including a high degree of individualization, intervention well in advance of surgery, focus on preoperative reduction over postoperative maintenance, harm reduction over complete abstinence and an avoidance of authoritarian approaches - are understandable, and warranted.

Most participants emphasized the potential importance of motivation and willpower (broadly defined as e.g., drive, desire, commitment to change, self-control) in efforts to reduce preoperative substance use. Indeed, many suggested that high levels were the *only* reasons they or their peers would make attempts at (but necessarily succeed in) reducing substance use prior to surgery. The salience of motivation as a behavioural determinant for substance use is well known (motivation is often the key target e.g., *motivational interviewing*; Miller & Rollnick, 1995), with motivation, and related constructs often having been theorised as the most proximal determinant of health behaviour (e.g., the Theory of Planned Behaviour; Ajzen, 1991). The preponderance of support for goal setting related strategies in this study, including tapering goals and planning to overcome barriers, may be the related to the fact that these strategies are typically conceived, and have been demonstrated to be, the antecedents of high motivation (Locke & Latham, 2002; Spinola, Park, Maisto & Chung, 2016)[33].

Self-determination theory (e.g., Deci & Ryan, 2000) conceives lack of motivation as *amotivation*; a state associated with low self-efficacy and a perception that costs of change outweigh benefits (Hardcastle et al., 2015). It also proposes change is unlikely when individuals are coerced or pressured (i.e., extrinsically motivated) and more likely when desired (i.e., intrinsic motivation; their own choice, based on their own values and interests). In support, O’Toole et al. (2006) found that the largest reported reason for entering treatment was physical health concerns (consistent with participants here suggesting motivation would be boosted due to health) and 100% of participants whose treatment motivation shifted from extrinsic to intrinsic completed treatment, versus 38.4% whose extrinsic motivation remained static (see also: Ryan, Plant & O’Malley, 1995). Given many participants suggested that motivation *could* be enhanced, it follows that *amotivated* individuals may need to be equipped with sufficient capabilities to achieve preoperative reduction (e.g., fast track to rehabilitation services), be in full knowledge of the benefits of preoperative reduction and be instilled with the belief that it is achievable. Despite a contingent of participants who supported heavy-handed approaches to intervention (e.g., not allowing substance users to have surgery), these approaches may be dangerous; undermining intrinsic motivation. Highly motivated patients' goal setting may be enhanced by setting specific, measurable, attainable, realistic and timely (SMART) goals. Goal achievement appears higher when goals are specific (e.g., reduce 5ml methadone a week prior to surgery) and difficult (if self-efficacy is high) (Webb et al., 2010).

Participants often suggested that they may not disclose their substance use upon referral, or at the time of preoperative assessment. This has been observed in past research. Islam et al. (2013) found that one-third of 2395 intravenous substance users accessing healthcare services only partially disclosed their substance use to staff (another third did not at all; see also qualitative research e.g., Abraham, 2017; McNeely et al., 2018). One reason identified in the present study may be that healthcare staff do not address the topic, perhaps because they do not see it as a priority, perhaps because they have no standardised guidelines to deal with it. This is unfortunate; several published guidelines exist (Rosenblatt & Mekhali, 2005; Hernandez, Birnbach & Zundert, 2005; Huxtable, Roberts, Somogyi & Macintyre, 2011), and previous authors have highlighted and stressed the importance of obtaining information of preoperative patients' substance use (Bailes, 1998; Culver & Walker, 1999).

Similarly, if patients are not asked about their substance use, they may feel as though it does not matter and may be discouraged from reducing or abstaining prior to surgery. Validated substance use screening measures routinely applied upon GP referral or at preoperative assessment may be accurate, inexpensive, brief - and thus highly useful here[34].

A more pertinent reason for non-disclosure however, may be perceived stigma (identified in the above studies). Indeed, participants' reservation with healthcare staff as interventionists was based on a perceived lack of knowledge/training of dependency, and a perceived stigma (and perception of worst treatment). A systematic review of studies on the attitudes of health professionals towards substance users supported the notion that substance users are subjected to negative attitudes (van Boekel et al., 2013). Further, the review found that negative attitudes could negatively impact treatment. However, in line with a systematic review of interventions to reduce stigma this may be modifiable (Livingston et al., 2012). The perception that healthcare staff may have little knowledge of dependency may be supported too. For example, an interview study of nurse anaesthetists found that they openly admitted to being uncertain about symptomatology, interaction between anaesthetics and substances, and methods to help patients (Forsberg et al., 2018). There is also evidence that the more credible the perceived source of information or guidance, the more effective the health intervention (e.g., Durantini et al., 2006). Given the above, perhaps a complex preoperative intervention may not only be necessary for patients, but staff; i. for increasing screening, ii. improving/implementing guidelines, iii. to increase knowledge and confidence and iv. to reduce stigma.

Exposure to other substance users or places associated with substance use were seen as large barriers preventing preoperative substance use reduction. Cue exposure has been shown to reliably predict craving, substance use *per se*, the development of substance dependency, maintenance of substance use/dependency, and relapse into habitual substance use (i.e., *cue reactivity*). Broadly, theories of associative learning are thought to account for the mechanisms behind this phenomenon (Carter & Tiffany, 1999; Ferguson & Shiffman, 2009; Hogarth, Dickinson & Duka, 2010).

Participants recommended two types of strategies to overcome the effect of external triggers on behaviour: identification of, and pre-emptive planning to avoid cues, and coping strategies to help reduce the effect of cues on behaviour. The former, as with goal setting[35] may require a high degree of *a-priori* motivation and commitment, though there is reasonable evidence for its efficacy across a range of health behaviours (Hagger & Luszczynska, 2014). In the context of substance dependency, planning to refuse substances if offered, or planning to do an alternative activity at a time when substance use is typical may indeed be useful preoperative strategies[36] (for an overview see Prestwich, Conner & Lawton, 2006). Regarding participants' second recommendation (skills to resist substance use seeking and use in the presence of cues) several strategies may be useful (for a brief overview, see Dharmadhikari & Sinha, 2015[37]). Boosting self-efficacy may be one highly effective strategy to increase the efficacy of coping skills (Bandura & Locke, 2003), and teaching coping skills strategies may be a highly effective way to increase self-efficacy (for an overview: Kadden & Litt, 2012). This self-efficacy and coping relationship is explained by the cognitive-behavioural model of the relapse process; relapse follows a high-risk situation when one perceives their coping strategies as ineffective (low self-efficacy), relapse is less likely when one believes they have effective coping strategies (high self-efficacy) (Larimer, Palmer & Marlatt, 1999).

Aside from external triggers on behaviour, many participants reported that substance use craving and seeking was triggered by their inner emotional states; substance use was seen as a way of coping with psychological distress (substance use and psychological distress are shown to be mutually reinforcing; e.g Holahan et al., 2003). There was a significant degree of co-morbidly (*dual diagnosis*) in the sample; participants referred to psychiatric diagnoses such as depression (common in this population; Petry, Stinson & Grant, 2005). Not only is there evidence that substance use increases the risk of perioperative complications, but mental ill health too; thus, the risk to these participants may be compounded (see Chapter 3).

To reduce preoperative substance use, many participants suggested they would need to address their internal cue reactivity: mental health issues, boredom, general stressors including likely (at least partial) causes of mental distress (e.g., housing issues). Unfortunately, it may be unrealistic to address such a wide range of complex triggers routinely in the time-limited preoperative context. Preoperative interventions may therefore offer a *minimum* number of components: i. efficient screening for mental health or other practical issues promoting substance use, ii. signposting and/or fast tracks to services which may offer mental health/practical support, iii. boosting self-efficacy to improve coping skills in the presence of cues (and motivation generally) and *vice-versa*, and iv. prompt planning of cue avoidance when/if motivated. It is important to note that the latter two strategies may benefit from the context at hand; these techniques only need to be effective in a relatively short period of time (i.e., the preoperative period), circumventing perhaps the hardest and failure-prone part of the recovery process: post-change maintenance (Larimer, Palmer & Marlatt, 1999; Middleton, Anton & Perri, 2016).

Increased social support can have a range of positive physiological effects (e.g., on cardiovascular health; Uchino, Cacioppo & Kiecolt-Glaser, 1996). There is also evidence to suggest that individuals who have the support of their family/friends have more substance use treatment successful outcomes (e.g., Clark, 2001; Dobkin, Civita, Paratherakis & Gill, 2002). This was reflected in the current study. Again, key behavioural determinants that positive social support may bolster is self-efficacy and coping (Stevens et al., 2015; Kadden & Litt, 2011; which may increase motivation), though there are plethora of other *general* (e.g., stress reduction, exposure to norms, reduced loneliness) and *instrumental* (e.g., organising appointments) social support mechanisms that may positively impact on substance use (Thoits, 2011a; 2011b).

With the caveat of negative social influences i.e., triggers, participants in the present study suggested that having family/friends engaged in preoperative interventions would be helpful and knowing that complications could negatively impact upon their loved ones would be motivating. *Some* participants also suggested that mutual aid groups (e.g., Narcotics Anonymous) may be a useful way of being introduced to an abstinent group of friends. High self-efficacy and motivation may buffer against any cue-related barriers (e.g., discussing substances and being around users) inherent in mutual support meetings thus, speculatively, encouraging attendance or organising mutual support between substance users in the preoperative period *may* be therefore a worthwhile adjunctive intervention strategy, though leveraging family influence on behaviour, perhaps through involving them in the intervention (e.g., see Behavioural Couples Therapy; O'Farrell & Schein, 2011), may be particularly useful.

Participants favoured individualisation and one-to-one intervention approaches. The main limitation with individualised approaches is their high cost and intensity. Nevertheless, such strategies have been regarded (and demonstrated) as efficacious previously (e.g., Hser et al., 1999) and have been endorsed by service users in previous studies (e.g., Friedricks, Spies, Harter & Buchloz, 2016). Such approaches are more reactive and adaptable, a useful quality given that the efficacy of individual intervention strategies here was regarded as highly heterogeneous. In relation to theory outlined above, individualisation may be enhanced using theory-related psychometric instruments. For example, the Treatment Entry Questionnaire has shown to be a reliable and valid instrument for assessing self-determined motivation for substance use treatment (Urbanoski & Wild, 2012); the Inventories of Drinking/Drug-Taking Situations (Turner, Annis & Sklar, 1997) useful tools for assessing external triggers, and the Situation Confidence Questionnaire (Annis, 1988) likewise for trigger-specific coping. Using such instruments as the starting point for intervention may provide a useful way of i. standardising intervention protocols (e.g., to increase translation into practice through ease of training, perhaps reducing cost), ii. targeting strategies at salient issues (e.g., boosting intrinsic motivation if low) and iii. assessing the effect of such strategies on constructs theorized to be related to substance use (i.e., being able to easily assess progress).

Confounding the conclusions of this study were several limitations. Firstly, because participants were recruited from a treatment centre, they may reflect individuals most motivated to receive treatment; by being in treatment, they were by default making a step towards sobriety. It may be that those outside the treatment system represent a different population of users, who may have had different experiences, and opinions on determinants and strategies. Given that many participants had to attend the centre as prerequisite for opioid substitution prescription or other reasons of compulsion (e.g., court-mandated) the notion that these participants represent the most motivated is unlikely to be true (and often reflected in participants' candour). Relatedly, the sample was mostly male, thus conclusions may not generalise to both sexes. It is however the case that twice as many males than females may be substance-dependent in the UK (e.g., McManus et al., 2016), so the sample distribution of sex may simply reflect the population distribution. Participants in the present study were not pre-surgical patients. Participants therefore had to either draw on their past experiences, generalise from their current situation, or draw on second-hand accounts from their contemporaries. This is an issue; research does show that serious health scares may change behaviour in substance-dependent individuals (e.g., Pettersen et al., 2018). Participants were however quite adamant in their opinions and beliefs, and many had similar or past experiences with healthcare services, so were in a good position to, in the author's and participants' opinion, hypothesize about their future behaviour. Also, participants that discussed experiences with surgery or healthcare use in general did not have particularly unique insights; that is, it appears participants were quite homogeneous in their views regardless of past experiences. Recruiting a sample of *preoperative* substance-dependent individuals, would, as Chapter 4 attests, be a protracted process. Convenience sampling at a substance treatment centre was the only sampling strategy deemed realistic to recruit a sufficient number of participants in a reasonable time period.

In sum, the present study may provide useful information for future interventions; targetable determinants including low self-efficacy and motivation and endorsed intervention strategies such as goal setting and individualisation. In particular, this study has highlighted that future interventions may have to be complex and intensive, though preoperative cessation in this unique population may be achievable. All conclusions must, however, be tempered by the aforementioned limitations, including a mostly male, non-patient sample (discussing hypothesized behaviour) recruited from a treatment centre (where motivation may be higher).

7.5 Key Findings: Study 6

- Among substance dependent individuals, the preoperative period was often considered a teachable moment for behaviour change. Highly endorsed preoperative interventions strategies included goal setting and intervention individualisation. However, using fear to motivate cessation or reduction was largely considered ineffective.
- Participants highlighted that efforts to encourage preoperative substance use reduction would be complicated by a perceived sense of stigma and lack of substance use-related expertise within healthcare settings.
- Harm reduction strategies were considered more useful than efforts to promote complete abstinence. This was particularly the case for individuals whose motivation to quit was low.
- Preoperative substance use abstinence or reduction may be hampered by psychological determinants including: low motivation, low self-efficacy and internal cue reactivity (e.g. poor mental health). Environmental determinants such as external cues (interacting with areas and people associated with substance use) were considered important also.

CHAPTER 8. SUMMARY AND DISCUSSION

8.1 Thesis Aims and Summary

8.1.1 Background

There is mounting evidence that preoperative use of a variety of recreational substances is associated with considerable postoperative morbidity (including mortality) (section 2.3). This effect appears to be dose-dependent (e.g., Eliasen et al., 2013) and independent of possible confounding factors (e.g., age) (e.g., Menendez et al., 2015). Despite this, an in-depth literature review reported in Chapter 2 identified many important evidence gaps in the perioperative substance use literature.

Briefly, there appeared to have been no previous investigation of whether preoperative substance use can impact on postoperative mental health outcomes – despite evidence that both substance use and undergoing surgery can negatively impact on mental health, and that both substance use and low mental health have been observed to predict complications (see subsection 3.1.1). There were also no published studies investigating the prevalence of hazardous preoperative substance use in the UK and thus no statistics on patient characteristics that interventions may best focus on (see sections 2.4 and 4.1). There was also no investigation of whether preoperative assessment detection of patients at high risk due to substance use may be improved, and no previous study investigating whether validated measures are better predictors of complications than routine assessments (see sections 2.5 and 3.1). Further, and perhaps most importantly, reviews of preoperative interventions for alcohol use seemed to be out of date and absent for illicit substance use (see subsection

2.6.4). After a systematic search in Chapter 5, there appeared to have been a small number of trials aiming to assess whether interventions can be introduced to reduce preoperative alcohol (nine trials - though just three targeted alcohol *alone*) and other illicit substance use (two trials - though zero targeted illicit substance use alone, and one of these studies did not assess substance use outcomes). This contrasts with other behaviours with similar perioperative risk profiles which have been a focus of numerous trials such as smoking (Prestwich et al., 2017: twenty-two trials) and lack of physical activity (Kehler et al., 2017: eleven trials; Stephensen et al., 2018: twenty-four trials). Previous intervention trials also seemed to have ignored developments in the behaviour change literature; interventions appeared to be based on generalized strategies, and not based on primary research extracting salient behavioural determinants associated with the behaviour(s).

8.1.2 Aims and Studies

Mindful that it would be impossible to tackle *all* gaps outlined in Chapter 2 and identified in subsequent chapters, this thesis focused on those deemed most important and feasible. Broadly, this thesis may be considered a *needs assessment* wherein the nature and extent of the problem, for whom and at what levels the problem exists, probable causes of the problem (e.g., intervention targets) and what has been effective in addressing the problem, were investigated. As such, the thesis - with an eye to the local context of the research, had two overarching aims:

1. **Risk analysis:** To assess the risk of preoperative substance use (POSU).
2. **Intervention development research:** To inform preoperative intervention development for POSU.

These two aims were divided into six more focused aims:

1.a. Explore uninvestigated routes through which POSU may have deleterious outcomes.

1.b. Assess the local extent (prevalence) of POSU.

1.c. Assess patient characteristics that may be associated with POSU.

1.d. Assess the local detectability of POSU.

2.a. Identify, assess and critically appraise current interventions to counteract POSU.

2.b. To build upon limitations of previous interventions by conducting research to inform future interventions to counteract POSU (e.g., assessing determinants of POSU reduction).

To address these aims, results of six studies are presented. In Chapter 3, Study 1 linked and analysed two waves of longitudinal data to determine whether an association existed between hazardous preoperative alcohol use and poor postoperative mental health outcomes (1.a). Chapter 4 presented two studies, both conducted in two separate Leeds-based preoperative assessment clinics. The first (Study 2) assessed the prevalence of, and patient characteristics associated with, hazardous preoperative substance use - as well as briefly surveying patient views on intervention (1.b and 1.c). The second

(Study 3) also assessed prevalence and prevalence *x* patient characteristics, but also assessed whether routine assessment was missing patients at risk of complications through substance use (and thus potential intervention recipients), whether validated substance use measures could predict perioperative complications better than routine assessment and whether an index of polysubstance use was able to predict complications (1.a, 1.b, 1.c and 1.d). In Chapter 5, Study 4 systematically identified, outlined, described and where appropriate meta-analysed the literature on preoperative interventions for both alcohol and illicit substance use (2.a). In Chapter 6, Study 5 a brief COM-B based questionnaire for assessing and identifying determinants of preoperative alcohol use was designed, trialled on a sample of preoperative patients and psychometrically evaluated (2.b). Study 5 also tried to assess patient preferences regarding possible intervention formats and modes of delivery (2.b). In Chapter 7, Study 6 aimed to investigate determinants of preoperative substance use amongst substance-dependent individuals, as well as their preferred intervention strategies, format and modes of delivery (2.b).

8.2 Summary of Main Findings and Contributions to Knowledge

8.2.1 Chapter 3

Study 1 identified one route through which alcohol use may catalyse postoperative complications (or negatively impact on perioperative patients generally) and provided further potential rationale for the implementation of preoperative interventions; for the first time, Study 1 provided some initial evidence that hazardous preoperative alcohol use may deleteriously impact on postoperative wellbeing and depressive symptoms.

Here, an interaction term was generated representing respondents drinking more than two glasses of alcohol five to six days a week or more at baseline (equivalent to an AUDIT-C score ≥ 5 or at minimum approximately 15 alcohol units per week) *x* those having had (inpatient, outpatient or either) surgery in the preceding 12-months at follow-up (approximately 2.5 years post-baseline). In a fully adjusted (e.g., for baseline outcome scores, comorbidities and age) model with follow-up wellbeing as the outcome, inpatient surgery alone and hazardous drinking alone were both non-significant predictors, while inpatient surgery *x* hazardous drinking was significant; those with both factors present had significantly poorer wellbeing than those who did not. In equivalent models with depressive symptoms as the outcome, effects were similar. These effects were not observed amongst those having generally lower risk surgeries (outpatient surgeries), though largely held in analyses accounting for missing data using multiple imputation (while inpatient surgery *x* depressive symptoms became non-significant, *either* surgery *x* depressive symptoms remained marginally significant). Further, inspection of marginal means revealed that among respondents having inpatient surgery, baseline hazardous drinking was associated with a lower score of postoperative wellbeing and more depressive symptoms (small effect sizes) and the impact of having inpatient surgery on wellbeing and depressive symptoms was greater amongst baseline hazardous drinkers (small-medium effect sizes).

8.2.2 Chapter 4

Study 2 and 3 further highlighted (amongst other issues) the need for more development and trials of substance use related preoperative interventions - especially in the local context (and the UK more generally, where no previous substance use targeted interventions have been assessed; Chapter 5).

In the first known UK analysis, across two preoperative assessment clinics, Study 2 and 3 demonstrated that the prevalence of hazardous preoperative alcohol use (as defined by scores on a validated measure shown to predict complications previously) may be as common as one in three patients; that previous three months illicit substance use may be less prominent but highly associated with hazardous alcohol use and smoking; and that hazardous preoperative substance use, in general, was associated with certain patient characteristics (males, younger patients and those with lower co-morbidity scores). Study 2 also demonstrated that motivation for intervention participation may be low amongst substance users (though this was based on a small subsample), while Study 3 also demonstrated that routine preoperative assessment (versus validated measures) *may* be missing certain patients who may benefit from intervention and that routine measures of alcohol use were often poorly adhered to. There were, however, no notable differences between routine and a brief validated measure of alcohol use (AUDIT-C) at predicting complications, nor any indication that a validated polysubstance use index (the WHO ASSIST) could predict complications. Both of these findings may be partially explained due to a low complication event rate, thus lack of statistical power.

8.2.3 Chapter 5

In an update of previous alcohol focussed reviews, and the first known illicit substance focussed systematic review of the literature, Study 4 identified that previous preoperative substance use interventions were low in number, generally had low quality and had mixed efficacy.

Using a purposively sensitive search strategy and inclusive inclusion criteria, Study 4 identified just nine trials for inclusion. Of these, there were just five randomised controlled trials, of which just three focused solely on alcohol use. There were no illicit substance use-only interventions - and thus no focus on *specific* illicit substances. Interventions were mostly high risk-of-bias e.g., blinding and randomisation sequence reporting was absent from all studies (naturally this includes non-randomised studies by default). Most interventions were variations on *motivational interviewing* though just one study reported an intervention protocol (which would aid replication and translation to practice) and descriptions of actual intervention techniques were often vague and hard to interpret. No intervention appeared to be based on determinant elicitation research within the perioperative context. Regardless, approximate behaviour change techniques were coded, though the small number of studies was not suitable for meta-regressions assessing whether intervention features could predict efficacy. There was some evidence across studies that interventions could be introduced to reduce postoperative alcohol use, though i. surprisingly just three studies measured *preoperative* alcohol use, ii. behavioural-only interventions did not have a significant pooled effect, and iii. two small trials using the pharmaceutical disulfiram were by far the most effective - both achieving complete preoperative abstinence. These latter two trials, when pooled, had large significant effects on postoperative complications - though behavioural-only interventions had non-significant effects (favouring controls). There was no robust evidence that illicit substance use could be modified.

8.2.4 Chapter 6

Study 5 developed a brief COM-B based questionnaire for assessing and targeting determinants of preoperative alcohol use, after iteration finding a psychometrically sound questionnaire which was able to predict preoperative alcohol use scores. There was also *some* insight into patient preferences regarding intervention deliverers and formats.

In the first known investigation aiming to identify targets for preoperative alcohol use interventions, perioperative-specific items representing COM-B model domains were generated by a team of researchers. Through correspondence and debate, these were reduced to a select few felt best to represent the model and integrated into a questionnaire. Patient feedback revealed that the questionnaire was understood and acceptable. After a number of preoperative patients completed the questionnaire, analysis found that a shortened 13-item version represented COM-B domains well in a confirmatory factor analysis; the questionnaire had high convergent validity, high internal reliability, though questionable discriminant validity. All six sub-domains were significantly associated with AUDIT-C scores (though not ASSIST scores) with *reflective motivation, physical capability* and *physical opportunity* predicting scores after controlling for all other subdomains. Patients generally had no strong preferences between intervention deliverers, though nurses, GPs and surgery team members were the highest among AUDIT-C hazardous patients. One-to-one and group sessions were the most favoured intervention formats, though computer-based interventions were by far the least rated.

8.2.5 Chapter 7

Study 6 is the first known study to assess substance-dependent individuals' barriers and facilitators to perioperative substance use reduction, as well as their preferred interventions features. A variety of considerations and directions for future interventions were identified.

Determinants of preoperative substance use reduction included individual self-efficacy, motivation, ability to cope with internal and external cues, as well as issues such as perceived stigma in healthcare. Participants also discussed and endorsed many strategies and methods to help overcome barriers such as intervening as early as possible before surgery, setting substance use reduction goals, and adapting interventions to individuals' circumstances and needs. Preoperative behaviour change in this population was found to be highly complex, though as many participants suggested, achievable. This may be especially true given that the preoperative period is a unique window of time whereby a subset of individuals may be inherently motivated by physical health concerns, and abstinence or reduction is only required for a limited period. It is also true however that many participants where highly cynical of efforts to promote preoperative reduction for certain individuals. For these, harm reduction may be the central focus of intervention, though efforts to enhance motivation may be worthwhile.

8.3 Key Thesis Limitations

Despite many novel contributions, this thesis has several potential limitations. Aside from study limitations identified within each chapter discussion, this section will outline those most important in the context of the thesis as a whole. Directions to tackle identified limitations are expanded upon in section 8.4.

Perhaps one of the most prominent limitations is the fact that the intervention development research conducted, while potentially useful, is essentially incomplete. It would have been useful for the thesis to have a completed intervention protocol ready for a pilot trial. There may be many further studies necessary before a trial is justified however (explored further in section 8.4). For instance, it is still not clear how one would integrate the COM-B questionnaire - which may be used to identify within-patient factors which may be useful to target (Chapter 6), into routine practice. It also not clear who would be best to deliver interventions, when and where would be the best time and place for intervention (though for both of these, there was some patient-focussed insight in Chapter's 6 and 7) and whether delivering tailored interventions may be acceptable to both patients and deliverers. It may also be the case that determinants identified in Chapters 6 and 7 are only relevant to the context of Leeds (as with prevalence estimates in Chapter 4). This was acknowledged from the start of thesis. Indeed, while interventions may be generalised between countries, cultures, time and place - their strategies may need to be adapted to address issues unique to the recipient population. Lastly, as required in the Behaviour Change Wheel framework (see subsection 6.1.1), the best behaviour change techniques (BCTs) used to modify identified determinants are unknown.

A second limitation may be the sample sizes in some studies. For example, in Study 5 analyses involving the COM-B questionnaire, estimates had wide confidence intervals - indicating imprecision. Similarly, in Studies 2 and 3 few illicit substance users were identified and an unknown - but likely very small proportion of substance-dependent patients were recruited. In Study 3, partly due to an insufficient sample size but partly (or perhaps largely) due to an insufficiently sensitive perioperative outcomes measure, two key research questions remained unanswered: i. can routine practice be improved upon through inclusion of validated substance use measures? And ii. can a polysubstance use index identify at-risk patients? Throughout the thesis, one of the main issues was trying to gain access to patients. This was a difficult process, requiring several layers of approval. The time limitations of the thesis meant pragmatic decisions regarding the length and target sample sizes of studies had to be made - which ultimately may have had a negative effect on inferential analyses.

A number of further limitations stemmed from the fact that patients and service users were the target participants of this thesis. This thesis had to, rightly, be mindful of practical and ethical considerations regarding participant and staff burden. For instance, by having patients' complete questionnaires at preoperative assessment (e.g., Study 3), which may be a highly emotionally sensitive time (possibly life-changing and highly stressful; see Chapter 3), it was felt best to keep their active participation short. Keeping participation short was highly necessary for staff also; delaying patients too much may have had knock-on effects - derailing the daily schedule and increasing proceeding patients' waiting times. This meant that questionnaires had to be short and that additional potentially useful data (e.g., for identifying potential intervention recipient characteristics) had to be deprioritised (e.g., assessment of socio-economic status, or other behavioural risk factors). Of course, if an aim was to integrate new questionnaires into routine practice, these questionnaires would have to be short in the preoperative context regardless - but assessing the utility of short questionnaires may have been improved by also delivering more intensive or probing assessments (e.g., DSM interviews) and comparing between them (e.g., AUDIT-C versus DSM sensitivity and specificity). Keeping patient participation short was also partly the reason for a lack of patient follow-up in Study 5 and patient *contact* follow-up in Study 3. In the case of the former, further insights into the questionnaire may have been made (e.g., temporal reliability) - the latter, a more patient-centred, holistic (e.g., quality of life) and potentially more sensitive (Woodfield et al., 2016) assessment of complications may have been achieved. Of course, steps to follow up on patients would have been made had issues with routine data in Study 3 been anticipated (e.g., ethical approval would have been sought to contact patients postoperatively). Limitations related to recruiting patients also meant that secondary datasets were sought to address certain research questions - which, by nature, are likely not to include all variables of interest (Study 1 and 2).

8.4 Implications for Future Research and Practice

Aside from directions outlined in Chapter 2 not directly addressed in this thesis (e.g., prospective studies investigating the effect of *specific* illicit substances on perioperative outcomes are greatly needed), there are several ways future research may build on the present studies. There may also be several ways routine practice may learn from the present findings.

Future trials, and perhaps routine practice, should find many useful directions in the systematic review presented in Study 4. For instance, practitioners may note that disulfiram appears highly useful for achieving preoperative abstinence (and in turn reducing complications). This, of course, tempered by the fact that this substance is recommended only for use in those *most* at risk (due to serious side effects) and that even amongst these individuals, they may need initial levels of high motivation for compliance (Fuller et al., 1986; Kalra, De Sousa & Shrivastava, 2014; Pettinati et al., 2008). Future researchers may also note and address the lack of quality in previous trials, lack of clear reporting of intervention components, lack of alcohol or specific substances as an intervention focus (meaning perioperative health outcomes may be confounded by the effect of change in other health behaviours), the lack of *preoperative* behaviour measurement and often lack of assessment of perioperative health outcomes. Both future research and practitioners may wish to note also that there is very limited evidence for effectiveness of behavioural interventions in this context. Adopting intervention strategies used in most previous studies, therefore, cannot be unequivocally recommended. However, given that a reduction in preoperative substance use may incur perioperative benefits (Gordon, 2018; Tønnesen et al., 2009) and substance focussed behavioural interventions have succeeded in other contexts (e.g., primary care; Kaner et al., 2018) - new strategies based on best practice behaviour change intervention development frameworks (e.g., the Behaviour Change Wheel; Michie et al., 2013) may improve outcomes.

Indeed, future trials may benefit from more intervention development research. As such it would be useful for future studies to confirm the construct validity of the COM-B questionnaire in Study 5 in a larger sample (or assess determinants, and thus provide intervention targets, from other theories or frameworks), to further investigate patient preferences with regard to strategies and determinants (perhaps through in-depth qualitative work) and further confirm insights provided in Study 6 (perhaps through - though challenging recruiting a sample of *preoperative* substance-dependent patients). For the latter, service designers should be mindful that communication between preoperative assessment and addiction treatment centres may be highly useful; such centres may have more resources to implement more intensive and tailored interventions (desired by participants; Study 6). For those at most risk, referral from preoperative assessment to such centres may allow for an efficient way of exposing patients to intervention. Clinicians based at the centre may be able to feedback to patients' surgical care team as to their progress. In this paradigm, the surgical care team, theoretically, would be able to better predict any substance-related complications based on patients' cessation progress and implement preventative measures as necessary.

Integrating *any* preoperative intervention into routine practice may be a complex process - and may have to occur at multiple levels. While much attention may be paid to patients' needs for behaviour change, NHS staff may be equally as important to involve in research. If we take a potential candidate preoperative interventionist: patients' general practitioner (GP) at the time of referral to surgery, a complex intervention may therefore have to focus on GP behaviours that comprise a brief intervention including GP alcohol use screening and strategy giving behaviours (e.g., prompting a patient to set weekly alcohol use goals). Future research, therefore, may have to *intervene on interveners* - perhaps following semi-structured interviews identifying COM-B determinants of intervention. Indeed, in this example, GPs may feel they do not have the knowledge of the impact of preoperative substance use on perioperative outcomes (psychological capability), the means to intervene (e.g., having enough time; physical opportunity) or the social opportunity (e.g., feeling confident about raising the issue of substance use with patients without fear of causing offence, for example). All of which may be intervention targets.

Future trial designers may note that assessing the best BCTs to alter particular determinants of preoperative substance use may be inferred from previous research or assessed through primary research. For example, by identifying BCTs effective in modifying theory-related constructs in relevant published meta-analyses (e.g., Prestwich, Kellar, Conner, Lawton, Gardner & Turgut, 2016) or by conducting or appraising studies involving expert consensus methods e.g., Delphi procedures (e.g., Garnett et al., 2015). Potentially the most insightful, but perhaps most far away, is the accumulation of more trials in the preoperative context - after which future meta-analyses may be better placed than Study 4 to identify whether certain BCTs are associated with higher efficacy.

Implications from Study 3 for preoperative assessment staff include: to be mindful that i. patients may be underreporting their substance use, ii. routine measures may underestimate the number of patients who may benefit from intervention, and iii. adherence to routine measures may be preferable to idiosyncratic descriptions (e.g., "*social drinker*"). The first point may be true if the difference in identified prevalence rates between study measures and routine were explained by reluctance to disclose to the latter (perhaps due to concerns around cancellation of surgery), and the second point perhaps only speculatively (e.g., for alcohol: if findings found in previous large studies are extrapolated here e.g., Bradley et al., 2011). Adherence to measures may be improved by inclusion of more streamlined and structured (preferably validated) checkbox measures. Lastly, assessors, and other healthcare staff alike should note the high perceived level of stigma felt amongst substance-dependent individuals (e.g., Study 6). While it is highly likely that the vast majority of staff hold non-discriminatory views, there may be a minority who do and unintentional stigmatisation (e.g., use of offensive language; assumptions about an individuals' character or background) (both highlighted in van Boekel et al., 2013). There may therefore be some use in interventions to reduce stigma (which may be effective with healthcare staff: Livingston et al., 2012) though methods to reduce *perceived* stigma amongst substance-dependent individuals may be more useful to investigate (e.g., how can well-meaning staff mitigate this perception?).

In general, the choice of lifestyle behaviour measures used in routine practice (as in Study 3) seem to be cursory and unscientific (which seems to be representative after inspection of many other UK clinics' assessment forms; though this could be the subject of an empirical investigation). For instance, as in Appendix C, the Study 3 clinic did not contain a measure of physical activity, and did not include validated measures of sleep, alcohol or illicit substance use. To improve the predictability and thus potential utility of measures of behaviour in this context, it may be useful to see whether (as was attempted here for alcohol only) routine versus other behavioural measures can better predict adverse events. If score-based measures were used, clinically relevant cut-offs could be identified and used to flag patients that may benefit from intervention.

Future studies could greatly improve on Study 3. Given that there was a failure to detect significant effects of alcohol use/polysubstance use on complications - but that effect sizes were in the predicted directions, the first, and most obvious suggestion, is to recruit a much larger sample. This , combined with outcomes including patient contact follow-up (e.g., for recovery or quality of life outcomes), integration of standardised complication measures (completed by dedicated researchers) into each patient's perioperative pathway (with Clavien Dindo grading; see subsection 1.4.1) and a host of healthcare utilisation measures (e.g., readmission, length of stay), would likely lead to more robust conclusions. In this 'perfect' Study 3, a randomised selection of preoperative assessors (alongside efforts to mitigate contamination - perhaps through a cluster design) would have either a validated substance use measure or continue using routine measures. Comparing between the two may eliminate speculation that mismatch in 'detection' rates may be explained through unwillingness to disclose to healthcare staff versus a researcher. Further, patients may complete, for instance, blood-tests (e.g., for illicit substances) or DSM interviews which may be used as a gold-standard comparison of detection. Routine versus study measures may then be compared to see which have better specificity/sensitivity at predicting detections on the gold-standard measures. Lastly, a host of other variables may be assessed to identify more patient characteristics that may be associated with substance use; theoretically, the more one knows about the intervention target population, the more one can tailor the intervention to their needs.

While addressing several aims already, the aforementioned ‘perfect’ Study 3 (or other prospective studies in general) could also provide an assessment of the proposed affect-related ‘cycle of postoperative morbidity’ proposed in Study 1. Indeed, while Study 1 found very initial evidence that hazardous preoperative alcohol use may impact on postoperative affect - it is the case that Study 1 had some significant limitations (e.g., a long length of follow-up which may have reduced effect sizes, and a non-validated alcohol measure) and that future studies are needed. Here, future studies may include preoperative and postoperative (validated) measures of both substance use and low affect (e.g., depressive symptoms, anxiety, stress, wellbeing), as well as measures of potential confounds (e.g., surgical severity) and postoperative health outcomes. As such, models could investigate whether i. substance use and low affect at baseline are associated, ii. whether baseline substance use could predict postoperative low affect (and vice-versa), iii. whether both low affect and substance use could predict complications, iv. mediation models investigating substance use could predict complications *through* changes in affect (and vice-versa), and v. whether complications could predict reduced affect (and whether this low affect could increase substance use as a coping strategy). Such research may provide, for example, explanations for the observed effects of mental health on perioperative outcomes, as well as provide more rationale for routine preoperative interventions - perhaps aimed at reducing presurgical anxiety and substance use.

8.5 Conclusion

Mounting research suggests that perioperative use of a variety of substances, most prominently alcohol, may increase the incidence of postoperative complications. This may not only physically harm patients but may also cause them, and their surgical team, significant mental distress. Complications - which incur significant costs to our financially strained NHS, may therefore be reduced through reducing patients' substance use. As a needs assessment, and limitations withstanding, this thesis has highlighted and addressed several key gaps in the perioperative substance use literature. These include demonstrating that preoperative alcohol use may have significant negative effects on postoperative affect, that hazardous preoperative substance use may be highly prevalent among UK surgical patients, that this prevalence may be underestimated by routine assessment, and that previous interventions have been low efficacy and high risk of bias. Further, this thesis has identified several potential intervention targets and features which may improve future intervention outcomes. Future studies may use suggestions made throughout this thesis to build upon the present findings. Ultimately this may lead to better preoperative interventions which may be more successful in mitigating perioperative patient harm.

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Table A1. A Non-Comprehensive List of Common Surgical Terms.

Prefix/suffix	**Refers to**
Prefixes	
Angio-	Blood vessel
Arthr-	Joint
Cardio-	Heart
Colono-	Large intestine colon
Colpo-	Vagina
Cranio-	Cranium
Cysto-	Bladder
Encephal-	Brain
Fascio-	Fascia (sub-dermal connective tissue)
Gastr-	Stomach/abdomen
Gloss-	Tongue
Hepat-	Liver
Hyster-	Uterus
Lamino-	Lamina
Lapar-	Abdominal cavity
Laryng-	Larynx
Lobo-	Lobe
Mammo-	Breast
Myo-	Muscle tissue
Nephro-	Kidney
Oophor-	Ovary
Orchid-	Testicle
Pallido-	Globus pallidus (in the brain)
Rhino-	Nose
Thoraco-	Chest
Uretero-	Ureter
Vas-	Vas deferens (part of the male reproductive system)
Suffixes	
-centesis	Puncturing
-clasia	Crushing/breaking
-desis	Fusing
-ectomy	Removal* (synonymous with 'resection')
-opsy	Looking at
-oscopy	Viewing with a scope
-stomy	Creating a hole
-tomy	Incising
-pexy	Fixing or securing
-plasty	Modifying or reshaping
-rrhaphy	Strengthening

Notes. *Which could be parts of the relevant area; Prefixes may be stacked e.g., a cystolaminohepatectomy would be a removal of parts of the bladder, lamina and liver.

Table B1. Sample Characteristics: Inpatient Surgery *x* Hazardous Alcohol Use.

Characteristic (95% CI)	**Inpatient surgery: yes (1523)**		**Inpatient surgery: no (16928)**	
	Hazardous alcohol use: yes (200)	**Hazardous alcohol use: no (1317)**	**Hazardous alcohol use: yes (2355)**	**Hazardous alcohol use: no (14530)**
Mean age	66.86 (65.28-68.44)	69.27 (68.46-70.07)	66.45 (65.86-67.04)	67.51 (67.23-67.79)
Gender				
Male	155 (81%, 73-87)	573 (43%, 39-47)	1744 (77%, 74-79)	5850 (38%, 37-40)
Female	45 (19%, 13-27)	744 (57%, 53-61)	611 (23%, 21-26)	8680 (62%, 60-63)
Marital status				
Divorced	16 (8%, 4-15)	80 (6%, 4-8)	148 (7%, 5-8)	925 (1%, 5-7)
Married (living together)	148 (76%, 67-83)	897 (63%, 59-67)	1835 (74%, 71-76)	10042 (64%, 63-65)
Married (living separated)	2 (0%, 0-2)	14 (1%, 1-3)	19 (1%, 1-2)	173 (1%, 1-2)
Registered partnership	5 (1%, 0-3)	11 (0%, 0-1)	27 (1%, 0-1)	238 (1%, 1-1)
Never married	7 (5%, 2-11)	71 (7%, 5-10)	129 (8%, 6-10)	808 (7%, 6-7)
Widowed	22 (10%, 6-17)	244 (22%, 19-26)	197 (10%, 8-12)	2343 (21%, 20-22)
Mean years of education (from ISCED)	10.25 (9.46-11.04)	9.92 (9.55-10.28)	10.43 (10.15-10.70)	9.99 (9.87-10.10)
Mean number of health conditions	1.77 (1.52-2.01)	2 (1.87-2.14)	1.43 (1.36-1.51)	1.59 (1.55-1.63)
Mean BMI	26.47 (25.86-27.09)	27.06 (26.65-27.47)	26.67 (26.43-26.90)	26.57 (26.45-26.69)
BMI: Underweight	0	12 (1%, 1-2)	20 (1%, 1-2%)	169 (1%, 1-1%)
BMI: Normal	65 (31%, 23-40)	453 (35%, 31-39)	837 (34%, 32-37)	5636 (39%, 37-40)
BMI: Overweight	106 (55%, 46-64)	567 (42%, 38-46)	1101 (47%, 44-50)	5960 (41%, 40-43)
BMI: Obese	29 (14%, 9-22%)	267 (22%, 18-25)	377 (18%, 15-20)	2566 (19%, 18-20)
Physical activity				
Never vigorous nor moderate	17 (11%, 6-18)	162 (15%, 13-19)	142 (7%, 6-92)	1259 (12%, 11-13)
Other	182 (89%, 82-94)	1155 (85%, 81-87)	2123 (93%, 91-94)	13268 (88%, 87-89)
GALI				
Limited	81 (42%, 34-52)	583 (42%, 38-46)	799 (35%, 32-38)	5818 (44%, 43-45)
Not limited	119 (58%, 48-66)	734 (58%, 54-62)	1556 (65%, 32-38)	8711 (56%, 55-57)

Characteristic (95% CI)	Inpatient surgery: yes (1523)		Inpatient surgery: no (16928)	
	Hazardous alcohol use: yes (200)	Hazardous alcohol use: no (1317)	Hazardous alcohol use: yes (2355)	Hazardous alcohol use: no (14530)
Smoking				
Current	61 (32%, 24-41)	206 (14%, 12-17)	686 (29%, 27-32)	2519 (15%, 15-16)
Stopped	53 (38%, 30-47)	707 (27%, 24-31)	727 (37%, 34-40)	8214 (23%, 22-24)
Never	86 (30%, 22-39)	404 (58%, 54-62)	942 (34%, 31-37)	3796 (62%, 60-63)
Hazardous alcohol use				
Yes	200 (100%)	-	2355 (100%)	-
No	-	1317 (100%)	-	14530 (100%)
Country				
Austria	7 (1%, 1-3)	150 (4%, 4-5)	90 (1%, 1-2)	854 (3%, 2-3)
Belgium	37 (3%, 2-5)	239 (4%, 3-4)	370 (3%, 3-3)	2081 (3%, 3-3)
Denmark	10 (1%, 1-2)	75 (1%, 1-2)	165 (2%, 1-2)	940 (2%, 2-2)
France	42 (32%, 24-41)	148 (19%, 16-22)	407 (27%, 25-30)	1282 (17%. 16-18)
Germany	12 (14%, 8-24)	153 (35%, 31-39)	153 (17%, 15-20)	1249 (29%, 28-31)
Greece	9 (1%, 1-2)	58 (1, 1-2)	172 (2%, 2-2)	2021 (4%, 4-4)
Italy	32 (28%, 20-37)	107 (16%, 13-19)	372 (28%, 26-31)	1220 (19%, 17-20)
Netherlands	23 (5%, 3-8)	107 (4%, 3-5)	292 (5%, 4-6)	1326 (5%, 5-5)
Spain	16 (12%, 7-19)	100 (11%, 9-14)	201 (13%, 11-15)	1140 (13%, 12-14)
Sweden	3 (0%, 0-2)	128 (3%, 2-3)	36 (0%, 0%-0%)	1872 (4%, 3-4)
Switzerland	9 (2%, 1-4)	52 (2%, 2-3)	97 (2%, 2-2)	545 (2%, 2-3)
Mean CASP BL	36.41 (34.97-37.85)	36.86 (36.10-37.63)	36.79 (36.28-37.29)	36.97 (36.75-37.19)
Mean CASP FU	34.82 (33.30-36.34)	36.39 (35.59-37.19)	37.04 (36.57-37.51)	36.81 (36.59-37.04)
Mean EURO-D BL	2.30 (1.76-2.84)	2.61 (2.33-2.89)	2.14 (1.98-2.30)	2.34 (2.26-2.42)
Mean EURO-D FU	2.92 (2.25-3.59)	2.98 (2.68-3.27)	1.99 (1.82-2.16)	2.28 (2.21-2.36)

Notes. Raw *n* figures are unweighted whereas confidence intervals (95% CI) were calculated accounting for sample weighting; BL: baseline; FU: follow-up; All percentages are rounded to the nearest integer; Missing data (% of total sample): inpatient surgery = 57 (0.3), marital status = 19 (0.1), years of education = 398 (2.2), BMI = 272 (0.5), physical activity = 36 (0.2), GALI = 29 (0.2), hazardous alcohol use = 51 (0.3), smoking = 34 (0.2), number of chronic conditions = 38 (0.2), CASP BL = 6681 (36), CASP FU = 1219 (6.6), EURO-D BL = 302 (1.6), EURO-D FU = 451 (2.4).

Table C1. AUDIT-C Perioperative Risk Cut-Offs *x* Other Patient Characteristics (Study 2).

	No risk (0)	**Low risk (1-4)**	**At risk (5-8)**	**High risk (9-12)**	**Uni OR**	**Multi OR 1**	**Multi OR 2**
Total	46 (23.5%; 17.7-30)	88 (44.9%; 37.8-52.1)	55 (28.1%; 21.9-34.9)	7 (3.6%; 1.4-7.2)			
Mean age	53 (47.9-58.1)	57.6 (53.9-61.3)	54.9 (50.3-59.6)	44.9 (31.9-57.8)	*p* = .19, *eta*^{2} = .02 (0-.07)	* No risk: *ref* Low risk: 1.03 (1-1.05) At risk: 1 (0.98-1.03) High risk: 0.96 (0.89-1.03)	ns
Gender					***	***	***
Male	21 (25.6%; 16.9-36.7)	24 (29.3%; 20-40.5)	32 (39%; 28.6-50.5)	5 (6.1%; 2.3-14.3)	No risk: 0.55 (0.28-1.09) Low risk: 0.32 (0.18-0.59) At risk: 2.53 (1.34-4.79) High risk: 3.64 (0.69-19.23)	No risk: *ref* Low risk: 0.32 (0.14-0.73) At risk: 1.67 (0.71-3.95) High risk: 15.72 (0.57-435.84)	No risk: *ref* Low risk: 0.23 (0.08-0.64) At risk: 0.91 (0.31-2.69) High risk: 4.28e +9 (6.22e+8-2.95e+10)
Female	25 (21.9%; 15-30.9)	64 (56.1%; 46.5-65.3)	23 (20.2%; 13.5-28.9)	2 (1.8%; 0.3-6.8)	*Ref*		

	No risk (0)	Low risk (1-4)	At risk (5-8)	High risk (9-12)	Uni OR	Multi OR 1	Multi OR 2
Smoker					***	***	***
Current	8 (19.1%; 9.1-34.6)	15 (35.7%; 22-52)	12 (28.6%; 16.2-44.8)	7 (16.7%; 7.5-32)	No risk: 0.72 (0.31-1.69) Low risk: 0.62 (0.30-1.25) At risk: 1.03 (0.48-2.20) High risk: (all smokers)	No risk: *ref* Low risk: 1.02 (0.39-2.66) At risk: 1.40 (0.51-3.82) High risk: (all smokers)	No risk: *ref* Low risk: 0.88 (0.32-2.40) At risk: 1.41 (0.49-4.06) High risk: (all smokers)
Former	8 (14.8%; 7.1-27.7)	26 (48.2%; 34.5-62)	20 (37%; 24.6 - 51.3)	-	*Ref (former + never)*		
Never	30 (30%; 21.5-40.1)	47 (47%; 37-57.2)	23 (23%; 15.4-32.7)	-			
Illicit substance user					***	ns (p = .07)	**
Yes	-	-	-	3 (100%; 31-100)	All high risk	All high risk	All high risk
No	46 (23.8%; 18.1-30.6)	88 (45.6%; 38.5-52.9)	55 (28.5%; 22.4-35.5)	4 (2.1%; 0.7-5.6)	-	-	-
Type of surgery					ns (p > .20)	-	ns
Bariatric	-	1 (33.3%; 1.8-87.5)	2 (66.7%; 12.5-98.2)	-	-	-	-
Colorectal	2 (100%; 19.8-100)	-	-	-	-	-	-
General	14 (35%; 21.1-51.7)	17 (42.5%; 27.4-59)	8 (20%; 9.6-36.1)	1 (2.5%; 0.1-14.7)	-	-	-

	No risk (0)	Low risk (1-4)	At risk (5-8)	High risk (9-12)	Uni OR	Multi OR 1	Multi OR 2
Hepatobiliary	1 (14.3%; 0.8-58)	3 (42.9%; 11.8-79.8)	3 (42.9%; 11.8-79.8)	-	-	-	-
Thoracic	3 (17.7%; 4.7-44.2)	6 (35.3%; 15.3-61.4)	7 (41.2%; 19.4-66.6)	1 (5.9%; 0.3-30.8)	-	-	-
Gynaecology	10 (25%; 13.3-41.5)	23 (57.5%; 41-72.6)	6 (15%; 6.3-20.5)	1 (2.5%; 0.1-14.7)	-	-	-
Urology	11 (18.3%; 9.9-30.9)	24 (40%; 27.8-53.5)	22 (36.7%; 24.9-50.2)	3 (5%; 1.3-14.8)	-	-	-
Uro-Gynae.	3 (23.1%; 6.2-54)	8 (61.5%; 32.3-84.9)	2 (15.4%; 2.7-46.3)	-	-	-	-

Notes. * $p < .05$. ** $p < .01$, *** $p < .001$; ns = non-significant; OR = odds ratio; 95% confidence intervals in parentheses; Ref = reference category/level; Uni ES = univariate effect size (OR unless otherwise specified); Multi OR 1 = multivariate effect size for univariate predictors $p < .20$; Multi OR 2 = multivariate effect size for model including all variables.

Table C2. Current Illicit Substance Users: Yes versus No *x* Other Patient Characteristics (Study 2).

	Non-user	**Current user**
Total	193 (98.5%; 95.6-99.7)	3 (1.5%; 0.3-4.4)
Mean age	55.6 (53.2-58.1)	35.7 (33.4-38.1)
Sex		
Male	80 (97.6%; 90.7-99.6)	2 (2.4%; 0.4-9.3)
Female	113 (99.1%; 94.5-99.1)	1 (0.9%; 0.1-5.5)
Smoker		
Current	39 (92.9%; 79.5-98.1)	3 (7.1%; 1.9-20.6)
Former	54 (100%; 91.7-100)	-
Never	100 (100%; 95.4-100)	-
AUDIT-C		
Non-hazardous (0-4)	134 (100%; 96.5-100)	-
Hazardous (≥5)	59 (95.2%; 85.6-98.7)	3 (4.8%; 1.3-14.4)
Type of surgery		
Bariatric	3 (100%; 30-100)	-
Colorectal	2 (100%; 19.8-100)	-
General	40 (100%; 89.1-100)	-
Hepatobiliary	7 (100%; 56.1-100)	-
Thoracic	16 (94.1%; 69.2-99.7)	1 (5.9%; 0.3-30.8)
Gynaecology	39 (97.5%; 85.3-99.9)	1 (2.5%; 0.1-14.7)
Urology	59 (98.3%; 89.9-99.9)	1 (1.7%; 0.01-10.1)
Uro-Gynae.	13 (100%; 71.7-100)	-

Table C3. Complications Outcome: Complication Types, Subtypes and Extracted Codes.

Type	Subtype	Code and description
Delirium	Delirium	F05.0: Delirium not superimposed on dementia, so described
		F05.1: Delirium superimposed on dementia
		F05.8: Other delirium
		F05.9: Delirium, unspecified
	Delirium due to substance use	F10.4: Mental and behavioural disorders due to use of alcohol: Withdrawal state with delirium
		F11.4: Mental and behavioural disorders due to use of opioids: Withdrawal state with delirium
		F12.4: Mental and behavioural disorders due to use of cannabinoids: Withdrawal state with delirium
		F13.4: Mental and behavioural disorders due to use of sedatives or hypnotics: Withdrawal state with delirium
		F14.4: Mental and behavioural disorders due to use of cocaine: Withdrawal state with delirium
		F15.4: Mental and behavioural disorders due to use of other stimulants, including caffeine: Withdrawal state with delirium
		F16.4: Mental and behavioural disorders due to use of hallucinogens: Withdrawal state with delirium
		F17.4: Mental and behavioural disorders due to use of tobacco: Withdrawal state with delirium
		F18.4: Mental and behavioural disorders due to use of volatile solvents: Withdrawal state with delirium
		F19.4: Mental and behavioural disorders due to multiple drug use and use of other psychoactive substances: Withdrawal state with delirium
	Alcohol dependence with withdrawal (but without specific mention of delirium)	F10.3: Mental and behavioural disorders due to use of alcohol: Withdrawal state
	Hepatic encephalopathy	K70.4: Alcoholic hepatic failure

Type	Subtype	Code and description
		K72.0: Acute and subacute hepatic failure K72.1: Chronic hepatic failure K72.9: Hepatic failure, unspecified
Cardiovascular	Stroke	I60.0: Subarachnoid haemorrhage from carotid siphon and bifurcation I60.1: Subarachnoid haemorrhage from middle cerebral artery I60.2: Subarachnoid haemorrhage from anterior communicating artery I60.3: Subarachnoid haemorrhage from posterior communicating artery I60.4: Subarachnoid haemorrhage from basilar artery I60.5: Subarachnoid haemorrhage from vertebral artery I60.6: Subarachnoid haemorrhage from other intracranial arteries I60.7: Subarachnoid haemorrhage from intracranial artery, unspecified I60.8: Other subarachnoid haemorrhage I60.9: Subarachnoid haemorrhage, unspecified I61.0: Intracerebral haemorrhage in hemisphere, subcortical

Type	Subtype	Code and description
		I61.1: Intracerebral haemorrhage in hemisphere, cortical I61.2: Intracerebral haemorrhage in hemisphere, unspecified I61.3: Intracerebral haemorrhage in brain stem I61.4: Intracerebral haemorrhage in cerebellum I61.5: Intracerebral haemorrhage, intraventricular I61.6: Intracerebral haemorrhage, multiple localized I61.8: Other intracerebral haemorrhage I61.9: Intracerebral haemorrhage, unspecified I63.0: Cerebral infarction due to thrombosis of precerebral arteries I63.1: Cerebral infarction due to embolism of precerebral arteries I63.2: Cerebral infarction due to unspecified occlusion or stenosis of precerebral arteries I63.3: Cerebral infarction due to thrombosis of cerebral arteries I63.4: Cerebral infarction due to embolism of cerebral arteries I63.5: Cerebral infarction due to unspecified occlusion or stenosis of cerebral arteries I63.6: Cerebral infarction due to cerebral venous thrombosis, nonpyrogenic I63.8: Other cerebral infarction I63.9: Cerebral infarction, unspecified

Type	Subtype	Code and description
		I64.X: Stroke, not specified as haemorrhage or infarction
	Transient ischaemic attack	G45.8: Other transient cerebral ischaemic attacks and related syndromes
		G45.9: Transient cerebral ischaemic attack, unspecified
	Cardiac arrest	I46.0: Cardiac arrest with successful resuscitation
		I46.1: Sudden cardiac death, so described
		I46.9: Cardiac arrest, unspecified
	Myocardial infarction	I21.1: Acute transmural myocardial infarction of inferior wall
		I21.2: Acute transmural myocardial infarction of other sites
		I21.3: Acute transmural myocardial infarction of unspecified site
		I21.4: Acute subendocardial myocardial infarction
		I21.9: Acute myocardial infarction, unspecified
		I22.0: Subsequent myocardial infarction of anterior wall
		I22.1: Subsequent myocardial infarction of inferior wall
		I22.8: Subsequent myocardial infarction of other sites
		I22.9: Subsequent myocardial infarction of unspecified site
		I24.9: Other acute ischaemic heart diseases

Type	Subtype	Code and description
	Deep vein thrombosis	I80.1: Phlebitis and thrombophlebitis of femoral vein
		I80.2: Phlebitis and thrombophlebitis of other deep vessels of lower extremities
	Pulmonary embolism	I26.0: Pulmonary embolism with mention of acute cor pulmonale
		I26.9: Pulmonary embolism without mention of acute cor pulmonale
Pulmonary	Infectious pneumonia	J10.0: Influenza with pneumonia, seasonal influenza virus identified
		J11.0: Influenza with pneumonia, virus not identified
		J12.0: Adenoviral pneumonia
		J12.1: Respiratory syncytial virus pneumonia
		J12.2: Parainfluenza virus pneumonia
		J12.3: Human metapneumovirus pneumonia
		J12.8: Other viral pneumonia
		J12.9: Viral pneumonia, unspecified
		J13.X: Pneumonia due to Streptococcus pneumoniae
		J14.X: Pneumonia due to Haemophilus influenza
		J15.0: Pneumonia due to Klebsiella pneumoniae
		J15.1: Pneumonia due to Pseudomonas
		J15.2: Pneumonia due to staphylococcus
		J15.3: Pneumonia due to streptococcus, group B
		J15.4: Pneumonia due to other streptococci
		J15.5: Pneumonia due to Escherichia coli
		J15.6: Pneumonia due to other Gram-negative bacteria

Type	Subtype	Code and description
		J15.7: Pneumonia due to Mycoplasma pneumoniae
		J15.8: Other bacterial pneumonia
		J15.9: Bacterial pneumonia, unspecified
		J16.0: Chlamydial pneumonia
		J16.8: Pneumonia due to other specified infectious organisms
		J17.0: Pneumonia in bacterial diseases classified elsewhere
		J17.1: Pneumonia in viral diseases classified elsewhere
		J17.2: Pneumonia in mycoses
		J17.3: Pneumonia in parasitic diseases
		J17.8: Pneumonia in other diseases classified elsewhere
		J18.0: Bronchopneumonia, unspecified
		J18.1: Lobar pneumonia, unspecified
		J18.2: Hypostatic pneumonia, unspecified
		J18.8: Other pneumonia, organism unspecified
		J18.9: Pneumonia, unspecified
	Aspiration pneumonia	J69.0: Pneumonitis due to food and vomit
	Respiratory tract infection	J20.0: Acute bronchitis due to Mycoplasma pneumoniae
		J20.1: Acute bronchitis due to Haemophilus influenzae
		J20.2: Acute bronchitis due to streptococcus
		J20.3: Acute bronchitis due to coxsackievirus
		J20.4: Acute bronchitis due to parainfluenza virus
		J20.5: Acute bronchitis due to respiratory syncytial

Type	Subtype	Code and description
		J20.6: Acute bronchitis due to rhinovirus J20.7: Acute bronchitis due to echovirus J20.8: Acute bronchitis due to other specified organisms J20.9: Acute bronchitis, unspecified J21.0: Acute bronchiolitis due to respiratory syncytial virus J21.1: Acute bronchiolitis due to human metapneumovirus J21.8: Acute bronchiolitis due to other specified organisms J21.9: Acute bronchiolitis, unspecified J22.X: Unspecified acute lower respiratory infection J44.0: Chronic obstructive pulmonary disease with acute lower respiratory infection J10.1: Influenza with other respiratory manifestations, seasonal influenza virus identified J11.1: Influenza with other respiratory manifestations, virus not identified
Wound related	Superficial or deep	T81.4: Infection following a procedure, not elsewhere classified [includes post-procedural abscesses]
	Prosthesis, implant or metalwork infection	T82.6: Infection and inflammatory reaction due to cardiac valve prosthesis T82.7: Infection and inflammatory reaction due to other cardiac and vascular devices, implants and grafts

Type	Subtype	Code and description
		T83.5: Infection and inflammatory reaction due to prosthetic device, implant and graft in urinary system T83.6: Infection and inflammatory reaction due to prosthetic device, implant and graft in genital tract T84.5: Infection and inflammatory reaction due to internal joint prosthesis T84.6: Infection and inflammatory reaction due to internal fixation device [any site] T84.7: Infection and inflammatory reaction due to other internal orthopaedic prosthetic devices, implants and grafts T85.7: Infection and inflammatory reaction due to other internal prosthetic devices, implants and grafts
	Wound dehiscence	T81.3: Disruption of operation wound, not elsewhere classified
Infection	Urinary tract infection	N39.0: Urinary tract infection, site not specified [default code, used when only “UTI” stated]
	Pyelonephritis	N10.X: Acute tubulo-interstitial nephritis N11.0: Nonobstructive reflux-associated chronic pyelonephritis N11.1: Chronic obstructive pyelonephritis N11.8: Other chronic tubulo-interstitial nephritis N11.9: Chronic tubulo-interstitial nephritis, unspecified N12.X: Tubulo-interstitial nephritis, not specified as acute or chronic

Type	Subtype	Code and description
	Obstructive uropathy with infection	N13.6: Pyonephrosis
	Urethritis	N28.8: Other specified disorders of kidney and ureter
	Cystitis	N30.0: Acute cystitis
		N30.1: Interstitial cystitis (chronic)
		N30.2: Other chronic cystitis
		N30.3: Trigonitis
		N30.4: Irradiation cystitis
		N30.8: Other cystitis
		N30.9: Cystitis, unspecified
		N33.0: Tuberculous cystitis
		N33.8: Bladder disorders in other diseases classified elsewhere
	Urethritis	N34.0: Urethral abscess
		N34.1: Nonspecific urethritis
		N34.2: Other urethritis
		N34.3: Urethral syndrome, unspecified
		N37.0: Urethritis in diseases classified elsewhere
		N37.8: Other urethral disorders in diseases classified elsewhere
	Cellulitis not at surgical site	L03.0: Cellulitis of finger and toe
		L03.1: Cellulitis of other parts of limb
		L03.2: Cellulitis of face
		L03.3: Cellulitis of trunk
		L03.8: Cellulitis of other sites
		L03.9: Cellulitis, unspecified

Table C4. Demographic and Surgery Characteristics of the Study 3 Sample (*n* = 273).

Variable	Mean (SD; 95% CI)	Variable sub-categories	*n* (%; 95% CI)
Age	50.64 (16.73; 48.6-52.60)	25th percentile	37
		50th percentile	51
		75th percentile	63.8
Gender		Male	130 (48; 42-53.9)
		Female	141 (52; 46.1-58)
BMI	28.95 (6.08; 28.2-29.6)	Underweight (<18.5)	2 (0.8; 0-1.9)
		Normal weight (18.5–24.9)	64 (25.1; 19.8-30.4)
		Overweight (25–29.9)	91 (35.7; 29.8-41.6)
		Obese (≥30)	98 (38.4; 32.5-44.4)
Physical activity (TAM-2 score*)	5383 (6744; 4580-6190)	At least some weekly strenuous activity	79 (29.6; 24.1-35.1)
		No weekly strenuous activity	189 (70.8; 65.3-76.2)
		At least some weekly strenuous or moderate activity	184 (68.9; 63.4-74.5)
		No weekly strenuous or moderate activity	84 (31.5; 25.9-37)
Co-morbidity (ASA-PS)	2.12 (0.82; 2.02-2.22)	I	64 (24.8;19.5-30.1)
		II	109 (42.2; 36.2-48.3)
		III	77 (29.8; 24.3-35.4)
		IV	9 (3; 2-6)
Surgery complexity**		Minor	20 (7.5; 4.3-10.7)
		Intermediate	78 (29.3; 23.9-34.8)
		Major	60 (22.6; 17.5-27.6)
		Extra major	48 (18; 13.4-22.7)
		Complex	60 (22.6; 17.5-27.6)
Surgery type**		Abdomen (excluding urinary and reproductive organs)	10 (3.8; 1.5-6.1)

Variable	**Mean (SD; 95% CI)**	**Variable sub-categories**	***n* (%; 95% CI)**
		Abdominal wall	*2*
		Oesophagus	*1*
		Other organs (mainly digestive)	*3*
		Rectum/anus	*4*
		Bones, joints and connective tissues/tendon muscle	30 (11.4; 7.5-15.2)
		Bone (non-specific)	*3*
		Connective tissue/tendon muscle	*3*
		Elbow	*2*
		External fixation/traction	*1*
		Foot	*1*
		Fractures	*8*
		Hand	*3*
		Hip, leg and pelvis – fixation/arthrodesis	*3*
		Knee	*2*
		Shoulder	*4*
		Brain, cranium and intracranial organs	18 (6.8; 3.8-9.9)
		Brain	*8*
		Cranium	*3*
		Nerves	*4*
		Other	*3*
		Ear, nose and throat	29 (11; 7.2-14.8)
		Fibre optic endoscopic procedures (GA or LA)	*1*
		Larynx and trachea	*3*
		Middle ear and mastoid	*8*
		Nasal sinuses	*5*
		Nose and nasal cavity	*4*
		Throat	*8*
		Endoscopic gastrointestinal procedures	7 (2.7; 0.7-4.6)
		Face, mouth, salivary and thyroid	34 (12.9; 8.8-16.9)
		Face and jaws	*7*
		Mouth cavity	*2*

Variable	Mean (SD; 95% CI)	Variable sub-categories	*n* (%; 95% CI)
		Neck	*4*
		Palate	*1*
		Salivary glands	*2*
		Teeth	*11*
		Thyroid and parathyroid glands	*4*
		Tongue	*3*
		Female reproductive organs	7 (2.7; 0.7-4.6)
		Uterus/adnexa	*6*
		Vagina/perineum	*1*
		Skin and subcutaneous tissue	11 (4.2; 2.2-7.6)
		Flaps and free skin grafts	*2*
		Lesions of skin	*8*
		Repair	*1*
		Spine, spinal cord and peripheral nerves	84 (31.8; 26.2-37.4)
		Nerve roots	*1*
		Nerves	*1*
		Other nerve blocks	*1*
		Other procedures (spinal)	*1*
		Spinal column (including intervertebral discs)	*63*
		Spinal cord	*17*
		Thorax and intra-thoracic organs	6 (2.3; 0.5-4.1)
		Heart – cardiac surgery	*4*
		Heart – cardiology	*1*
		Urinary system and male reproductive organs	3 (1.1; 0-2.4)
		Bladder	*1*
		Genitalia	*2*
		Vascular system	27 (10.2; 7.1-14.5)
		Abdominal vessels	*1*
		Head and neck	*10*
		Ileo-femoral vessels	*5*

Variable	**Mean (SD; 95% CI)**	**Variable sub-categories**	***n* (%; 95% CI)**
		Non-specific	*3*
		Renal vessels	*1*
		Varicose veins	*7*

Notes. * TAM-2: total sum of 3 x reported minutes per week of mild, 5 x moderate and 9 x strenuous activities; ** As per AXA procedure codes; ASA-PS: American Society of Anaesthesiologists physical status score; BMI: Body Mass Index; TAM-2: Total Activity Measure 2; Missing data frequencies per variable (n) are as follows: age (3), gender (2), BMI (18), TAM-2 (6), ASA-PS (15), surgery type (9), surgery complexity (8).

Table C5. Substance Use Characteristics of the Study 3 Sample (*n* = 273).

Variables	**Mean (SD; 95% CI)**	**Variable sub-categories**	***n* (%; 95% CI)**
AUDIT-C (total score)	3.89 (3.01; 3.53-4.25)	Non-drinker (0)	54 (19.8; 15.5-24.9)
		Non-hazardous drinker (1-4)	98 (35.9; 30.4-41.8)
		At-risk drinker (5-8)	103 (37.7; 32.2-43.6)
		High risk drinker (9-12)	18 (6.6; 3.7-10)
AUDIT-C (hazardous drinker score)		Hazardous drinker (≥ 5)	121 (44.3; 38.4-50.2)
		Non-hazardous drinker (< 5)	152 (55.7; 49.8-61.6)
AUDIT-C (alcohol use frequency score)	1.96 (1.38; 1.80-2.12)	Never	54 (19.8; 15.1-24.5)
		Monthly or less	61 (22.3; 17.4-27.2)
		2-4 times per month	43 (15.8; 11.4-20.1)
		2-3 times per week	72 (26.4; 21.2-31.6)
		4+ times per week	43 (15.8; 11.4-20.1)
AUDIT-C (alcohol use average amount score)	1.01 (1.23; 0.86-1.16)	1 or 2 drinks	131 (48; 42.1-53.9)
		3 or 4 drinks	64 (23.4; 18.4-28.4)
		5 or 6 drinks	37 (13.6; 9.5-17.7)
		7 or 9 drinks	25 (9.2; 5.8-12.6)
		≥ 10 drinks	16 (5.9; 3.1-8.7)
AUDIT-C (alcohol binge frequency score)	0.92 (1.10; 0.79-1.05)	≥ 6 drinks: never	135 (49.5; 43.6-55.4)
		≥ 6 drinks: less than monthly	59 (21.6; 16.7-26.5)
		≥ 6 drinks: monthly	51 (18.7; 14.1-23.3)
		≥ 6 drinks: weekly	22 (8.1; 4.9-11.3)
		≥ 6 drinks: daily or almost daily	6 (2.2; 0.5-3.9)
Cigarette smokers	Cigarettes per day: 11.84 (8.60; 9.89-13.80)	Current	75 (27.5; 22.2-32.8)
		Former	85 (31.1; 25.7-37)
		Never	113 (41.4; 35.5-47.5)

Variables	**Mean (SD; 95% CI)**	**Variable sub-categories**	***n* (%; 95% CI)**
E-Cigarette users		Yes	18 (6.6; 4-10.3)
		No	253 (93.4; 89.7-96)
ASSIST: global continuum of risk score	17.47 (13.45; 15.90-19.10)	25^{th} percentile	7
		50^{th} percentile	13
		75^{th} percentile	25
ASSIST: lifetime substance use score	7.01 (5.04; 6.41-7.61)	25^{th} percentile	3
		50^{th} percentile	6
		75^{th} percentile	9
ASSIST: alcohol risk score	4.40 (4.43; 3.88-4.93)	25^{th} percentile	2
		50^{th} percentile	4
		75^{th} percentile	6
ASSIST: alcohol use frequency		Never	66 (24.2; 19.2-29.7)
		Once or twice	35 (12.8; 9.1-17.4)
		Monthly	36 (13.2; 9.4-17.8)
		Weekly	100 (36.6; 30.9-42.6)
		Daily	36 (13.2; 9.4-17.8)
ASSIST: tobacco risk score	5.32 (7.82; 4.39-6.25)	25^{th} percentile	0
		50^{th} percentile	0
		75^{th} percentile	12
ASSIST: cigarette use frequency		Never	190 (69.6; 63.8-75)
		Once or twice	3 (1.1; 0.2-3.2)
		Monthly	1 (0.4; 0-1.2)
		Weekly	5 (1.8; 0.6-4.2)
		Daily	74 (27.1; 21.9-32.8)
ASSIST: cannabis risk score	0.47 (2.47; 0.18-0.76)	25^{th} percentile	0
		50^{th} percentile	0
		75^{th} percentile	0

Variables	Mean (SD; 95% CI)	Variable sub-categories	*n* (%; 95% CI)
ASSIST: cannabis use frequency		Never	258 (94.5; 91.1-96.9)
		Once or twice	4 (1.5; 0.5-3.9)
		Monthly	1 (0.3; 0.1-3.9)
		Weekly	5 (1.8; 0.8-4.3)
		Daily	5 (1.8; 0.8-4.3)
ASSIST: cocaine risk score	0.11 (1.04; 0-0.23)	25th percentile	0
		50th percentile	0
		75th percentile	0
ASSIST: cocaine use frequency		Never	268 (98.2; 95.8-99.4)
		Once or twice	4 (1.5; 0.4-3.7)
		Monthly	1 (0.4; 0-1.2)
ASSIST: sedatives risk score	0.01 (0.24; 0-0.04)	25th percentile	0
		50th percentile	0
		75th percentile	0
ASSIST: sedatives use frequency		Weekly	1 (0.4; 0-1.2)

Notes. AUDIT-C: Alcohol Use Disorder Identification Test – Consumption; ASSIST: Alcohol, Smoking and Substance Involvement Screening Test; ASSIST scores for substances with no identified last 3-month users are not presented; ASSIST cut-offs for risk taken from reference and do not necessarily *perioperative* risk, but risk to health generally; Missing data frequencies (n) are as follows: E-Cigarette users (2).

Table C6. AUDIT-C Perioperative Risk Cut-Offs x Other Patient Characteristics (Study 3).

	No risk (0)	**Low risk (1-4)**	**At risk (5-8)**	**High risk (9-12)**	**Uni OR**	**Multi OR 1 (*ref: no risk*)**	**Multi OR 2 (*ref: no risk*)**
Total	54 (19.8; 15.5-24.9)	98 (35.9; 30.4-41.8)	103 (37.7; 32.2-43.6)	18 (6.6; 3.7-10)			
Mean age	52.3 (48.2-56.4)	56.3 (53.3-59.4)	46.2 (43.1-49.3)	39.6 (29.6-49.6)	*** *eta*^{2} = 0.10 (0.04-0.16)	** Low risk: 1.02 (0.99-1.05) At risk: 0.99 (0.97-1.02) High risk: 0.95 (0.90-1.00)	* Low risk: 1.01 (0.98-1.05) At risk: 0.98 (0.95-1.01) High risk: 0.95 (0.89-1.00)
Gender					*****	******	*****
Male	29 (22.3%; 15.9-30.4)	36 (27.7%; 20.6-36.1)	54 (41.5%; 33.3-50.3)	11 (8.5%; 4.7-14.7)	No risk: 1.40 (0.77-2.56) Low risk: 0.49 (0.29-0.81) At risk: 1.38 (0.84-2.25) High risk: 1.77 (0.66-4.71)	Low risk: 0.44 (0.20-0.97) At risk: 1.11 (0.50-2.46) High risk: 2.68 (0.54-13.37)	Low risk: 0.44 (0.19-1.05) At risk: 1.07 (0.45-2.55) High risk: 2.24 (0.41-12.15)
Female	24 (17%; 11.6-24.2)	62 (44%; 35.9-52.4)	48 (34%; 26.6-42.3)	7 (5%; 2.4-10.1)	*Ref*		
Smoker					ns (p > .20)	**-**	ns
Current	18 (24%; 15.5-35.2)	20 (26.7%; 17.7-38)	31 (41.3%; 30.6-53)	6 (8%; 3.6-17)	No risk: 1.42 (0.75-2.70) Low risk: 0.73 (0.41-1.30) At risk: 1.22 (0.73-2.05) High risk: 1.42 (0.51-3.96)	-	-

	No risk (0)	Low risk (1-4)	At risk (5-8)	High risk (9-12)	Uni OR	Multi OR 1 (*ref: no risk*)	Multi OR 2 (*ref: no risk*)
Former	15 (17.6%; 10.8-27.5)	36 (42.4%; 32.1-53.3)	29 (34.1%; 24.7-45)	5 (5.9%; 2.4-13.6)	*Ref (former + never)*	-	-
Never	21 (18.6%; 12.4-27)	42 (37.2%; 28.7-46.6)	43 (38.1%; 29.5-47.5)	7 (6.2%; 2.9-12.6)			
Illicit substance user					***	*	ns
Yes	3 (15.8%; 4.6-42.2)	2 (10.5%; 2.3-37.1)	8 (42.1%; 21.1-66.5)	6 (31.6%; 13.7-57.3)	No risk: 0.75 (0.21-2.66) Low risk: 0.19 (0.04-0.86) At risk: 1.22 (0.47-3.13) High risk: 9.31 (3.01-28.75)	Low risk: 0.08 (0.00-1.34) At risk: 0.84 (0.16-4.26) High risk: 3.67 (0.40-33.42)	-
No	51 (20.1%; 15.6-25.5)	96 (37.8%; 32-44)	95 (37.4%; 31.6-43.6)	12 (4.7%; 2.7-8.2)	*Ref*		-
Mean $\log_{10}$ TAM-2	3.4 (3.2-3.6)	3.5 (3.4-3.6)	3.5 (3.4-3.6)	3.5 (3.4-3.7)	ns ($p > .20$), $eta^2 = 0.01$ (0-0.03)	-	ns
ASA-PS					***	**	**
I	9 (14.1%; 7.3-25.2)	12 (18.8%; 10.8-30.5)	37 (57.8%; 45.1-69.5)	6 (9.4%; 4.2-19.7)	*Ref*		
II	22 (20.2%; 13.6-28.9)	42 (38.5%; 29.8-48.1)	41 (37.6%; 28.9-47.2)	4 (3.7%; 1.4-9.5)	No risk: 1.55 (0.66-3.60) Low risk: 2.71 (1.30-5.68) At risk: 0.44 (0.23-0.83) High risk: 0.37 (0.10-1.36)	Low risk: 0.96 (0.29-3.13) At risk: 0.35 (0.12-1.02) High risk: 0.44 (0.06-3.37)	Low risk: 1.03 (0.29-3.69) At risk: 0.45 (0.14-1.41) High risk: 0.24 (0.03-2.30)

	No risk (0)	Low risk (1-4)	At risk (5-8)	High risk (9-12)	Uni OR	Multi OR 1 (*ref: no risk*)	Multi OR 2 (*ref: no risk*)
III	20 (26%; 17.2-37.1)	35 (45.5%; 34.5-56.9)	17 (22.1%; 14-33)	5 (6.5%; 2.7-14.9)	No risk: 2.14 (0.90-5.12) Low risk: 3.61 (1.67-7.81) At risk: 0.21 (0.10-0.43)	Low risk: 0.73 (0.21-2.57) At risk: 0.18 (0.06-0.61) High risk: 1.08 (0.12-9.54)	Low risk: 0.94 (0.24-3.61) At risk: 0.24 (0.07-0.87) High risk: 0.75 (0.09-6.50)
IV	-	6 (66.7%; 26.2-91.9)	1 (11.1%; 0.9-62.6)	2 (22.2%; 3.9-67)	Low risk: 8.67 (1.89-39.68) At risk: 0.09 (0.01-0.77) High risk: 2.76 (0.46-16.41)	All > no risk	All > no risk
Mean BMI	30.1 (28.1-32.1)	29.6 (28.3-30.8)	27.8 (26.8-28.8)	28.8 (25.1-32.5)	ns (p = .10), eta^2 = 0.02 (0-0.06)	See *notes*	See *notes*
Surgery complexity					ns (p = .13)	ns	ns
Minor	2 (10%; 2.2-35.5)	9 (45%; 23.8-68.2)	8 (40%; 20-64)	1 (5%; 0.6-32.3)	*Ref*	-	-
Intermediate	13 (16.7%; 9.8-26.9)	27 (34.6%; 24.7-46)	28 (35.9%; 25.9-47.3)	10 (12.8%; 6.9-22.5)	No risk: 1.80 (0.37-8.72) Low risk: 0.65 (0.24-1.75) At risk: 0.84 (0.31-2.30) High risk: 2.79 (0.34-23.22)	-	-
Major	9 (15%; 7.8-26.8)	17 (28.3%; 18.2-41.3)	31 (51.7%; 38.8-64.3)	3 (5%; 1.6-14.8)	No risk: 1.58 (0.31-8.06) Low risk: 0.48 (0.17-1.37) At risk: 1.60 (0.57-4.48) High risk: 1.00 (0.10-10.20)	-	-

	No risk (0)	**Low risk (1-4)**	**At risk (5-8)**	**High risk (9-12)**	**Uni OR**	**Multi OR 1 (*ref: no risk*)**	**Multi OR 2 (*ref: no risk*)**
Extra major	11 (22.9%; 12.9-37.4)	21 (43.8%; 30.1-58.4)	14 (29.2%; 17.8-44)	2 (4.2%; 1-15.9)	No risk: 2.68 (0.54-13.37) Low risk: 0.95 (0.33-2.72) At risk: 0.62 (0.21-1.84) High risk: 0.83 (0.07-9.66)	-	-
Complex	16 (26.7%; 16.8-39.6)	24 (40%; 28.1-53.2)	18 (30%; 19.5-43.1)	2 (3.3%; 0.8-12.8)	No risk: 3.27 (0.68-15.71) Low risk: 0.81 (0.29-2.26) At risk: 0.64 (0.22-1.84) High risk: 0.66 (0.06-7.64)	-	-
Type of surgery					**	ns	ns
Abdomen	2 (20%; 3.7-62.2)	3 (30%; 7.6-69)	5 (50%; 18.1-81.9)	-	No risk: 0.50 (0.05-4.98) Low risk: 0.86 (0.10-7.51) At risk: 5.00 (0.42-59.66)	-	-
Bones, joints and connective tissues/tendon muscle	1 (3.3%; 0.4-22.2)	12 (40%; 23.5-59.1)	15 (50%; 31.9-68.1)	2 (6.7%; 1.5-24.7)	No risk: 0.07 (0.01-0.95) Low risk: 1.33 (0.21-8.46) At risk: 2.50 (0.27-23.36) High risk: 0.36 (0.03-4.72)	-	-

	No risk (0)	**Low risk (1-4)**	**At risk (5-8)**	**High risk (9-12)**	**Uni OR**	**Multi OR 1 (*ref: no risk*)**	**Multi OR 2 (*ref: no risk*)**
Brain, cranium and intracranial organs	5 (27.8%; 10.9-54.7)	4 (22.2%; 7.7-49.5)	8 (44.4%; 22.2-69.1)	1 (5.6%; 0.6-35.5)	No risk: 0.77 (0.11-5.61) Low risk: 0.57 (0.08-4.35) At risk: 4.00 (0.39-41.51) High risk: 0.29 (0.02-5.60)	-	-
Ear, nose and throat	3 (10.3%; 3.1-29.1)	10 (34.5%; 18.9-54.3)	9 (31%; 16.3-51)	7 (24.1%; 11.4-44)	No risk: 0.23 (0.03-1.84) Low risk: 1.05 (0.16-6.78) At risk: 2.25 (0.23-22.14) High risk: 1.59 (0.16-16.02)	-	-
Endoscopic gastrointestinal procedures	2 (28.6%; 4.2-78.5)	1 (14.3%; 1-74.3)	2 (28.6%; 4.2-78.5)	2 (28.6%; 4.2-78.5)	No risk: 0.80 (0.08-8.47) Low risk: 0.33 (0.02-5.03) At risk: 2.00 (0.13-29.81) High risk: 2.00 (0.13-29.81)	-	-
Face, mouth, salivary and thyroid	8 (23.5%; 11.8-41.5)	11 (32.4%; 18.3-50.5)	14 (41.2%; 25.4-59)	1 (2.9%; 0.4-19.8)	No risk: 0.62 (0.09-4.01) Low risk: 0.96 (0.15-6.04) At risk: 3.50 (0.37-33.31) High risk: 0.15 (0.01-2.83)	-	-

	No risk (0)	**Low risk (1-4)**	**At risk (5-8)**	**High risk (9-12)**	**Uni OR**	**Multi OR 1 (*ref: no risk*)**	**Multi OR 2 (*ref: no risk*)**
Female reproductive organs	2 (28.6%; 4.2-78.5)	-	4 (57.1%; 15-90.9)	1 (14.3%; 1-74.3)	No risk: 0.80 (0.08-8.47) At risk: 6.67 (0.49-91.33) High risk: 0.83 (0.04-17.00)	-	-
Skin and subcutaneous tissue	1 (9.1%; 0.9-53.7)	3 (27.3%; 7.2-64.6)	5 (45.5%; 16.8-77.4)	2 (18.2%; 3.5-58)	No risk: 0.20 (0.01-2.88) Low risk: 0.75 (0.09-6.47) At risk: 4.17 (0.36-48.44) High risk: 1.11 (0.08-15.53)	-	-
Spine, spinal cord and peripheral nerves	22 (26.2%; 17.8-36.8)	35 (41.7%; 31.4-52.7)	27 (32.1%; 22.9-43.1)	-	No risk: 0.71 (0.12-4.15) Low risk: 1.43 (0.25-8.24) At risk: 2.37 (0.26-21.28)	-	-
Thorax and intra-thoracic organs	2 (33.3%; 4.2-85.1)	22 (33.3%; 4.2-85.1)	1 (16.7%; 0.9-81.4)	1 (16.7%; 0.9-81.4)	*Ref*	-	-
Urinary system and male reproductive organs	-	1 (33.3%; .08-99.7)	2 (66.7%; 0.3-99.9) -	-	Low risk: 1.00 (0.06-18.92) At risk: 10.00 (0.40-250.43)	-	-

	No risk (0)	Low risk (1-4)	At risk (5-8)	High risk (9-12)	Uni OR	Multi OR 1 (*ref: no risk*)	Multi OR 2 (*ref: no risk*)
Vascular system	3 (11.1%; 3.3-31.1)	16 (59.3%; 39-76.8)	7 (25.9%; 12.2-46.8)	1 (3.7%; 0.5-24.5)	No risk: 0.25 (0.03-2.00) Low risk: 2.91 (0.45-18.74) At risk: 1.75 (0.17-17.69) High risk: 0.19 (0.01-3.61)	-	-

Notes. * $p < .05$, ** $p < .01$, *** $p < .001$; ns = non-significant; OR = odds ratio; 95% confidence intervals in parentheses; Ref = reference category/level; Uni ES = univariate effect size (OR unless otherwise specified); Multi OR 1 = multivariate effect size for univariate predictors $p < .20$; Multi OR 2 = multivariate effect size for model including all variables; TAM-2: total (physical) activity measure (higher = more activity) - note log transformation to mitigate skew; ASA-PS: American Society of Anaesthesiologists physical status score; BMI: body-mass index; note that multivariate analyses were conducted without covarying both BMI and ASA-PS scores, results here are those including ASA-PS scores.

Table D1. COM-B Factor Loadings.

Factor	**Item**	***B (β)***	***B* 95% CI**
Physical capability	*I can cope with the negative physical effects of drinking less*	0.62 (0.86)	0.50-0.75
	I find it physically challenging to drink less	0.82 (0.95)	0.68–0.97
Psychological capability	*I can drink less*	0.76 (0.90)	0.62–0.91
	I know why it is important to drink less	0.65 (0.77)	0.50–0.79
	I could resist alcohol	0.83 (0.69)	0.61–1.05
Physical opportunity	*There are lots of opportunities for me to drink*	1.41 (0.88)	1.15–1.66
	I have lots of time to drink	1.43 (0.79)	1.13–1.74
Social opportunity	*People I spend time with drink often*	1.49 (0.92)	1.21–1.77
	I often feel pressured to drink	0.82 (0.67)	0.59–1.04
Reflective motivation	*I plan to drink less*	1.02 (0.70)	0.72–1.32
	If I drank less I would do better after the operation	1.12 (0.75)	0.81–1.42
Automatic motivation	*I need to drink*	1.00 (0.70)	0.73–1.27
	I can stop myself from drinking impulsively	1.14 (0.87)	0.89–1.39

Notes. B = unstandardized estimate, β = standardised; all *Z* scores $p < .001$.

Table D2. COM-B Factor Covariances.

Subdomain		Estimate (SE)
Phys. capability	Psych. capability	0.56 (0.08)
	Phys. opportunity	0.29 (0.11)
	Soc. opportunity	0.34 (0.10)
	Ref. motivation	0.43 (0.11)
	Auto. motivation	0.51 (0.10)
Psych. capability	Phys. opportunity	0.49 (0.10)
	Soc. opportunity	0.38 (0.11)
	Ref. motivation	0.28 (0.12)
	Auto. motivation	0.53 (0.10)
Phys. opportunity	Soc. opportunity	0.91 (0.06)
	Ref. motivation	0.69 (0.09)
	Auto. motivation	0.65 (0.08)
Soc. opportunity	Ref. motivation	0.49 (0.12)
	Auto. motivation	0.68 (0.08)
Ref. motivation	Auto. motivation	0.37 (0.13)

Notes. SE = standard error; all Z scores $p < 0.05$.

Table D3. COM-B Ratings Correlated with AUDIT-C and ASSIST Scores.

Measure	Subdomain	Coefficient	95% CI	99% CI
ASSIST	Phys. capability	-0.23*	-0.40- -0.03	-0.45–0.03
	Psych. capability	-0.17	-0.35-0.03	-0.40–0.09
	Phys. opportunity	-0.33***	-0.49- -0.14	-0.54– -0.08
	Soc. opportunity	-0.39***	-0.55- -0.22	-0.59– -0.16
	Ref. motivation	-0.42***	-0.56- -0.24	-0.61– -0.18
	Auto. motivation	-0.28**	-0.45- -0.09	-0.50– -0.03
AUDIT-C	Phys. capability	-0.21*	-0.39- -0.02	-0.44–0.04
	Psych. capability	-0.25*	-0.42- -0.06	-0.47–2.98e-3
	Phys. opportunity	-0.39***	-0.55- -0.22	-0.59– -0.16
	Soc. opportunity	-0.48***	-0.61- -0.31	-0.65– -0.25
	Ref. motivation	-0.37***	-0.52- -0.19	-0.57– -0.13
	Auto. motivation	-0.31**	-0.47- -0.12	-0.52– -0.06

Notes. * p < .05, ** p < .01, *** p < .001.

Table D4. ASSIST Regression Statistics.

Predictor	***B* (95% CI)**	***β* (95% CI)**
Phys. capability	-0.31 (-0.83–0.20)	-0.14 (-0.36–0.09)
Psych. capability	0.13 (-0.19–0.45)	0.09 (-0.14–0.32)
Phys. opportunity	-0.21 (-0.54–0.12)	-0.19 (-0.49–0.11)
Soc. opportunity	-0.19 (-0.57–0.19)	-0.14 (-0.43–0.14)
Ref. motivation	-0.24 (-0.54–0.05)	-0.18 (-0.40–0.04)
Auto. motivation	-0.00 (-0.33–0.33)	-9.42e−4 (-0.24–0.23)

Notes. *B* = unstandardized estimate, *β* = standardised; * *p* < .05, ** *p* < .01, *** *p* < .001.

Table D5. AUDIT-C Positive vs. Negative Patients' Intervention Format/Deliverer Scores.

AUDIT-C	**Item**	**Mean (SD)**	**Mean difference (95% CI)**	***d***
	Format			
Positive	Computer based	5.49 (2.18)	0.91 (0.22-1.61)	0.50
Negative		6.40 (1.30)		
Positive	Group-based	6.87 (0.58)	-0.13 (-0.42-0.16)	-0.18
Negative		6.74 (0.85)		
Positive	Guided workbook	6.51 (1.12)	-0.08 (-0.54-0.37)	-0.07
Negative		6.43 (1.19)		
Positive	One-to-one	6.95 (0.40)	-0.07 (-0.28-0.14)	-0.14
Negative		6.87 (0.61)		
Positive	Phone helpline	6.76 (0.67)	-0.15 (-0.48-0.19)	-0.18
Negative		6.62 (0.97)		
	Deliverer			
Positive	Alcohol counsellor	6.40 (1.47)	-0.21 (-0.86-0.44)	-0.13
Negative		6.19 (1.79)		
Positive	GP	6.91 (0.44)	-0.14 (-0.39-0.11)	-0.24
Negative		6.77 (0.76)		
Positive	Nurse	6.95 (0.40)	-0.09 (-0.31-0.12)	-0.18
Negative		6.85 (0.62)		
Positive	Self-guided	6.55 (1.34)	-0.29 (-0.88-0.30)	-0.20
Negative		6.26 (1.59)		
Positive	Surgery team	6.71 (1.13)	-0.09 (-0.55-0.37)	-0.08
Negative	member	6.62 (1.19)		

Table E1. Barriers and Facilitators: Theme Quotations.

Theme	Sub-theme 1	Sub-theme 2	Sub-theme 3	Example quotations
Motivation & Willpower				
	Prime importance of motivation			**Aiden**: *"…listen, once you're that far gone, you're that far gone, I've been there me sen* [self] *on gear and what have you, and it's like, when your mind's set, I've even got people who'll bring me heroin down t' hospitals, and gone in t' toilets, got it together and done it in me groin and what have you. So, if you're that set in your ways, there's no way they can stop you."* **Matt**: *"Most people are on it on a* [methadone] *script anyway, aren't they? But most people just use the script to balance themselves out until they get some money to score, really, that's what most people use it for, they're just not interested in stopping."* **Matt:** *"I don't think none of this b*llocks works really, I don't, I think, like I say you get to a point where you've had enough. In my experience, all these recovery groups and all that, sitting down and talking about drugs makes me want to use drugs. "* **Ethan**: *"I think a lot of it's down to myself because I sort of like, had strong willpower to try, you know, do something about it.* **Jenny**: *"I think with me it was like, it's like doing stuff, motivating yourself to do certain things* [other than use substances].*"*

Theme	Sub-theme 1	Sub-theme 2	Sub-theme 3	Example quotations
	Moderators of motivation & willpower			
		Social influence		**James:** *"I think if it was something that was life-threatening or something in that manner and I think that I needed to do this, you know, then yeah, I think* [I would be motivated to reduce] *yeah, because I've got a wife and I've got family and, you know, things like that. There are people that care about me."*
				Jacob: *"One of the key areas of me finally coming here* [a drug and alcohol treatment centre] *to sort my Codeine addiction out was to speak to my girlfriend about it* […] *she basically helped me make the right decision in coming here in the first place."*
		Withdrawal symptoms		
		Health conscientiousness		**Lucas:** *"Well, it depends what sort of surgery you was having, what it was, I suppose. Well, I suppose any sort of surgery, if it were going to affect that surgery course you would* [affect motivation], *yeah."*
				Charles: *"…if it were a more serious operation, then obviously it would have a bigger effect on you for using."*
			Fear for health	**Owen:** *"Yeah, well in that context* [surgery] *I'd have to reduce, yeah."*
				Susan: *"Well, obviously I'm going to surgery because I need to go to surgery, so the outcome's going to be better for me, so I need to help myself* [to reduce]*..."*
				Ryan: *"…there's a lot of people, you know, that have come close to losing legs and stuff, and that's been about the time they've become totally abstinent because, you know, it's pretty serious sh*t if you're heading towards losing your leg…"*

Theme	Sub-theme 1	Sub-theme 2	Sub-theme 3	Example quotations
			Disregard for health	**Aiden:** *“With surgery cos it’s, surgery’s irrelevant, innit, they do what they’ve got to do, you do what you’ve got to do. So, if your minds set for, if you’re in heroin, amphetamine or whatever, you’ll go and do it. It dun’t matter what a doctor says”*
Interaction with healthcare				
	Stigma			**Rosie:** *“…they do see addicts as a drain on the system, especially in Accident and Emergency, or when you're having a thousand pound operation because your habit has caused your health problem…”* **Mason:** *“Before they knew they were alright, and then I told them* [that they are heroin dependent]*, because I had to tell them because I was staying in, and it were like, everything changed and that, they were coming in gloved up and that as if I had AIDS…”*
	Healthcare ignore substance use			**Hazel:** “*…when you go for them pre-op they just ask you* […] *if you smoke and stuff, there’s never no question about… I mean they ask you about medication. When people ask me about medication I always forget to mention the Methadone.”* **Chris:** *“I had no signposting, no advice whatsoever, it were just sort of ‘Don't use, stick to your Methadone, we're aware of it’, and that were sort of it.”* **Ethan:** *“I can’t remember owt said about alcohol, it were mainly like, you know, like your fitness and stuff like that and did I smoke?”*
	Disclosing substance use to healthcare			
		Moderators of disclosure		

Theme	Sub-theme 1	Sub-theme 2	Sub-theme 3	Example quotations
			Stigma	**Ryan:** *"*[The paramedics] *were absolutely so like... didn't bat an eyelid, they were like you're just a person that's got a problem, there's no judgement or anything. And that, that has led me like be open and so I was very open, I just said 'yeah, I'm on Methadone'* [to a nurse at the hospital].*"*
			Fear of surgery delay or cancellation	**Joe:** *"It depends what state of mind you're in doesn't it? If it's something that you know you absolutely have to have you know and it's a case of well you might die if you don't, you might keep quiet"*
				Rachel: *"I don't know, I think she thought she wouldn't have been able to have the operation.. that's what she had in her head.. so she panicked and didn't tell them, and then she's come home and told me and shes panicked more thinking something's gonna happen to her then because she's not told them."*
Hopelessness & cynicism				**Jenny**: *"Some people that I know probably wouldn't like doing anything. Even if you locked them up they would still try and get it in there or whatever, you know, to try and do it, and they wouldn't be bothered* [about their health].*"*
	Disregard of health			
	Low self/other belief			**Aiden:** *"Surgery's irrelevant, innit, they do what they've got to do, you do what you've got to do. So, if your minds set for, if you're in heroin, amphetamine or whatever, you'll go and do it. It dun't matter what a doctor says to you or anyone, if your minds set for that gear* […] *nothing, even old bill can't stop you."*
				Aiden: *"No, because if your minds set, your minds set, innit? Nobody can change it, only you yourself, dun't matter how many people stand in front of you and say, "You're going to die if you do this", if your minds set, you go, "So what? Do you think I give a f*ck?"*

Theme	Sub-theme 1	Sub-theme 2	Sub-theme 3	Example quotations
Triggers				**Chloe:** *"I'd say like for me personally it's like social media when I see friends out drinking, you know* […] *and being on my own and not socialising as much I think that's, that's a thing that'd probably trigger me to use, to go out and overdrink and you know, whatever else."*
	Internal triggers			
		Mental ill health, trauma & mood		**Hazel:** *"I've been using drugs since I were 11, at the moment it's a bit of erratic, it comes with me depression, and goes"*
				Ryan: *"someone's got mental health problems and they feel a lot of anxiety from that so they take drugs to reduce the anxiety and the drugs they become tolerant so they use more drugs,* […] *they use more money, so they've got more money problems and they've got more anxiety coming off the money problems..."*
		Boredom		**Leo:** *"I play games on the computer and I was told to find more games, so I've found more games* […] *just to occupy the time, because boredom's the big thing"*
				Elijah: *"I think it's a lot to do, a lot to do with, it's a lot to do with boredom* […] *That is the big factor really, is that boredom fear."*
				Rachel: *"But when I keep myself at home bored not doing nothing it's just a different story, it's hard, you start thinking about sh*t"*

Theme	Sub-theme 1	Sub-theme 2	Sub-theme 3	Example quotations
	External triggers	People & places		**Joe:** *"…it wouldn't be a good idea to hang out with other people who are using before your surgery because that's yeah, another trigger. As daft as it sounds, coming here [a drug and alcohol treatment service centre] is a trigger you know."* **Rob:** *"…so to tell someone that, you know, their family uses drugs and their friends use drugs and blah, blah, blah, and then all of a sudden they're sat on their own, the only thing that can fill that gap really is NA [Narcotics Anonymous] and stuff like that, so NA, so cut off everybody, go to NA, stay clear"* **Matt:** *"In my experience, is that all these recovery groups and all that, sitting down and talking about drugs makes me want to use drugs…"* **Noah:** "*There's always some*[one] *there that's out of his head on thingy* [..] *that* [says] *when you're going out, 'we're going to score, we're going to score'. There's someone else there that knows someone to score off and* [says] *'come with me and I'll go get you some', and that's what happened with me, so that's why I don't bother with the groups really…"*
		Idiosyncratic triggers		**Charles:** *"When I'm working, I seem to have access to a little bit more money, so you've always got money there and it's not an issue to have to go and get the money to buy the drugs, so..."* **Elijah:** *"the money, the moment you get some money in your pocket, knowing that you can't afford it, yeah, but you still go and get it…"* **Jacob:** *"My main cue is driving past a pharmacy. I've got no emotional issues at the moment, I'm very happy in my home life, so, yeah, just driving around, seeing a pharmacy is normally what spurs me on…"*

Theme	Sub-theme 1	Sub-theme 2	Sub-theme 3	Example quotations
Social influences				
	Family and/or friends as a facilitator			**Susan:** *"I need to stop doing what I'm doing to get this surgery* […] *I've got two children to think about..."*
				Jacob: *"One of the key areas of me finally coming here* [to a drug alcohol treatment service] *to sort my Codeine addiction out was to speak to my girlfriend about it. I found out she was supportive* […] *you know, she basically helped me make the right decision in coming here in the first place."*
				Dave: *"But once I admitted it, then we got it all sorted, she had me to the doctor's, basically she dragged me all over the place."*
				Charles: *"I think, a lot of the time, for meself, it's just seeing other people's, like I've got a brother who's in a relationship, he's got money, he's got his own house, do you know what I mean, he's happy, and obviously I tend to think that I'm missing out on a lot of things, so..."*
	Loneliness, lack of support barriers			**Rob:** *"Some might have a girlfriend, some might have a wife but most end up on their own, I didn't realise that until I started going into recovery and hearing people talk that we all end up in same place…"*
				Noah: *"…it helps to talk doesn't it as well, helps to talk to someone about it, I don't have many friends or owt anymore, I've lost all of them from me heroin addiction, so yeah it helps to talk to therapist."*

Theme	Sub-theme 1	Sub-theme 2	Sub-theme 3	Example quotations
	Family and/or friends as a barrier			**Rob:** *"…'sit in barber's chair long enough, you'll get your hair cut', do you know what I mean? And that's exactly what it is. So if you put yourself round drugs, you're probably going to use if you've had a problem…"*
Habit & automaticity				**Elen:** *"…it's like built into you, you know and you're telling yourself all the way there you don't want to go [and buy heroin] but you're still going and getting* [it]*."*
				Joe: "*I can ride them* [cravings] *out, they call it surfing the emotion* […] *I can do that but then it gets to a point with me where, and I'm telling myself I don't want to go* [and buy heroin] *but I'm still going you know"*
				Matt: *"If you've got an habit you've got to use haven't you? It's not like you can think, 'oh I'm having surgery today, I won't use.' You've got to* [use]*…"*
				Jack: *"Unless you've been in this position that I'm in and you're craving that thing, it's like some people crave chocolates, some people crave cream cakes, you know what I mean, they've got to eat"*
				Jack: *"…I did 3½ months, I think it were, without a drink and then I thought I could beat it* [...] *I thought I'll just have a taste, I had a taste and I didn't like it but I finished it, just a habit..."*
				Lucas: *"…I think that nearly every time I have one* […] *I think to meself, when I've had it, I think what a waste of time that was…"*

Theme	Sub-theme 1	Sub-theme 2	Sub-theme 3	Example quotations
Preoperative reduction easier than postoperative maintenance				**Mike:** *"…I mean I would have stopped drinking but I'd have had it in my mind that after the surgery I'll start again."* **Rob:** *"…I'd stop taking methadone, I would, I'd want to live that much that it would, overnight it would change me, I can't guarantee that I'd stay off it once I'd come through the thing, but I would stop for the f*cking operation."*

Table E2. Strategies: Theme Quotations.

Theme	**Sub-theme**	**Example quotations**
Setting goals		
	Goal setting, planning and tapering	**Ryan:** *"…small, manageable goals rather than saying, 'you know what, tomorrow I'm going to be clean, off everything, never going to touch it again'* […] *you're setting yourself to be disappointed* […] *you're setting up expectations which will, they're going to be violated and then it's going to make you feel worse, you know."*
		Charles: *"I have stopped using a couple of times before, and, yeah, it's definitely, definitely worked, like sitting down and working out what those triggers are and trying to keep yourself away from them or change certain things."*
	Self-monitoring	**Charles:** *"I don't know whether it's you haven't got time or you don't really want to like tell yourself what you are using so, but, yeah, I've never really, I've never really been one to keep a record of what I'm doing."*
Providing risk information		
	Motivation and information	**Logan:** *"…if they said you'd die if you didn't have this surgery* […] *it depends, if they said it now, I might because I'm wanting to stop, I'm wanting to change it,* […] *but the majority of my life I'd just say, 'F*ck it, I'll take me chances', kind of thing."*
		Charles: *"…sitting down and speaking to somebody and explaining that there are, do you know what I mean, there could be implications of you using on top, when you're going in for your operation. I think it's going to be a massive issue, because, like I say, I just don't think people, I don't think people realise."*

Theme	Sub-theme	Example quotations
	Methods to increase impact of risk information	**Noah:** *"…keep going with them I think, to finally get through to them, yeah. You'd have to be, it'd have to take a bit of time, it'd take a good few month I'd have thought."* **Jack:** *"I listen to what the doctor says, you know what I mean, or the nurse says and I show respect because they're doing a great job, you know what I mean…"* **Hazel:** *"Yeah, because half of them nurses and that they haven't got a clue like, and I've even been on a ward where I'm the only one who's taking it and they haven't got a clue…"* **Ryan:** *"…you don't want to scare people because if you scare people you make them stressed and that might make them start using more, you see."* **Ryan:** *"…whoever does the intervention has to be very well-informed about the subject* […] *what helps me is that, I suppose it can sort of scare people away but when I'm given sort of facts about the physical impact drugs can have and stuff can have, and how that might undermine my operation* [it is/would be beneficial]*"* **Sam:** *"I think actually demonstrate the risks, show, maybe show pictures, you know like you see on cigarette boxes now, it shows the, the implications of smoking* […] *graphs, maybe more, more visual that's more of an impact on the patient."*
Heavy-handed approaches		**Matt:** *"Well they should do, they should f*ck 'em off, mate and then give somebody the surgery that deserves it and that'll appreciate it and won't just carry on using and f*ck the rest of their life up."* **Lucas:** *"I think that's what they should do, I really do, just say you either stop that or we're not treating you because what's the point…"* **Ryan:** *"…You've got to sort of create a sort of welcoming and inviting sort of atmosphere really"* **Dave:** "[if surgery was withheld] *all they're going to do is just go out and drink even more."*

Theme	Sub-theme	Example quotations
Addressing stress, distress & mental health		**Will:** *"…I'm dying to get off the methadone and out of this place, so I can get into a service without the drugs.. because I believe all the time I'm here they're not really addressing my mental health…they're just addressing my drug use…"* **Logan:** *"I suppose, seeing a psychologist first might help, or something else rather than just, straight away, like asking them, 'Oh, do you want to stop completely?"* **Ryan:** *"…look at the sort of whole context of using and any sort of issues that might be contributing to it. Social issues, housing issues, problems with benefits, domestic violence, you know, mental health."* **Dave:** *"Well, my main problem what kept me triggering me off were me and me ex were always arguing and me son ended up in foster care…"*
Avoiding & removing triggers		**Charles:** *"…when I've, I have stopped using a couple of times before, and, yeah, it's definitely, definitely worked, like sitting down and working out what those triggers are and trying to keep yourself away from them…"* **Mike:** *"I went to a barbeque on Saturday night, felt a bit uncomfortable but I took myself out of the situation by going for a walk* […] *because I've learned that* […] in [a drug and alcohol treatment service] *they went through the coping strategies and things I can do"* **Ryan:** *"…going out and doing things that interest me, stimulating like my natural level, levels of enjoyment, getting enjoyment from things that I naturally enjoy without having to put chemical inside me, reinvigorating those areas of my life…"*
Flexibility & individualization		
	Efficacy of certain strategies highly depend on individuals	**Matt:** *"…everybody's different, what will work for one person won't work for everybody will it"* **Elen:** *"everybody's different and respond different to different techniques"* **Will:** *"…it all depends on the person. Everyone's different"* **James:** *"I think* [all strategies are] *worth* […] *a go and things are going to be different for different people, you know, everybody's going to react in different ways to different things."*

Theme	Sub-theme	Example quotations
	Preferred one-to-one, personal interventionist and plan	**Hazel:** *"…when you go for your pre-op and, you know, like you're on Methadone or whatever, maybe if they have someone there from the drug team and then between you all you could put a plan together couldn't you?"*
Harm reduction strategies more realistic than complete abstinence		**Ryan:** *"But, you know, if you could say to people, I think if you gave across the idea, look, eighteen weeks, you know, you could stop completely but even if you reduce a bit, that'd be great, that would get rid of that tension I think, that's one avenue for getting rid of that tension, you know."*
Pre-surgery an opportune time to motivate detox and/or rehab attendance		**Chris:** *"…maybe after the assessment, I think the time in between surgery it would have been helpful for me to be detoxed, it would have been because I still, you know, I still came out after the surgery and spending time in hospital, I still came out with 60ml Methadone problem and I were using on top as well so..."* **Chris:** *"If it were up to me there'd be people who are going in for elective surgery would be detoxed, you know would be detoxed and go into that procedure clean and with a fresh bite of the cherry, you know a fresh new life. However, like I say, I don't think funding would allow that, you know, maybe it needs some more money piling into it."*
Aiding memory		**Chloe:** *"Constant reminder yeah I think that would be good."* **Oliver:** *"I do that with appointments and things like that, put them up, you know, on top of the fireplace, so when I pass them and I look at them, then I think…"*
Just talking to someone		**Rachel:** *"that's all a lot of people need, just people to listen and follow up on stuff I think…"* **Noah:** *"I try and keep her out of the drugs, you know what I mean, she hates drugs me mum and that, these people* [at the drug and alcohol treatment centre] *know all about the drugs and my mum doesn't know owt about it, these people know about all the drugs, so you've got someone to talk to and then they know exactly what you're on about…"*

Table E3. Formats: Theme Quotations.

Theme	Sub-theme 1	Sub-theme 2	Quotation
Interventionists			**Rob:** *"I've known* [name] *for fifteen year, maybe even longer, so she's seen me go through my addiction, she's seen me at me worst, she's seen me get better, she's seen me up and down, so I think, I think it's handy to know your Drug Workers."* **Mason:** *"…but a doctor or a nurse, yeah, I'd definitely take it on board because they're in that for a reason, aren't they, that's their job and they know what they're doing, so..."* **Jack:** *"I listen to what the doctor says, you know what I mean, or the nurse says and I show respect because they're doing a great job, you know what I mean…"* **Hazel:** *"Yeah, because half of them nurses and that they haven't got a clue like, and I've even been on a ward where I'm the only one who's taking it and they haven't got a clue, they're asking me, you know what I mean, what it does to you and stuff like that, because they're not used to dispensing it and working with it, so you know what I mean, they're a bit stunned, yeah."* **Ryan:** *"I think that it would be wonderful if the doctors knew, and everyone in the hospitals knew the mechanics of addiction and also the physiological side of sort of Methadone and stuff, because my friend was there and he was having lots of antibiotics and they were interfering with the Methadone. So is the withdrawal a lot and you know, it's not good to put someone in, in withdrawal and it can, you know, I think in very limited numbers, it does put a strain on the body."* **Mason:** *"Like up here as well, because up here who've never done drugs, but I like the ones who've been on it, you know, and become workers, cos they know what you're about and what they've done to get off it themselves and stuff, so I get a few tips and that."* **Rob:** *"…because to be around clean people that know what you've been through, know what you're going through, fantastic if it works."*

Theme	Sub-theme 1	Sub-theme 2	Quotation
Timing			**Joe:** *"Well someone who's been doing it for 20 years isn't going to sort it out in 13 weeks, you know."* **Jenny:** *"…if it's in the space of like a week or two I don't think that it would make much difference anyway* […] *not for the amount of like years that I done it for."* **Mike:** *"…maybe say a couple of month before..."* **Noah:** *"…it'd have to take a bit of time, it'd take a good few month I'd have thought."* **Lucas:** *"…definitely weekly, well at least once a week"* **Leo:** *"…it's got to be once a week"*
Group sessions			**Rob:** *"I rang someone up at two o'clock in the morning and the lad was asleep, and he got up, answered his phone and spent an hour talking to me. I didn't use."* **Noah***:* *"Just like people coming in and they're on heroin anyway, some people can come in and then they're showing their phone numbers and stuff…"* **Noah:** *"I were clean and someone asked me to go score with them…"* **Mason:** *"…it wasn't for me because they talk about drugs too much, and if it gets put in me head then I want to go and do it after, so I try to minimalise it…"*
One-to-one sessions			**Mason:** *"Yeah, I don't like groups, me, you get all kind of riff-raff in there, but yeah, one-on-one, because if there's loads of people in there you think they all judge you and stuff, yeah, I find it difficult…"*

Theme	Sub-theme 1	Sub-theme 2	Quotation
Other modes of delivery			
	Opioid substitution		
		Useful for withdrawal symptoms	**Noah:** *"…they'd need to do a detox really wouldn't they, like Methadone script and like come off it pretty quickly till they get weaned down, weaned down, and within 18 weeks, yeah, of course they could…."* **Ryan:** "[on the benefits of attending a substance us treatment centre] *…on a very dark physical level they prescribe Methadone, which stops you from having severe withdrawal symptoms. They also, beyond that* […] *they look at the sort of whole context of using and any sort of issues that might be contributing to it."* **Mason***: "Oh yeah, once I get off it, never touch owt to get back on it, hopefully, because I know what it does to you. I've been years trying to get off this stuff, it's just hard, even when you stop your Methadone* [laughs] *parts are still there, it's damn hard, I find it hard, anyway."* **Lucas:** *"…the heroin I've sorted it out, I've got that sorted, you know, I'm medicated for that, I don't need to go near that ever again…"* **Aiden:** *"I'm getting detoxed off Methadone, I've had enough of it, I don't touch gear now, I haven't touched it for ages."*
		Substitution can be counterproductive	**Joe:** *"…getting Methadone you know when people are still using is a joke, you know and I'm an addict saying that. I think there's no incentive then for them to give clean samples and be clean* […] *I feel like I'm taking someone else's support really because I don't need to, you know to be taking Methadone every day. I also think it's a big factor in why people have a problem for so long, because they rely on it."* **Matt:** *"…most people just use the script to balance themselves out until they get some money to score, really, that's what most people use it for, they're just not interested in stopping."*

Theme	Sub-theme 1	Sub-theme 2	Quotation
	Information leaflets		**Joe:** *"You know, not just leaflets, talking information, that sort of thing. If you give people leaflets then they just tend to take them and not read them don't they? That sort of thing."* **Chris:** *"I mean, there's lots of ways to deliver information isn't there, I mean I find, well I found from personal experience that you know, if you're given a leaflet you know, you end up using it as roach material for the spliff* [cannabis cigarette], *you know what I mean?"*
	Alcohol medication		**Jack:** *"Antabuse* [disulfiram] *when I was using Antabuse it were, it were good, it were good because I knew if I went anywhere near alcohol I were going to be in this state."*

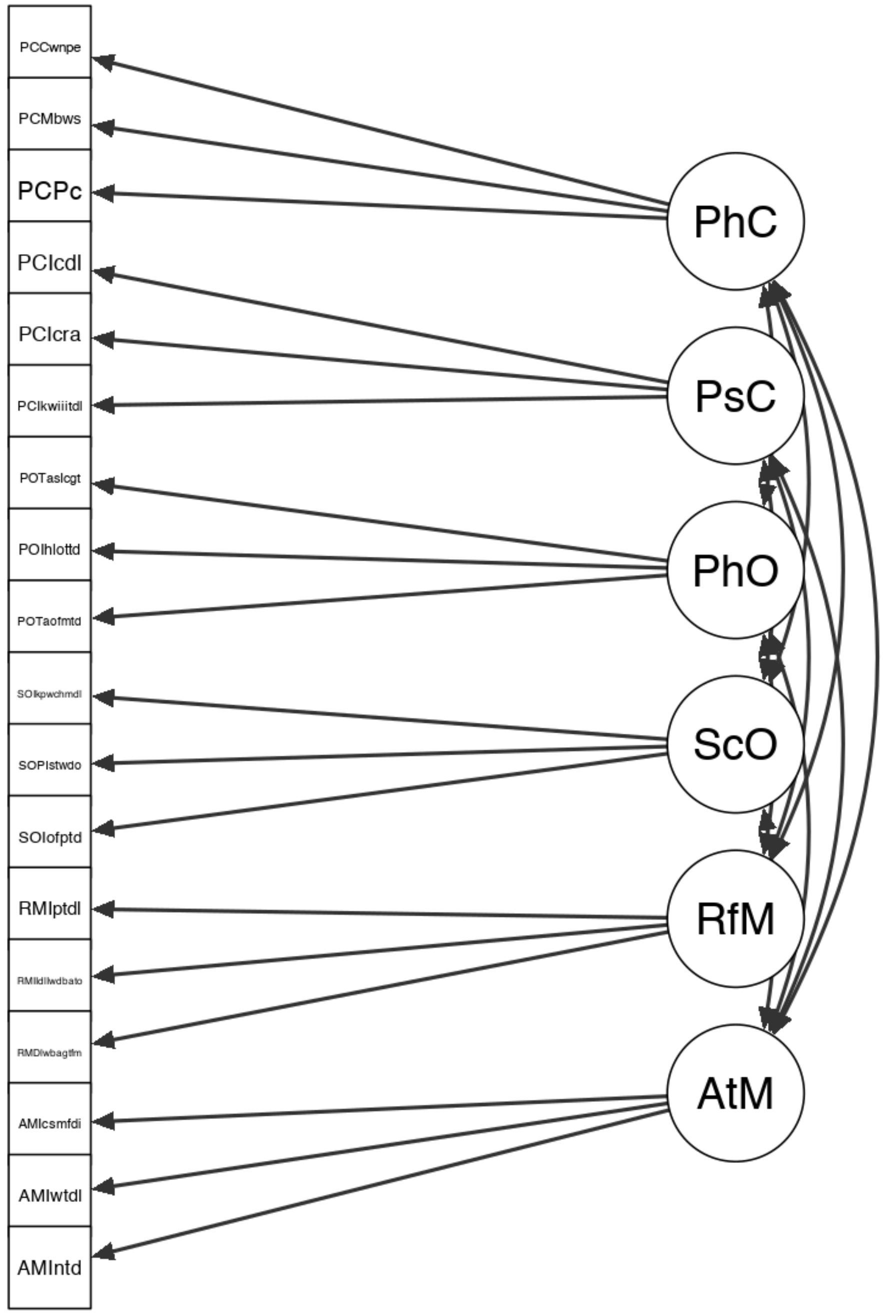

Figure A1. Model 2: COM-B Subdomains as Latent Constructs.

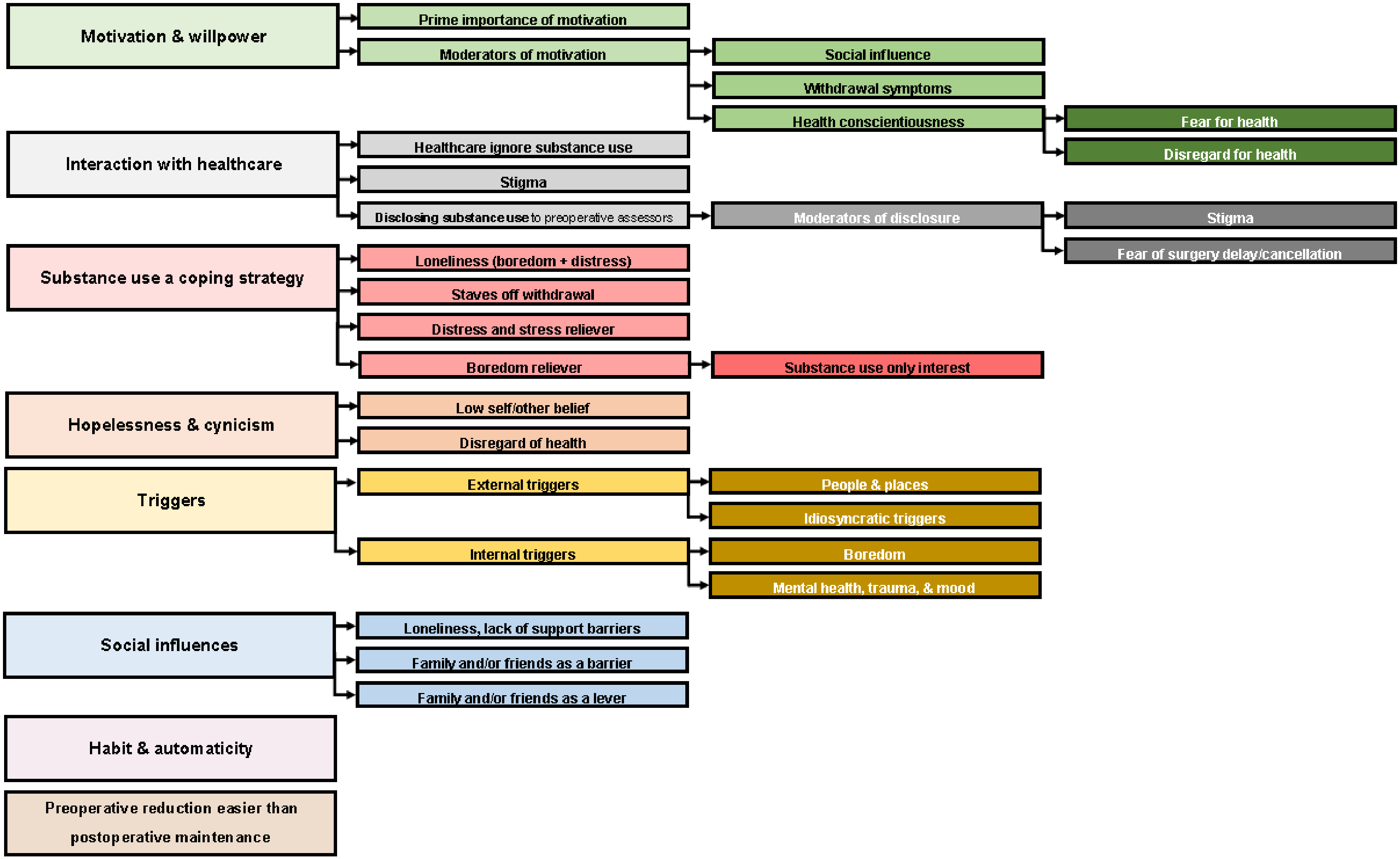

Figure B1. Schematic Representation of Themes Related to Barriers and Facilitators.

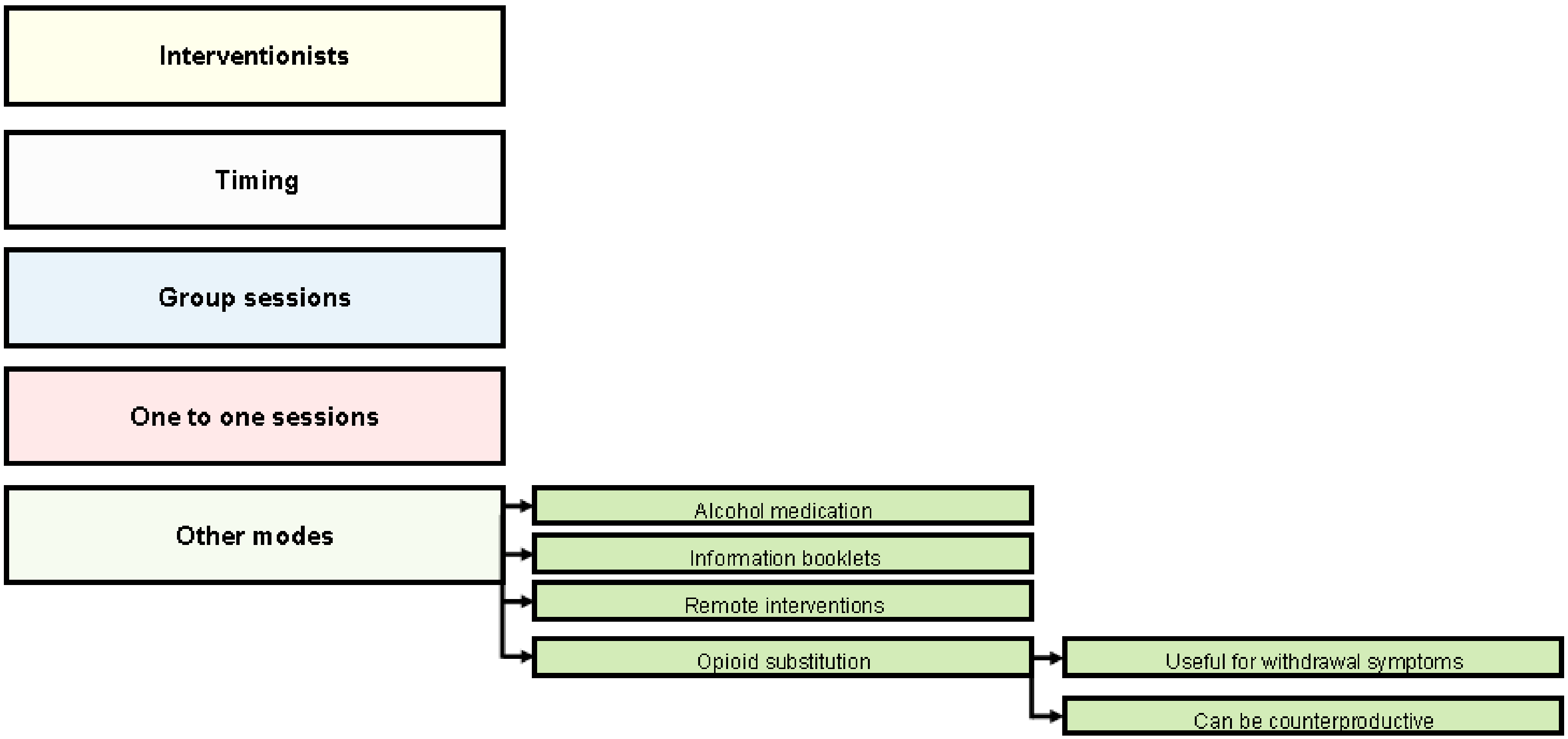

Figure B2. Schematic Representation of Themes Related to Intervention Formats.

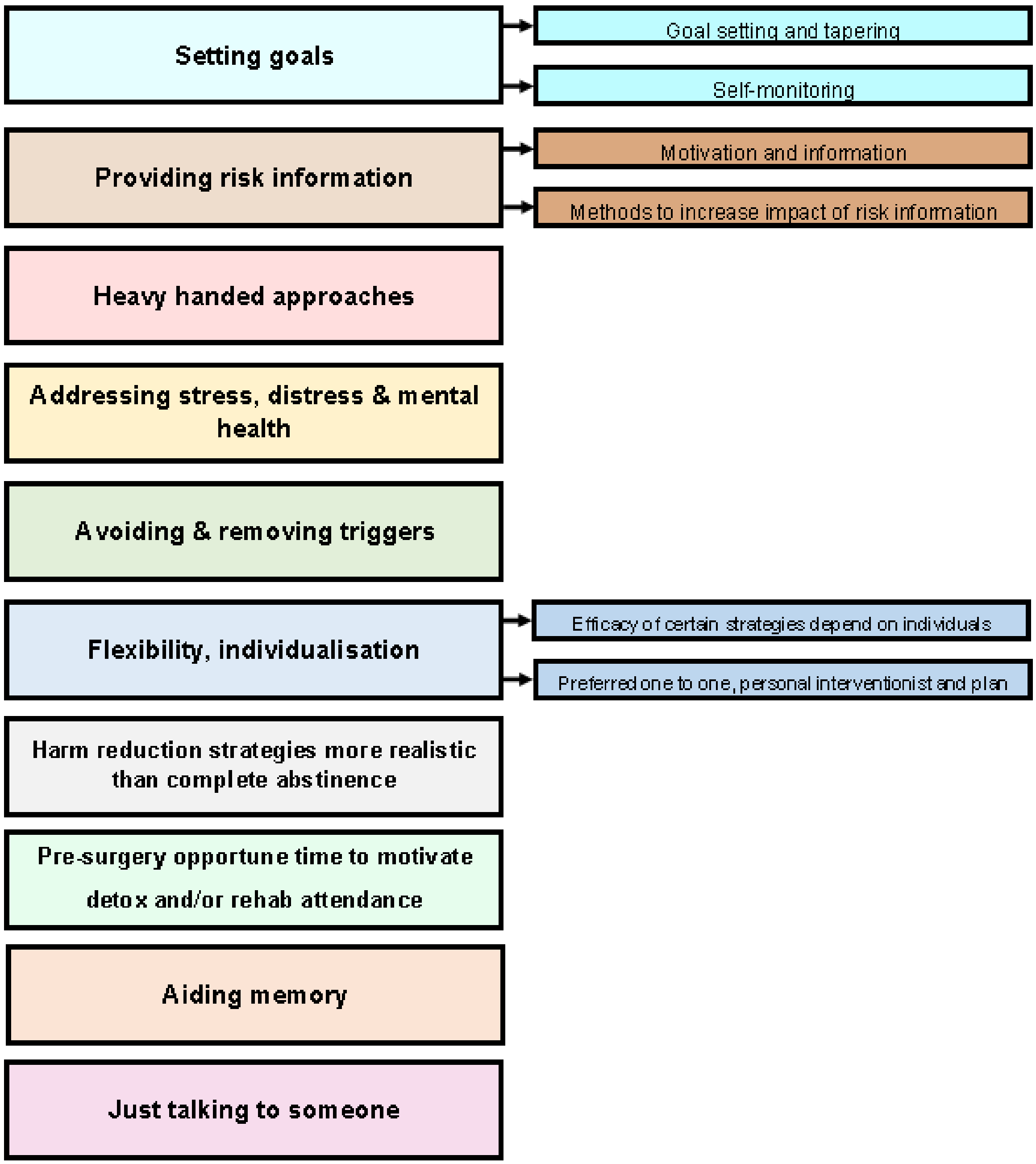

Figure B3. Schematic Representation of Themes Related to Intervention Strategies.

APPENDIX A: NICE RECOMMENDATIONS FOR PREOPERATIVE TESTING

ASA Grades (American Society of Anesthesiologists Physical Status Classification System)	
ASA 1	A normal healthy patient
ASA 2	A patient with mild systemic disease
ASA 3	A patient with severe systemic disease
ASA 4	A patient with severe systemic disease that is a constant threat to life

Test	ASA 1	ASA 2	ASA 3 or ASA 4
Minor surgery (**examples**: excising skin lesion; draining breast abscess)			
Full blood count	Not routinely	Not routinely	Not routinely
Haemostasis	Not routinely	Not routinely	Not routinely
Kidney function	Not routinely	Not routinely	Consider in people at risk of AKI[1]
ECG	Not routinely	Not routinely	Consider if no ECG results available from past 12 months
Lung function/arterial blood gas	Not routinely	Not routinely	Not routinely
Intermediate surgery (**examples**: primary repair of inguinal hernia; excising varicose veins in the leg; tonsillectomy or adenotonsillectomy; knee arthroscopy)			
Full blood count	Not routinely	Not routinely	Consider for people with cardiovascular or renal disease if any symptoms not recently investigated
Haemostasis	Not routinely	Not routinely	Consider in people with chronic liver disease • If people taking anticoagulants need modification of their treatment regimen, make an individualised plan in line with local guidance • If clotting status needs to be tested before surgery (depending on local guidance) use point-of-care testing[2]
Kidney function	Not routinely	Consider in people at risk of AKI[1]	Yes
ECG	Not routinely	Consider for people with cardiovascular, renal or diabetes comorbidities	Yes
Lung function/arterial blood gas	Not routinely	Not routinely	Consider seeking advice from a senior anaesthetist as soon as possible after assessment for people who are ASA grade 3 or 4 due to known or suspected respiratory disease
Major or complex surgery (**examples**: total abdominal hysterectomy; endoscopic resection of prostate; lumbar discectomy; thyroidectomy; total joint replacement; lung operations; colonic resection; radical neck dissection)			
Full blood count	Yes	Yes	Yes
Haemostasis	Not routinely	Not routinely	Consider in people with chronic liver disease • If people taking anticoagulants need modification of their treatment regimen, make an individualised plan in line with local guidance • If clotting status needs to be tested before surgery (depending on local guidance) use point of care testing[2]
Kidney function	Consider in people at risk of AKI[1]	Yes	Yes
ECG	Consider for people aged over 65 if no ECG results available from past 12 months	Yes	Yes
Lung function/ arterial blood gas	Not routinely	Not routinely	Consider seeking advice from a senior anaesthetist as soon as possible after assessment for people who are ASA grade 3 or 4 due to known or suspected respiratory disease

AKI, acute kidney injury
[1]See recommendation 1.1.8 of the NICE guideline on acute kidney injury
[2]Note that currently the effects of direct oral anticoagulants (DOACs) cannot be measured by routine testing.

APPENDIX B: EXAMPLE PREOPERATIVE ASSESSMENT FORM (LEEDS, UK)

Patient name .... Hospital / NHS number..

Observations

Date	BP ►	Pulse	Resp	SPO2	Weight ►►	Height	BMI ►►

Please answer either Yes or No for all questions on pages 6, 8 and 10 with a tick ✓ in the corresponding box. If you are unsure what the question means please leave blank. A nurse will go through your answers with you in more detail.

Medical History	Yes	No	Nursing Assessment
Cardiovascular System (Heart)			
Do you have or have you ever suffered with angina/chest pain?			NYA Classification
Have you ever had a heart attack?	►		
Have you had rheumatic /scarlet fever / heart murmur?			
Do you get short of breath?			
Do you have or have you had any problems with your blood pressure (high or low)?			
Is there a close blood relative history of heart problems?			
Have you had heart surgery?			
Do you have any form of heart disease? *(IHD, PVD, CVD, Aneurysm)*	►		
Do you take or have you taken Warfarin / Aspirin / Clopidogrel / Ticagrelor / Dabigatran / Rivaroxaban in the past?	►		
Do you suffer with palpitations / racing heart / irregular heartbeat?			
Do you have a pacemaker?			
Do you or any blood relative have a history of thrombosis (blood clots) in the lungs or legs	►		
Do you get swollen ankles/			
Other			
Respiratory System (Chest and Lungs)			
Do you get short of breath when you lie flat, walk or climb stairs?	►		Dyspnoea Grade
Do you have problems with your breathing? e.g. Asthma / Chronic Obstructive Pulmonary Disease / Bronchitis / Tuberculosis	►		
Do you suffer from other chest problems? *specify*	►		
Do you have a persistent cough?			
Have you ever been told that you appeared to stop breathing whilst you were sleeping?			
Do you or have you ever had a tracheostomy?			
Do you require Oxygen at home?			
Other			

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APPENDIX C: PREOPERATIVE ASSESSMENT FORM LIFESTYLE BEHAVIOURS SECTION (LEEDS, UK)

Patient name .... Hospital / NHS number.......................................

Discharge arrangements

Post discharge arrangements

Do you have a responsible person to collect you from hospital *(D/C -on the day of your surgery)* Yes ☐ *D/C* No ☐

Contact name..

Do you have a responsible and able person to look after you for at least 24 hours Yes ☐ *D/C* No ☐

Do you have a) telephone? Yes ☐ *D/C* No ☐

b) difficulty accessing toilet? Yes ☐ *D/C* No ☐

Do you have sole responsibility for the continued care of a child / adult or pet? Yes ☐ No ☐

If yes you will need to make provisions for their care during hospitalisation

Do you understand implications of day case? Yes ☐ *D/C* No ☐ N/A ☐

Method of transport home....................... Lives within one hour of hospital Yes ☐ *D/C* No ☐

Discharge Risk assessment

Do you live in a House ☐ Bungalow ☐ Flat ☐ Residential home ☐ Nursing home ☐

Risk to discharge	Yes	No	
Do you live with family / friends and are you well supported		▶	Please specify
Do you know where you will be going to stay post surgery		▶	
Will you be dependant on a family member or friend for care post discharge	▶		
Are other people / agencies / services involved in your care at home	▶		
Do you have existing SAP documentation at home *If yes please bring with you on admission*		▶	
Will your current care arrangements need to be adjusted or will you require additional support when you get home	▶		
Will you require nursing / residential home placement	▶		
Will you require social services or will there be complex discharge arrangements	▶		
Are you able to mobilise independently		▶	▶ Indicates risk

Existing SAP documentation at home ☐ SAP requires completing ☐

Nursing specialist assessment completed Yes ☐ No ☐ D/C

Lifestyle history

	Yes	No	
Do you smoke? (number per day)			
Have you been offered smoking cessation advice?			
Do you drink alcohol (number of units per day)?			
Do you use non prescription drugs or recreational drugs?			
Do you regularly use any form of pain relief?			
Do you feel you have any sleep related problems?			

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APPENDIX D: PROPOSED MANAGEMENT OF HAZARDOUS SUBSTANCE USING PATIENTS (ADAPTED FROM NEUMANN & SPIES, 2015)

General algorithm and clinical pathway for patients with substance use disorders
Structured AUD, NUD and DUD screening

- Do you drink alcohol? yes:
    - Alcohol Use Disorder Identification Test (AUDIT), or
    - abbreviated version, AUDIT-C or
    - NIAAA screen for risky drinking e.g. How many times in the past year have you had…
      -5 or more drinks in a day (men)
      -4 or more drinks in a day (women) (One standard drink = 12–14g in the (US)
    - Plus CAGE (if dependence is of interest)
- Do you consume drugs, yes:
    - DSM-IV criteria or ICD criteria
- Do you smoke? Yes
    - Fagerström

If questionnaire results are negative, history not available, questionnaire screening not applicable or reliable and patient undergoing major surgery, critical ill etc.

- Consider collateral information
- Consider the use of markers
  Laboratory testing:
  AUD: CDT, GGT, MCV, EtG, Peth
  NUD: CO-Hb, Cotinin
  DUD: substance or metabolite testing in urine, saliva or blood (depending on substance)
- Comprehensive assessment of comorbidity

If patient is positive

- Synopsis of clinical findings (Screening, history, physical examination, questionnaires, marker, collateral information) =>
- Diagnosis (ICD 10, DSM 4/5) =>
- Consider and discuss specific interventions, include the informed patient into the decision making process (shared decision making), psychoeducation, if appropriate
  Prophylactic, preventive Intervention =>
    - (Preventive) treatment
        - Pharmacological withdrawal prophylaxis,
        - Substitution,
        - Stress reduction…
        - Treatment (e.g. AWS, detoxification, rehab, self help groups…)
        - Abstinence
    - Risk communication,
        - brief Interventions, e.g. Motivational Interviewing
        - FRAMES
            - Feedback
            - Responsibility
            - Advice
            - Menu of behavioral change
            - Empathy
            - Self - efficacy
- Monitor for complications
- Monitor for continuous risky/unrisky use

If preventive treatment not necessary:

- Inform, endorse, confirm
- Maintenance or supportive therapy in former substance users,
- Reevaluation of substance use screening negative patients in special medical conditions

APPENDIX E: MULTIPLE IMPUTATION ANALYSIS RESULTS (STUDY 1)

Wellbeing (CASP-12)

Model 1. $F(4, 349.2) = 912.47$, $p <.001$; df min = 59.49, df max = 424, df average = 208.14. Hazardous drinking ($b = .29$; 95% CI: -.04-.63; $p = .09$); inpatient surgery ($b = -.40$; 95% CI: -.85-.06; $p = .09$); hazardous drinking *x* inpatient surgery ($b = -1.06$; 95% CI: -2.15-.03; $p = .056$).

Model 2. $F(22, 3430.6) = 309.97$, $p <.001$; df min = 40.28, df max = 3703.81, df average = 933.42. Hazardous drinking ($b = .26$; 95% CI: -.07-.59; $p = .12$); inpatient surgery ($b = -.39$; 95% CI: -.83-.05; $p = .08$); hazardous drinking *x* inpatient surgery ($b = -1.05$; 95% CI: -2.10-.005; $p = .05$).

Model 3 (inpatient surgery). $F(28, 4266.6) = 265.57$, $p <.001$; df min = 28.65, df max = 2034.40, df average = 716.02. Hazardous drinking ($b = .21$; 95% CI: -.11-.53; $p = .20$); surgery ($b = -.15$; 95% CI: -.59-.29; $p = .50$); hazardous drinking *x* surgery ($b = -1.07$; 95% CI: -2.10-.04; $p = .04$).

Model 3 (outpatient surgery). $F(28, 4258.9) = 266.20$, $p <.001$; df min = 33.41, df max = 8612.88 df average = 1287.43. Hazardous drinking ($b = .04$; 95% CI: -.30-.38; $p = .81$); surgery ($b = -.37$; 95% CI: -.98-.23; $p = .22$); hazardous drinking *x* surgery ($b = -.18$; 95% CI: -1.38-1.01; $p = .76$).

Model 3 (either surgery). $F(28, 2318.6) = 247.87$, $p <.001$; df min = 25.27, df max = 824.28, df average = 215.96. Hazardous drinking ($b = .15$; 95% CI: -.20-.50; $p = .40$); surgery ($b = -.20$; 95% CI: -.61-.22; $p = .35$); hazardous drinking *x* surgery ($b = -.64$; 95% CI: -1.49-.20; $p = .13$).

Model 3 (inpatient surgery): Between marginal means effect sizes. If hazardous alcohol use: no, surgery: yes versus no = Hedges' $g = -0.07$; 95% CI: -0.12- -0.01. If hazardous alcohol use: yes, surgery: yes versus no = Hedges' $g = -0.23$; 95% CI: -0.37- -0.08. If surgery: yes, hazardous alcohol use: yes versus no = Hedges' $g = -0.11$; 95% CI: -0.26–0.03. If surgery: yes and hazardous alcohol use: yes, versus if surgery: no and hazardous alcohol use: no = Hedges' $g = -0.17$; 95% CI: -0.31- -0.03.

Depressive symptoms (EURO-D)

Model 1. $F(4, 5881.2) = 575.10$, p <.001; df min = 352.72, df max = 16949.40, df average = 4732.09. Hazardous drinking (b = -.21; 95% CI: -.32- -.09; p < .001); inpatient surgery (b = -.43; 95% CI: .25-.60; p < .001); hazardous drinking *x* inpatient surgery (b = .28; 95% CI: -.13-.69; p = .18).

Model 2. $F(22, 14400.2) = 140.27$, p <.001; df min = 561.88, df max = 16459.20, df average = 6794. Hazardous drinking (b = -.09; 95% CI: -.21-.02; p = .12); inpatient surgery (b = .41; 95% CI: .23-.58; p < .001); hazardous drinking *x* inpatient surgery (b = -.30; 95% CI: -.10-.71; p = .14).

Model 3 (inpatient surgery). $F(28, 15584) = 120.93$, p <.001; df min = 568.45, df max = 16511.67, df average = 7225.52. Hazardous drinking (b = -.06; 95% CI: -.18-.05; p = .28); surgery (b = .33; 95% CI: .16-.51; p < .001); hazardous drinking *x* surgery (b = .32; 95% CI: -.08-.72; p = .12).

Model 3 (outpatient surgery). $F(28, 2873.8) = 247.64$, p <.001; df min = 29.62, df max = 4343.31, df average = 596.72. Hazardous drinking (b = .13; 95% CI: -.23-.49; p = .47); surgery (b = -.35; 95% CI: -.96-.25; p = .24); hazardous drinking *x* surgery (b = -.26; 95% CI: -1.78-1.26; p = .73).

Model 3 (either surgery). $F(28, 15587.4) = 122.07$, p <.001; df min = 479.24, df max = 18197.57, df average = 7103.0-3. Hazardous drinking (b = -.08; 95% CI: -.20-.04; p = .20); surgery (b = .35; 95% CI: .21-.49; p < .001); hazardous drinking *x* surgery (b = .29; 95% CI: -.03-.62; p = .07).

Model 3 (inpatient surgery): Between marginal means effect sizes. If hazardous alcohol use: no, surgery: yes versus no = Hedges' g = 0.17; 95% CI: 0.12-0.23. If hazardous alcohol use: yes, surgery: yes versus no = Hedges' g = 0.33; 95% CI: 0.19-0.47. If surgery: yes, hazardous alcohol use: yes versus no = Hedges' g = 0.08; 95% CI: -0.06–0.23. If surgery: yes and hazardous alcohol use: yes, versus if surgery: no and hazardous alcohol use: no = Hedges' g = 0.25; 95% CI: 0.12-0.

APPENDIX F: PERIOPERATIVE AUDIT-C RISK CATEGORY RESULTS (STUDY 2 & 3)

Study 2

AUDIT-C: Perioperative Risk Cut-Offs

In univariate analyses, males versus females were more likely to be at risk (significant) and high-risk drinkers (non-significant), and less likely to be low risk (significant) and non-drinkers (non-significant) drinkers. Smoking status and illicit substance user status was also significantly associated with AUDIT-C cut-offs. Of those in the high-risk AUDIT-C category 100% (seven patients) were current smokers, and all illicit substance users were current smokers and in the high-risk AUDIT-C category. Low risk and non-drinkers appeared less likely to smokers versus non-smokers, but this did not meet statistical significance. Lastly, univariate analyses indicated no association between surgery type and AUDIT-C cut-offs and age, though age narrowly met the threshold for inclusion in the preceding multivariate model (p = 0.19).

In a multinomial logistic regression model (where non-drinker was the reference category) including all variables apart from surgery type ($\chi^2(12)$ = 60.88, p <.001, Nagelkerke's R^2 = 0.17), omnibus likelihood ratio tests indicated that all included predictors were significant apart from illicit substance use. There was some evidence that high and at-risk drinkers were more likely to be younger, male versus female and current versus non-smokers. Results were similar in a model including all predictors ($\chi^2(33)$ = 78.91, p <.001, Nagelkerke's R^2 = 0.23). In both models, non-significance across most variable levels indicated a possible lack of statistical power.

Study 3

AUDIT-C: Perioperative Risk Cut-Offs

In univariate analyses, the following variables showed significant differences: age, gender, illicit substance use, comorbidities and surgery type (and surgery complexity met the threshold for inclusion in multivariate models). Those in the high and at-risk AUDIT-C categories appeared to be younger than those in the no- and low-risk categories. Males versus females were also represented more in at-risk and high-risk categories, and less represented in the low-risk category. A larger proportion of illicit substance users versus non-users were in the at-risk and high-risk categories, with a lower proportion in the no- and low-risk categories. Overall, patients with more comorbidities were more represented in no- and low-risk categories (though the largest proportion of high-risk patients were seen in the highest comorbidity category, this was just two patients thus confidence intervals were very wide). It was difficult to identify trends between AUDIT-C scores and surgery types, though it was notable that despite being the most prominent form of surgery spinal surgeries had zero (0 out of 84 patients) AUDIT-C high risk patients. This is in contrast, for example, to ear nose and throat surgeries for which 31.2% of patients (7 out of 22) were high risk.

In a multinomial logistic regression model (where non-drinker was the reference category) including all predictors apart from smoking status, physical activity and BMI ($\chi^2(63) = 133.51$, $p < .001$, Nagelkerke's $R^2 = 0.26$), omnibus tests indicated that gender, age, comorbidities and illicit substance user status remained significant. Results indicated that increasingly high-risk patients were younger, male, and illicit substance users. Versus the lowest comorbidity category, all others appeared to have a lower number of at-risk patients. Results were almost identical in the fully adjusted model and in the BMI analyses (note that BMI was not significant in any multivariate analysis).

APPENDIX G: SYSTEMATIC SEARCH STRATEGY: EMBASE EXAMPLE

(STUDY 4)

1. EXP REVIEW/
2. (LITERATURE ADJ3 REVIEW$).TI,AB.
3. EXP META ANALYSIS/
4. EXP "SYSTEMATIC REVIEW"/
5. OR/1-4
6. (MEDLINE OR MEDLARS OR EMBASE OR PUBMED OR CINAHL OR AMEDs OR PSYCHLIT OR PSYCLIT OR PSYCHINFO OR PSYCINFO OR SCISEARCH OR COCHRANE).TI,AB.
7. RETRACTED ARTICLE/
8. 6 OR 7
9. 5 AND 8
10. (SYSTEMATIC$ ADJ2 (REVIEW$ OR OVERVIEW)).TI,AB.
11. (META?ANAL$ OR META ANAL$ OR META-ANAL$ OR METAANAL$ OR METANAL$).TI,AB.
12. 9 OR 10 OR 11
13. (RANDOM$ OR PLACEBO$ OR SINGLE BLIND$ OR DOUBLE BLIND$ OR TRIPLE BLIND$).TI,AB.
14. RETRACTED ARTICLE/
15. OR/13-14
16. (ANIMAL$ NOT HUMAN$).SH,HW.
17. (BOOK OR CONFERENCE PAPER OR EDITORIAL OR LETTER OR REVIEW).PT. NOT EXP RANDOMIZED CONTROLLED TRIAL/
18. (RANDOM SAMPL$ OR RANDOM DIGIT$ OR RANDOM EFFECT$ OR RANDOM SURVEY OR RANDOM REGRESSION).TI,AB. NOT EXP RANDOMIZED CONTROLLED TRIAL/
19. 15 NOT (16 OR 17 OR 18)
20. EXP COHORT ANALYSIS/
21. EXP LONGITUDINAL STUDY/
22. EXP PROSPECTIVE STUDY/
23. EXP FOLLOW UP/
24. COHORT$.TW.
25. EXP CASE CONTROL STUDY/
26. (CASE$ AND CONTROL$).TW.
27. EXP CASE STUDY/
28. (CASE$ AND SERIES).TW.
29. CASE REPORT/
30. (CASE$ ADJ2 REPORT$).TW.
31. (CASE$ ADJ2 STUD$).TW.
32. OR/20-31
33. EXP DRINKING BEHAVIOR/
34. EXP ALCOHOLISM/
35. ALCOHOL-RELATED DISORDER*.MP.
36. (DRINK* ADJ3 (BEHAVIOUR OR HAZARDOUS OR HARMFUL* OR DEPENDENCE)).MP.
37. (ALCOHOL* ADJ3 (DRINK* OR USE* OR INTAKE OR INTERVENTION* OR EDUCATION OR PROGRAM* OR ABUSE$ OR MISUSE$ OR PROBLEM$ OR DEPEND$ OR ADDICT$ OR DISORDER$)).MP.
38. DRUG DEPENDENCE/ OR EXP ADDICTION/ OR EXP BENZODIAZEPINE DEPENDENCE/ OR EXP CANNABIS ADDICTION/ OR EXP COCAINE DEPENDENCE/ OR EXP CONGENITAL DRUG DEPENDENCE/ OR EXP DRUG ABUSE PATTERN/ OR EXP DRUG MISUSE/ OR EXP DRUG SEEKING BEHAVIOR/ OR EXP GLUE SNIFFING/ OR EXP METHAMPHETAMINE DEPENDENCE/ OR EXP MULTIPLE DRUG ABUSE/ OR EXP NARCOTIC DEPENDENCE/
39. (DRUG ABUSE$ OR DRUG MISUSE$ OR DRUG PROBLEM$ OR DRUG DEPEND$ OR DRUG ADDICT$ OR DRUG DISORDER$ OR ILLICIT DRUG$).TI,AB.
40. ((NARCOTIC$ OR HEROIN OR OPIATE$ OR OPIOID$ OR OPIUM OR COCAINE$ OR CANNABIS$ OR MARIJUANA OR MARIHUANA OR HASHISH OR PHENCYCLIDINE OR BENZODIAZ$ OR BARBITURATE$ OR AMPHETAMINE$ OR MDMA OR HALLUCINOGEN$ OR KETAMINE OR LSD OR INHALANT$ OR SUBSTANCE$) ADJ3 (ABUSE$ OR MISUSE$ OR USE$ OR PROBLEM$ OR DEPEND$ OR ADDICT$ OR DISORDER$)).TI,AB.
41. 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40
42. EXP POSTOPERATIVE COMPLICATION/
43. EXP PREOPERATIVE CARE/ OR EXP PREOPERATIVE EDUCATION/ OR EXP PREOPERATIVE EVALUATION/
44. SURGERY/
45. (SURGICAL ADJ3 (SETTING* OR PATIENT* OR OUTCOME*)).MP.
46. (PREOP* ADJ3 (INTERVENTION* OR EDUCATION OR PROGRAM* OR STUD* OR TREATMENT* OR PREVENT* OR THER* OR SERV* OR COUNSEL* OR SUPP* OR INFO* OR CONSULT* OR CARE)).MP.
47. (PRE-OP*ADJ3 (INTERVENTION* OR EDUCATION OR PROGRAM* OR STUD* OR TREATMENT* OR PREVENT* OR THER* OR SERV* OR COUNSEL* OR SUPP* OR INFO* OR CONSULT* OR CARE)).MP.
48. (PERIOP* ADJ3 (INTERVENTION* OR EDUCATION OR PROGRAM* OR STUD* OR TREATMENT* OR PREVENT* OR THER* OR SERV* OR COUNSEL* OR SUPP* OR INFO* OR CONSULT* OR CARE)).MP.
49. (PERI-OP* ADJ3 (INTERVENTION* OR EDUCATION OR PROGRAM* OR STUD* OR TREATMENT* OR PREVENT* OR THER* OR SERV* OR COUNSEL* OR SUPP* OR INFO* OR CONSULT* OR CARE)).MP.
50. 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49
51. 12 OR 19 OR 32
52. 51 AND 50 AND 41

APPENDIX H: COM-B QUESTIONNAIRE (STUDY 5)

Please **rate** your agreement with each statement **from**

1 (strongly disagree)

2 (disagree)

3 (more or less disagree)

4 (neither agree/disagree)

5 (more or less agree)

6 (agree)

to

7 (strongly agree).

To rate, just circle your chosen number next to the statement e.g. ①. Please be honest in your responses and take the time to read the statements carefully.

Rate how the following statements may relate to you **drinking alcohol** ***between now and the day of your operation***.

I can cope with the negative physical effects of drinking less	1	2	3	4	5	6	7
I can stop myself from drinking impulsively	1	2	3	4	5	6	7
I know people who can help me drink less	1	2	3	4	5	6	7
I want to drink less	1	2	3	4	5	6	7
People I spend time with drink often	1	2	3	4	5	6	7
There are services I can get to that can help me drink less	1	2	3	4	5	6	7
I plan to drink less	1	2	3	4	5	6	7
My body would suffer if I drank less	1	2	3	4	5	6	7
I need to drink	1	2	3	4	5	6	7
I find it physically challenging to drink less	1	2	3	4	5	6	7
If I drank less I would do better after the operation	1	2	3	4	5	6	7
I know why it is important to drink less	1	2	3	4	5	6	7
Drinking less would be a good thing for me	1	2	3	4	5	6	7
There are lots of opportunities for me to drink	1	2	3	4	5	6	7
I often feel pressured to drink in social situations	1	2	3	4	5	6	7
I have lots of time to drink	1	2	3	4	5	6	7
I can drink less	1	2	3	4	5	6	7
I could resist drinking alcohol	1	2	3	4	5	6	7

Please provide any other comments relating to your thoughts and feelings regarding you drinking less between now and the day of your surgery:

Please rate: 1 = wouldn't be at all helpful, to 7 = would be very helpful

WHAT FORM MIGHT A PROGRAMME TO HELP YOU REDUCE DRINKING TAKE?

1. Group session(s)	1	2	3	4	5	6	7
2. A phone helpline	1	2	3	4	5	6	7
3. Computer based	1	2	3	4	5	6	7
4. A guided workbook	1	2	3	4	5	6	7
5. One-to-one session(s)	1	2	3	4	5	6	7

Any Others?

____

WHO MIGHT BE BEST TO DELIVER THE PROGRAMME?

1. General practitioners	1	2	3	4	5	6	7
2. A nurse	1	2	3	4	5	6	7
3. Surgery team member (e.g. anaesthetist or surgeon)	1	2	3	4	5	6	7
4. Anyone trained in alcohol use counselling	1	2	3	4	5	6	7
5. Self-guided with materials (e.g. online/a workbook)	1	2	3	4	5	6	7

Any Others?

____

APPENDIX I: SHORTENED INTERVIEW SCHEDULE (STUDY 6)

1. Opening (consent and demographic information)

Obtain consent

- Explain the nature and aims of the study, and what clients will have to do
- Explain that clients do not have to answer anything that they do not wish to
- Read out consent and have clients sign their names if they agree

Obtaining clients' demographic and substance use background

'How old are you?'

- Note the gender of the client

'Can you tell me a little about your experiences with substance use (e.g., what substances the client uses and how frequently?'

'Can you tell me a little bit about your health history?'

2. Main Interview

Discussing past experiences

'Have you had any past experience with elective surgery? (give examples, e.g., hip replacement)'

- 'Can you tell me about your experiences?
- 'Do you feel as though your substance use was a barrier to surgery?'
- 'Were you offered help to reduce your use of substances?
- 'Was it helpful?'

[improvise – follow up questions contingent on clients' responses]

Discussing future experiences

'Are you scheduled or due to be scheduled to have elective surgery in the future?'

- Probe client's fears and feelings toward the procedure/probe whether their substance use may be related to any fears

'If you were to have elective surgery, do you think you would be frightened or apprehensive about undergoing surgery?

- 'Do you think your substance use may be related to this fear?'

'Have any of your friends who use illicit substances undergone surgery?'

- 'If you can, can you tell me a little about their experiences?'

[improvise – follow up questions contingent on clients' responses]

Strategies/barriers

'What do you think would help you not to use drugs in the few days prior to surgery. How long could you abstain for?'

'What do you think would get in the way of you being abstinent or situations that would definitely make you use drugs during this time?'

'Do you have the capability to reduce or become abstinent prior to surgery?'

'Are there things you would need, or need access to reduce or become abstinent prior to surgery?'

'Would you be motivated to reduce or become abstinent prior to surgery?'

'Would knowledge of the risks be motivating to you?'

[Improvise – follow up questions contingent on clients' responses]

APPENDIX J: EXPANDED RESULTS (STUDY 6)

Barriers and Facilitators to Preoperative Substance Use Reduction

Theme A1: Motivation & willpower (169 codes, 205 references)

Whereas motivation may be considered broadly as an initial drive or desire to change behaviour, willpower (or *volition*) may be considered a commitment to behaviour change, over time (and thus an antecedent of high motivation). A near universal sentiment across participants – users of all substances and demographics - was the importance of these two interlinked behavioural determinants in regard to preoperative substance use reduction. Many participants framed low motivation and an absence of willpower as the most proximate and salient cause of past failures to reduce substance use (barrier), vice-versa for high motivation and strong willpower (facilitator). Many participants recognized the perioperative period as an important period of time to enhance motivation (a *teachable moment*) given that substance use reduction in this period may protect from additional and unnecessary perioperative complications. Given the high regard with which participants held motivation, efforts to boost motivation may be the most successful facilitators to capitalize on when developing a preoperative intervention for reducing substance use; increasing motivation may increase willpower, which in turn may decrease preoperative substance use. Some moderators of motivation and willpower were identified across interviews, that is, mind-sets, situations or other variables that may increase or decrease their salience in the preoperative period. These moderators are described in subthemes below, in addition to one subtheme highlighting the importance participants held motivation and willpower.

Prime importance of motivation & willpower. Most participants emphasized that individual motivation and willpower (e.g., drive, desire, commitment, self-control) to reduce prior to surgery would be the main moderators of success. It follows that low motivation, and weak willpower may be barriers to preoperative substance use reduction.

Many participants argued that, regardless of the resources available to them, of any strategies used by or with them, of any personal or environmental situation – low motivation, and thus low drive to reduce or quit substance use, was the sole reason for continued use, and would be so in the preoperative period. Especially among participants who stated that they were currently abstinent, a strong desire, and strong commitment to behaviour change were seen as primary reasons for successful reduction in their substance use, and again, would be so in the preoperative period.

Some participants argued that motivation and in turn willpower could be enhanced via intervention – and thus saw the potential benefit of external efforts to boost them. In addition, there were several variables which were seen as arbitrators of motivation. Understanding these may be a useful when devising strategies for preoperative interventions.

Moderators of motivation & willpower. Across interviews, several moderators of motivation and willpower were identified – and where particularly salient, grouped into lower level subthemes below.

Health conscientiousness. The most notable modifier of preoperative motivation and willpower was the degree to which participants regarded health as important, or the degree of risk participants were willing to accept to carry on using. It is important to note that the severity of the surgery was considered important; if surgery was minor, patients were more inclined to disregard health risks, if major, many stated they would be more motivated to reduce.

Fear for health (surgery a teachable moment). Many participants considered the thought of having surgery a daunting and potentially life-changing event. This was universal across users of all substances and demographics. For these individuals, the preoperative period was often regarded as a time where drive to reduce would be boosted inherently. Many participants provided examples of health scares they or their peers had experienced previously and the positive impact this had on motivation to reduce, suggesting that surgery may have a similar impact. Participants suggested that the preoperative period would be an opportune time to intervene to further boost motivation and to enhance willpower – in this way, the preoperative period was seen as a *teachable moment*. It is important to note that fear of health may also have counterproductive effects (see theme A3: *substance use as a coping* *strategy*)– so needs to be managed according.

Disregard for health (surgery irrelevant). A large number of participants suggested that, even if they explicitly knew that preoperative substance use would be risky (above and beyond use generally), they and their peers would carry on using regardless. Those considered most as likely disregard health risks in the preoperative period (by themselves and others) were typically alcohol and/or heroin dependent individuals. One participant suggested that many users are on "*self-destruct mode*" (**Alex**), another suggested that "[people] *use knowing it could kill them at any minute so they're not just going to stop just because they're having an operation*" (**Matt**). Many participants expressed an attitude articulated by the following: "*f*ck it, I'll take me chances*" (**Logan**). It was the opinion of many participants therefore that surgery is completely irrelevant to their substance use. For such individuals, perhaps any intervention should focus on harm reduction (e.g., using less risky routes of administration; reducing slowly etc) over aims to reduce acutely or achieve abstinence (see theme B7*: harm reduction strategies more realistic than complete abstinence*). A high disregard for health may reflect poor mental health, and substance use in full knowledge of abundant risks, a form of self-harm. Additional mental health related support may be necessary for these individuals; only when one strives for self-preservation over self-destruction would one alter their behaviour to achieve it.

Social influence. As outlined in more detail in theme A6 (social influences), many participants suggested that family/friends can increase motivation – directly (e.g., actively engaging in treatment) or indirectly (e.g., simply being on the users mind). An example of indirect influence includes motivation to reduce preoperative substance use to lower the risk of upsetting or emotionally harming family (through death or any other serious perioperative complication). An example of direct influence on motivation includes family helping convince users enter treatment.

Withdrawal symptoms. Naturally, substance use withdrawal, almost universally for users of alcohol or opioids, was considered a huge detriment to motivation and willpower. As in theme A3 (*substance use as a coping strategy*) substance use was often regarded as a way of simply dealing with the negative physical and psychological sequelae of abstinence. As such, any efforts to ease these symptoms were seen as a vital component to any potential intervention, preoperative or otherwise.

Theme A2: Interaction with healthcare (152 codes, 49 references)

A large area of discussion, across all interviews, revolved around barriers that may be integrated into, or specifically relevant to, the perioperative patient pathway. These issues include a perception of discrimination and inferior treatment experienced by substance users when accessing healthcare; and a lack of emphasis on substance use by healthcare services. These barriers may be considered systemic, in that they may require a change of routine practice, or additional training or guidance for NHS staff, to alter. Another issue was that of substance use disclosure to healthcare services; this may be considered a systemic (lack of disclosure due to perceived stigma) but also an individual barrier (lack of disclosure due to a desire to use substances without being denied surgery). The following three subthemes reflect the most commonly discussed barriers participants had either faced previously (or expected in the event of surgery) when interacting with the NHS.

Stigma. A large proportion of participants believed that they would encounter some degree of stigma or discrimination when interacting with healthcare services. Not only may this be a huge barrier in engaging with, and likely to reduce the efficacy of, potential perioperative interventions, but may be a significant barrier to accessing healthcare services in the first instance.

Participants often suggested that they felt as though they may be regarded as a burden, and a *“drain on the system”* **(Rosie)** by NHS staff. Participants suggested that because staff saw their health issues as *“self-inflicted”* **(Chris)** they resented having to treat them. One participant suggested that *“outdated ideas*” by staff could have a negative emotional impact on users **(Ryan)**. One example of outdated mannerisms was the use of *“non-PC* [politically correct]*”* language, such as the term *“drug abuser”* which has the potential to offend, even in the absence of any intent to do so (**Ryan**).

Linked with the perception that staff resent substance users, is the perception that staff actively may treat them differently – or more specifically, worse – than non-users. One participant suggested that this may manifest as having to wait a *"little bit longer"*, or simply not being *"looked after as well"* **(Charles)**. Two participants who were in hospital previously suggested that as soon as they disclosed their substance use, they felt as though staff wanted to "*chuck* [them] *out*" (**Mason)**.

Disclosing substance use to healthcare. Identifying patients who may benefit from a preoperative intervention for substance use relies on patients being open about their use. When discussing disclosure, there was significant variation in participant attitudes. A minority of participants stated they would be open about their dependency (e.g., to protect their health; because they see no reason not to; and because these individuals may be highly motivated to reduce substance use) and others would not be open under any circumstances (e.g., to avoid judgment; to continue using without being hassled; and because these individuals may have low motivation to reduce substance use). Most however suggested that they would under certain circumstances.

Moderators of disclosure. Circumstances that impact disclosure may be considered moderators: variables that increase or decrease the likelihood of disclosure. One example is a suggestion by two participants that routine substance testing prior to surgery would lead users to disclose. This may make some individuals uncomfortable however, and may be impractical for a number of reasons (e.g., individuals may simply refuse). Two lower level subthemes below highlight potential moderators of disclosure most often discussed by participants.

Stigma. As above, many participants stated they felt as though NHS staff resent users, and that users receive worse treatment. It follows naturally therefore that users would be wary about disclosing if they felt poorer treatment would follow, which was articulated by several participants. One participant suggested that a positive experience can have the opposite effect:

> **Ryan:** *"*[The paramedics] *were absolutely so like... didn't bat an eyelid, they were like you're just a person that's got a problem, there's no judgement or anything. And that, that has led me like be open and so I was*

very open, I just said 'yeah, I'm on Methadone' [to a nurse at the hospital]*."*

Fear of surgery delay or cancellation. Three participants suggested that the fear of surgery being cancelled or delayed would make users wary of disclosing substance use. One participant suggested that users may even risk serious complications in order to have surgery. Another highlights that the fear of missing surgery may outweigh the fear of potential complications:

> **Rachel:** *"I don't know, I think she thought she wouldn't have been able to have the operation.. that's what she had in her head.. so she panicked and didn't tell them, and then she's come home and told me and shes panicked more thinking something's gonna happen to her then because she's not told them."*

Healthcare ignore substance use. Of a number of participants who had previous experience undergoing a hospital procedure requiring preassessment, a common theme that emerged when discussing their experiences was how little emphasis was placed on their substance use dependency. Participants often stated that healthcare staff did not ask about substance use, or ignored the topic. Others highlighted that, even when their substance use was raised, it was often not discussed in any meaningful way; this included no advice or information on the perioperative risks of substance use and no attempts to intervene, or signpost to drug and alcohol services. This could lead to a perception that substance use in the preoperative period is not risky, does not matter, and may lead to users continuing to use as they would generally.

In contrast, one participant was denied gastric surgery and referred to a psychiatrist for intervention, after disclosing their substance use issues. However, this was with a private healthcare provider, and the participant just went elsewhere to have their procedure – a place where healthcare staff did not ask about substance use.

Theme A3: Substance use a coping strategy (82 codes, 94 references)

For many participants, and across users of all substances, using substances appeared to be a maladaptive coping strategy; a way to numb oneself to trauma, boredom, loneliness, low mood, anxiety and other ill mental health. Many of the issues discussed within this theme could be seen – at least partially, a result of substance use, such that a vicious cycle occurs; users may be using substances to cope with issues generated by using the substance. Each of the below subthemes reflect a common physical or mental state for which substances were used to alter, understanding and addressing each may present a facilitator to preoperative substance use reduction.

Loneliness (boredom plus distress). This subtheme, as outlined in theme A6 (*social influences*) below, highlights how important a feeling of loneliness – experienced by a large number of participants, was regarded as a trigger for substance use. Aside from the negative effects absence of any emotional or practical (e.g., money management) support that close relationships may bring, participants inferred or explicitly stated that loneliness may trigger substance use through boredom and low mood – and that the former may worsen the latter (see theme A5: *triggers*):

> **Rachel:** *"But when I keep myself at home bored not doing nothing it's just a different story, it's hard, you start thinking about sh*t."*

Staves off withdrawal. As in theme A1 (*motivation & willpower*), it goes without saying that symptoms of substance withdrawal are a significant barrier to abstinence or reduction for substance users generally. This was the case here, where many – particularly current or former heroin and alcohol dependent – participants suggested that this would be one of the primary reasons preoperative substance use reduction/abstinence may be hard to achieve. In relation to the current theme, substance use was considered an easy way of coping with the physical and mental suffering of withdrawal. Again, using substances to counter withdrawal may be considered a vicious cycle; the longer a substance is used, the higher the user's tolerance increases, leading to higher doses, which ultimately leads to worse withdrawal symptoms and a higher sensitivity to their onset.

Boredom reliever. As in theme A5 (*triggers*) below, boredom may act as a trigger for substance use. Many participants were not in employment or had no daytime commitments, so substance use was seen as a way to relieve themselves of boredom and pass the time**,** e.g., *"…and I've had the problem for the last ten years, since I retired."* **(Leo)**.

Substance use only interest. When discussing the issue of boredom, and substance use as method to cope with boredom, some participants highlighted that – even if they were in employment, or had the means to engage in other activities, substance use was their only interest, and that substance dependency may strip users' of their previous interests. In support, one participant highlighted how gaining new interests was vital in their recovery.

> **Jenny:** *"So like now I've got more interests like gym, you know like actually going out and stuff that's helped me psychologically."*

Distress and stress reliever. The majority of participants expressed that they often experience some form of psychological distress or stress. Again, as in theme A5 (*triggers*), participants suggested that this may be a trigger for substance use. Many participants explained that substance use is a method to cope with such emotions, serving as a quick fix and distractor. For some participants these emotions stemmed from past trauma, such as sexual abuse. For others, substance use was regarded as self-medication for current mental health problems, or a method of dealing with stressful life events. As mentioned previously, this issue may be compounded by the presence of withdrawal symptoms – which can cause a significant amount of mental distress. Substance use can also worsen mental distress, as in the following quotation:

> **Ryan:** "[it's a] *vicious cycle where, you know, someone's got mental health problems and they feel a lot of anxiety from that so they take drugs to reduce the anxiety and the drugs they become tolerant so they use more drugs, they use more drugs, they use more money, so they've got more money problems and they've got more anxiety coming off the money problems…"*

As in theme A1 (motivation & willpower), anxiety over, and fear of, undergoing surgery was seen as a major barrier to substance use reduction. Instead of decreasing substance use to reduce any potential additional perioperative risks, many participants suggested that this anxiety would actually increase preoperative substance use, as substance use would be considered a method of counteracting this fear. This again may lead to a vicious cycle:

> **File 31:** *"…it's sort of like 'oh yeah, shit, I'm having a big operation and I'm*

worried about it, what do I do when I'm stressed, I use', and then I'll use and then I'll think 'oh shit, I've used again, I've got that surgery coming up' and it's a vicious cycle, you know."

Theme A4: Hopelessness & cynicism (81 codes, 129 references)

A consistent theme across all interviews was the perception that reducing substance use in the preoperative period would be hindered by pessimistic attitudes and mind-sets; participants generally regarded their, or others users', situation as hopeless, in that they felt incapable of changing their behaviour, even in the event of an upcoming surgery. As a result, participants were highly cynical of efforts to reduce or abstain in this period of time. This theme is typified by the following quotation:

> **Jenny:** *"Some people that I know probably wouldn't like doing anything. Even if you locked them up they would still try and get it in there or whatever, you know, to try and do it, and they wouldn't be bothered* [about their health]*."*

This theme was further divided into two subthemes.

Disregard of health. Hopelessness manifested as a general disregard for health for a number of participants. As outlined previously in theme A1 (*motivation and willpower)* many participants were cynical about others' health conscientiousness, such that they believed that they would carry on using substances despite potential health risks – but optimistic about their own (the extent to which this may have been a product of social desirability is unknown). However, many participants were open in suggesting that the risk of perioperative complications would not be enough of a motivator to reduce. Most participants who expressed hopelessness, or perceived hopelessness in their peers, were previous or current alcohol and/or heroin users – substances particularly conducive to health issues.

Low self/other belief. Low self-belief may incur apathy and low engagement with potential interventions, and is an important barrier to overcome. Indeed, persistent amongst a large proportion of participants, across all ages and users of all substances, was a general expression of futility in regard to their own chance of success at reducing or abstaining from substances in the preoperative period. Participants also felt equally, if not more so, cynical about others' success. Illustrative quotes include: *"they could try* [to reduce] *but it wouldn't happen"* (**Jack**), *"me personally, I don't think I'd do it* [abstain] *for a couple of weeks"* (**Rachel**) and "*someone who's been doing it for 20 years isn't going to sort it out in weeks, you know*" (**Joe**).

Theme A5: Triggers (79 codes, 89 references)

This theme and issues within it were amongst the representative in relation to substance users universally – as opposed to participants in treatment for one particular substance.

This theme demonstrates the power of substance related stimuli and their effect on substance seeking. Participants readily argued that exposure to substance related cues or triggers in the preoperative period would hinder any efforts to reduce or abstain from substance use. Just one participant stated that cues do not affect their substance craving:

> **Lucas:** ***"****I'll tell you, in the time I stopped that heroin and I haven't touched heroin for 14 years, maybe a bit more, if somebody come in there and started smoking heroin there or loading it up and having a go it wouldn't bother me, it don't bother me at all, it really don't bother me, even the smell of it and all that, it just don't bother me."*

But later suggested that this may be due to the fact that they had achieved abstinence for a while, and thus suggesting that the effect of cues diminish over time:

> **Lucas:** ***"****I'd say after about 12 months, maybe a bit less than that, 10 or 12 months, it didn't bother me then, it didn't bother me."*

Participants provided many examples of their personal cues and triggers, as well as suggesting others that they perceived to be relevant to other users. These are grouped in two subthemes below.

Internal triggers*.* Participants often suggested that internal emotional states were responsible for cravings, acting as triggers. As in theme A3 (*substance use as a coping strategy*), this may be a result of a maladaptive coping strategy where substance use is used to distract or numb from negative emotional states. These internal states tended to be of two types.

Mental ill health, trauma & mood. Mental ill health and related low mood, often stemming from negative past experiences could be seen as the primary internal trigger for substance seeking, and a highly important barrier to substance use reduction:

> **Hazel:** ***"****I've been using drugs since I were 11, at the moment it's a bit of erratic, it comes with me depression, and goes"*

Life events that lead to low mood could be key triggers for substance use seeking, regardless of mental health issues:

> **Elen:** ***"****Before the surgery or completely? I don't know, I suppose if you had something traumatic happening in your life, in that period of time, you know, a death or something like that, something that might trigger the drinking off."*

Boredom. Four participants suggested that having nothing to do, and the resulting feeling of boredom was a trigger for substance seeking. One participant suggested that fear of experiencing boredom was important:

> **Elijah:** ***"****I think it's a lot to do, a lot to do with, it's a lot to do with boredom* […] *That is the big factor really, is that boredom fear."*

Another participant suggested that boredom may be a key determinant of negative mood, which as above, may lead to substance use:

> **Rachel:** ***"****But when I keep myself at home bored not doing nothing it's just a different story, it's hard, you start thinking about sh*t"*

External triggers*.* The most important triggers for substance use, based on the fact that most participants raised them and often discussed them in detail, were triggers external to the self. These triggers included interacting with certain people, being in certain places and seeing certain objects that were associated with substance use. Triggers could be grouped into two subthemes.

People & places. Perhaps the trigger regarded most pertinent amongst all participants was simply being around people who use substances. Similarly, and related, were places associated with substance use. One participant offered an example where they moved away from Leeds abstinent to attend a college course, but as soon as they returned they '*took the easy option*' to use heroin instead of "*putting the effort in*" to find a job (**Logan).**

A participant who stated that they were a current abstainer noted that "*I've had to cut out a huge section of my social circle sort of thing*" (**Mike).** Another highlighted that while users would have to cut certain people from their life to achieve abstinence – they may be vulnerable to loneliness, and would need to address this with things such as mutual aid groups. This is complicated by the fact that mutual aid groups i. increase exposure to other users, and ii. engender thoughts about using substances, which may trigger craving.

Idiosyncratic triggers. There were a number of external triggers that may have been suggested by just one or two participants that may not have fit with the *people & places* subtheme. While this may indicate that they may not be generalizable across participants in this sample, these represent how cues and triggers can be highly idiosyncratic.

Two participants suggested that money was a notable substance-related cue. Paydays may therefore be triggers for substance seeking. One participant suggested that something as simple as seeing a tin foil chocolate bar wrapper could trigger craving, due to its association with heroin injection. Another, a codeine user, stated that simply seeing any chemist (where the participant would typically procure their codeine) was their primary trigger. Exposure to social media, and images of others drinking was cited as a trigger for one alcohol dependent participant. Lastly, simply the time of day, because of previous or current habit, can be a cue to drink alcohol:

Theme A6: Social influences (70 codes, 120 references)

Many participants stressed the importance of social influences on their substance use generally, and the potential impact they would have on preoperative substance use. Social influences were mentioned as both barriers and facilitators to preoperative substance use reduction. This theme was relevant to users of all substances, and was divided into the following subthemes.

Family and/or friends as a facilitator*.* Many participants saw their family and/or friends as vital to any attempts to reduce substance use. This was often framed in a direct sense; family and friends can offer support in organizing appointments, helping open users' eyes to their situation, helping with money management and offering emotional support. Family and/or friends as facilitator was also framed in an indirect sense; participants suggested that they may think twice about resuming substance use in the preoperative period if there was an increased risk to themselves, and by a proxy, a higher risk of impacting their family:

> **Pp 28:** *"I need to stop doing what I'm doing to get this surgery […] I've got two children to think about..."*

Indeed, some participants suggested that admitting their current substance use situation to their family was often a trigger to seeking further help, or engaging more with current treatment - suggesting that fear of upsetting their family was a real driver to reduce. This is closely related to a fear of harming their relationship with loved ones through their substance use. For example, one participant suggested that the threat of losing his partner because of his substance use was a pivotal moment in his recovery. Similarly, a desire to repair broken relationships was often highlighted as a reason for participants' attendance at the drug and alcohol service from which they were recruited. Lastly, family were seen as a useful facilitator through a process of social comparison. For example, one participant suggested that seeing the benefits for others of not using substances, creates a desire to emulate them:

> **Charles: "***I think, a lot of the time, for meself, it's just seeing other people's, like I've got a brother who's in a relationship, he's got money, he's got his own house, do you know what I mean, he's happy, and obviously I tend to think that I'm missing out on a lot of things, so..."*

Loneliness, lack of support barriers. As above, family and/or friends were often regarded as a positive influence on preoperative substance use. It follows that the absence of this support network (and the lack of direct and indirect benefits) was seen as a negative influence for some participants. Some participants framed this as a vicious cycle; long-term dependence leads to broken relationships and thus solitude, solitude leads to loneliness, and loneliness leads to substance use. Further, substance use may be used a coping strategy (see theme A3: *substance use a coping strategy*) to combat the boredom and low mood associated with loneliness, and thus loneliness may become a trigger (see theme A5: *triggers*) for substance use. Narcotics Anonymous, and other mutual aid support groups were often suggested as a solution to the issue of loneliness – as were contact with drug and alcohol services.

Family and/or friends as a barrier. Social influences were by no means considered solely positive. As outlined in theme A5 (*triggers*) above, exposure to certain social circles and associating with individuals in active dependency introduces triggers and situations deleterious to substance use reduction or abstinence. Similarly, a poor homelife situation can lead to stress, which may also trigger substance use. One participant mentioned a situation where contact with his child was taken by child protective services (due to his girlfriend's arrest), and subsequent relapse because of it. It was also suggested by one participant that family members may act as enablers and actually hinder efforts to intervene – for example by buying and supplying illicit substances to the user.

Theme A7: Habit & automaticity (10 codes, 21 references)

Habit was often raised as a barrier to preoperative substance use reduction. This theme appeared to be equally relevant to users of all substances. Some participants framed their experience of habit as a loss of control, such that attaining and using substances was an automatic process, constraining free will. Indeed, refraining from substance use in the preoperative period was not considered an option available to them. For some participants, while they admitted they had an active desire to use substances, this was often suggested to be unrelated to how much they derived pleasure from taking the substance; active desire manifested as an automatic uncontrollable wanting or craving, in the absence of positive expectations.

> **Lucas:***"…I think that nearly every time I have one* […] *I think to meself, when I've had it, I think what a waste of time that was…"*

Theme A8: Preoperative reduction easier than postoperative maintenance (3 codes, 4 references)

This small theme reflects a consensus among a few current or previous users of crack cocaine, heroin and alcohol that preoperative reduction would be easier to achieve than maintaining abstinence or reduction postoperatively.

When probed why there was a difference between these time periods, one participant was unsure: *"So it's mad how you, and you think, 'Well, if you can do it for that, why can't you turn it round on a f*ckin' day-to-day basis?'"* (**Susan**). One participant suggested that their fear of surgery going wrong was a motivator to refrain from using methadone prior to surgery, and inferred that once this perceived risk was over, they would resume using substances. It may be therefore that fear of health could be a variable determining preoperative versus postoperative substance use; using substances in preoperative period may be perceived as a higher risk to health than in the postoperative period.

Preoperative Intervention Strategies

Theme B1: Setting goals (58 codes, 57 references)

Among the most discussed intervention strategies were those related to strategic setting and monitoring adherence to substance use related goals and specifying and following tapering regimens. As elaborated upon in the following two subthemes, participants were generally positive about setting manageable goals to reduce substance use, but expressed concerns about efforts to self-monitor intake.

Goal setting, planning and tapering. The vast majority of participants supported the use of gradual substance use reduction over abrupt cessation – which may be dangerous, unsustainable and very difficult to achieve. In this vein, participants generally preferred harm reduction strategies (stressing preoperative substance use reduction over complete abstinence; as in theme B7 [*harm reduction strategies more realistic than complete abstinence*]) such as the use of opioid substitution to counter withdrawal and taper (though participants did raise issues with this particular approach; as in theme C5 [*other modes of delivery*]). Participants much preferred small and manageable goals; small reductions in substance use over a longer period of time. One participant suggested that big unmanageable goals (e.g., abrupt cessation) are destined to fail, and thus engender disenfranchisement and low motivation. Participants also endorsed strategies based around avoiding exposure to cues and triggers to substance use, and strategies to resist the impact of such cues (e.g., practicing refusing drinks; replacing alcoholic drinks with others) (see theme B5: *avoiding & removing triggers*). Such strategies rely on a significant degree of forethought and planning, which participants held to be highly useful in general. Participants favoured personalized plans tailored to their particular circumstances (e.g., level of dependency, environment, mind-set; as in theme B6: *flexibility & individualization*) and felt that having a set surgery date would aid planning by giving a concrete target to reduce by.

Self-monitoring. Self-monitoring substance use intake is necessary to monitor adherence to set substance intake goals. While participants were optimistic about setting and meeting reduction goals, they were less optimistic about self-monitoring. Participants suggested monitoring may boring, time consuming, unrealistic and pointless; particularly for those with impaired memory due to large substance intake. Nevertheless, one participant suggested that self-monitoring provides a motivational boost when one can see how well they have achieved their goal.

Theme B2: Providing risk information (53 codes, 111 references)

The vast majority of participants understood there were risks of using substances prior to a surgical procedure. These participants typically held this to be common sense, though were less sure about the specific risks. Perhaps the strategy most commonly suggested by participants was receiving more in depth information about the risks of preoperative substance use; indeed, when asked what their ideal intervention would look like most suggested one-to-one weekly sessions with a trained substance use specialist, mainly comprised of risk information and general support.

Motivation and information. While risk information was highly regarded, the consensus among participants was that simply providing information was not enough – especially for long term users, and especially for users of heroin and/or alcohol. Participants stressed that knowledge of risks may not translate into motivation to reduce. As mentioned previously, many participants felt that only individual motivation would lead to preoperative substance use reduction – with many suggesting that information alone would not be able to engender this motivation. This is unsurprising, given that many participants told stories of continued use in the face of serious health scares.

Irrespective of whether information was considered able to bolster motivation, many participants suggested that information was useful regardless. Indeed, many participants desired to be informed on the specific consequences of their substance use; and some participants who had had surgery previously regretted not being informed of the risks (*"No, there were no, there were no help, not even any advice really."* **[Chris]**). Some participants also suggested that they had not considered that substance use prior to surgery would be an issue, so would appreciate forewarning.

Methods to increase impact of risk information. Participants suggested numerous ways risk information could be more effectively used as a strategy. Participants generally supported weekly intervention sessions, in which risk information could be repeated – in this way, one participant suggested information has "*got to be hammered home*" (**Leo**). As in theme C1 (*interventionists*) below, participants felt that risk information from interventionists with a high degree of specialist substance use knowledge would have more of an impact, as participants would trust their expertise. This extended to NHS staff such as doctors and nurses, though some participants felt that NHS clinical staff were not well trained in substance use, so were wary of their advice.

As mentioned previously, fear of surgery, and fear of complications, were often mentioned as risk factors for increasing substance use. It is important therefore that risk information is not used to scare users, but to inform them. It is unclear how this may be achieved, but monitoring users' level of fear, providing stress and anxiety support, increasing users' perceived control over their substance use and stating the risk in clear and digestible statistical terms may be useful.

> **Ryan:** *"…you don't want to scare people because if you scare people you make them stressed and that might make them start using more, you see."*

Participants also endorsed different delivery methods for risk information. Participants stated that visual representations of the likelihood of perioperative complications through graphs may increase the impact of the information. Using risk information as a method to support decisional balance (asking users to list the pros and cons of using) was also highly regarded, and a strategy familiar to participants.

Ryan: *"…whoever does the intervention has to be very well-informed about the subject…"*

Sam: *"I think actually demonstrate the risks, show, maybe show pictures…"*

Theme B3: Heavy-handed approaches (31 codes, 20 references)

There was a sharp divide between a minority of participants who believed services should take an authoritarian approach to substance use reduction, and a larger contingent favouring a more liberal approach.

Of the former, several participants suggested that surgery should be withheld from those not willing to reduce their substance use before surgery, regardless of the consequences. One participant suggested a system whereby patients are denied surgery if they are tested positive for substances prior to surgery. Another participant who *was* denied surgery due to their substance use suggested that this tactic worked – though they quickly resumed. In this camp were those that believed that interventions should be heavily reliant on scare tactics. One participant went as far to say that substance users should be restrained against their will. These participants tended to be older, and previously or currently dependent on opioids or alcohol.

In direct contrast to the above, many participants suggested that forced treatment is useless; favouring compassion over compulsion. Many participants felt that a welcoming, inclusive and warm relationship with an interventionist was to the interventions benefit. They also argued that only coming to their own decision to reduce would motivate them to do so, and that withholding surgery may actually lead to increased substance use due to stress. In fact, one participant suggested that withholding surgery from individuals with substance dependency issues would be discriminatory, and that they would feel stigmatised if they were denied surgery. A couple of participants compared the authoritarian approach to negative previous experiences with court-mandated treatment, which they suggested was generally ineffective and too focused on 'tick box' clean substance tests over treatment itself. The authoritarian approach also discounts participants' general preference for an emphasis of harm reduction over complete abstinence (as outlined in theme B7*: harm reduction strategies more realistic than complete abstinence*), which they felt was more realistic. In this way, forcing complete abstinence was considered *throwing the baby out with the bathwater*.

> **Ryan:** *"…You've got to* sort of create a sort of welcoming and inviting sort of atmosphere really"

Theme B4: Addressing stress, distress & mental health (30 codes, 26 references)

Often, participants suggested that substance use was used as a coping strategy to reduce negative emotional states associated with low mood, mental ill health and stress. As such, many participants frequently suggested that mental health intervention was vital as the primary, or as an adjunct, component for any intervention targeting substance use dependency. Accordingly, the ability of a preoperative intervention to identify, if not actively address, mental ill health and refer (and if necessary fast track) to services was considered highly desirable.

Participants also saw a lot of value in help with addressing stressful and triggering practical life issues such as access to government benefits, support with finding housing and legal issues. Any attempt to ease the users' life in general was considered a stress reliever, and thus a facilitator to substance use reduction.

In lieu of any ability of an intervention to substantially alter an individual's life circumstances, participants recommended several stress focused interventions they had received through their own treatment previously. Apart from one participant who highly recommended mindfulness practice, participants were vague in regard to the particular stress reduction techniques they favoured. The aforementioned mindfulness advocate also suggested that users may be reluctant to engage in the practice, but would benefit if they engaged with it: *"if they were like I were at first, 'it's a load of rubbish', then I don't think it would help them. If they opened themselves up to it then yeah, I think... it did me anyway"* **(Mike)***.*

Theme B5: Avoiding & removing triggers (30 codes, 50 references)

Given that exposure to particular internal states (e.g., boredom, low mood) and external situations (e.g., exposure to people or places associated with substance use) were seen as triggers for craving and substance use seeking, a large majority of participants endorsed cue avoidance or strategies to counter the triggering effects of cue exposure.

The most prominent trigger for substance use craving, seeking and use was being in a substance-related environment or in the presence of other substance users. Therefore, as in theme B1 *(setting goals)* above, the most endorsed cue-related intervention strategy across participants was simply being aware of cues that may trigger substance use craving, seeking and use, and avoiding them (planning). Participants suggested that this process could be aided and enhanced via structured guidance with an interventionist. Relatedly, several participants endorsed learned coping strategies aimed at tempering craving in the presence of triggering situations.

Boredom, or lack of things to do was also a major trigger for substance use. Participants suggested that a valuable intervention component would be to signpost users to events, distractions, clubs, and aid with job searching and finding volunteering roles. Being involved in activities other than substance was considered a facilitator to substance use reduction – any strategies aimed at getting users involved in such activities were therefore heavily endorsed.

Participants also frequently suggested that poor mental health, low mood and stress were triggers for substance use. As in theme B4 *(addressing stress, distress & mental health)* above, addressing the root cause through access to mental health services or intervention was considered vital.

Theme B6: Flexibility & individualization (20 codes, 32 references)

The majority of participants suggested that some degree of individualization of intervention strategies was necessary for any preoperative intervention. Participants highlighted that different individuals have different needs; with different life situations, different substance use histories and durations, and different levels of motivation. In this vein, analysis led to the two subthemes below.

Efficacy of certain strategies highly depend on individuals. Participants heavily stressed the highly heterogeneous nature of intervention efficacy. Over and over again, participants stated some variation of the following quotation: *"…everybody's different, what will work for one person won't work for everybody will it"* **(Matt)**; *"everybody's different and respond different to different techniques"* **(Elen)**; *"…it all depends on the person. Everyone's different"* **(Will)** and *"I think* [all strategies are] *worth* […] *a go and things are going to be different for different people, you know, everybody's going to react in different ways to different things."* **(James)**. Three participants further suggested that this was dependent on how *deep* their addiction was. This may be related to theme A1 (*motivation & willpower*) above, in that many participants suggested individual strategies do not matter at all – rather, individual motivation and willpower are the key determinants of reduction – which *deep*, or lengthy and health disregarding dependency, may diminish. Similarly, all strategies at times of high individual motivation may be somewhat effective – suggesting that intervention timing may be more important than the strategies themselves. Though, as above, it should not be discounted that several participants suggested that intervention can actually increase motivation. Further, the degree to which certain strategies work *even in times of high motivation* may still be highly variable – and therefore it would be useful to identify those most efficacious for each individual.

Preferred one-to-one, personal interventionist and plan. Because participants generally suggested that each individual responds to different strategies, it follows that they repeatedly showed preference for intervention strategies and formats that were personalized to some degree. This was mostly verbalized when discussing preference for one-to-one intervention sessions over groups, and a high degree of support for individualized planning strategies (as in theme C4: *one-to-one sessions*; and theme B1: *setting goals*).

Theme B7: Harm reduction strategies more realistic than complete abstinence (14 codes, 25 references)

A common sentiment amongst participants was that both intervention deliverers and receivers should manage their expectations; aiming for complete preoperative abstinence may be unrealistic, and that any steps - however small - to a reduction in use and/or a reduction of harm (e.g., through less risky routes of administration) should be strived for and praised. As in theme A1 (*motivation & willpower*) above, this may be especially the case for individuals with low or no motivation to reduce, of whom potential surgery may be inconsequential to their substance use habit.

Harm reduction strategies that were considered to be more readily achievable included a reduction in polysubstance use – that is, promoting abstinence for perhaps one of many substances the participant may use: *“myself, it's kind of Heroin and Valium, but crack and stuff like that* [are avoidable]*”* (**Logan**). This was closely related to heroin users’ highlighting how vital opioid substitution is for any intervention package. These users suggested that providing an easy route for heroin users onto medically managed non-contaminated and pre-dosed Subotex (buprenorphine) or methadone prescriptions would be beneficial for surgery – and would allow hospital staff to better determine any potential interaction effects with anaesthetics. One participant suggested that users should be made aware of which opioids may have the lowest risk profiles in relation to surgery, so they may be more inclined to use them instead of those more harmful.

Theme B8: Pre-surgery an opportune time to motivate detox and/or rehab attendance (9 codes, 24 references)

Many participants suggested that the preoperative period would be an ideal time to enter into inpatient detox and/or a rehab community. These participants were exclusively current or previous dependent alcohol and/or heroin users. Participants suggested that given the additional risks of using substances in the preoperative period, it would be useful to have a system whereby they could be fast tracked into these services (which typically have a waiting list). Participants typically held detox and rehab as the gold standard intervention strategy but warned that relapse was common without a strong commitment to abstain (thus additional support may be required). One participant suggested even a short detox – being admitted to hospital perhaps a week prior to surgery would be useful. Another suggested that a detox, combined with a successful surgery, could kick start a clean life thereafter.

> **Chris:** "*If it were up to me there'd be people who are going in for elective surgery would be detoxed* […] *and go into that procedure clean and with a fresh bite of the cherry, you know a fresh new life.*"

Theme B9: Aiding memory (6 codes, 8 references)

The topic of aiding memory was discussed fairly frequently across interviews. Some, but not all, participants suggested that having reminders of a surgery date, or certain appointments, would help keep substance use reduction at the forefront of their mind, and remind them of their goal of reducing prior to surgery**.** Suggested memory aids included text messages, weekly calls with a substance use counsellor or calendar entries. Two participants also suggested that having family or friends remind them of their goals, and/or organize appointments (and thus free up cognitive resources) may be beneficial also.

Theme B10: Just talking to someone (4 codes, 8 references)

Five participants suggested that just having a non-judgmental confidant to talk to about substance use would be beneficial. Four of these suggested that such an individual would not be a friend or family member, such that they may be unemotionally invested, or provide more objective guidance. The main benefit participants felt such individuals would offer is helping take *"weight off your shoulders"* (**Mason)** and to just be listened to: *"that's all a lot of people need, just people to listen and follow up on stuff I think…"* (**Rachel**). As in theme C1 (*interventionists*) it was suggested that this individual would best be a trained substance use counsellor or a previous substance user.

Preoperative Intervention Formats

Theme C1: Interventionists (94 codes, 122 references)

When questioned about preferences concerning different behavioural intervention formats, the most discussed element across interviews was the person delivering the intervention; participants saw the interventionist as an integral part of an interventions success, indeed, the relationship between the participant and interventionist often seemed to be regarded as more important than particular intervention strategies. In this vein, participants suggested that a preoperative intervention would be more effective if there was a warm, comfortable and open relationship between the interventionist and user. A relationship built over a long period of time may be preferred, but unrealistic in the preoperative period. Regardless, not having to see multiple interventionists prior to surgery and thus allowing a more personal relationship to develop may be a useful strategy.

Participants had mixed opinions on NHS staff delivering substance use interventions prior to surgery. A number of participants suggested that intervention at preassessment by a preoperative nurse would be useful. Indeed, participants suggested that nurses and other clinical staff might have more impact given their perceived authority as health workers.

Conversely, a number of participants took the complete opposite view. These participants felt that clinical staff were undertrained in regard to substance use, and thus not equipped to intervene. This view may be explained by experiences of stigma, or perceived stigma; if staff are not willing to treat users with respect, then it is unlikely that they i. would be able to sympathise with, and/or address, barriers to substance use reduction, and ii. have received training with handling such patients.

Similar to above, one participant suggested that they distrust NHS staff because they may not have first-hand experience of their issues*: "they've never been on the, they've never had this gear, took the gear, so what they're going to tell you is what they've read from books and whatever"* **(Elijah)**. This was related to a common preference: interventionists who were either previous users, or specialists with much experience with substance use clients. In relation to the former, participants suggested that interventionists who were former user could serve as role models, and may offer tricks and tips that only first-hand experience would confer. Seeing them in their role may show that abstinence is possible, and simply interacting with them may therefore be motivating. On the whole, participants suggested they would be more optimistic about interventions by, and at, centres (such as the one they were recruited from) exclusively focused on reducing substance use. This may be because such environments are free of perceived stigma, may have staff with more expertise specifically in dependency, and may have, as above, staff with previous experience of dependency. Referral to such services from, or having representatives of such services accompany users at preoperative assessment may therefore be vital.

Theme C2: Timing (25 codes, 22 references)

With the exception of one participant in treatment for cannabis, participants generally held the view that intervention should occur well in advance of surgery (*"…maybe say a couple of month before..."* **[Mike];** *"…it'd have to take a bit of time, it'd take a good few month I'd have thought."* **[Noah])** – suggesting that acute reduction may be unrealistic, dangerous and pointless. Indeed, one participant, who had had surgery previously, suggested that a 13-week window was not sufficient for them to reduce:

> **Joe:** *"Well someone who's been doing it for 20 years isn't going to sort it out in 13 weeks, you know."*

Stepped reduction of methadone dosage for heroin users was a strategy supported by some participants. This naturally requires a long period of time to achieve, as withdrawal symptoms are kept at bay through small incremental reductions over a long period of time (typically 5ml a week) – though the length of time depends on the dose at which the user is stabilized (typically: low = <40mg, high = >80mg).

Most participants also suggested that any behavioural intervention would benefit from weekly sessions up to the date of surgery (*"…definitely weekly, well at least once a week"* **[Lucas];** *"…it's got to be once a week"* **[Leo])**. One participant suggesting that reduction has: *"got to be hammered home"* **(Leo)**

Taken with the above, participants generally favoured highly intensive approaches to intervention; many regular sessions over a long period of time. Given that participants also preferred one-to-one sessions with substance use specialists (see theme C1 [*interventionists*] above), any intervention perceived as most useful would demand a high amount of resources.

Theme C3: Group sessions (15 codes, 16 references)

Group-based intervention sessions, over one-to-one sessions, are more economical to deliverers in regard to time and money – so are the most common form of behavioural interventions typically used for substance use treatment. Across interviews however, the perceived potential efficacy of preoperative group-based intervention sessions was mixed to negative.

Some participants highlighted positive previous experiences with group-based intervention formats such as Narcotics Anonymous (NA). In these cases, over and above the in-group meetings themselves, participants praised elements such as being introduced to a network of abstinent peers (and having their support) (see theme B10: *just talking to someone*):

> **Rob:** *"I rang someone up at two o'clock in the morning and the lad was asleep, and he got up, answered his phone and spent an hour talking to me. I didn't use."*

More often than not however, participants highlighted many issues inherent in group-based interventions; the most prominent that group-based sessions can expose users to cues that may trigger substance use craving (see theme A5*: triggers***).** These triggers may be external; interacting with other substance users, and being in an environment associated with substance use, increases the chance that the participant will crave thus seek and use substances. These triggers may also be internal; some participants outlined their struggles with social anxiety, which group sessions – through the pressure to be open about deeply personal issues - may increase. As above, participants suggested that substance use was often a response to mental distress.

As in theme B6 *(flexibility & individualization)* above, participants were also much more inclined to prefer intervention sessions that were personalised – which is by nature not a prominent feature of group-based sessions. Lastly, one participant suggested that group sessions may only be useful once a reduction or abstinence has been achieved, as the effect of cues may diminish over time.

Theme C4: One-to-one sessions (6 codes, 24 references)

Across participants, and by a large margin, one-to-one interventions sessions were preferred over other intervention formats. As above – many participants saw many flaws in group-based sessions, which one-to-one sessions largely avoid. Reasons for this preference included more in-depth and confidential conversations, more individualization and personalization, less chance of embarrassment and less exposure to people that may trigger craving. All participants asked to outline their ideal preoperative intervention suggested weekly one-to-one intervention sessions, mostly composed of considered risk information and practical support (e.g., signposting to mental health services; delivering motivational interviewing).

Theme C5: Other modes of delivery (18 codes, 14 references)

While one-to-one and group-based face-to-face interventions were the most discussed among participants, the relative pro and cons of other or additional formats were discussed also. Those most prominent are outlined in subthemes below.

Opioid substitution. Given that all but one current or previous heroin user in the sample had previously - or where currently - receiving a form of opioid substitution treatment as an adjunct to behavioural intervention (either methadone or buprenorphine), these participants frequently reflected on the perceived cost and benefits of this treatment method.

Useful for withdrawal symptoms. On the one hand, many participants suggested that substitution was an invaluable and gold standard method of intervention. Participants highlighted that substitution alleviated any withdrawal symptoms, thus physical and mental suffering and craving for illicit opioids (*"*[buprenorphine] *counter-acts the symptoms because mainly it's not about the addiction it's about the symptoms that you get from wanting* [heroin] *and craving* [heroin]*"* **[Ppt 1]**). One participant suggested that the physical component of heroin dependency needs to be suppressed before targeting the root causes, or other determinants of continued use.

In support, others suggested that that in the absence of any other determining factors, opioid substitution – at a dose that allows stabilisation (enough to nullify opioid withdrawal completely) completely eradicates any compulsion to use heroin again. In the context of surgery therefore, many participants regarded opioid substitution – at an appropriate dose, and with enough time to taper, a valuable tool to target the physical component to heroin dependency. However, because dependency and continued substance use is not simply borne out of the need to address withdrawal alone, behavioural interventions targeting determinants – be they psychological, environmental or social, may be necessary also.

Substitution can be counterproductive. Apart from the inherent issue of opioid substitution as a preoperative intervention (that the use of any substance in the preoperative period may increase the likelihood of perioperative complications) many participants highlighted other problems with the approach.

Participants often suggested that substitution could become a crutch; a way of staving off withdrawal at times when heroin is unavailable. Participants suggested that substitution may also reduce motivation to reduce opioid use in general – users may be happy being maintained on the prescription and become complacent and unengaged with intervention. Participants also highlighted that tapering from methadone is incredibly difficult, with many users having multiple cycles of tapering and relapsing over years. In a time-limited period, a significant degree of motivation on the part of the user would be required to reduce. One participant suggested that themselves, and most people they knew, probably would not stick to any taper schedule. Because tapering off the prescription would be necessary in the preoperative period, all the above issues present significant difficulties. In this way, opioid substitution may be counterproductive to preoperative reduction.

Information leaflets*.* With regard to leaflets as a format for delivering information, opinions were mixed. Two participants suggested that most people would just ignore them – suggesting face-to-face information would have more impact. Conversely, two participants stated that they would be useful in addition to more intensive intervention.

Remote interventions*.* The few participants who discussed remote interventions (e.g., phone or web-based interventions) were highly sceptical of their potential efficacy. One participant described the concept as "*annoying"*, another suggested*: "I won't do phone calls I like to see* [interventionists] *and that, see what they're about."* (**Mason**).

Alcohol medication. Those who had previously used alcohol medication (e.g., disulfiram) typically described them as useful for reducing cravings. Two participants mentioned that they entered treatment (with the service from which they were recruited) partially to receive a disulfiram prescription. One of these also expressed frustration that clinicians are sometimes unwilling to prescribe the medication.

> **Jack:** "*Antabuse* [disulfiram] *when I was using Antabuse it were, it were good, it were good because I knew if I went anywhere near alcohol I were going to be in this state."*

ENDNOTES

[1] Considered a procedure with little risk of conferring any serious or permanent injury. As defined by the Concise Dictionary of Modern Medicine: "*Any surgical procedure that can be performed in a brief period of time (usually < 1 hour under local anaesthesia) and does not under normal circumstances constitute a major hazard to life or function of organs or body parts. Minor surgery does not generally require hospitalisation and may be performed electively, usually by a general surgeon in a secondary-care hospital setting.*"

[2] Considered a procedure with some or high risk of conferring some degree of serious morbidity or risk to life. As defined by the Concise Dictionary of Modern Medicine: "*Any operation: (1) Within or upon the contents of the abdominal, pelvic, cranial or thoracic cavities; or (2) Which, given the locality, condition of patient, level of difficulty or length of time to perform, constitutes a hazard to life or function of an organ or tissue. Major surgery usually requires general anaesthesia, a period of hospitalisation of varying length (often a week) and may be performed by a general—board-certified—surgeon in a secondary care hospital, or by a surgical subspecialist in a tertiary care hospital.".*

[3] Indeed, by not forcing the NHS to ensure this target, the ex-health-secretary Jeremy Hunt was accused of breaking the law by the opposition Labour party (Campbell, 2017).

[4] A tongue-in-cheek example provided by the authors include "*the inability to walk after the amputation of the leg*."

[5] Before this new definition was later further evaluated, deemed highly useful for its intended purpose and thus unaltered in 2009 (Clavien et al., 2009).

[6] As outlined a report by the International Association for Ambulatory Surgery (Lemos, Jarrett & Philip, 2006), when compared with inpatient surgery, day case surgery has several advantages to patients and hospitals alike: less risk of hospital acquired infection (be that wound infection or MRSA); less stress and life-disruption for patients; a release of beds for those who may need them more; and a between 10-70% reduction in costs when day case care replaces

inpatient care. Patients who have the same procedure twice or more, once as a day case procedure and once as an inpatient procedure tend to favour the former (Lemos et al., 2006). As such, the NHS has aimed to increase the proportion of procedures performed as day cases – with a great degree of success. A report by The Kings Fund (Appleby, 2015) suggests that the NHS has saved £2 billion from 1998 to 2013 from replacing inpatient with day case procedures and suggests that day cases will make up 87% of all procedures by 2023/2024. This rise is no doubt in part due to innovations in shorter acting anaesthetics and minimally invasive surgical techniques.

[7] The authors suggest that the mechanism for this phenomenon is unknown, but likely explained to some degree by a combination of the direct effects of the complication(s) and a prolonged systematic inflammatory response (which is associated with many surgery-related factors e.g., trauma, anaesthesia, and is associated with a greater risk of several significant ailments).

[8] A world-renowned neurosurgeon named Henry Marsh has recently brought such issues to the public eye, with bestselling memoirs including *Do No Harm: Stories of Life, Death and Brain Surgery* and *Admissions: A life in Brain Surgery* providing an honest and reflective account of the emotional trauma associated with the profession.

[9] Developed by NCEPOD following a 2011 report (Findlay et al., 2011) recommending the development of rapid methods to detect preoperative patient risk, and a systematic review finding that previous calculators had significant limitations (Moonesinghe et al., 2013) e.g., the Surgical Risk Calculator and Revised Cardiac Index.

[10] Recently, the ASA classification system been altered to include the influence of lifestyle factors on perioperative outcomes (Doyle & Garmon, 2017; though there is no evidence to suggest that this alteration has been adopted in practice, and the SORT calculator guidelines do not include this new definition).

[11] As stated in a short piece by Nicholson, Coldwell, Lewis and Smith (2013), there are likely several benefits from having nurses perform what used

to be a role reserved for doctors - not least a reduction in cost and increase in efficiency. However, a systematic review by Hines, Munday and Kynoch (2015) identified few experimental trials on several outcomes though some low-quality evidence suggesting that nurse-led preoperative assessment may reduce surgery cancellations, non-attendance and patient anxiety – while also improving patient preparation, though little to no evidence of benefits for patient morbidity or mortality. Future studies are greatly needed.

[12] "*the process of enhancing an individual's functional capacity before scheduled surgery, aimed at improving the patient's tolerance to upcoming physiological stress*" (Danjoux & Kothmann, 2015)

[13] This latter point does not hold for substance-dependent individuals however (who tend to be older and have a large degree of comorbidity) - thus special emphasis is placed on these individuals in Chapter 7.

[14] i.e., the observation in many studies (though not always consistently) that abstinent individuals have a higher prevalence of health conditions when compared to low or moderate alcohol users. With increasingly higher alcohol use, this benefit not only reduces but a higher prevalence of health conditions is observed in the heaviest drinkers above abstinent individuals.

[15] UK example: http://www.forms4care.com/XForm/LoadForm?patientId=2&formName=Pre-Operative-Assessment&view=read&formInstanceId=example-instance.

[16] *Ibid*.

[17] Note that while this may be the *ideal* circumstance, intervention as early as possible may present unique challenges i.e., the maintenance of behaviour change and increased expense (if repeated sessions). The timing of interventions, therefore, must be a pragmatic decision based on a balance between the physiological benefits of long-term reduction or abstinence and any practical issues relating to the success or feasibility of the intervention.

[18] This is a journal article written in the Danish language. Note that the key findings were translated to the author of thesis by a Danish-speaking (Swedish) colleague (SB).

[19] A systematic review by Ghoneim and O'Hara (2016) illustrates that the results above hold true across a wider range of surgeries and demonstrates that the relationship between depression and surgical recovery includes a wider range of harmful consequences (including increased risk of mortality).

[20] This paper uses data from SHARE Waves 1 and 2 (DOIs: 10.6103/SHARE.w1.611), see Börsch-Supan et al. (2013) for methodological details. The SHARE data collection has been primarily funded by the European Commission through FP5 (QLK6-CT-2001-00360), FP6 (SHARE-I3: RII-CT-2006-062193, COMPARE: CIT5-CT-2005-028857, SHARELIFE: CIT4-CT-2006-028812) and FP7 (SHARE-PREP: N°211909, SHARE-LEAP: N°227822, SHARE M4: N°261982). Additional funding from the German Ministry of Education and Research, the Max Planck Society for the Advancement of Science, the U.S. National Institute on Aging (U01_AG09740-13S2, P01_AG005842, P01_AG08291, P30_AG12815, R21_AG025169, Y1-AG-4553-01, IAG_BSR06-11, OGHA_04-064, HHSN271201300071C) and from various national funding sources is gratefully acknowledged (see www.share-project.org).

[21] Informal anecdotal evidence, after the study was completed, found this to be true after correspondence with some nursing staff.

[22] The present study coincided with a nationwide increase in surgery delays: https://www.bbc.co.uk/news/health-43300995 (QualityWatch, 2018).

[23] As outlined by Prestwich et al. (2015) poor use of theory (e.g., using only parts of a theory), increased awareness and use of "*stringent methodological procedures*" (e.g., those more conscientious about using theory, may be more conscientious regarding the quality of their research - for example, by using masked designs, which by definition are used to reduce the intervention effect size by e.g., reducing the effect of placebo) and employing a mishmash of theories (ironically, but intuitively, too much integration of theories may lead to no coherent theory) may all undermine a fair, and empirical comparison between interventions claiming to use theory and those ignoring theory.

[24] This allows covariances between latent factors to be directly interpreted as correlation coefficients.

[25] Note that all below analyses were conducted *excluding* items outlined in Table 6.2. Results were very similar when including all items.

[26] $F(6, 95) = 10.39$; $p < .001$; $R^2 = .40$. After controlling for the effects of all other subscales, *physical opportunity* (β = -0.39, 95% CI: -0.66- -0.13, p = .004), *physical capability* (β = -0.25, 95% CI: -0.45- -0.06, p = .01) and *reflective motivation* (β = -0.22, 95% CI: -0.41- -0.02, p = .03) were significant.

[27] Opioids (such as heroin) are typically cited as those most highly associated with dependency potential and adverse health outcomes (e.g., Nutt, King & Phillps, 2010). It has been estimated that 52% of individuals accessing drug and alcohol services from 2016-17 did so for opioids, or opioids plus another substance (Public Health England, 2017).

[28] e.g., of those in contact with drug and alcohol services, an estimated 43% of opioid users also used crack cocaine, and 20% had adjunctive problematic alcohol use (during 2016-17) (ONS, 2017).

[29] For example, heavy alcohol use has been demonstrated to predict major depressive disorder (MDD) and MDD to predict perioperative complications but MDD is rarely mentioned in analyses of the relationship between alcohol use and surgical complications (see Chapter 3).

[30] Conventions outlined in COREQ (COnsolidated criteria for REporting Qualitative research) (Tong, Sainsbury & Craig, 2007) are followed throughout this chapter.

[31] Indeed, the thrust of this approach is employed by many governments (as a reactionary intervention e.g., cigarette packaging with graphic images of health conditions, or as preventative intervention e.g., emphatically and only emphasizing the risks of illicit substance use to school children).

[32] See also prominent theories of health behaviour e.g., Protection Motivation Theory and the Health Belief Model (see Conner & Norman, 2005).

[33] This is reflected in the counselling approach of motivational interviewing (found successful in some contexts: Lundahl, Kunz, Brownell,

Tollefson & Burke, 2010, unsuccessful in others: Li, Zhu, Tse, Tse & Wong, 2016), where specific goal setting, planning and making a commitment to behaviour change form the last stage of the intervention, after preceding techniques have been applied to promote motivation.

[34] However, in one unique study Tønnesen et al. (2010) showed that an intervention to increase GPs screening, referral and brief intervention of hazardous preoperative alcohol users to substance use treatment failed. The authors targeted and tailored their intervention towards possible barriers that they identified in a literature search (e.g., lacking confidence/knowledge, too time consuming), but did not engage in any direct elicitation research. Conducting sufficient elicitation research may have allowed the researchers to better focus on barriers which may be more amenable to change.

[35] Action planning (or *implementation intentions*) and goal setting are similar techniques, and both feature in the *goals and planning* section of the behaviour change technique taxonomy; Michie et al., 2013).

[36] Tiffany (1990) proposes that substance use behaviours are encoded in memory as *sequences of behaviours*. Over time, substance-dependent individuals learn a set of various behavioural sequences (*action plans*) that can be used to overcome predicted obstacles to substance use (e.g., lack of money). These sequences become automatic through repetition and are triggered by substance-related cues (both cues and sequences are stored in memory as *automatized action schemata*). Adaptive, conscious action plans may disrupt this process; "*by identifying the situations in which addictive behaviours could or do occur, implementation intentions might be used to promote alternative action plans that are incompatible with the previous addictive behaviour.*" (Prestwich, Conner & Lawton, 2006).

[37] These include *mindfulness* (mindfulness-type interventions have shown to be efficacious for substance use. These are a broad grouping of (brief or more intensive) meditation-like techniques that, at their core, aim to bolster awareness of, and control reactions to, the consequences of exposure to external cues (e.g., craving) (see Garland & Howard, 2018).