DOCTOR OF MEDICINE

Long term outcomes of methadone substitution therapy (OST-M) for opiate dependency
the effect of patient characteristics and co-morbidities

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Brian A. Kidd

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University of Dundee Medical School

Long term outcomes of methadone substitution therapy (OST- M) for opiate dependency: the effect of patient characteristics and co-morbidities.

By

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This thesis is dedicated to my father, Alistair Kidd.

Abstract

Aims and objectives

Substance misuse is a chronic relapsing condition associated with high morbidity and mortality. Treatment attempts to reduce harms associated with drug use and to promote recovery and has developed considerably in the last 30 years. Opioid substitution therapy using methadone (OST-M) is an effective treatment for opioid dependency. Though the effectiveness of OST-M in delivering harm-reduction is well evidenced, evidence demonstrating recovery is limited as is understanding of those factors influencing progress. In this context, national policy makers and stakeholders have repeatedly questioned the value of OST-M as a substance misuse treatment and, at times, have sought to limit its use. Rigorous, long term outcome studies of UK subjects are required to improve clinical outcomes in OST-M subjects and to ensure ongoing availability of evidence-based treatments.

In this context, the study had two main objectives: to demonstrate that standard clinical information systems can deliver rich, valid datasets to support outcome research; to use these data to explore the relationships between a selection of baseline variables (patient characteristics, comorbid conditions, the nature of substance misuse and the treatment received), the clinical process and long term outcomes achieved in a large cohort of OST-M patients in a standard NHS treatment setting.

Methods and materials

Standard clinical information, collected over 7 years, was linked with validated data from a range of databases. A large representative sample (76% of the OST-M treatment population in a region) was described in detail. Follow-up data were retrieved from clinical casenotes (4 years) and linked datasets (4-7 years) and collated to create a database for analysis. Variables for analysis were selected following a review of the published literature. Univariate analyses were undertaken to demonstrate statistically significant associations between baseline and follow-up variables. Significant variables were then entered into multiple regression analyses to develop predictive models for selected outcomes. Any

predictive models were then subjected to cross-validation to determine their predictive power in novel datasets.

Key results

Many highly significant associations were shown. Significant personal (demographic) factors included: age, gender, having children, having conflict in personal relationships, educational level achieved and being in employment. It was notable that the area lived in (of three districts) was strongly associated with a wide variation in clinical process and outcomes achieved. Whether treated in primary care or specialist services, the medical treatments received, the level of non-NHS support and patient satisfaction showed strong associations with outcome. Baseline illicit drug use was also strongly associated with outcome.

Multiple regression analyses found that despite these highly significant associations, strong predictive models of long terms outcome could not be demonstrated. Where weak models were created - predicting drug use (by self - report); drug use (positive tests); family stability - cross validation showed these had no predictive value in novel datasets.

Conclusions

Standard clinical information, linked with relevant NHS datasets can give rich and comprehensive data suitable for research of large representative samples over long time periods. This study represents one of the largest OST-M populations ever described in the UK with longer follow-up periods than most of the published literature.

In this study strong associations were found between a range of independent and dependent variables over 4-7 years. These findings broadly reflected the evidence base. However, the associated variables could not generate strong useful predictive models of long term outcome. This could reflect issues of study design or data quality.

This type of approach should be further developed in the field of substance misuse research. Issues of data quality would require to be addressed to maximize the value of these datasets. Further research is required to develop better understanding into key factors influencing long term outcomes of treatment in substance misuse.

Abbreviations

ACMD	Advisory Council on the Misuse of Drugs
ADHD	Attention Deficit Hyperactivity Disorder
ASI	Addiction Severity Index
BRT	Buprenorphine Replacement Therapy
CM	Contingency Management Approach
CRA	Community reinforcement Approach
CSP	Chronic severe pain
CTN	Clinical Trials Network OST- M
DTTO	Drug Treatment and testing Order
EIU	Effective Interventions Unit of the Scottish Executive
GMS	General Medical Services
GP	General Practitioner
GROS	General Register office for Scotland
HCV	Hepatitis C Virus
HIC	Health Informatics Centre
HIV	Human Immunodeficiency Virus
ISD	Information Services Division of the Common Services Agency. NHS Scotland
IVDU	Intravenous Drug User
LAAM	Levo alpha acetyl methadol
MAP	Maudsley Addiction Profile
MM	Methadone Maintenance*
OST- M	Methadone Replacement Therapy *
NDTMS	National Drug Treatment Monitoring System
NHS	National Health Service
NTA	National Treatment Agency
ORT/OST	Opiate Replacement/Substitution Therapy*

OTI	Opiate Treatment Index
PTSD	Post Traumatic Stress disorder
QoL	Quality of Life
RCGP	Royal College pf General Practitioners
RCT	Randomized Controlled Trial
SACDM	Scottish Advisory Committee on Drug Misuse
SHHD	Scottish Home and Health Department
SPS	Scottish Prison Service
SUP	Substance Use Problem
R&D	Research and Development
SUMIT	Substance Misuse Information Tayside
TARS	Tayside Arrest Referral Scheme
TMC	Tayside Methadone Cohort
UKDPC	UK Drugs Policy Commission
UNODC	United Nations office on drugs and crime

*The published literature in this field uses a number of terms – often interchangeably - to describe the use of prescribed opioid drugs to replace or substitute those illicit drugs being used as part of a drug problem. These include: *Opioid replacement therapy (ORT); opioid substitution therapy (OST); methadone maintenance (MM).* In publications addressing these treatments, the opioid/opiate used may be described (methadone, buprenorphine, diamorphine) though at times this may not be clear. Also, some research projects are unclear regarding whether they are addressing a *maintenance* approach (a process of prescribing a substitute which involves period of stable prescribing – but also, clinically – led increases or reductions) or a *detoxification* approach (a time-limited medical treatment, aimed at safely alleviating symptoms of withdrawal with a clear end-point that the subject is no-longer dependent).

In this thesis, to avoid confusion, the term *Opioid Substitution Therapy using Methadone* (OST-M) is used for all methadone research in the literature review. If specific *detoxification* approaches or different opioids are the subject of any study this is made clear in the text.

Signed Declaration

I hereby certify that I, Brian A. Kidd, am the author of this thesis, that all references cited in this manuscript have been cited by me, that this thesis is a record of work carried out by me and that it has not been submitted in any previous application for a higher degree

Signature of candidate Date:

I hereby certify that the candidate has fulfilled the conditions of Ordinance and regulations for the degree of MD in the University of Dundee

Signature of Supervisor Date:

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Signature of Supervisor Date:

Chapter 1. The treatment of opiate dependency in the UK – a political analysis

No science is immune to the infection of politics and the corruption of power.… The time has come to consider how we might bring about a separation, as complete as possible, between Science and Government in all countries. I call this the disestablishment of science, in the same sense in which the churches have been disestablished and have become independent of the state.

Jacob Bronowski - Encounter (1971)

Dogbert: So, Since Columbus is dead, you have no evidence that the earth is round.
Dilbert: Look. You can Ask Senator John Glenn. He orbited the earth when he was an astronaut.
Dogbert: So, your theory depends on the honesty of politicians.
Dilbert: Yes... no, wait

Scott Adams -Dilbert comic strip (1989).

A strategic approach to problem drug use in the UK

Introduction

The use of psychoactive substances precedes recorded history and some suggest may even have contributed to human neurodevelopment (Hill & Newlin 2002). The problematic use of such substances has also been described for centuries but from the second half of the 20th century has been acknowledged as a large and increasing public health problem across the world, evoking responses from international and national institutions aiming to reduce the harm caused by substance use (United Nations Office on Drugs and Crime [UNODC], 2008; Babor et al 2010). Substance misuse can have complex impacts on the individual, with potential effects on physical and psychological health as well as social functioning. Its worst effects often impact on the most excluded and disadvantaged in society. Central to any response to address substance misuse, it is important that policy-makers take cognisance of the best available information and research evidence, use this objectively and avoid the temptation to bring moral or political judgements to bear.

Addressing substance misuse in the United Kingdom (UK)

In its final report, the independent UK Drug Policy Commission (UKDPC) states:

"Drug policy is currently a mix of cautious politics and limited evidence and analysis. This is coupled with strident and contested interpretations, both of the causes of problems and the effects of policies. In fact, for as long as there has been a drug policy, there have been gaps in the evidence as well as uncertainty about how to understand and act on the evidence that we do have" (UK Drug Policy Commission [UKDPC] 2012[1])

This statement is extremely relevant when we consider the current state of flux around the treatment of opioid dependency in the UK.

The way we manage people experiencing substance use problems in the UK has changed dramatically over the last 25 years (Kidd & Sykes 1999; Kidd 2010). This change has often been driven by fears regarding the safety and health of society as a whole rather than specific concerns for the individual's needs or wishes. Large changes in policy direction, service capacity or clinical process can occur swiftly – reflecting political will or the emergence of a new drug-related threat. The inconsistent quality of information available to inform how we should best manage such problems raises challenges at all levels. Simply understanding the magnitude of the problem to be addressed is problematic. Assessment of the size of "hidden populations" is innately complicated and uses indirect sampling models to estimate prevalence (Frischer & Taylor 1999; Hickman et al 1999; Hay 2000). In the UK, information about those who are accessing services is supplied by the Criminal Justice System (CJS), National Health Service (NHS) and various social care agencies. But the different countries, regions and even districts within the UK have developed diverse methods of data collection or have in place differing mechanisms of governance for such systems (Information Services Division [ISD] 2012; Health & Social Care Information systems 2011). This makes the interpretation of findings or comparison between geographical areas or treatment approaches challenging – even in the UK, where one major service element, the NHS, has traditionally delivered a substantial element of the care process – medical treatments.

Substance misuse brings many detrimental effects on health and society. During the last quarter of a century, the substance misuse problem in the UK has increased greatly in terms of raw numbers as well as its effect on society (ISD 2012; Health & Social Care Information systems 2011). The demands this places on key public institutions including the NHS and CJS make it imperative that scientific scrutiny of the available interventions and clinical treatments to address the problem is as robust and objective as possible.

Information, experimental change and evaluation

The 2012 UKDPC report, cited above, goes on to give a critique of the current state of information systems to inform the best way to manage drug problems in the UK. The report states:

"The way we collect analyse and use evidence in UK drug policy has often been inadequate and this has held back cost-effective policies that could have improved the lives of millions of people" (UKDPC 2012[1]).

They recognise that full blown Randomized Controlled Trials (RCTs) may not always be required to demonstrate effectiveness but also acknowledge that, when such scientific rigour is seen as less relevant, *"too often we have slipped to the other extreme and relied simply on anecdote".* The report authors have the view that, in the drugs field, evidence is not given the same position as in other health and social care areas. Instead, *"evidence is often treated as a stakeholder whose interests should be taken into account, rather than a tool that is useful for all participants."* This is clearly an issue which could stand in the way of progress and the UKDPC makes a plea for a "*new and more mature relationship with evidence".* Examples of the change required would include: having a willingness to be guided by evidence and avoidance of *"cherry-picking"* of the evidence when the outcomes are politically challenging; recognising different levels and forms of evidence; being clear regarding the objectives of any intervention being evaluated and accepting both negative and positive results from evaluations of new initiatives or pilot studies.

The issues raised by these examples echo a long-standing view, expressed in numerous advisory documents for successive governments, that good quality information, a culture of

evaluation and objective analysis and support for a coordinated programme of research would place policy–makers in a stronger position when difficult strategic decisions are required.

In Scotland, for example, significant increases in service funding were supported by the first Scottish Executive in 1999 after a long period when new funding for treatment was largely unavailable. The Scottish Advisory Committee on Drug Misuse (SACDM) set up a research sub-committee, supported by the Effective Interventions Unit (EIU) – a newly created and innovative support unit, tasked with producing authoritative evidence for the substance misuse field in Scotland - and co-opted leading Scottish academics to advise on how best to evidence the government's strategic aims. Regarding treatment, this final report stated:

"There is a commitment within the UK and Scottish drug misuse strategies to develop effective drug misuse treatment services. This aim is currently hampered by the lack of detailed information on the effectiveness of drug misuse services within Scotland. Where research has been undertaken into the provision of methadone this would appear to have an important role in the treatment of opiate dependent drug misusers. However, it is not possible to say within Scotland what the long term impact of drug misuse treatment services is. There is a need to develop a programme of drug misuse treatment evaluation that is both comprehensive in its coverage across Scotland and in its inclusion of the range of treatment modalities that are currently available within Scotland." (McKeganey & McIntosh 2000)

Despite this advice, some 13 years later, Scottish ministers have continued to struggle when questioned regarding the effectiveness of Scottish treatment services (Chief Medical officer for Scotland, 2012). There is clearly a need to address this deficit in information and intelligence.

The changing political map in the UK

At the same time as the treatment of substance misuse has been evolving so dramatically, there has been a shift in the political balance in the UK, with disaggregation of national governments to Scotland, Wales and Northern Ireland in the late 1990s. As responsibility for local government, health, social care and criminal justice policy has been devolved, to some

degree, to these new national administrations, there has been a divergence in the approaches taken to prevent the development of substance use problems or to intervene to manage them. In 2012 the implications of this political divergence has been highlighted further, with six different political parties – including two coalitions - in power across four administrations. Meantime, the Westminster (UK) government retains responsibility for all UK legislation regarding controls over drugs with abuse potential (Crown Office 1998). With substance misuse an area which is strongly influenced by socio-political drivers, this situation raises risks regarding the consistency of service delivery across the UK.

It is important to recognise that, as this political turmoil is acted out in the UK, there is a broad consensus around the world regarding how substance misuse is best understood and addressed (UNODC, 2008). However, even with this consensus in place, in the UK there is ongoing debate regarding the nuances of what services should be achieving when they treat substance misusers – at times coloured by a moral judgement within society expressed through the media and periodically influenced by politicization of the drugs debate. This is not a new phenomenon. Indeed, there has been a tension between clinical opinion and political will in the UK for over 100 years with regard to these issues. There is also a long-standing trans-Atlantic perspective, with consecutive US governments keen to publicly support a "war on drugs" and an approach to drug treatment which is more skewed towards abstinence and rehabilitation than harm reduction or risk management.

European approaches have, as a rule, engendered a more pragmatic approach. For example the European Union Drugs Strategy (2005-12) stated its [demand reduction] aims as achieving:

"Measurable reduction of the use of drugs, of dependence and of drug-related health and social risks through the development and improvement of an effective and integrated comprehensive knowledge-based demand reduction system including prevention, early intervention, treatment, harm reduction, rehabilitation and social reintegration measures within the EU Member States. Drug demand reduction measures must take into account the health-related and social problems caused by the use of illegal psychoactive substances" (Council of the European Union 2004)

It is in this strategic context that the new devolved administrations in the UK have recently redefined their expectations of treatment for substance misuse.

Current UK and Scottish Government Strategies

In the last 4 years, both the Scottish and UK Governments have brought forward new strategies to address the drug problems experienced across the country. These strategies have some similarities – with both seeing the status quo as in need of major change and claiming to aspire to deliver an enhanced culture of recovery for drug users seeking treatment.

When considering what can be achieved, the Scottish strategy – *The Road to Recovery* – states:

> "*In practice recovery will mean different things at different times to each individual… [It]... might mean developing the skills to prevent relapse…rebuilding broken relationships... Milestones may be as simple as gaining weight... or building self-esteem. What is key is that recovery is sustained*." (Scottish Government 2008)

There is acknowledgement of the achievements to date of the long-established harm reduction approaches but also an aspiration to move the balance of care towards more individualized progress which better supports the reintegration of substance misusers into their own communities.

The UK (Westminster) Government's strategy - *Drug Strategy 2010. Reducing Demand, Restricting Supply, Building Recovery: Supporting People to Live a Drug-Free Life* – addresses drug problems in England and Wales. It places more responsibility on the legal system to control illegal drug availability. It does also point towards a recovery agenda for treatment-seeking individuals, stating:

"A fundamental difference between this strategy and those that have gone before is that instead of focusing primarily on reducing the harms caused by drug misuse, our approach will be to go much further and offer every support for people to choose recovery as an achievable way out of dependency…..The causes and drivers of drug and alcohol dependence

are complex and personal. The solutions need to be holistic and centred around each individual, with the expectation that full recovery is possible and desirable." (Home Office 2010)

These strategies make it clear that, during this period, the focus of treatment is changing substantially in the UK for the first time since the 1980s. If we do not put these current developments into an historic context we are in danger of revisiting old arguments – pitting the pragmatism of "harm reduction" against the aspiration of "abstinence" - repeatedly with no likelihood of resolution. At worst, this could mean that evidence-based treatments, known to be effective at reducing drug-related harms and death, may become less available to substance misusers in the UK, largely for socio-political reasons. At best, it points to a continuation of the shabby stigmatization of a highly vulnerable group within society which is at high risk of a range of morbidities, social disadvantage and premature death.

The following section will briefly summarize how policy has evolved in the UK in recent decades.

UK Drugs policy: a recent history

The approach to managing drug problems in the UK has long been the subject of political and clinical debate. The main points of this discussion are summarised briefly below. A more detailed analysis is contained in a number of publications (e.g. Royal College of Psychiatrists 1987; Stark, Kidd & Sykes, 1999; Strang & Gossop 2005).

20th Century – opium and the British System of care up to the 1960s

The main illicit drug problems in the UK have been dominated by the use of opioids in recent years. Opioids can be defined as:

"any of a group of substances that resemble morphine in their physiological or pharmacological effects, especially in their pain-relieving properties"
https://wwwcollinsdictionary.com/dictionary/english/opioid

Opiates are naturally occurring opioids, specifically associated with the opium poppy. Opiates can be defined as:

" an addictive drug made from the opium poppy that has morphine-like, soothing effects" http://www.yourdictionary.com/opiate

For over a century, the problems associated with illicit opioid use in the UK were managed under an approach known as *The British system.* The *British System* could be seen as having been in place as early as the 18th century. At this time Britain was a global superpower and its active opium trade in the east meant that opium and its derivatives were readily available within the UK. Inevitably, British subjects became addicted to opiates, and doctors would attempt to alleviate their suffering, often by prescribing opioid drugs. This practice was not seen as problematic by society and was essentially free of governance until the early 20th century. The first world war saw initial governmental controls appearing which, for the first time, made the possession of some substances, such as cocaine, illegal for the general public, though doctors were still seen as legitimate suppliers of these substances if they were medically required (Berridge, 1984).

However, it is felt that the modern view of the *British System* is best captured in the work of the Rolleston Committee of 1926 (Departmental Committee on morphine and heroin addiction, 1926). The *British System* is often understood to be an approach to the problem of opioid addiction which was person-centred, avoided the kind of confrontational difficulties seen in the USA (where there had been a strong abstentionist bias) and allowed doctors to help people to overcome any problems associated with their substance use, often by offering them a safe and legal supply of prescribed opioid drugs. An alternative analysis suggests that at its start, the problem to be addressed was minimal - as there were very few problem substance users - and the approach of replacement prescribing which was embodied in the *British System* has been described as *"a system of masterly inactivity in face of a non-existent problem"* (Downes, 1988). What is clear, is that the drug users accessing medical care at that time – which continued up to the 1960s - were demographically very different from the current stereotype, described as *"more likely to be*

female, middle-aged or elderly, and from the middle classes; a substantial minority were themselves doctors or allied professionals." (Strang & Gossop 2005).

There is no doubt of the tidy pragmatism contained in the *British System*. But there is also the worrying seed of a reductionist approach to dealing with the complex problems associated with substance misuse by using simply medical approaches. When the Rolleston Committee recommendations are examined it is clear that replacement prescribing by doctors of opioid drugs is proposed as only a part of the solution and not the solution in itself. There is an assumption that the physicians will also be helping individuals to address associated problems and a sense that improvement (or recovery) is implicit in this approach. This important point becomes relevant in the context of the current debate.

The 1960s – social control of an expanding challenge

The *British System* was the basis of the approach to address substance use problems until the 1960s when a sudden increase in problematic drug use – particularly through injecting in younger people and centred on London - saw a reaction from the UK Government to increase controls over this new and expanding problem. In response, two Department of Health committees within 4 years made recommendations to government on how to address heroin and cocaine use – reflecting the speed of this change (Ministry of Health 1961; 1965). A Home Office committee also considered responses to reports of increasing cannabis use during the same period (Home Office cannabis report, 1968). From this point, increasing controls over the manufacture, storage and movement of a range of "controlled" drugs and a move to reduce General Practitioners' prescribing of opioids became the norm. Instead, replacement prescribing of opioids – such as prescribed pharmaceutical diamorphine (heroin) - became a more specialist activity and government strategy became more aimed at helping individuals detoxify from their addiction (Royal College of Psychiatrists, 1987). Though a group of individuals continued to access prescribed heroin from doctors, a drive towards detoxification/abstinence was broadly supported through the 1960s and 1970s until the appearance of blood borne virus problems in injecting drug users heralded another change of direction.

1980s: Blood-borne virus infection, HIV and AIDS – the re-birth of UK harm reduction

Hepatitis B infections had raised initial public health concerns in the late 1970s, but it was the link with HIV which drove real change in the strategic approach to drug misuse. In the face of compelling evidence that injecting drug users had a high prevalence of HIV infection in parts of Scotland (Robertson et al 1986; Robertson, Bucknall & Wiggins 1986), the McLelland Committee recognised that the public health risk of HIV was potentially greater than the risk of substance misuse. In response their landmark report made recommendations to increase availability of prescribed opioid replacement treatments – such as methadone – and to take forward the delivery of limited needle exchange schemes for injecting drug users (Scottish Home & Health Department, 1986). In England, a similar process was proposed and in the name of harm reduction – a pragmatic treatment approach which promoted the achievement of a range of intermediate goals rather than focussing solely on the achievement of abstinence - new community treatment teams were developed to address the rapidly increasing challenge (Advisory Council on the Misuse of Drugs [ACMD], 1988). General Practitioners (GPs) were again encouraged to prescribe opioids to reduce the likelihood of illicit substance use (ACMD, 1989). The first substantial UK treatment guideline in 1991 made replacement prescribing with methadone a real consideration for all doctors if dealing with injecting opioid dependent drug users (Department of Health, Scottish Home & Health Department, Welsh Office 1991).

The next 15 years saw a c-change in delivery. Achieving a reduction in drug-related harm was now the focus of treatment interventions for illicit drug users. As this approach developed and clinicians, service commissioners and politicians grew more comfortable with the concept of harm-reduction, the idea spread into more and more areas of the substance misuser's life. Clinical professionals moved their focus away from the goal of rehabilitation of substance users, instead developing a more pragmatic focussed approach which aimed to reduce injecting, and the associated biological, psychological and social risks that this activity brought with it.

The 1990s to the new Millennium – Expansion of "harm reduction" into social care

As the 1990s progressed, the prescribing of replacement opioids started to become a credible solution for a widening range of social ills – such as drug-related criminal activity. Criminal Justice departments started to invest in treatment services for criminals. For example, Arrest Referral Schemes were first launched in the UK in 1996 and focussed on hard-to-reach individuals, with the aim of giving immediate access to treatment [prescribing] which was thought to have potential in reducing criminal activity (Effective Interventions Unit [EIU], 2002[1]). Recognising the close link between recidivist crime and illicit drug use, Drug Treatment and Testing Orders (DTTOs) were initially piloted in the UK in 1998. They linked sentencing with mandatory treatment (meaning opioid replacement prescribing and testing) – often as an alternative to custody. Though, following evaluation (Home Office 2000; Scottish Executive 2002[2]) they were superseded in England, they have been retained in a modified form in Scotland. Another huge development was that in the mid-1990s it became more acceptable for medical staff inside Scottish prisons to treat drug users using treatments more in line with available community treatments when they had previously received only symptomatic relief if treated at all (Scottish Prison Service [SPS], 1994).

Nor was this move towards broadening harm reduction limited to the Criminal Justice System. Concerns about pregnant drug users, their children and the broader child & family implications of substance misuse also drove a change in the area of child protection. Soon opioid replacement was being proposed as an essential element of managing risk to children in the families of drug misusers (Scottish Executive, 2001).

There followed a clear change of emphasis in the treatment process. Previously, the process of care for substance misusers involved a comprehensive assessment of need. Experienced professionals would determine the nature of the substance use disorder through objective assessment and would offer one of a range of treatment approaches, tailored to that person's needs and strengths as part of an ongoing programme of care. Now there was an expectation that services would give rapid access to (mainly) opioid substitution therapies aimed at stabilisation of drug use and harm reduction rather than detoxification or

abstinence. Opioid substitution therapy had become the treatment of choice for a whole range of physical, psychological and social issues which may be affected by drug use.

But early in the new millennium, this harm reduction approach, which seemed to herald a significant change in the nature of the debate around how best to address substance misuse, was gradually seen by some in the UK as part of the problem rather than the solution. New performance management structures for English services were set up by the English National Treatment Agency (NTA) – a special health authority tasked with improving effectiveness of treatment for substance misusers. Aiming to improve substance misuse services in England, the NTA focused its attention on reducing delays to accessing treatment and measures of treatment retention - rather than the delivery of improved outcomes. Training of doctors (such as General Practitioners) and other professionals in the field almost exclusively emphasized the medical (prescribing) aspect of care with training concerning the development of skills around psychological support and delivery of social interventions given little prominence. Indeed, the 1999 updated national treatment guideline gave little mention of the place for so-called *"wraparound services"* (Department of Health et al, 1999). Reports of activity showed that more and more people were starting on opioid replacement therapy – mainly with methadone - in the UK, with services being accessed by record numbers (ISD, 2002).

Critics of harm reduction in general and methadone in particular began to publicly portray this approach as detrimental to progress, claiming that users received methadone – the most commonly used substitute drug - but no additional support to progress – becoming *"parked"* on methadone. This negative view started to gain media and political support. With very high proportions of drug users in treatment on methadone (and by the millennium, the newly introduced alternative, high dose Buprenorphine) and availability of detoxification, abstinence orientated approaches or non-prescribed alternatives reducing, a sense of confrontation developed (Kidd, 2010).

"The New Abstentionists" and "The Great Debate" 2008

In 2008, the journalist Mike Ashton published his critique *The New Abstentionists* as a special insert in *Druglink* the house journal of the organisation Drug Scope (Ashton, 2008). This followed an interview on the BBC Radio 4 "Today" programme, in which the Chief Executive of the NTA – following publication of that organisation's annual report - had been asked how many people had successfully completed treatment in England in the previous year. His answer of *"3%"* had become a major news story, with the media debate suggesting that the UK drug treatment programme was failing. Ashton's article critically analysed the evidence to date on treatment effectiveness and, concluding that the evidence for harm reduction approaches was sound, raised concerns that there was a political shift around the UK, with politicians of all colours struggling to hold a firm line in support of harm reduction - instead being beguiled by claims that abstinence-based approaches could turn the tide of increasing numbers of problematic drug users and improve treatment effectiveness.

The article stimulated considerable interest and rekindled the previously dormant 'either/or' - abstinence or harm reduction - debate in the UK. In response, the Drug Scope charity organized three *Great Debates* across the UK. The purpose of these events was to allow those dealing with these issues – service delivery staff, commissioners, service users and their families - to hear opinions from those who held polarized views - and to participate in a facilitated discussion on the topic. It is questionable whether these events were successful - in that the records of the discussions suggest they simply allowed rather fixed views to be aired in, what was at times, a hostile and polarized environment. A summary document was published which tried to ensure the discussion was articulated in an objective and balanced manner (Roberts, 2009). The *Great Debate* may however, have ensured that, as UK governments developed their plans, they had some awareness of the potential pitfalls of holding simplistic views regarding the relative merits of abstinence or harm reduction approaches.

An international perspective – the recovery consensus statements 2007/8

In 2007 The Betty Ford Institute in the USA had carried out a process to develop a consensus statement on *"recovery"* - aiming to give a working definition which people involved in the field at all levels could see as relevant to their practice (Betty Ford Consensus Panel, 2007). In the context of the new invigorated (but polarized) discussion in the UK, this initiative gave an opportunity for those from the different schools of thought in the UK to work together to develop a consensus view of what all services should be trying to deliver. The UK Drug Policy Commission progressed this work, publishing their consensus statement in 2008 (UKDPC, 2008). The following draft statement was agreed by the UKDPC group:

> *"The process of recovery from problematic substance use is characterized by voluntarily sustained control over substance use which maximizes health and wellbeing and participation in the rights roles and responsibilities of society"*

The statement was then taken into the field for comment by a wide group of stakeholders - including service users, professionals and strategists. A consistent view from this process was that the statement did seem to capture the correct tone - allowing many views of addiction to be seen as relevant - and potentially opening the discussion to allow a more diverse range of interventions, with more individual significance, to become available. The Royal College of General Practitioners' (RCGP) consulted its own membership. They found that 74% of their members, who had involvement with and training in the treatment of drug users, were supportive of the statement (RCGP, 2008).

In summary, the ability of substance misusers to recover was being actively debated and a focus of this debate became the value (or otherwise) of Opioid Substitution Therapy – OST – and the drug most commonly used in the UK for this purpose, methadone.

The treatment of opioid dependence – Methadone and Opioid Substitution Therapy (OST)

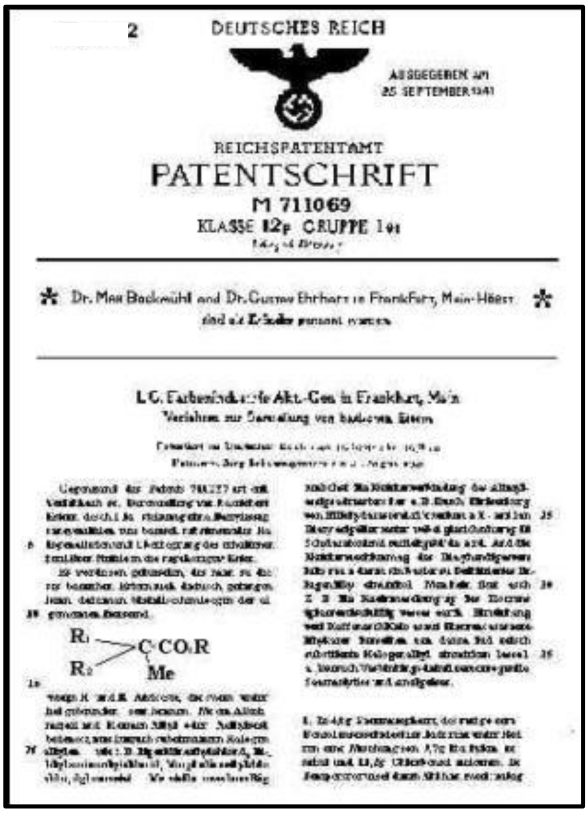
Opioid Substitution Therapy has been a central element of the medical response to opiate dependency for many years and, as described earlier, had formed the basis of the *"British System"*, in which doctors pragmatically supported their patients, who had become addicted to opioid drugs, by prescribing a safe supply of these drugs to allow them to carry out their

responsibilities. The early days of the British System saw doctors prescribing opium and morphine, and later diamorphine. In recent years however, the most prominent prescribed medication used in OST across the world and in the UK is 6-Dimethylamino-4, 4-Diphenyl-3-Heptanone - or methadone – a long-acting synthetic opioid.

Methadone

Methadone was first developed in 1937 in Germany (Figure 1) by scientists seeking a synthetic opioid analgesic to address an acute shortage of opium in that country at a time when there was a strong political drive to make the German state more independent of world trade. However, it was not widely used as in early tests it was found to promote behaviours which were not desirable in the military environment. Nor was the drug made freely available to the civilian community. These early developments and links with Fascism have developed to an almost mythological level. It was named Dolophine in the USA by the Eli Lilly company – and opponents to its use still mis-name it Adolphine, believing (wrongly) that it was named after Adolf Hitler, seeing this as a reason to be doubtful about its place in clinical care (Herman, Stanclif & Langrod 2000; Gerlach 2004).

Figure 1. early German Methadone patent


2 DEUTSCHES REICH

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After the Second World War, all German patents and research records were requisitioned and expropriated by the allies. The records of the research work on methadone and other opioid drugs were confiscated by the U.S. Department of Commerce Intelligence, investigated by a Technical Industrial Committee of the U.S. Department of State and taken to the USA. (Council on Pharmacy and Chemistry of the American Medical Association, 1947). In 1949 researchers in Kentucky showed methadone to be effective at helping heroin addicts in short term detoxification programmes (Isbell & Vogel 1949). However, trials repeatedly showed high levels of relapse once an addict had detoxified and it was some years before methadone's potential was realised (Brecher, 1972).

In the post war period, heroin addiction flourished in some parts of the USA – such as New York City (Andima, Krug & Bergner, 1973). Opiate overdose became the most common cause of death for young adults in New York and criminal activity relating to heroin use was widespread (Halpern & Rho 1966). Debate regarding a policy to address this issue in the USA progressed through the 1950s and early 1960s. In 1964, investigation of methadone maintenance therapy began as a research project at The Rockefeller University under the direction of Drs. Vincent Dole and Marie Nyswander whose seminal work progressed understanding of the potential of methadone OST and its potential mode of action (Dole & Nyswander, 1965; Dole, Nyswander & Kreek, 1966; Dole, 1988).

Early use in the UK

Methadone use was reported as early as the 1940s in the UK – when it was being trialled as a potential analgesic (Prescott & Ransome, 1947). In the 1960s use of illicit drugs was increasing and raising concerns for the government. Illicit methadone use was one feature of this change. By the end of 1968, when Home Office notification of addicts became compulsory in the UK, 297 people had been notified as addicted to methadone. By 1969, this number had risen to 1687. In the UK at this time, methadone was not subject to significant controls over prescribing and by the end of 1969, in central London, there were serious concerns about availability of illicit methadone. This may have originated from poorly controlled medical prescribing and diverted supplies of injectable methadone were being extensively used alongside diamorphine tablets (or "jacks") also prepared for injecting - "jacking up" (Edwards & Busch, 1981). Previous sections of this chapter have shown how

national strategic responses aimed to reduce availability of prescribed opioid drugs – with a move towards less OST and more detoxification or abstinence-orientated treatments. Coincidentally, in some areas of the UK, clinicians began to reconsider maintenance prescribing. For example a Glasgow study in 1975 reported that when new patients were not prescribed methadone they did as well as those who were prescribed - except for criminal behaviour (Paxton, Mullin & Beattie 1978). The value of OST was being brought into question.

But in the 1980s a second step-change in illicit drug use occurred in the UK. This time there was a much broader geographical spread, beyond the cities and also associated with a much wider population of poorer, working class drug users who were less prone to inject drugs – smoking them instead – "chasing the dragon" (Home Office, 1986). The initial national response was to continue to offer detoxification programmes – often using short term or time limited prescribed methadone. However, blood-borne virus infection – in particular the appearance of HIV/AIDS in the public consciousness changed how drug use would be managed for decades (Figure 2).

Figure 2. AIDS Public Health Poster (c1987)

The emergence of a potential link between HIV infection and injecting drug use – first identified in Edinburgh – re-energized the place of OST in general and methadone in particular (Robertson et al 1986). An expert committee reviewed the evidence with a view to identifying effective interventions to address this threat in Scotland and the resulting McLelland report (Scottish Home and Health Department [SHHD], 1986) proposed that services should aim for intermediate goals on the path to abstinence, in order to reduce drug-related harms. These goals included: stopping or reducing injecting with unsterile equipment; taking drugs more safely (by mouth or inhalation); and taking prescribed (legal) rather than illicit drugs. Echoing the Mclelland Committee findings, the 1988 ACMD report on HIV prevention stated that:

"...HIV is a greater threat to public and individual health than drug misuse. The first goal of work with drug misusers must therefore be to prevent them acquiring or transmitting the virus. In some cases this will be achieved through abstinence. In others, abstinence will not be achievable for the time being and efforts will have to focus on risk reduction. Abstinence remains the ultimate goal but efforts to bring it about in individual cases must not jeopardise any reduction in HIV risk behaviour which has already been achieved." (ACMD 1988)

This phenomenon reversed the abstinence-orientated prescribing policy of the preceding years as it legitimised longer-term opioid prescribing (OST) to enable users to stop injecting. As described above, the concept of "harm reduction" in the UK later developed to encompass other emerging potential injection-related health risks – such as Hepatitis C infection – but also to include more social outcomes such as attempts to reduce criminal activity or improve employability.

International opinion and OST

International debate continues regarding how society may balance the needs of illicit drug users and their families or communities with other national priorities or philosophies – especially with regard to the use of OST. Though a review of the research evidence base is contained in Chapter 3, in-depth analysis of the broader policy debate is beyond the scope of this thesis. A helpful summary is contained in the publication *Drug Policy and The Public Good* (Babor et al 2010). In the *Summary and Conclusions* chapter, a number of potential

mechanisms – including medical, social, criminal justice and legislative approaches – to address drug-related harm are summarized. They however specifically address the place of OST. Making the importance of OST as part of an effective drug policy clear, the authors state:

"We emphasise services for opiate dependent individuals because our review found that: 1. the services available for this population, especially OST, have the strongest supporting evidence; 2. opiate use poses a high risk of overdose death; and 3. injection drug use has in many societies produced an ensuing epidemic of AIDS and other infectious diseases. Services for opiate users therefore could have a relatively large effect on population indicators of drug-related harm." (Babor et al 2010)

Evidence-based clinical practice in the UK 1991-2007

Any discussion about recovery in the context of problematic substance use must be considered against considerable recent development in terms of evidence-based clinical practice in the UK. The UK has developed clinical guidance for medical and other staff since 1991, when the first "*Orange Guideline*" made it clear that methadone prescribing was appropriate as a harm reduction measure and outlined the best practice for delivery of replacement prescribing and detoxification treatments (Department of Health et al., 1991). This guideline saw many changes in services across the country – but also revealed inconsistencies from area to area. For example, in Scotland the services available in the two largest cities – only 40 miles apart - were completely different. Edinburgh, in the wake of their HIV epidemic, was developing comprehensive services incorporating specialist psychiatry services and GP-based OST services (Greenwood, 1990). In Glasgow however, GPs were unlikely to consider delivery of OST (Kidd & Ralston 1993).

The guidance for clinicians was updated in 1999 (Department of Health et al., 1999). That version reflected a much improved evidence base as treatment was evolving rapidly across the world and UK experience in the newly-developed services across the country was identifying the potential challenges around such services and offering practical solutions. Requirements that doctors delivered appropriate types of treatments which reflected their training and experience were emphasised, as were the implications should doctors not fulfil

their obligations to the drug using population. As the evidence base developed further a new guideline for clinicians appeared in 2007 (Department of Health et al., 2007). This is the current live guidance for clinicians in the UK.

2007 " Orange Guidelines"

The 2007 UK treatment guideline was the most comprehensive yet. It was produced by a diverse committee of clinicians (from a range of professions), as well as service users and treatment providers from a range of philosophies and backgrounds. Government officials and advisors were also involved in the process. Though in essence the guideline represents a report by an expert group, for the first time in the UK, the process of guideline development was supported by the commissioning of systematic reviews of the research evidence base. These were taken forward by the National Institute for Health and Clinical Excellence (NICE). NICE Guidelines and Technology Appraisals covering all the key medical and psychological interventions were considered by the guideline group (NICE, 2007a; 2007b; 2007c; 2007d). The group also took into account any live guidance or evidence bases in other associated areas of work, such as pain management and mental health dual diagnosis. In this environment of scrutiny, this was the first national treatment guideline to comprehensively address the evidence base for the effectiveness of psychosocial interventions for substance misusers. It was also timely that, at a time when medical care for drug users was under public scrutiny, the guideline emphasised the need for high levels of clinical governance and quality standards in this area of work.

England: NTA - Models of Care 2002-6

Paradoxically, at the same time as it was being criticised for failing to deliver recovery, the NTA had been developing high quality guidance for commissioners, services and staff to improve delivery of a more person-centred approach to care in England. First published in 2002 - but continuously evolving - the *"Models of Care"* guidance had the potential to address some of the concerns, voiced by service users, that all roads led to methadone. Instead, the guidance required services to fully and holistically assess need and help service users to access the interventions they required (NTA, 2006). Advice about improved care planning ensured that staff would regularly review a person's progress against their agreed goals and created an environment in which commissioners were required to ensure a full

range of options was available in their area. The NTA commissions treatment services for substance misuse across England and holds services to account against tight standards regarding access to services. At the same time, they have developed validated, useful clinical tools which can be used to assess improvement - even in those for whom abstinence is a challenge. They have also published additional reports which signpost how future service delivery may be improved in the UK.

Example (England) - NTA – outcomes for those leaving services 2010

In 2010, the NTA produced a report based on follow up data relating to nearly 50, 000 cases in treatment in England (NTA, 2010). This report had used novel methods to follow up people in treatment. The NTA had required treatment providers across England to supply reports using a common format – thus allowing the NTA to collate the data collected from many diverse agencies. The system (NDTMS – the National Drug Treatment Monitoring System) could then supply key data on follow-up over many years. In this study, the NTA had linked these clinical data to criminal justice data in central data systems as well as testing/screening data in the Drug Test Records allowing them to identify where people re-entered either a treatment or justice system after discharge. The 2010 report contains data on two cohorts discharged in 2005/6 and 2006/7.

In 2005/6, they found that they could include 41,475 cases who had been discharged. Of these, 3353 had been discharged having completed a programme as drug free; 6417 had completed a programme but were not drug free. The vast majority - 31,705 - had an unplanned discharge. In the next 4 years, however, 19,047 (46%) did not return to either treatment or the criminal justice system while some 22,428 (54%) did return. Of those who did, 11, 641 (52%) had returned via a treatment route while 10,787 (48%) returned via a criminal justice route. Of the criminal justice cases, 7,025 (65%) had re-entered treatment as part of this contact. The report concluded that the nature of discharge (planned/unplanned) seemed to be less important than may have been expected. In 2006/7, 43,893 cases were included in a repeat of this analysis.

As well as giving indications of the outcome of treatment over time, these reports hint at mechanisms which could be used to manage clinical information across the treatment

system, using routine clinical data, to more comprehensively assess outcomes and the effectiveness of treatment interventions.

UK 2010: A new government and a new strategy

In 2010, a new UK government was elected – a Conservative/Liberal Democrat coalition. The previous Labour government had been in power for over 12 years and had inherited the harm reduction approaches put in place by the previous Conservative government in face of the HIV epidemic in the 1980s. This approach had been strongly supported across the political divide with high levels of investment from consecutive governments seeing huge developments in the field in England and Wales. This new coalition government quickly brought forward a new national strategy *Reducing Demand, Restricting Supply, Supporting Recovery* (Home Office, 2010). In the context of a government focused on dealing with austerity by cutting public spending, this strategy emphasised the enforcement aspect of drugs strategy as well as the potential of returning recovering drug users to productive work. Regarding treatment there was more bullish language regarding recovery. The strategy was the first in the UK for nearly 20 years to play down the harm reduction aspect of treatment. It stated: *"instead of focusing primarily on reducing the harms caused by drug misuse, our approach will be to go much further and offer every support for people to choose recovery as an achievable way out of dependency."*

The strategy made it clear that there was to be a stronger emphasis on more people progressing from treatment with OST, stating: *"Our ultimate goal is to enable individuals to become free from their dependence; something we know is the aim of the vast majority of people entering drug treatment. Supporting people to live a drug-free life is at the heart of our recovery ambition."*

However, there does seem to be some acknowledgement that OST is a strong component of the system, stating: *"Substitute prescribing continues to have a role to play in the treatment of heroin dependence, both in stabilising drug use and supporting detoxification. Medically-assisted recovery can, and does, happen. There are many thousands of people in receipt of such prescriptions in our communities today who have jobs, positive family lives and are no longer taking illegal drugs or committing crime."*

"Recovery Orientated Drug Treatment"

In this setting the NTA was asked to set up a new expert group to bring forward advice on the delivery of a more recovery-orientated approach to treatment. This work was published in the summer of 2012 (NTA, 2012). The task of this group was: *"to describe how to meet the ambition of the Drug Strategy 2010 to help more heroin users to recover and break free of dependence".*

Acknowledging the progress made in the previous 10 years, the report also recognised that this report was timely. It stated: *"Previous drug strategies focused on reducing crime and drug-related harm to public health, where the benefit to society accrued from people being retained in treatment programmes as much from completing them. However, this allowed a culture of commissioning and practice to develop that gave insufficient priority to an individual's desire to overcome his or her drug or alcohol dependence."*

The report emphasised those significant harm reduction achievements of previous strategies, including the achievement of less drug deaths and BBV infections than many neighbouring countries. However, the report intended to *"ally safe, evidence-based recovery-orientated practice to the public health and wider social benefits we already accrue from treatment."* It went on to describe how this could be achieved – emphasising the need for quality assurance of OST treatments to ensure consistent high quality prescribing; introducing the need to build *"recovery capital";* delivering individualised, tailored care programmes based on individual need; using the techniques of *"phasing and layering"* of interventions – essentially delivering the most relevant interventions at the correct time as part of an individual's recovery plan.

So through considerable investment in a central governance structure, delivered by the NTA, English services had seen improvements in performance – but crucially had also started to produce detailed information on outcomes. The emphasis was now on improving the quality of service delivery to improve the likelihood of substance misusers progressing through treatment towards re-integration and recovery.

Scotland: development of "The Road to Recovery"

While the English system of care was evolving as described above, Scotland was also responding to the drivers of concerns over Blood Borne Virus spread and the criminal justice pressures relating to substance misuse. Devolution of powers to the newly formed Scottish Parliament in 1998 brought direct control for much of drug policy to Scotland.

A brief history of strategy in Scotland

Scotland's strategic drive to managing substance misuse began with the HIV epidemic of the 1980s. Prior to this, there were clear parallels with the UK in terms of how services were arranged and delivered. The McLelland Committee report (SHHD, 1986) had introduced the expectation that harm reduction interventions would be made available in Scotland. However, the subsequent development of services was patchy across even those areas in which injecting drug use was rife.

In 1994, a Task Force report formed the basis of the first national strategic approach to drug use in Scotland (Drugs in Scotland. Meeting the Challenge, 1994). Under a Conservative Secretary of State, the Task Force report strongly reiterated the prominence of harm reduction in general and opiate replacement therapy in particular in the Scottish response. It required the creation of local Drug Action Teams – partnership groups involving senior accountable public officers, with responsibility to address local need – with the aim of improving consistency of delivery across the country. The report also launched an advisory committee for ministers – the Scottish Advisory Committee on Drug Misuse (SACDM). SACDM aimed to ensure and policy development was supported by up to date expert opinion. There was little new funding to support developments however, and at a time when the public sector in Scotland saw little growth, there was minimal coordinated improvement nationally.

The Labour party took power in the UK government in 1997 and quickly moved to introduce a Scottish Parliament (Crown Office, 1998). Drug misuse was placed in the Justice Department and the first Scottish "drugs minister" – Angus Mackay, Deputy Justice Minister - successfully argued for a huge investment to improve services to address drug problems in

Scotland. In 1999, “Mackay’s Millions” – a total new investment of £100m - was announced alongside a new Scottish Strategy – *Tackling Drugs in Scotland - Action in Partnership* (Scottish Executive, 1999). This strategy was closely aligned with the UK strategy and essentially aimed to sharpen up local accountability, reflected in the new administration. However, it made no moves to change the harm reduction ethos of treatment services. The considerable financial investment had a huge impact on Scottish services for substance misuse. Year on year increases in available spending saw massively increased service capacity and activity until 2010.

SACDM Methadone Review 2007

In 2007, in response to the methadone-related death of a child, the Labour first minister, Jack McConnell, announced a review of the use of methadone in Scotland. The Scottish Advisory Committee on Drug Misuse (SACDM) convened a process involving three elements: a survey of service users' views of their methadone treatment; a query to all NHS Boards in Scotland regarding numbers in treatment, outcomes achieved and governance of practice; an expert review group to assess these findings as well as the international evidence and to produce a report for ministers. The review was published in 2007 (SACDM Methadone Project Group, 2007). It found that few NHS Boards could be clear how many people were in treatment nor had any real means of demonstrating how effective their programmes were. Service users mainly reported that they found access to methadone treatment helpful - but were concerned about a lack of choice in terms of treatment options – either to allow progress from prescribed methadone or to give access to detoxification. The expert group, citing the 2007 National Treatment Guideline and associated NICE reviews, re-iterated the place for methadone in treatment. It also made clear that inconsistency of delivery and quality issues needed to be addressed to ensure optimal care was being offered in Scotland. The methadone review was delivered to the new minority SNP administration [following Scottish elections in 2007] and its findings were welcomed by ministers.

The document points towards an improved mechanism for the delivery of care in which the service user’s need is central but it also acknowledges that a high proportion of Scottish treatment seeking substance misusers are opioid/opiate dependent and, for them, substitute prescribing remains the treatment of choice. It stated: *“...replacement*

prescribing with methadone remains the main plank of medical treatment for opiate dependency…The challenge with methadone is to optimize delivery of harm reduction whilst ensuring that progress to recovery is encouraged, facilitating a way out of methadone treatment whenever appropriate."

Recognising that the report had brought an opportunity to refresh the approach to substance misuse in Scotland, SACDM then requested a further review, which would consider more broadly the full range of treatment elements required to improve the prospects of recovery for substance misusers in Scotland. This next report would aim to put replacement prescribing into the context of a person with a holistic range of needs.

Essential Care 2008

The result was *Essential Care* (SACDM, 2008). This was published in 2008 as the product of a large multi-disciplinary and multi-agency expert group. The report echoed a number of international guidance documents in the substance use field - but also considered learning from other areas facing similar challenges in effecting change - such as the mental health recovery field. The report had a number of key messages. It expected that all substance misusers should be able to access a full range of evidence-based interventions. These should be consistent across the country but would be locally commissioned. Availability of services supporting a continuum of care was essential, with improved processes of service commissioning, effective performance-management improving delivery and an expectation that a full range of specialist services should be available in every locality. The role of more generic services – such as mental health services, pain services and social work - in addressing the needs of substance users was also emphasized. The Executive Summary of the document stated: *"Substance users have the right to the same quality of care as the rest of us."*

The Road to Recovery – 2008 Achieving political consensus

The Scottish Government published its new strategy to address problematic substance use in 2008 (Scottish Government, 2008). At this time, the SNP had formed a minority government. Yet, in this period where polarization around the philosophy of drug treatment

was the norm, the SNP administration successfully took their strategy through the Scottish Parliament - it was accepted unanimously - suggesting the pragmatic approach it contained was acceptable to a broad range of political opinions. This achievement was a striking contrast with the sense of political struggle in England. The document used the new language of *recovery* but clearly rejected the view that this was a move away from support for harm reduction. To make this point they quoted the United Nations Office on Drugs and Crime:

> *"Harm reduction has often been made an unnecessarily controversial issue, as if there were a contradiction between treatment and prevention on the one hand and reducing the adverse health and social consequences of drug use on the other. This is a false dichotomy. They are complementary."* (UNODC, 2008)

What was new about the strategy was a practical approach to addressing the apparent lack of availability of treatment, the sense of a reduced range of options (medical, psychological and social) available for users and the concern about people being *'parked'* on methadone without any attempt to better engage these people in approaches which could improve their prospects. There was an expectation that service users should be encouraged to engage in their own recovery, based on their own needs and strengths. Services needed to become more aspirational for their patients. Asserting the need for a more personalized approach to care, the strategy stated:

> "*In practice recovery will mean different things at different times to each individual… [It]... might mean developing the skills to prevent relapse…rebuilding broken relationships... Milestones may be as simple as gaining weight... or building self-esteem. What is key is that recovery is sustained*."

The treatment strategy was based on the key Scottish documents described above, which aligned Scottish practice with the national and international evidence base. At this point, Scottish strategy was seen as leading the move towards improving the prospects of delivering real recovery to more people in treatment while deftly balancing the harm-reduction needs of many accessing treatment.

Delivering Outcomes – Scottish Delivery Reform 2009

So often, Government Strategies are published and expectations run high - before faltering as the next political wave pulls the attention of officials towards another initiative. The publication of *The Road to Recovery* however, heralded the initiation of a major process of reform in the way services would be coordinated and delivered. A 'Delivery Reform Group' - comprising members of key Advisory Committees - embarked on a redesign of delivery arrangements, culminating in the publication of the new *Framework for Delivery* report (Scottish Government, 2009). This document was endorsed by the NHS Scotland Executive and Health Minister, Drugs Minister (Deputy Justice Minister) and Confederation of Scottish Local Authorities (COSLA). In tandem, the national audit office - Audit Scotland - published a critique of the effectiveness of the local Drug and Alcohol Action Teams (DAATs), highlighting their inconsistencies and recommending improved local commissioning based on needs assessment. In response, a new arrangement - requiring DAATs to be transformed into Alcohol and Drug Partnerships (ADPs) was required by October 2009 (Audit Scotland, 2009). Reporting of performance was to be aligned with generic performance management systems for the first time. Previously, DAATs had reported separately to government officials on specific areas of performance, relating specifically to the use of ring-fenced resources, earmarked by central government for local use. The new system acknowledged that action to address substance misuse was unlikely to be effective if not closely linked to broader local strategies to address areas such as social exclusion and health inequalities. Consequently, the new arrangements placed ADPs inside local Community Planning Partnerships, with the NHS partner becoming subject to new "HEAT" targets on access to services (NHS Scotland's performance management tool) and local authorities required to report on delivery of local outcomes as part of their new "Single Outcome Agreements". The Government had also made available a *Substance Misuse Outcomes Toolkit* to aid local outcome development (SACDM, 2009). This would allow performance in the area of substance use to be seen alongside performance in more mainstream areas of the local plan. This major development aimed to ensure that such areas as housing, education and broader community services would participate more vigorously in the response to problem substance use.

New financial resources to support improvements continued to increase significantly in Scotland for the years 2008/9 and 2009/10 to support the proposed changes. Meantime the Government reviewed all governance structures to ensure they were fit for purpose (increasing potential to release funds to improve care). A number of specific national initiatives were also launched. They created a specialist "support function" – employing experienced substance misuse staff to work as national delivery officers- to help local ADPs to deliver on their new agenda. National voluntary sector providers were funded to deliver and develop a Scottish Drugs Recovery Consortium which aimed to increase the profile of the recovery movement and, through working with local systems of care, improve recovery opportunities for substance misusers across Scotland. Finally, in a bold change, signalling a desire to see government policy scrutinized objectively, the Scottish Government announced the creation of an independent Scottish Drug Strategy Delivery Commission (DSDC). This body would replace SACDM and hold the Government to account on its own strategic delivery. DSDC would set its own agenda – reflecting priorities contained within the 59 objectives in the Road to Recovery strategy.

The DSDC published its first report in 2011 (Scottish Drug Strategy Delivery Commission 2011) and has engaged government in a process aimed at improving performance in key priority areas such as child protection, effective prevention activity and the criminal justice response to the new "legal highs". Regarding recovery, this report acknowledged that the aspirations contained in the Road to Recovery were proving slow to be realised. The DSDC gave clear recommendations to the Scottish Government to improve prospects for those in treatment for substance misuse. These included the need to develop better information systems to report on activity, performance and outcomes (DSDC 2011). At this stage, the Scottish strategic process had appeared objectively to be progressing well and though there was a delay in delivering adequate information on recovery, the SNP Government was supported by a strong cross-party consensus in the Scottish Parliament.

Re-politicization of the Scottish debate 2012 – coming full circle

In the late summer of 2012 the Registrar General's office published its annual report on drug deaths in Scotland for the year 2011 (General Register Office for Scotland [GROS], 2012). Drug deaths had been increasing steadily in Scotland for many years and in 2011

deaths increased by 20% from the previous year to a total of 584. Crucially, GROS reported that heroin and/or morphine were implicated in, or potentially contributed to, 206 (35%) of the deaths while methadone was implicated in, or potentially contributed to, 275 (47%) of the deaths. For the first time, methadone (*the treatment*) was associated with more deaths than heroin (*the problem)*.

There was an immediate political and media backlash. Having initially reported the drug deaths figures objectively, a number of media outlets, led by the *Daily Record* newspaper reported a coordinated series of strong anti-methadone stories. They stated that: *"State prescribed heroin substitute is not the answer. Drug and drink related deaths reach record levels*" - emphasising that methadone had contributed to more deaths than heroin (*Daily Record* 18th August, 2012). This quickly moved into a confrontational position and was reporting negatively on many aspects of methadone prescribing. Focusing on the profits made by community pharmacies, the *Daily Record* stated: *"Revealed: £36million bill to provide methadone to drug users. Chemists across Scotland are raking in tens of thousands of pounds of taxpayers' money to dish out the heroin substitute to addicts."* (Ferguson, 2012, 12th August).

Within a month this stance had developed into the clearly stated view that the Scottish drug strategy was failing. At this stage, opposition politicians were also being quoted as having concerns. In September 2012, efforts in the Scottish press to portray methadone treatments negatively included citing examples of tragedies from England. For example, on 5thSeptember the Daily Record reported on a toddler's death in Bristol (*Daily Record* 050912). They were soon able to report a rift in the national political consensus. On 10th September, the Daily Record stated: *"Majority of MSPs believe Scotland is losing the war on drugs. A study has revealed 60per cent of MSPs believe the current approach is ineffective in tackling drug misuse. Only 35per cent think it is working"* (*Daily Record* 100912). This piece cited a report based on a survey of 55 MSPs which had been carried out by the UK Drug Policy Commission prior to the publication of the Scottish Drug death statistics. The UKDPC had published its report on 9th September (UKDPC, 2012). The report had stated that: three in five (60%) MSPs felt that Scotland's current policies were not effective in tackling the problems caused by illicit drugs; more than two thirds (70%) of MSPs said that drug policy

did not make enough use of evidence and research, and a similar majority (68%) agreed that Scotland should have more powers over policy about drugs. The UKDPC report and associated media coverage heralded a new period of political unrest regarding the direction of drug strategy in Scotland. MSPs from the main opposition parties began a concerted effort to gather information from Government sources and NHS Boards regarding activity and outcomes in the treatment of substance misuse. The situation worsened as it became clear that the Government still struggled to supply valid information regarding activity and outcomes. The media campaign also continued and by October, the BBC was reporting *"Political unity 'broken' on Scotland's drugs policy"* (BBC 31/10/12).

This pressure on government was effective. In October 2012 the current Minister for Community Safety and Legal Affairs, Ms Rosanna Cunningham, announced that she was to ask the Chief Medical Officer for Scotland to commission a review of the use of methadone in Scotland (Scottish Government News Release 051012). The Minister seemed to continue to support methadone replacement therapy when she stated:

"Prescribed drug treatment has saved many thousands of lives in Scotland. It is the responsibility of the professionals to determine the most appropriate treatment for each person seeking medical help with addiction problems".

News reports were less balanced, however (Figure 3). The Daily Record reported that:

"Scottish Government order review of £36m methadone programme thanks to Daily Record campaign. An independent expert panel will review the use of the controversial heroin substitute after a Record campaign revealed how addicts were left stuck on methadone for more than 30 years" (*Daily Record* 051012).

Figure 3. Screenshot of Daily Record online article 051012

Scottish Government order review of £36m methadone programme thanks to Daily Record campaign

AN independent expert panel will review the use of the controversial heroin substitute after a Record campaign revealed how addicts were left stuck on methadone for more than 30 years

Methadone

THE Government have ordered a top level review of Scotland's scandalous £36million methadone programme, thanks to the Daily Record. An independent expert panel led by Chief Medical Officer Sir Harry Burns will probe the use of the controversial heroin substitute.

The BBC was more balanced in its coverage, stating:

"Ministers have ordered a review of the way heroin addicts are treated. It will gather evidence on substitute drugs such as methadone, and is part of the Scottish government's national drugs strategy. It emphasises recovery from addiction - rather than the previous policy allowing addicts to use alternatives to heroin to stabilise their lives. It is hoped the review will help doctors offer a full range of treatments, including methadone. Since the

1980s, methadone has been at the heart of the drug treatment strategies of successive governments" (Alderson, 2012 October 5th)**.**

In an attempt to clarify the concerns and to restore consensus in parliament, a parliamentary debate took place in November 2012. (Scottish Parliamentary debate 081112). This debate showed that the previous consensus regarding the facts around harm reduction and recovery was, in fact, largely intact. One political party – Scottish Labour - was an isolated critic of the current government approach but was already reducing the inflammatory and stigmatizing language it had used over the previous months. The proposed methadone review was already underway and was welcomed by the political majority. The following day the Daily Record reported:

"Daily Record's methadone campaign tops the agenda at Holyrood. Taxpayers are being hit for more than £36m a year - with no record of whether it is working or not" (*Daily Record* 091112).

The second report in the same day stated:
"The methadone problem is causing huge devastation but we must look at it in a rational manner. Millions of pounds of public money are spent administering methadone to more than 22,000 drug abusers across Scotland. There are currently no accurate statistics to tell us what success – or not – the programme is having. No one knows how many addicts are helped to kick heroin. But we do know methadone contributed to 275 of the 584 drug deaths in Scotland last year – more than heroin itself."

Further example screen shots of the online media coverage of this debate are contained in Appendix 8.

Lessons learned - the place of evidence

The socio-political debates around substance misuse and the focus of drug strategies have repeatedly shown themselves to be relatively immune to what evidence and scientific study does exist. Regarding policy, the recent UKDPC report *A Fresh Approach to Drugs* (UKDPC

2012) cites repeated UK government reports over a long period, highlighting a lack of availability of evidence across the drugs field (House of Commons Science and Technology Committee, 2006; Wagstaff & Maynard, 1988). In Scotland repeated reports on [for example] drug deaths (Zador et al, 2005), methadone effectiveness (SACDM, 2007) and the delivery of services more conducive to recovery (DSDC, 2011) have recommended that the Scottish Government should support research and evaluation using improved information systems. The DSDC report specifically highlighted for ministers and officials the risks of not having this information available. It was in this hiatus that the most recent political attack on evidence-based treatments has occurred, bringing the place of OST into question.

Even if evidence is available, governments may find it difficult to respond to advice which, though evidence-based, is felt to be unsavoury politically. This issue was demonstrated clearly during the public disagreement between the Chairman of the Advisory Council on the Misuse of Drugs (ACMD) and the (then) Home Secretary over drug classification. Ultimately the Chairman, a leading academic in the field of addictions research, was relieved of his position and accused ministers of *"devaluing and distorting the scientific evidence over illicit drugs by their decision last year to reclassify cannabis from class C to class B against the advice of the ACMD"* (Travis, 2009 30th October). But there are more worrying consequences. After the 2010 General Election, the new Coalition government brought forward proposals to amend legislation which had previously required them to seek scientific advice when developing drugs policy (Jha, 2010 5th December).

This problem regarding the balance of evidence and policy, could however be readily resolved. The UKDPC report gives a valid framework which, if applied, would facilitate a more objective approach to drug policy generally in the UK. The authors state: *"To make progress on tackling the problems associated with illicit drug use, we need a new and more mature relationship with evidence".* They identify 5 areas where they feel improvements are necessary. These are:

- Willingness to be guided by evidence – requires avoidance of "cherry picking" evidence to avoid difficult political issues
- Recognition of different forms of evidence – requires policy makers to be able to distinguish between better and poorer quality evidence

- Clarity on objectives – this requires those considering evidence to be aware of the specific objectives an intervention is aiming to deliver on
- Overcoming the desire for trials to deliver positive results – this reflects the political sensitivity of trials or pilot projects. these can be seen as the first wave of government policy and if they "fail" can be seen as a negative outcome.
- Awareness of alternative policies – this reflects the need for governments to be aware of opportunity costs and to be prepared to invest in what they know while researching what they don't.

This statement is moot. A first expectation is that policy-makers are prepared to agree on the quality of the evidence base – including its strengths and weaknesses. The second is that they have an understanding of what this evidence base is relaying. The third is to encourage a culture of objectivity. However, it is equally important that the academic and clinical establishment are able to acknowledge when the evidence base is less compelling and, in such circumstances, should promote the development of an improved evidence base, open to objective scrutiny and debate, which ensures the treatments available are those most likely to deliver the best outcomes.

In Conclusion

This introductory chapter has set this thesis in context. In particular, it has made the following points:

- The use of psychoactive substances is a common activity since pre-history
- Substance misuse has been known to be hazardous for centuries but has evolved into a major international public health challenge in the 20th Century
- International consensus is in place, supported by international institutions, regarding the treatment approaches most likely to reduce the harms associated with opioid misuse. Opioid Substitution Therapy (OST) is a key element of this approach and methadone, a synthetic opioid developed in the 1930s, has been shown to be a highly effective substitute drug since the late 1960s
- Over 20 years, the UK has developed evidence-based treatment guidance and created standards of care, reflecting the international evidence base
- The purpose of treatment of substance misuse in the UK has evolved considerably over the last 25 years as the evidence base has developed. From the 1980s, consecutive governments of all political types have supported the broad thrust of *harm reduction.* Now, there is a drive to better facilitate progress towards *recovery*.
- Politically, the UK is becoming more diverse as legislative power and governance is devolved to local administrations, more accountable to their own populations. Local area developments bring variation.
- Alongside this devolution, local expert groups have produced advice for successive governments regarding how the evidence base can best support their aspirations. As these political systems diversify further, local data will be essential to inform locally relevant developments.
- Valid, high quality information is essential if outcomes are to improve. This includes information on activity and process, evaluation of service effectiveness and hypothesis-driven research. The evidence available must be evaluated objectively with policy makers capable of determining when evidence is robust or not. The recent UKDPC framework gives a helpful guide on the issues to be addressed if evidence is to positively influence treatment effectiveness.

Chapter 2. The Key Longitudinal Studies

> Things do not change; we change.
>
> *Henry David Thoreau (1817 - 1862)*

> For one swallow does not make a summer, nor does one day; and so too one day, or a short time, does not make a man blessed and happy
>
> *Aristotle (384-322 BC)*

> Hardly had the glow been kindled by some good deed on your part or by some little triumph over your rivals or by a word of praise from your parents or mentors when it would begin to cool and fade leaving you in a very short time as chill and dim as before.
>
> *Samuel Beckett (1906–1989)*

Introduction

Substance misuse is a chronic relapsing condition and achieving long-term recovery requires people to make major changes in their lifestyles, behaviours and relationships (McLellan, Lewis, O'Brien & Kleber, 2000). As in any behavioural change, this process is cyclical and involves periods of contemplation/preparation, action and relapse. Recovery may be influenced by biological, psychological and social factors and the recovery cycle may be repeated for many years – even for a lifetime (Koob & Volkow 2010). For some, it has been suggested that this process can be spontaneous and may not require additional support from services (Best et al, 2010). There is however, clearly a view, supported by the evidence base, that for many, making effective care and treatment available can influence the outcome, reducing drug-related harms and facilitating recovery (Vielleux et al, 2010).

If we are to understand the factors which may be important in promoting success, it is essential that treatment programmes are evaluated in a meaningful way. One key aspect of the research required to demonstrate recovery will be that it is longitudinal and follows up subjects over a sufficient time period – often for many years. As the treatment of substance misuse has evolved from the late 1960s, national programmes of research around the world have attempted to inform the development of effective treatment approaches through prospective longitudinal studies which have followed, sometimes very large cohorts of treatment – seeking substance misusers, over long periods in the UK, USA, and Australia.

Longitudinal studies

Types of study

Longitudinal studies can help understanding of the natural history of any chronic relapsing condition. This approach also has the potential to bring improved insights into the potential long term risks and benefits of treatments for these chronic diseases. The studies can be of two types.

- A prospective study identifies the subjects at the beginning of the research process, before treatment is initiated and then follows them up over time, with changes observed over this time period. Often hypotheses are in place to be tested, using valid scientific methods.
- A retrospective study identifies subjects at a later stage and retrospectively assesses factors or processes which may have influenced an observed outcome.

There are clearly, however, potential problems in longitudinal studies - issues of Internal validity (reflecting methodological challenges) and issues of external validity (reflecting challenges of interpretation of any findings).

Internal validity

Prospective studies - Key methodological challenges with these studies include selection bias, issues regarding comparisons – comparing different clinical groups - and the length of the study required to be able to determine meaningful outcomes (especially in chronic conditions). This final issue becomes more relevant in relapsing conditions as any observation at one time point (for example abstinence) may be followed by a significant change (relapse). The research method applied may mean such changes are not identified or measured accurately.

Retrospective studies - Retrospective studies bring additional issues which can raise questions regarding the quality of the research and challenge its findings. Often, the data collected in retrospective studies were not collected for the study purpose, or the mechanism of collection did not take a future research project into account. This can mean that studies are hampered by missing data. There can also be the challenges of "recall bias"

– if subjects are being interviewed about aspects of their past history or bias regarding the interpretation of the information supplied.

External validity

The interpretation of findings must recognise that the research should be relevant to a particular population or environment to be a valuable evidence base which can inform practice. Studies carried out at different times, using particular subjects in different cultures, systems or environments will mean that findings are not necessarily generalizable to the population of interest and they should therefore be interpreted with caution. For example, in the substance misuse field, studies of male ex-servicemen in the 1970s in the federally-controlled substance misuse systems of the USA, will have limited relevance to the management of a modern GP-based UK shared-care scheme, supported by a small local voluntary sector provider.

There are additional challenges when we try to interpret the findings of these studies. What definitions are chosen and the means of measuring the key factors or outcomes may bias the results. For example, in substance misuse, clarity regarding the drugs being used or assessing the extent of any addiction or dependence may not be straightforward. Reported drug use may not be reflected in objective assessments. Self-reports of avoidance of injecting behaviour or risk may be challenged by presence of active injection sites on physical examination. Reported abstinence from benzodiazepines may be challenged by positive drug screens. This is well illustrated by the fact that different researchers and studies have tackled one of the few apparent absolutes in this field – abstinence–differently. Studies have measured abstinence through direct objective assessment through urine testing (Hser, Hoffman, Grella & Anglin, 2001); some have used more indirect measures of the supposed consequences of drug use (Haastrkup & Jepsen, 1988) or have recorded subjects' self-report of drug use/abstinence (Simpson, 1981). These differing dependent variables mean that comparison is impossible between studies. This issue has been regularly identified in a number of recent Cochrane reviews of substance misuse treatments and will be discussed further in Chapter 3.

The studies

This chapter will focus in some detail on the three large UK prospective studies of recent years. This section will consider the National Treatment Outcome Research Study (NTORS), Drug Treatment Outcomes Research Study (DTORS) and Drug Outcomes Research in Scotland (DORIS) studies. The second section will very briefly summarize the main findings of the large prospective studies carried out in the USA and Australia – the Drug Abuse Treatment Outcome Study (DATOS) and the Australian Treatment Outcome Study (ATOS). It is also valuable to consider earlier work from the USA which preceded the DATOS study and informed early quality improvement in the field of opiate replacement therapy such as the Drug Abuse Reporting Programme - DARP (1969-73) and Treatment Outcome Prospective Study - TOPS (1979-81). The chapter will describe the main findings of these key longitudinal studies and consider how their findings may inform the current thesis. The studies are summarized in Tables 1 and 2.

As well as these studies, there have been a number of additional cohorts described of treatment – seeking, opiate dependent subjects in the UK and across the world in the last 40 years. Some (e.g. Stimson & Oppenheimer, 1982) describe the treatment of substance users prior to the modern development of harm-reduction concepts and, though of considerable historic interest, offer little to the development of current clinical practice. Others (e.g. Hser et al, 2001) are cited elsewhere in the thesis as they have comprehensively observed the course of substance users' careers over decades and informed the development of more focused prospective studies and RCTs considering the relative merits of specific interventions or treatment approaches.

One aspect of the current study was to test the concept of using standard clinical data to objectively assess outcomes over time as well as the potential predictive value of those characteristics commonly assessed by clinicians. The cohort studies chosen in this review were selected as they aimed to address similar issues, in modern clinical settings and with specific consideration of OST with methadone.

Table 1. Longitudinal Studies - UK

Study	Country	Dates & duration	Notes
The National Treatment Outcome Research Study – NTORS	**UK (England)**	**1996-2001** **5 year follow up**	Prospective Longitudinal cohort study of 1075 subjects inducted from 54 services in 4 treatment modalities: • specialist in-patient treatment • residential rehabilitation programmes • community-based methadone maintenance • methadone reduction/detox programmes *Data collected:* at intake; 6/12; one year and at 2-3 years and 4-5 years after intake. 763 reviewed at 1yr. 496 at 5 years. **Conclusions:** "Treatment works". Showed improvements in terms of reduced drug use and crime, increased abstinence, and health. 1year improvements were maintained at 5 years. Time in treatment was an important positive factor. Concern regarding poor outcomes on alcohol and stimulants.
The Drug Treatment Outcomes Research Study -DTORS	**UK (England)**	**2009** **13 month follow up**	Prospective longitudinal study of 1796 subjects from 342 agencies across England. Type of agencies not defined – but in line with NTA "menu" of treatment options. Also qualitative study and cost-effectiveness element *Data collected* : intake, 3-5/12 (1131 cases) & 11-13/12 (504) **Assessment is essentially of process and <u>not</u> outcome** **Conclusions:** Despite increased demand and changes in drug use patterns since NTORS, services still effective and reducing harms, improving health and wellbeing. Services responsive and patients satisfied. Cost effectiveness high.
Drug Outcomes Research in Scotland - DORIS	**UK (Scotland)**	**2001-2004** **33 month follow up**	Prospective longitudinal study of 1033 subjects in a range of treatments (including prison). These were: • Opiate replacement • Other replacement • Counselling/non-medical • residential rehabilitation • detoxification *Data collected* : at baseline (MAP), 8, 16 and 33 months Also qualitative element to the study **Conclusions:** Mainly focussed on achievement of abstinence and not harm reduction. Concluded Scottish services poorer than English (NTORS) at achieving abstinence.

Table 2. Longitudinal Studies – USA and Australia

Study	Country	Dates & duration	Notes
Drug Abuse Reporting Programme - DARP	**USA**	**1969-1972** **(select data <1981)** **12 year follow up for some elements** **Mean 6yr follow up of over 6000 cases**	Prospective Longitudinal Cohort Study of 43,943 subjects from 52 agencies in 4 modalities (+controls): methadone maintenance; therapeutic communities; out-patient drug – free; out-patient detoxification Data collected at intake and then 2 monthly **Conclusions:** Demographic and sociological characteristics only limited importance. Length of time in treatment and behaviour in treatment most important
Treatment Outcome Prospective Study - TOPS	**USA**	**1979-1981** **Maximum** **5 years follow up for some elements – up to 4270 cases**	Prospective longitudinal study of 11,759 subjects from 41 services (10 cities) in 4 treatment groups: methadone maintenance; detoxification; residential care; op drug-free. Subjects interviewed: intake & 1, 3, 6, 9 and 12 months. After leaving treatment, follow-up at 3/12, 1,2 & 3-5years. **Conclusions:** Drug abuse treatment reduces illicit drug use and criminal activity. Time in treatment important factor
Drug Abuse Treatment Outcome Study - DATOS	**USA**	**1991-1993** **3 month follow up & 12 month s follow up post discharge** **5 year follow up of 2966 cases**	Prospective longitudinal study of 10,010 subjects from 96 services in 4 treatment groups: methadone maintenance; residential long term; residential short term; out-patient drug-free. Data collected: 1 & 3/12 in treatment and 1yr post treatment **Conclusions:** Drug use reduced >50% in all groups with methadone treatment affecting opiate use most. Retention and aspects of engagement (influenced by service characteristics) also affected outcomes
The Australian Treatment Outcome Study - ATOS	**Australia**	**2003-2006** **3 & 12 month follow up with a 3 year follow up for one sample (NSW)**	Prospective longitudinal study of ~615 new patients – 535 entering 3 treatment types: methadone maintenance - 201 cases; detoxification – 201 cases; residential settings – 133 cases Data collected: 3 & 12/12 (and 24 & 36/12 for NSW sample) **Conclusions:** Drug use associated risks and crime reduced across all modalities at 3 months and was maintained to 3 years. Time in treatment positively affected outcome except in detoxification. Depression negatively affected outcome.

National Treatment Outcome Research Study (NTORS) – UK (England) 1996-2001

NTORS was the first major prospective study in the UK and is clearly relevant today. It must be recognised that the study commenced at a time when recovery was not a priority for services – harm reduction was seen as the clear goal and national strategies across the UK were focussed on increasing capacity of harm reduction services – in particular Opioid Substitution Therapy using methadone (OST-M). The 1999 National Treatment Guideline was still 3 years from publication and service development was at an early stage, with large inconsistencies in service delivery across the UK.

NTORS was a UK government (Department of Health) funded national prospective study which followed from and was modelled on, prospective studies in the USA that in the 1980s and 90s had demonstrated the impact of a range of treatments on outcomes in substance use. NTORS recruited 1075 subjects who were at the point of entering 54 different drug treatment programmes across England. The study recognised the difficulties in terms of generalising US research in the UK – citing potential differences in terms of UK substance users as well as the variation in treatment modalities available in different localities. The research design was a prospective, longitudinal cohort study of new self-selecting treatment-seeking subjects recruited as they entered four different residential or community-based treatment modalities across the UK. These modalities were: specialist in-patient treatment; residential rehabilitation programmes; community-based methadone maintenance and methadone reduction (detoxification) programmes. The modalities were chosen to best represent the modes of treatment delivery commonly available across the UK. There were no controls. The study was described as *naturalistic* with causal relationships inferred through measurement of key variables in the different treatment modalities at different points through the treatment journey. Data were collected at intake to the study, six months, one year then subsequently at 2-3 years and 4-5 years after intake.

Purpose of NTORS

The study aimed to address a very wide range of questions, including: describing the characteristics of those entering treatment; types and severity of problems experienced by subjects; changes in substance use problems in treatment; any changes in other drug-

related problems; were these changes maintained over time; relationships between the characteristics of substance misusers and the outcomes they achieved in treatment; describing the main components of treatment programmes; assessing relationship between treatment structure and process and outcome achieved?

Recruitment

Some 54 services were recruited to the study, comprising 8 in-patient units; 15 residential rehabilitation facilities; 16 methadone maintenance services and 15 methadone reduction/detoxification services. The study recruited subjects based on set criteria. These were: this was a new treatment episode; the subject had a primary drug problem (not alcohol); they had a UK contact address; they were not a previous client of that project. NTORS recruited 1075 subjects. Their distribution was: 122 (11.3% of cohort) in specialist in-patient facilities; 286 (26.6%) in residential rehabs; 458 (42.6%) in methadone maintenance programmes; 209 (19.4%) in methadone reduction programmes.

Description of the study population – baseline data

The study population has been described in detail (Gossop et al, 1996; Gossop et al, 1998). The population was 74% male and the vast majority defined as “white-UK”. Nearly half were in relationships/co-habiting and nearly half had child-care responsibilities. Some 20% were in temporary accommodation and 80% were unemployed. The most commonly reported substance use problem was long-term opioid dependence with heroin the most frequently used drug (>80%) while 49% had used illicit methadone in the 90 days prior to intake. Some 81% used two or more types of drugs and over 50% used stimulants. The average duration of use was 9 years while 25% had used heroin for 13 years or more. Three quarters were using “regularly” – weekly or more. Mean heroin use was reported as 2/3g daily but 25% used 1g or more daily. Some 62% were injecting drugs. In the 3 months prior to recruitment 68% had drunk alcohol with an average weekly alcohol consumption of 51 units for men and 45 units for women. Three quarters of daily drinkers used 10 units per day or more with the average for this group being 24 units per day. Criminal activity was assessed. Some 61% of the cohort were responsible for a reported 70,728 crimes. Over half (52%) reported at least one non drug-dealing offence. The most common reported offence was shoplifting. Three quarters had been arrested in the previous 2 years – a total of 4,466 arrests. Health issues

were assessed. Of the NTORS cohort, 48% had been to A&E and 25% had been admitted to a general hospital bed in the previous 2 years. Depression and anxiety were described as "common" with 29% reporting suicidal thoughts in the 3 months prior to recruitment. Some 10% had received in-patient psychiatric care in the previous 2 years for problems other than addiction while 14% had been treated by community psychiatric services. Some 70% had seen their General Practitioner in the 2 years prior to recruitment.

Client differences by modality at intake ($p<0.05$)

There were no gender differences. Those choosing to enter methadone reduction, however, were younger, had shorter drug histories and more simple/less complex drug use histories associated with less risk-taking. Those accessing residential facilities were found to describe, in general, a more serious range of problems with longer heroin careers. They were more likely to use stimulants or have a heavy alcohol intake and showed evidence of more needle sharing/risk taking behaviours. This latter group also had worse offending histories.

Follow up studies – 6 months and One year

Six month follow up saw considerable improvements in all groups (Gossop et al 1997[1]; Gossop et al 1997[2]). At one year outcome data was available on 769 subjects (71% of the original cohort), of whom 753 successfully completed a follow up interview. A further 16 subjects had died during that year (Gossop, Marsden & Stewart, 1998). There were significant improvements in drug use and risk-taking across the cohort. There were significant differences in outcome, reflecting treatment modality attended. The residential facilities often saw greater improvements – particularly regarding alcohol use. There was huge variation in service performance however, in all modalities, with the worst performing services showing virtually no impact on drug use. There were 16 deaths - mainly attributed to overdose. There was one suicide and one AIDS-related death. Crime fell in both groups to similar amounts.

Authors' conclusions – 1 year follow up

The authors concluded that at 1 year, treatment was effective with subjects more likely to be abstinent and to reduce their use of drugs and risk-taking as well as criminal activity. They raised concerns regarding the poor general impact of treatment on drinking behaviour

and health outcomes. They discussed why different individuals access different types of services and considered the way that treatment pathways could better facilitate engagement and retention. They particularly emphasised that methadone maintenance programmes had more success in this regard. The issue of the huge service variation (3 fold from best to worst) raised issues of consistency of practice and quality of commissioning in the UK. This finding also makes interpretation and generalization of the results a challenge.

Follow up studies - Five years (Gossop, Marsden & Stewart, 2001)

A sample of 650 cases from the NTORS cohort was defined using a degree of scientific rigour to ensure proportions represented, as closely as possible, the original cohort for 5 year follow up. Some 496 of the 650 selected cases were interviewed (76%). This represents 46% of the original cohort. With regard to drug use, the 1 year success already described was maintained at 2 and 5 years. Less subjects were using any drugs and those still using were using less frequently in all settings. Injecting fell overall by nearly half, as did sharing of injecting equipment. Alcohol use reduced in the residential group but showed no change in the methadone group.

The Drug Treatment Outcomes research Study (DTORS) – UK (England) 2009

This study could be seen as a follow-up from NTORS – but was more focused on short term service performance, aiming to determine how treatment services were responding to changing demographics, developments in drug use presentations to services and higher numbers presenting for treatment in England since NTORS. The study recruited a weighted representative sample of 1796 subjects presenting to 342 different agencies across England and followed them up twice: at 3-5 months after induction - 886 (49.3%) subjects and at 11-13 months - 504 subjects (28%). A qualitative assessment and economic evaluation were included in the study report (Barnard et al, 2009).

Subjects

The subjects are described in the baseline report (Jones et al, 2007). Again they were mainly described as male and white UK - though more subjects were presenting form other ethnic groups. Descriptive analyses found that ethnicity and recent drug use at presentation

showed some associations. Those describing crack cocaine as their primary drug problem were less likely to be White (77%) and more likely to be Black (12%) than those whose primary problem drug was reported as heroin (91% White, 2% Black). Compared to NTORS, Criminal Justice was now a more common source of referrals with 35% referred by this route. Balance of drug use had also changed since NTORS. In the four weeks prior to baseline interview 62% of subjects had reported using heroin, 44% had used crack cocaine, 25% benzodiazepines and 50% alcohol. Some 37% reported injecting drugs recently, and 48% of the injectors (17.9% of respondents) had shared equipment in the past four weeks. Seventy-six per cent of opioid users reported poly-drug use in combinations with other opioids, benzodiazepines or alcohol with over a third injecting. Some 9% had overdosed in the previous 3 months. Crime was common. In the previous 12 months, 73% reported committing an offence.

Follow up findings (Jones et al, 2009)

The study was essentially an audit which explored the standards expected from services as part of the treatment process. It reported that services were responding well to increased demand. Over 80% of subjects had an agreed care plan in place within 3 weeks of assessment, and the majority reported being happy with the care process. At first follow-up 89% had started at least one treatment modality/episode or completed treatment with a median wait of just 7 days to starting. Some 75% had started their treatment within 22 days. At 2nd follow up (11-13 months) 81% were retained or had completed their treatment. However, new or inexperienced patients did less well in structured treatment approaches. Improvements were greatest in the first 12 weeks though some improvement continued for 3-8 months. Little significant improvements were identified thereafter. Regarding outcomes achieved, this study addressed relatively short term outcomes and found that, overall, drug use and drug-related harms reduced in that early period. Employment, home stability and ability to take on childcare responsibilities also improved (by self-report only) at each stage while crime reduced.

Conclusions

The main findings of the study were that *"drug treatment is still effective in reducing a range of harmful behaviours associated with problem drug use and it is cost-effective."*
Commenting on the care process, the authors stated that *"the majority of treatment seekers received care-co-ordinated treatment, expressed satisfaction with their care, were retained in treatment beyond three months".* All outcomes were based on patient self-report with reports not offering any objective assessments or measures to confirm the reported outcomes. However, the report stated that treatment was associated with *"significant and substantial reductions in drug use and offending as well as improvements in social functioning."*

Drug Outcomes research in Scotland (DORIS) – UK (Scotland) 2001-2004

This Scottish outcome study started in 2001 and had a research design similar to the earlier National Treatment Outcome Research Study (NTORS) in England. DORIS recruited a cohort of 1033 drug misusers who were entering a range of 5 types of drug treatment services. A baseline assessment was undertaken using a standardized assessment tool. Subjects were then reviewed in "sweeps" at 8, 16 and 33 months thereafter. Additional qualitative data were also collected. The aim of the study was to establish whether drug users in treatment progressed, what outcomes were being achieved and what types of treatment services were associated with the best outcomes.

On entering the DORIS study, researchers accessed a sample representing some 1 in 12 of all substance misusers entering treatment in Scotland in 2001. Of those invited to participate, 89% accepted and undertook a baseline interview. Using a standardized assessment of dependence, they found (unlike NTORS) that there were no significant differences in the groups accessing different treatment types.

Outputs& reports

A number of reports and publications were produced from the DORIS study. These included papers on drug users' aspirations from drug treatment (McKeganey, Morris, Neale & Robertson, 2004), the treatment needs of prison and community based drug users (Neale &

Saville, 2004; Neale, Robertson & Saville, 2005), employability (Kemp & Neale, 2005), experiences of trauma and abuse amongst treatment-seeking drug misusers (McKeganey, Neale, &Robertson, 2005), drug users' life problems and overdose (Neale &Robertson, 2005), drug users and assault (Neale, Bloor, & Weir, 2005).

Results

Unlike the NTORS publications, none of the reports addressed changes in drug use from the perspective of a harm-reduction outcome (i.e. assessing changes in drug use and drug-related harms). One paper in particular - *Abstinence and drug abuse treatment: Results from the Drug Outcome Research in Scotland study* (Mckeganey et al 2006) – reported only on achievement of abstinence in different treatment modalities at 33 month follow up. This paper reported 33 month outcomes on 695 subjects (67% of the DORIS cohort). The authors reported that 88% of respondents had used heroin in the 90 days prior to 33 month follow up assessment. Some 60% had injected and 11% overdosed in that period. They found that only 5.9% of females and 9% of males were abstinent at 33 months follow up and this group was heavily skewed towards those who had been accessing residential rehabilitation programmes. When the definition of "abstinence" was aligned with that used in NTORS, the authors reported that, of residential rehabilitation patients, 35.9% (NTORS) and 33.3% (DORIS) would be abstinent for 90 days. For OST (methadone replacement) patents, 24.3% (NTORS) compared with only 11% (DORIS) would be abstinent for 90 days.

Conclusions

The authors focused on abstinence outcomes concluding that *"There is a need to establish why so few drug users in contact with the methadone programme in Scotland appear able to become drug free 33 months after having contacted this service."* They went on to plea for improved access to residential rehabilitation in Scotland and felt there was a need to address *"why it is that such a small proportion of drug users receiving methadone maintenance within Scotland appear to be able to achieve a 90-day drug-free period."*

Discussion – conclusions from large longitudinal studies in the UK

Both NTORS (1996-2001) and DTORS (2009) were commissioned by UK Government departments to assess effectiveness of treatment services in England. NTORS remains the

study which has contributed the longest follow-up period and its positive findings have guided UK treatment policy for over ten years. Implications regarding treatment retention and time in treatment are important at delivering improved outcomes and that these should be areas of improvement for services. The study also recognises the continuing challenge of ongoing alcohol use and gives a sense of different interventions better matching an individual's needs – with more complex cases seeming to do better in more intensive (often residential) environments. The follow up study, DTORS, focused on treatment process and showed that the major changes in service delivery in England in the intervening 10 years had not seen an overt deterioration in service performance. Indeed, in the relatively brief follow up period of up to 13 months, people presenting to services seemed to be accessing their treatment of choice very quickly and were being retained well with positive outcomes reported – though improvements did not continue beyond 8 months.

In contrast, the DORIS study in Scotland was not Government funded – but was commissioned by an independent trust. The Scottish Executive Effective Interventions Unit (a unit whose aim was to improve the quality of information and evidence available to frontline staff) supported the project in kind through a steering group and practical support regarding recruitment and delivery. The outputs from the project have tended to focus on the issue of abstinence and have asserted that Scottish services may not be meeting the expectations of service users. This view has resulted in the DORIS outputs becoming a focus for dispute between those supporting differing philosophies – harm reduction or abstinence. Criticism of the authors' interpretation of their findings by international authorities (e.g. Newman, 2005) has reduced the influence of this work – one of the few substantial longitudinal studies reported on Scottish subjects.

In conclusion – these UK studies have given an indication of the effectiveness of the treatment system in England and NTORS in particular has laid down a strong baseline from which more detailed research questions could be developed regarding treatment outcome. The emphasis on process in DTORS (it is essentially a service quality audit), its short timeframes and the absence of objective, measureable outcome assessments make it less powerful and it clearly adds little to the evidence base regarding treatment outcomes. The differing treatment and service commissioning environment in Scotland during the same

period makes generalising some of the English findings questionable. The DORIS study reports have not addressed key questions about effectiveness of Scottish treatment systems in terms of levels of drug use or drug-related harm.

International Longitudinal studies

A number of international longitudinal studies have given an indication of treatment effectiveness. Though they are now historic and have issues regarding the generalizability of their findings to UK practice, they do address issues of principle, have the advantage of very large numbers followed up for long periods and should inform hypothesis-driven research in the UK.

Drug Abuse Reporting Programme (DARP) USA (1969-72 – with some subjects to 1981)

This early longitudinal study examined data from 4 treatment groups – methadone maintenance, therapeutic communities, outpatient drug-free (counselling & abstinence), outpatient detoxification – and non-treatment controls. Some 43,943 clients from 52 services were assessed at intake and 2 monthly thereafter (with post-treatment follow ups for up to 12 years for some samples). This was a large comprehensive and carefully constructed naturalistic longitudinal study, supported by Federal funding and assessing services across the USA. For the first time, DARP identified factors influencing outcome and in particular showed that time in treatment (retention) was a key factor. There are over 100 reports describing the process and various findings. A summary is available (Simpson & Sells, 1982).

Findings at 1 year: Among the group of daily opioid users, post-treatment prevalence for daily drug use declined in all groups, including controls. Non-opioid use (excluding marijuana and alcohol), criminal involvement and employment levels also improved following treatment across the modalities. Time spent in any treatment significantly predicted post-treatment outcomes.

Findings at 6 years: The longer term follow-ups revealed a challenge for this type of project as people moved in and out of different modalities and it became difficult to attribute any change to a specific modality. Any significant differences between the treatment modalities, observed in the first 3 years after DARP, became insignificant by Year 6. Some 61% of the original sample had ceased daily opioid use for at least a year by this time and this improvement in drug use was accompanied by improvements in other outcome indicators including crime, employment, non-opioid drug use and alcohol use. (Simpson, Joe & Bracy, 1982).

Findings at 12 years (Simpson & Sells, 1990): This follow up study examined a number of outcomes and process measures. ***Treatment history*****:** the sample had averaged more than 6 treatment episodes in their lifetime. Subsequent treatment episodes saw a "gravitation" towards methadone maintenance as the treatment of choice. ***Relapse rates*****:** Almost three quarters of the sample reported at least one relapse to daily opioid use though only 41% ever had a continuous episode of daily use lasting over 2 years. Relapse was most likely in the first 3 months after ceasing to use, but of those who abstained for 3 months or more, 80% were still abstinent 12 months later. ***Ceasing illicit drug use*****:** At Year 12 of DARP, 75% had not used any illicit opioids daily for at least one year, 67% had not used opioids for at least 3 years and 61% had not used opioids at all. ***Criminal involvement*****:** Some 95% of the males had been arrested during their lifetime, 91% had been imprisoned at some point in their lifetime, with 60% having spent a year or longer imprisoned.

Conclusions: The main findings of this study were:

- the length of treatment was extremely important with at least 3 month contact required to instil positive changes in outcome
- post -treatment outcome improved with increased time in treatment
- Methadone maintenance, therapeutic communities and drug-free groups showed no differences in outcome – but <u>all</u> showed better outcomes than those not in treatment (controls) or the detoxification groups.
- Differences between treatment groups diminished over time
- At 12 years 63% of subjects had not used illicit opioids daily for 3 years

This study is large and has follow up elements over several years for some subjects making its findings powerful indicators of treatment effectiveness. Its weaknesses (in terms of UK practice) include that it is set in a US sample and care system – making generalizability limited. Also, as the study progressed, subjects accessed a range of treatments, essentially "infecting" specific groups and making interpretation of relevant factors very difficult. The study did show that many patients reduce their drug use and that retention is an important factor influencing positive outcomes.

Treatment Outcome Prospective Study (TOPS) USA (1979-81)

The TOPS study was again Federally funded and aimed to expand on the findings of DARP by providing a framework for more specialized studies, such as those dealing with changing drug use patterns, the effect of comorbidity on outcomes, the impact of legal involvement on treatment and the overall cost-effectiveness of drug abuse treatment. This study examined data from 4 treatment groups – methadone maintenance, detoxification, residential care and outpatient drug-free. Some 11,759 clients entering 41 services were recruited. Subjects were interviewed on accessing the service and then at 1, 3, 6, 9 and 12 months. After leaving treatment, some selected subjects were followed-up at 3 months 1 year, 2 years and 3-5 years.

Findings (Hubbard, Rachal, Craddock & Cavanaugh, 1984)
Treatment was found to be effective in reducing daily opiate use and other illicit drug use during and after treatment, a finding that supported DARP results. Drug use patterns in the USA had changed in the decade following DARP, with less daily use of opioids and more poly substance use (primarily involving stimulants and cocaine). However, 77% of the TOP sample still reported opioids as their primary drug problem. The study found that subjects with legal involvement or where there was legal pressure to enter treatment were just as likely as those without such pressure to benefit from that treatment. Indeed, the study showed that those with legal involvement stayed in treatment slightly longer. When costs associated with crime were calculated, drug misuse treatment was found to be cost effective. Among methadone maintenance programmes, some specific factors of programme delivery were associated with more positive findings. Programmes with flexible

dosing policies, specialized personnel, frequent urine monitoring, and more comprehensive services - in terms of frequency of contact and more favourable patient satisfaction reports - were more likely to have higher client retention rates.

Conclusions

The detoxification cohort was removed from study due to persistently poor outcomes. All remaining treatment modalities showed dramatic reduction in drug use and criminal activity over the first 3 months. At 1 year after treatment there was a clear reduction in drug use, crime and mental health issues if subjects were retained in treatment for 3 months or more. There were no differences reported in outcomes comparing those in methadone maintenance or residential programmes. Over 50% of subjects were abstinent from heroin at 1 year post treatment. The researchers concluded that time in treatment was the most important predictor of outcome. Significant changes in regular heroin use were seen only after 1 year in treatment.

This study has the same strengths and limitations overall as DARP when its findings are applied to UK practice. However, the study has duplicated the finding of DARP that detoxification was significantly less effective than other interventions in these subjects. Also, time in treatment – especially the first 3 months – was a strong indicator of future outcome. Significant changes in illicit opioid use took over one year to appear.

Drug Abuse Treatment Outcome Study (DATOS) – USA (1991-1993)

Following on from the lessons of DARP and TOP, DATOS was designed to *"capture a longitudinal snapshot of drug abuse patterns and treatment responses in the USA"* (Simpson & Curry, 1997). A naturalistic design recruited from a large number of treatment programmes with the aim of identifying changes in treatment populations and service delivery over the study period. Key observations included: reductions in opiate use and increases in cocaine use in the treatment-seeking population; considering the implications of an emerging ageing treatment population; reductions in the availability of a range of health and social care services for this population across the USA (Flynn et al 1997).

Subjects

Intake Sample: A total of 10,010 clients entering 96 different treatment programs, offering four treatment types – methadone maintenance; residential long term; residential short term; out-patient drug-free - during 1991-1993. *Follow-up Sample:* Some 4,229 (42%) of the eligible clients who completed the two-stage intake interviews were selected for follow-up (using a stratified random design to ensure they were representative of the baseline sample). Some 2,966 subjects were successfully interviewed at follow up, representing 52% of the proposed follow up sample and 22% of the baseline sample. No significant differences were found between intake and follow-up samples with regard to gender, ethnicity, and age. Data was collected at 1 and 3 months while in treatment and then at 12 months post treatment.

1 year findings (Hubbard et al 1997)

Clients treated in all modalities studied in DATOS showed large and significant improvements during the 1-year follow-up period. Overall, major outcome indicators for drug use, illegal activities, and psychological distress were each reduced on average by about 50%. There were significant outcome differences between those admitted to different types of treatment (as well as variations between programmes of the same type). Outcome differences also reflected the length of time subjects remained in treatment. Again, the length of time in treatment (retention) was directly related to improvements in follow-up outcomes for all modalities except short-term in-patient care.

A model to explore essential elements of *"treatment readiness"* and *"engagement indicators"* as potential predictors of retention and outcomes was tested in the different therapeutic settings (Joe, Simpson & Broome, 1999). They demonstrated that well-motivated clients developed better relationships with their counsellors and stayed in treatment longer. Those who attended more counselling sessions and discussed a broader range of topics stayed longer in the out-patient drug free and long term rehabilitation groups. Those with more severe background problems (hostility or cocaine use) had difficulty developing a working relationship with their counsellors, attended fewer sessions, and discussed fewer topics. One study also examined client "*confidence in treatment"* and "*commitment to recovery"* as indicators of engagement after 3 months and found that those

with higher motivation at admission developed more confidence and commitment to treatment, as did those who had better relationships with counselling staff and who attended more counselling sessions. (Broome, Simpson & Joe, 1999).

Conclusions: The main findings of this study were:
Again the study is based on a US sample and treatment environment. Again the original sample is substantial – though the follow up elements are small and the follow up periods more limited than in DARP and TOP. Overall, they found that most treatment approaches had an effect on illicit drug use with methadone maintenance having the main effect on opioid use specifically. Treatment retention was again strongly associated with positive outcomes – longer periods in treatment had the most effect. The study looked in-depth at "softer" issues relating to the client or treatment process. Aspects of patient motivation and engagement seemed to have some effect on treatment outcomes (Simpson & Brown, 1999).

Australian Outcome Treatment Study (ATOS) 2003-6

ATOS was the first large-scale longitudinal study of treatment outcome for heroin dependence to be conducted in Australia. This longitudinal prospective study aimed to describe the characteristics of people entering treatment for heroin dependence. The study examined the treatments received and 3 and 12 month outcomes achieved – in terms of drug use, criminal behaviour and mental health as well as assessing the associated costs. Longer term outcomes at 24 and 36 months were also examined in a specific follow up sample. The sample sizes reported as assessed in various associated publications vary from 495 (Darke et al, 2009) to 615 (Williamson, Darke, Ross & Teesson, 2007), 745 (Ross et al, 2006) and 825 (Teesson et al, 2006). IT is not clear why such variation is observed. Of these publications, the Teesson paper gives the most detailed description of the methods used and states that the sample was some 825 active heroin users entering 38 agencies offering three treatment modalities: 277 entering maintenance; 288 detoxification and 180 residential rehabilitation. Eighty non-treatment controls were also assessed. The clinical measures used examined drug use and risk behaviours, treatment history, criminality, general health, health service utilisation, and psychopathology – using the Opiate Treatment Index tool (Darke et al 1992). Self-report was used to determine changes in illicit drug use –

there is no report of objective testing. A health economic evaluation was also included. After baseline assessment, subjects were followed up at 3 months. The various reports give differing follow up rates which range from 80% at 12 months to 70% at 3 years.

Findings at 1 year

Some 80% of the original sample were interviewed at 1 year. There were substantial reported reductions in heroin and other drug use across all treatment modalities. The majority of those who had entered treatment reported being heroin abstinent at 1 year compared to the non-treatment controls. Reductions in poly drug use were also reported in the treatment samples. Major reductions in risk-taking, crime and injection-related health problems were reported across all treatment groups with less marked reductions reported in the control group. Psychopathology was assessed to be significantly reduced among the treatment modalities compared to controls. Positive outcomes at 1 year were associated with more treatment days experienced over the 1 year follow-up period - described as *'treatment dose'* and fewer treatment episodes - described as *'treatment stability'*.

Findings at 3 years

Some 94.5% of the baseline sample completed at least one follow-up interview over a 36-month follow-up period. The proportion reporting heroin use in the preceding month decreased from 99% to 35% from baseline to 24 months. This rate then remained stable to 36 months. This reduction in reported heroin use was accompanied by reductions in self-reports of other drug use and in risk-taking, crime and injection-related health problems. There were also improvements in assessed general physical and mental health. Positive outcomes were associated with more time in maintenance therapies and residential rehabilitation and fewer treatment episodes. Time spent in detoxification was not associated with positive outcomes. Major depression was also associated consistently with poorer outcome (Teesson et al 2008).

Conclusions: The main findings of this study were:

The study reflects a treatment sample in Australia – which, it could be argued has more similarities in terms of service delivery with the UK than the US services. The numerous but diverse published reports make sample sizes difficult to clarify – but there seems to have

been at least 70% of the sample followed up at 3 years. Only self-report was used to determine drug use outcomes, apparently with no objective drug testing. From these reports, reductions in drug use, associated risks and crime were observed at 3 months and maintained over 36 months. These outcomes were related to time in treatment (except in the case of the detoxification group). Depression appeared to negatively affect outcome in all groups.

Summary and commentary - the national longitudinal studies

What do these studies tell us?

There are consistent finding in all of these studies. They generally show that being in treatment is associated with clinical improvements. In most modalities, those in treatment do better than those not in treatment in terms of drug use and the associated risks, overall health and crime. Staying in treatment seems to be an important indicator of better outcomes. In NTORS, improvements are generally seen at 1 year and seem to be broadly maintained to 5yrs for those reviewed. DORIS raises differences between Scotland and England regarding abstinence-based outcomes. DATOS has raised the issues around the drug user's ability to engage with treatment services (or the services' ability to facilitate engagement). ATOS shows that co-morbid mental health issues (in this case depression) may impact on the outcome achieved.

Limitations

There are limitations to the conclusions which can be drawn from such research. The limitations include:

- ***Relevant to the UK? –*** The UK health system is very different from that in the USA or Australia. While some findings of these national studies should inform study development in the UK, it is essential that UK research – reflecting the specifics of the delivery of services locally – demonstrates that any findings are generalizable to the UK treatment system.

Also, the NHS across the UK is now taking on very different characteristics. This reflects different and diversifying government priorities. National governance of drug treatment has

been the norm in England for some years. Local governance remains the Scottish government's preferred approach – though recent HEAT targets have seen considerable improvements in measureable performance nationally. Also, it is now likely that General Practice contracts will vary across the UK, with a Scottish General Medical Services contract now being discussed with doctors' representatives. The care of substance misusers is not part of the GP "General Medical Services" (GMS) contract currently and this is likely to be an area for debate in future negotiations in Scotland. In such circumstances, generalizability of research from different health systems in the UK becomes a serious issue.

- ***Size and representativeness of the sample*** - While the total numbers of individuals entering these studies is high, the number entering each intervention is relatively low. For example, those entering an OST programme in NTORS is 458. Some 279 entered OST in DORIS and in ATOS this group consists of only 201 cases. By follow up (even in the early stages) these samples reduce considerably.

In the case of NTORS, these subjects were recruited from 54 different services increasing the likelihood that factors relating to specific service culture, process or performance (the issues touched on in DATOS) can impact on outcome. Though sampling processes are described, which aim to ensure that the groups are representative at each stage, in some of the studies, the issue of sample size and representativeness impacts on the generalizability of any findings. ATOS appears to have achieved high levels of follow up though the associated reports are difficult to interpret regarding final numbers.

- ***Selection of participants*** – The samples are generally drawn from self-selecting populations presenting themselves to discrete treatment modalities – not randomized to a different treatment or condition as would normally be the case in primary research. The studies do not differentiate whether the intervention being accessed would best match to that individual's clinical presentation. If local services are not comprehensive – for example offer only detoxification or OST- M options, subjects may be accessing inappropriate treatment for their needs. [This would not be an unusual situation in parts of the UK – especially in the 1980s and 90s. In Glasgow, for example, formal OST programmes were only commenced in 1994. Prior

to this, few patients would receive OST and all from general practice.] Those involved in the studies must give informed consent – adding a further selection bias to the study of what is a relatively small proportion of a very heterogeneous population. Since DARP, the US studies commented specifically on the effects of each treatment episode contaminating the final outcome at follow up, making interpretation regarding which intervention was driving any observed change very difficult.

- ***Follow-up periods –*** NTORS is the only UK study to have a substantial follow up period – 5 years - which can realistically reflect the natural history of a treatment-seeking substance misuser. DTORS has a follow up period of only 13 months while DORIS achieves 33 month follow-up for some selected elements of the study. In Australia, ATOS' main study report relates to a 12 month follow up – though one geographical area followed a sub-sample up for 3 years. The report generalises from these findings which may overstate the significance of their results. The US studies follow a similar approach – with the main analyses relating to relatively short follow up periods (DATOS 15 months) but with sub-samples followed up for longer periods – up to 5 years in DATOS and 12 years in DARP.

- ***Controls –*** These studies generally lack matched control groups. Only ATOS had a non-treatment control. This may be inevitable in such studies for ethical or practical reasons – though some more localised research of large numbers of subjects has used waiting-list controls to assess effectiveness of forms of OST- M delivery (e.g. Schwartz et al, 2006). This lack of controls prevents comparison with the experimental results (i.e. the proposed effect of the intervention) and weakens the power of the scientific findings. The observations from such studies should be used to inform the design and execution of hypothesis-driven controlled trials to give strong research evidence of what does and does not work.

Discussion - limitations

The limitations reflect many issues. It must be recognised that these national studies were one element of a research process which was "catching up" with a potential global disaster – the spread of HIV in the intravenous drug using population. Harm reduction approaches

had a developing evidence base as well as pragmatic face validity and national governments were responding to the public health challenge. Support for research exploring treatment effectiveness was welcomed by clinicians and academics and was often driven by clinical pressure and lobbying. However, when a clinical challenge also has substantial political perspectives – for example, cash-strapped health services investing in delivery of interventions to reduce harm in an excluded and stigmatized patient group - clinicians and researchers may overplay their hand. Nor has this challenge abated.

Evidencing treatment effectiveness in Scotland and England

Demonstrating treatment effectiveness may be complicated by the difficulty in determining the best way to measure positive outcomes in a harm-reduction environment or one where patients progress along a recovery continuum which may take several years and be characterised by fluctuating periods of progress and relapse. In such a chronic relapsing condition, even demonstrating the outcome "drug free" offers a challenge to researchers who may demonstrate improvement in a narrow area of drug use but little effect in terms of broader recovery. Consequently, measures of drug use and injecting risk must be enhanced by attempts to describe improvements in social functioning or health status or are replaced by measures of service use or "proxy" outcomes – such as treatment retention. Objective and consistent measurement of these outcomes presents a real difficulty for researchers in this field in terms of obtaining comparable data as well as interpreting complex findings.

The direct challenge to the Scottish Government strategy, described in Chapter 1, reflects, to some extent, a lack of convincing evidence – from formal research or local/national reporting - for the effectiveness of Scottish treatment services and specifically, a lack of prioritization of high quality research into the effective treatment of substance misuse in Scotland.

This deficiency can be further illustrated by reviewing research activity in this field. The Chief Scientist's Office (CSO) for Scotland publishes reports of all research funded by CSO on an annual basis (Chief Scientist for Scotland [CSO], 2012). This report shows that, since the publication of *the Road to Recovery* in 2008, the CSO has received reports of only 6 research studies, funded by that office, relating to substance misuse. Of these, one was focused

specifically on Hepatitis C - but in a drug using population. During this same period, the CSO received reports of 216 studies on other topics. Only 2.7% of CSO funding, under all headings, was in the area of substance misuse.

Also, a gap in availability of valuable routine clinical information has been identified in a recent report by the Information Services Division (ISD) of the NHS which undertook a consultation on information needs in the field of substance misuse across Scotland (ISD, 2012[2]). When interviewing a range of stakeholders, the issue of treatment effectiveness was high on the agenda. The report states: *"Effectiveness of interventions was a prominent response to this question... Some interviewees focussed on knowing interventions' effects while others discussed ways to determine effectiveness. Effectiveness can be measured in several ways and different interviewees had different priorities. A common concern was that at present there was a lack of awareness of the effectiveness of interventions that are being used across Scotland."*

In particular, there were real concerns about demonstrating meaningful outcomes. One interview clearly raised the question of ISD – who collate national statistics on behalf of the government - supporting an ongoing process of service evaluation (not unlike the studies cited above): *"For large cohorts of service users, you could evaluate new treatments, in effect a natural experiment, which would be valuable given the difficulty in carrying out randomised controlled trials for methodological reasons and political reasons."* The ISD consultation report concluded that: *"Perhaps the most prevalent need identified, one that sits at both the population and individual levels, was a clear understanding of what works. This could be the effectiveness of interventions; what treatment works and what does not. But there was more than this, it extended out to needing to identify which policies worked and why, which patient journeys generated positive outcomes, what could be considered a 'positive outcome'."*

The NHS in England is advised on decisions regarding which treatments should be available, by the National Institute for Health and Clinical Excellence – NICE (National Institute for Clinical Excellence Establishment and Constitution Order, 1999). The purpose of the

organisation was originally to avoid “postcode lotteries” and to ensure equity of access to evidence-based medical treatments across the country. NICE is required to “provide independent, authoritative and evidence-based guidance on the most effective ways to prevent, diagnose and treat disease and ill health, reducing inequalities and variation” and its guidance – which includes an assessment of cost – effectiveness of the intervention in question - is required to be followed by local Health Authorities and Primary Care Trusts in England and Wales.

In the case of treatment for substance misuse, the most recent national treatment guidelines for the UK (Department of Health 2007) were supported by NICE systematic reviews or technology appraisals covering all the main treatment approaches (NICE 2007 a-d). This should have given a degree of security to treatment availability in this field in England and Wales. However, only three years later, in 2010, a new government was compelled to further explore the evidence on treatment effectiveness – reflecting their view that there was a need to understand better what treatments were most likely to deliver the desired outcome of *recovery* - and how delivery of services would facilitate this. The resulting expert report - *Medications in recovery: re-orientating drug dependence treatment* (National Treatment Agency, 2012) re-iterated the existing evidence base – but was unable to point to any novel research which promised improved progress towards recovery. The document declared: *“If we stick closely to the compelling evidence for effective OST, and the existing guidance based upon that evidence, we will deliver many of the improvements needed”.* It went on: *“ We strongly support continued reference and adherence to the existing NICE drug misuse guidance (reviewed and unchanged in 2010-11) and to the more practitioner-orientated 2007 Clinical Guidelines”.*

Even the supplementary Appendix C (Bell, 2012) which reviewed the evidence to date, recognised that firm evidence regarding recovery was lacking and described in aspirational terms the need to better recognise so-called “*recovery capital”* and some proposed changes to improve care planning and review. The evidence of effectiveness of such approaches in improving delivery of recovery outcomes is clearly yet to appear.

In Conclusion

Large national longitudinal studies can give valuable information about the effectiveness, risks and benefits of treatment and can support descriptive research. If well planned and constructed, they can also address key research questions. However, the studies to date, have many limitations and should be followed by high quality hypothesis-driven research which takes forward the many valid issues they raise. Few such studies have been taken forward in the UK setting.

In this environment, in the UK, there is clearly an opportunity to develop processes which collect high quality clinical information on large numbers of those in treatment. Such systems could collect data using validated tools of recognised value to the field. Such data collection systems would facilitate the development of programmes of research, addressing hypothesis–driven studies to answer the many unanswered questions which must be understood if recovery is to become a reality.

The next chapter will describe a review of the research literature, which will inform the development of hypotheses for testing.

Chapter 3. Predicting outcomes – a literature review

It is a capital mistake to theorize before you have all the evidence. It biases the judgment.
Sir Arthur Conan Doyle -A Study in Scarlet (1887)

"…Yeah?...well, you know, that's just like..ah your opinion, man"
The Dude - The Big Lebowski (Ethan & Joel Coen, 1997)

Introduction

This chapter describes a literature review which aimed to generate hypotheses for testing. The published international literature relating to factors impacting on outcome for those in receipt of Opioid Substitution Therapy using methadone (OST-M) was reviewed:

1. To identify key independent variables (predictors) impacting on the outcome of OST-M treatment.
2. To identify relevant dependent variables (outputs and outcomes) which are valid indicators of treatment effects in OST-M

Methods

Search terms

The project planned to use data available in a regional database of methadone-prescribed patients in Scotland - the Tayside Methadone Cohort database (described in detail in Chapter 4). The database contained baseline clinical data collected in 2005 and follow-up data from a range of sources, collected over the next 7 years. The literature review focused on those factors which were available within this database with the aim of generating testable hypotheses. The literature review would direct the selection of specific independent variables (predictors) and dependent variables (outputs and outcomes).

Identification of studies:

An electronic keyword search was conducted using the following databases:

- EMBASE (1974-April 2012 inclusive);
- Ovid Medline(R); Ovid Medline (R) in-process and other non-indexed citations (1946-April week 2 2012);

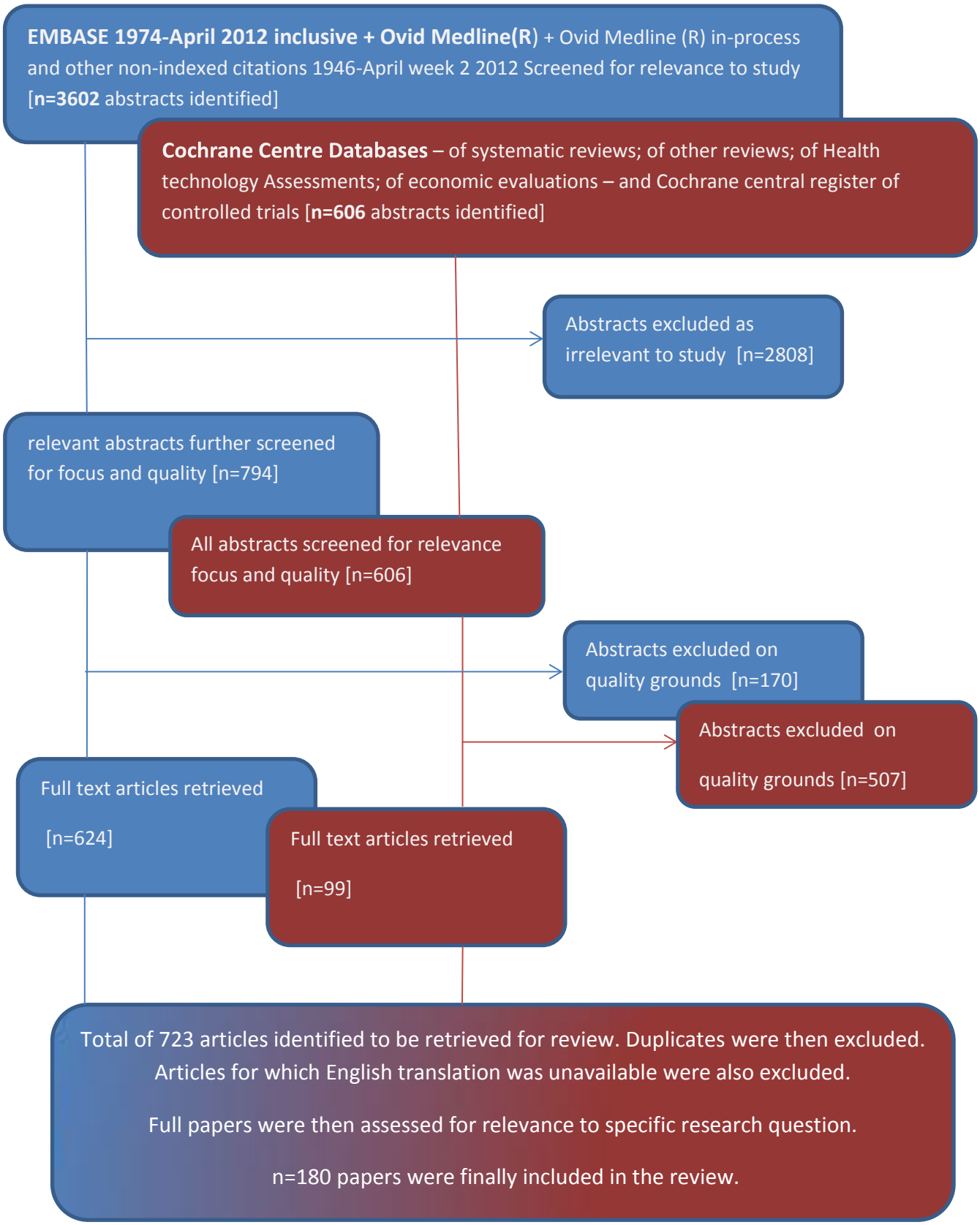
- Cochrane library - database of systematic reviews; database of other reviews; Health Technology Assessments; economic evaluations; controlled trials.

Searches were limited to publications relating to research in humans. Though publications in all languages were sourced, only those for which an English translation was readily available were used. Keywords and results are summarized in Table 3 and Figure 4.

Table 3. Results of Literature search

Keywords	Databases searched	Results
Opioid related disorders	***Cochrane Database***	
	Cochrane database of systematic reviews (contains 7163 articles)	23 identified and abstracts screened 8 papers selected for review
	Cochrane database of other reviews (contains 16,773 articles)	30 identified and abstracts screened 10 papers selected for review
	Cochrane database of Health technology Assessments (contains 10,997 articles)	12 identified and abstracts screened 4 papers selected for review
	Cochrane database of economic evaluations (contains 11,720 articles)	11 identified and abstracts screened 2 papers selected for review
	Cochrane central register of controlled trials (contains 670,154 articles)	530 identified and abstracts screened 75 full papers selected for review
	Cochrane Database totals	***99 full papers to be reviewed***
Methadone and outcomes	EMBASE 1974-April 2012 inclusive; Ovid Medline(R); Ovid Medline (R) in-process and other non-indexed citations 1946-April week 2 2012	1358 articles identified. 350 abstracts selected and screened 294 full papers selected for review
Methadone and comorbidity		198 articles identified 81 abstracts selected and screened 71 papers selected for review
Substance misuse, opiate/opioid, dependency and comorbidity		393 articles identified 89 abstracts selected and screened 62 papers selected for review
Opiate addiction and comorbidity *Opioid addiction and comorbidity*		436 articles identified 93 abstracts selected and screened 74 papers selected for review
Methadone and pain		858 articles identified 61 abstracts selected and screened 33 papers selected for review
Methadone and anxiety		325 articles identified 91 abstracts selected and screened 71 papers selected for review
Methadone and ADHD		15 articles identified 15 abstracts selected and screened 7 papers selected for review
Methadone and PTSD		19 articles identified 14 abstracts selected and screened 12 papers selected for review
	EMBASE/MEDLINE totals	***624 full papers to be reviewed***

Figure 4. Consort diagram (summary) of literature review process



Selection of relevant studies/papers

All outputs from the electronic keyword searches were initially screened online and those not relevant to this study excluded. Exclusion criteria included:

- papers not focusing on OST-M
- papers in which methadone was not a significant factor in the analysis
- papers in which the OST-M treatments were clearly intended for short term or detoxification purposes
- papers considering treatment in residential/in-patient facilities

Some articles included community-based OST - M alongside others which were within the exclusion groups. In these cases a pragmatic judgement was made based on the relevance to the current project. If at this stage an article clearly did not meet these pre-defined criteria it was rejected. Duplicate articles were also removed from the output of each electronic search at each stage. Finally, reference lists of the selected papers were searched manually for any additional key references not identified from the initial electronic search. These additional lists were taken through the same procedures as above and, if required, accessed and included in the review.

Review of relevance and quality of retrieved articles

Full text articles were accessed online via the NHS e-library, sourced directly from local university libraries or through the University of Dundee inter-library loan system. Many of the retrieved articles identified were purely descriptive in nature. Many published papers assessed associations between variables in a cross-sectional sample of a study population and addressed a wide range of dependent and independent variables. Few were found to have a follow-up element to the study or to test a specific, focused hypothesis. The electronic search also identified a large number of “review” or “editorial” articles. Some of these had followed a rigorous/systematic method to review the existing research while others were less rigorous and more selective. A pragmatic judgement was made regarding their inclusion in the literature review.

Summary of studies identified

Some 180 articles were ultimately included for critical appraisal as part of in this review. Of these, 19 were systematic reviews. Of the remaining 161 studies, only 90 (55%) had any longitudinal follow up element. The remainder were descriptive studies or simply identified associations between variables in a cross-sectional survey of subjects at a single time point. Of the 90 with follow–up elements, the majority – some 64 studies (71% of the identified studies with follow up elements, 39% of the total) - had follow-up periods of up to one year (mean 8.64 months; range 3 months-1year). Only 26 studies - 29% of those with follow-up and 16% of all identified relevant studies - had follow up periods of more than 1 year (mean 5.86yrs; range 1.5-30yrs). The most common duration of follow up (mode) was only 2 years.

Although rarely acknowledged as an issue, relatively short follow up periods in the research evidence base have been commented on previously in a number of recent Cochrane Reviews of OST-M. For example, in the 2009 Cochrane review of *Methadone maintenance versus no therapy*, follow up periods in the research cited ranged from only 45 days to 2 years (Mattick, Breen, Kimber & Davoli 2009). The 2011 Cochrane review of the effect from added psychosocial interventions reviewed evidence from studies of 6-48 weeks (all under one year) duration with a mean of only 17 weeks (Amato, Minozzi, Davoli & Vecchi 2011). The 2003 Cochrane review of the relative effect of methadone dose drew its conclusions based on evidence from studies of 7-53 weeks duration (Faggiano, Vigna-Taglianti, Versino & Lemma, 2003).

Opiate dependency is a chronic relapsing condition with a natural history which suggests that at least 5 years of illicit drug abstinence is good indicator predicting future stable abstinence (Hser, 2007). In such circumstances, it is surprising that so few well-constructed studies have attempted to clarify how treatment can affect long term prospects of recovery.

Effectiveness of Methadone Replacement Therapy (OST- M) – Systematic reviews

All studies reviewed address the use of methadone as the opioid substitute. For the purposes of the review, this will be summarized as *OST-M*. This term will also be used for

those studies using other specific terms - such as *methadone maintenance therapy* (MMT). These reflect the same treatment type – and do not reflect a specific reduction or detoxification intervention.

The literature search identified 19 systematic reviews considering the effectiveness of Opiate Substitution Therapies. Most of these consider Methadone and Buprenorphine (Subutex® and Suboxone®) while a few also consider the drug *Levo-alpha acetyl methadol* - LAAM. The reviews are summarised in Table 4 (p83).

Patient characteristics affecting outcome

The reviews identified address a number of key questions.

Is OST-M associated with improved outcomes?

An early review and meta-analysis considered the effectiveness of OST-M in reducing illicit opiate (heroin) use, HIV risk behaviour and criminality (Marsch, 1998). Marsch reviewed 43 studies. Of these: 11 studies (involving 2,056 participants) had used ongoing illicit opiate (heroin) use as the outcome measure; 24 studies (7,173 participants) used criminal activities as the outcome measure; 8 studies (at least 1,797 participants) used reports of HIV risk behaviours as the outcome measure. The author concluded that there is a consistent, statistically-significant relationship between OST-M and the reduction of illicit opiate use, HIV risk behaviours and drug and property-related criminal behaviours. The effectiveness of OST-M was felt to be most apparent in its ability to reduce drug-related criminal behaviours. OST-M was described as having had a moderate effect in reducing illicit opiate use and drug and property-related criminal behaviours, and a small to moderate effect in reducing HIV risk behaviours.

A UK-based review of community OST-M (or buprenorphine) considered 48 RCTs – 14 of methadone, 20 buprenorphine and 14 comparing both (Simoens et al, 2005). The authors concluded that the results supported the effectiveness of community maintenance treatments with methadone or buprenorphine. The authors raised issues which they felt might bias some of the trials. These included: use of different treatment groups in the

studies; variable drug dosing in different studies; high drop-out rates; small sample sizes; short treatment duration. Despite these concerns, the reviewers felt that the studies supported the view that community maintenance treatment with methadone or buprenorphine was effective in terms of treatment retention, abstinence and reduction in illicit opiate use. However, there was considerable variation between the studies in terms of the reported results achieved. They also concluded that both methadone and buprenorphine were more effective at higher doses.

In 2007, the UK's National Institute for Health and Clinical Excellence in the UK published a technology appraisal which reviewed the evidence of effectiveness of OST using methadone or Buprenorphine (Connock et al 2007; NICE 2007a). This was part of a range of reviews being undertaken to support delivery of updated clinical guidance for UK doctors (Department of Health, 2007). Following the standardized processes for these exercises, an expert group took evidence from a wide range of stakeholders – including the pharmaceutical industry, service users and clinicians. They also reviewed 31 existing systematic reviews and 28 additional RCTs as well as 11 economic evaluations. They noted: there were no RCTs from the UK – with the majority originating in the USA. The RCTs reviewed usually used fixed dosing, very restrictive delivery (e.g. supervised consumption), had no additional psychosocial interventions and short follow up (<1yr). They commented that fixed doses did not reflect normal clinical practice and stated that *"none used all of the appropriate parameters, effectiveness data, perspectives and comparators required to make their results generalizable to the NHS.."*. They also felt there was insufficient evidence to draw conclusions regarding cost effectiveness. However, in balance they still felt they could conclude that OST-M supports retention, reduced opiate use, reduced HIV risk behaviours and sero-conversions, reduced mortality and reduced criminal activity. They also stated that higher fixed doses were more effective than lower fixed doses.

In 2009 a Cochrane Review examined all RCTs comparing OST-M with placebo or a non-pharmacological therapy (Mattick , Breen, Kimber & Davoli, 2009). They reviewed 11 RCTs (1969 subjects) of which only two were double blind. Outcomes were assessed from 45 days to 2 years maximum. The authors commented on the lack of any evidence on some key outcomes of interest (such as deaths, social outcomes) and the relationship between

medical and psychosocial treatments. They also felt that the methodological failings of much of the research made generalising from the evidence base *"impossible".* They concluded however, that OST-M does improve retention and does reduce heroin use though they could not conclude that it reduces criminal activity.

A systematic review of the evidence for a range of treatment options for opioid dependence aimed to "synthesize the current status of opioid dependence treatment" (Veilleux et al, 2010). They reviewed existing systematic reviews from the Cochrane database and supplemented this with additional meta-analyses of RCTs published since the most recent Cochrane reviews. Again the authors raised the challenge of carrying out a meta-analysis as studies used a broad range of methods and approaches – including differing subjects, outcomes and durations. They felt that there was a need to broaden quality research to better scrutinize more clinical outcomes including abstinence. Citing 155 studies, involving 28,999 subjects, they commented on effectiveness of OST-M. They concluded that OST-M improves treatment retention, reduces opioid use and reduces withdrawal symptoms in opioid dependent individuals. They identified what they saw as clear evidence of dose effects – with higher doses more effective at delivering these desired outcomes.

In 2012, the British Association of Psychopharmacology published an update of its 2004 advice for UK clinicians on the treatment of a range of substance use disorders (Lingford-Hughes, Welch, Peters & Nutt, 2012). This advice was based on a rigorous systematic review of the literature over 3 years, overseen by an invited expert panel. They sourced previous systematic reviews from credible sources (e.g. Cochrane database) and other RCTs when possible. The authors commented on the complexity of the evidence base – reflecting the heterogeneity of research subjects, lack of clarity of the research question in many studies and small sample sizes or short follow up times. The evidence base was also largely from the US health system making generalizability to the UK a concern. They acknowledged that at times the strength of recommendations made was extrapolated from relatively low grade evidence or expert consensus (given an "s" status – a *standard of care*).

With regard to OST-M, they concluded that it improves treatment retention, reduces heroin use, shows a trend towards reducing mortality and reduces injecting related risk behaviours

- but not sexual risk behaviours. Higher doses seemed to be more effective at achieving these outcomes. There was no evidence for an added effect from psychosocial interventions nor for an effect on criminal activity.

In Conclusion – systematic reviews on effectiveness of OST-M

In summary then, a series of systematic reviews has repeatedly concluded that availability of OST-M is associated with improved retention, reduced illicit opioid/heroin use and reduced HIV risk behaviours – related to injecting. Higher doses are felt to be more effective. There is less consensus, in these reviews, regarding the effect on criminal activity and mortality. These reviews have consistently commented on methodological issues regarding the studies carried out affecting relevance to the UK. These concerns include: lack of UK-based research; research is often lacking a clear research question; studies cited often have small numbers with short term follow-up periods; heterogeneous populations are offered diverse treatment approaches which are difficult to compare; use of fixed dosing and rigid delivery systems (e.g. supervision of methadone dispensing); OST-M is often delivered with no additional psychosocial interventions.

OST-M dose effects

Many of the reviews cited above have commented on a dose effect - with higher doses being more effective than lower doses.

A Cochrane review was undertaken in 2008 to comprehensively assess the evidence regarding the effect of OST-M dose on outcome (Faggiano et al, 2008). They reviewed 21 studies including 11 RCTs (all from the USA and using follow up periods of <1yr). The studies included some 5994 subjects. Controlled prospective studies (CPS) were also cited. These CPS can follow patients up for up to 10 years. Again, the authors acknowledged the issue of heterogeneity of subjects, inconsistency of sampling etc. – which affected the quality of the research. They also recognised that the short follow up period of RCTs reduced the relevance of the review findings. There was insufficient evidence to comment on some outcomes – such as mortality, criminal activity and social outcomes. They did, however conclude that higher doses OST-M (60-100mg) were more effective at retaining patients and reducing opioid and cocaine use.

Evidence for specific outcomes – the purpose of treatment

Some reviews have considered evidence that OST-M can deliver specific outcomes along a continuum of progress towards ultimately being entirely drug free (abstinent). The key first step of retention in treatment has been addressed in the reviews cited above. The next key (harm reduction) outcome would be reduction in risk behaviours and reduced Blood Borne Virus (BBV) infections and sero-conversions.

Preventing blood-borne virus (BBV) transmission

The effectiveness of drug treatment in preventing HIV spread in intravenous drug users was explored in a review by Sorensen & Copeland (2000). They reviewed 33 studies including over 17,000 participants. They identified serious methodological problems in the literature including: a lack of control groups in many longitudinal studies; questionable validity of self-report of risk behaviours (often the basis of reports that treatment is successful); concern regarding the representativeness of the samples (differences in demographics between in-treatment and out-of-treatment IDUs in comparative studies; self-selected treatment samples; highly selected samples; small sample sizes). Other issues included: short follow-up periods in longitudinal studies and high attrition rates. Despite these concerns regarding the science, they concluded that there is clear evidence that OST-M reduces HIV risk behaviours, particularly needle use.

A recent Cochrane Review aimed to assess the effect of oral OST on risk behaviours and HIV sero-conversions (Gowing et al, 2011). They could not be highly selective due to the lack of RCTs - so included all types of original studies. Some 38 studies incorporating 12,400 subjects were included. The authors noted that most studies were *"at high risk of bias".* They also stated that *"The lack of data from randomized controlled studies limits the strength of the evidence presented in this review".* They concluded, however, that OST reduces opioid use, intravenous use, needle sharing and HIV sero-conversion. They also felt there may be an effect on sexual risk behaviours for HIV.

Though not technically a systematic review, a recent UK study aimed to examine the effect of harm reduction availability and Hepatitis C (HCV) sero-conversion (Turner et al, 2011). The researchers carried out a meta-analysis and pooled analysis on data for 2986 subjects

from six areas in the UK over 8 years. They used questionnaire information to determine availability of OST and needle exchanges locally. Some 40 new HCV cases were identified in the period. The study concluded that improved access to both OST and needle exchange was associated with a considerably reduced rate of HCV sero-conversion.

Reductions in Illicit drug use and abstinence

A meta-analysis was carried out to identify risk factors for continued drug use in patients treated for *"opiate abuse"* in a range of interventions, including OST-M (Brewer et al, 1998). Some 69 studies were examined. Ten variables were felt to show statistically significant and longitudinally predictive relationships with continued use while in treatment. These included: high level of pre-treatment opiate/drug use; having a history of prior treatment for opiate addiction; having a treatment history where there has been no prior abstinence from opiates; abstinence from/light use of alcohol (heavier use of alcohol was more likely to be associated with at least a period of abstinence from opiates than light use or abstinence from alcohol); history of depression; describing experiencing high levels of stress; being unemployed or having employment problems; the level of association with substance abusing peers; only having a short period of treatment; leaving treatment prior to completion.

One review specifically explored abstinence from opioid use in subjects on OST-M programmes (Kornor & Waal 2005). This review estimated opioid abstinence rates and explored possible relationships with characteristics of the patients or treatment programmes they had received. There are quality issues regarding the clarity of this review and the conclusions drawn. Twelve studies (incorporating 9,718 subjects) met the inclusion criteria for the review. The designs of these studies, however, were not clear from the study report, although the authors did report that most were "follow-up studies". Two of the studies appeared to be randomised controlled trials. Follow-up ranged from 1 month to 103.2 months. Overall, 33% of patients in the studies had a period of abstinence from opioids for an average of 2 years following detoxification. The rates of abstinence ranged from 22% to 86%. It is not clear how the authors appraised the evidence retrieved, but they concluded that OST maintenance programmes may be suitable for a subgroup of patients. They did state that further research was needed to better tailor programmes to achieve the

goal of abstinence from illicit opioids. Regarding the characteristics of the treatment programmes - abstinence rates were higher in patients who volunteered to participate in detoxification programmes. Methadone dose and psychosocial support were not found to be related to abstinence rate in this review**.** Regarding the characteristics of the subjects - age, ethnicity and educational level were shown to have a positive relationship with abstinence rate in some studies, but not others. Similarly, duration or severity of dependence, detoxification difficulties, social problems and involvement in criminal behaviour were shown to have a negative relationship in some studies, but not others.

Recovery and broader treatment outcomes

A review of the evidence regarding improvements in the Quality of Life (QoL) of drug users in treatment was reported in 2010 (de Maeyer, Vanderplasschen & Broekaert, 2010). The authors reviewed 38 studies which had assessed QoL as at least one measure of treatment effectiveness. Some 16 studies followed up those on some form of OST. A further 11 studies compared QoL in opioid users and non-opioid users while 8 longitudinal studies considered changes in the QoL over time in various treatment modalities. The OST studies found that QoL was very low on entry but improved with treatment. This improvement occurred early but then deteriorated again after only a few months (though normally not to pre-treatment levels). There were no definitive differences between OST types/drugs in the nine studies which made these comparisons. The authors concluded that services must address more than the drug use as other factors are likely to affect QoL. They felt that OST has a significant effect on QoL in the early stages of treatment and though this tends to deteriorate, improvement is sustained beyond the level found on entry.

There have been two recent publications, which are relevant to the use of OST-M in the UK treatment setting, specifically reporting reviews of the evidence supporting *recovery*. Both are highly selective and were commissioned by new governments launching new drug strategies which had emphasised a recovery ethos over harm reduction.

One published review explored the research evidence for improved recovery (Best et al 2010). This review was commissioned by the Scottish Government to support their national drug strategy which had the stated aim of improving recovery outcomes for substance

users. The authors described a systematic review of the published literature which identified 205 relevant articles. The process of critical appraisal was not well defined in this review and a number of descriptive articles by experts in the recovery field are widely cited. The authors note that much of the evidence is from overseas (almost exclusively the USA) and is from other areas of addiction such as alcohol or the broader mental health field – so may not translate well into the field of opioid dependence. The authors make a number of broad statements regarding their belief around the recovery evidence base and emphasise the lack of relevant systematic research in this area in the opioid dependent population in the UK. They conclude that in opioid dependency, *"sustained recovery is the norm"* [though there is no evidence presented from quantitative research to support this view]. They point out that pathways towards achieving this outcome are *"individualistic"* and identify the phenomenon of *"recovery capital"* - positive attributes in a person's life - as *"the best predictor"* of recovery outcomes. They also define an identifiable range of *"barriers"* to recovery. They conclude that structured treatment has a part to play but emphasise that social support is also required if opioid dependent individuals are to progress from serious problem drug use.

The Best review gives a helpful overview of the quality of evidence addressing the elements which constitute the specific outcome of *recovery* from substance misuse. However, the report makes statements about recovery which clearly cannot be based on the evidence presented. They do conclude that there is a dearth of high quality research evidence available to assess potential for recovery in the opioid dependency field in the UK.

In 2012 the English National treatment Agency (NTA) published their report *Medications in Recovery: Re-orientating Drug Dependence Treatment* (NTA, 2012). Like the Best review in Scotland, this was commissioned (alongside a number of reviews on various approaches to treatment) by the new UK Government in order to respond to a perceived need to reconsider how treatment should be focussed in England. [In the UK, though drug control legislation is a UK Government responsibility, disaggregation and creation of the Scottish Parliament has made Criminal Justice and Health strategies a devolved power. Consequently, national strategies and delivery plans for Scottish and English services are subject to different governance and accountability arrangements. The NTA oversees

treatment delivery in England & Wales only.] The report was sponsored by ministers and produced by an invited expert group of stakeholders from a range of backgrounds including leading academics in the field in the UK and was supported by authorities from the USA.

As an Appendix to the report, a small sub-group of senior clinicians prepared a review of the literature to date - *Opioid Substitution treatment and its effectiveness: review of the evidence* (Bell, 2012). Recognising that recovery may be supported by less sound, high-quality research, the author states that the review *"seeks to integrate, as far as is possible, the discourse of evidence-based practice (built on observation and measurement), with the humanitarian, recovery-based discourse based on values (such as responsibility, choice, and empowerment)".* The approach taken was *"to identify the broadly-agreed objectives of treatment, and to review the empirical evidence as to the effectiveness of OST. The paper then reviews the factors associated with variations in treatment effectiveness.."*
No search strategy or agreed process of exclusion/inclusion of references, nor critical appraisal process is included in the review. The review was ultimately attributed to one author. As such, the report represents the views of a select group/individual (albeit a group including recognised clinical experts in the UK addiction field).

The review re-iterates the published evidence base regarding the many harm reduction benefits of OST described in this thesis. However, the authors are less optimistic regarding the evidence for improvements in those areas relating to long term recovery. Areas addressed include:

- *Quality of Life* –They conclude that measureable improvements in quality of life have been seen in the short term but there is little evidence for this being sustained beyond the early (6 month) phase of treatment;
- *Re-integration to society* - The review could identify no compelling quantitative research in this area. Qualitative research methods have raised the ambivalence of those on methadone, who recognised that being on methadone may improve the conditions for recovery – as users are not in a constant state of withdrawal – but the stigma and control associated with methadone treatment has negative effects too. Thematic analyses have identified key themes which potentially contributed to

improvements in quality of life. These were: availability of good caring relationships; having an occupation; independence; having a meaningful life.

- *Achieving abstinence* - This issue was contextualised in the review – recognising that the philosophy of OST recognises the chronic relapsing nature of addiction and does not necessarily hold abstinence at its centre. The review discusses the implications of developing a *"recovery focus"* in OST. The authors acknowledge that *"therapy requires a rationale"* and recognise the paradox of committing an individual to long term maintenance medical therapy when one aim is to help them take control of the challenge of their own lives. The historic evidence base is cited – and shows the challenge of offering effective counselling/therapeutic approaches in this group. The authors state that a recovery focus can *"provide direction and structure"* for the service user and clinician. The person's own community is also seen to have a role to play. However, the authors recognise the challenge of delivering recovery. Citing Moos (2003), they state *"individuals need long-term social supports and personal psychological resources to sustain recovery. Formal treatment can be a powerful factor in building these social supports and psychological resources to facilitate positive change, but on its own it typically does not have a lasting influence."*

What is the effect of how the OST- M is delivered?

Some reviews have considered whether the mechanisms of treatment delivery affect outcomes in OST- M.

One metanalysis reviewed 143 studies to explore the impact of programme [delivery] factors on treatment outcomes (Prendergast, Podus & Chang, 2000). They concluded that the heterogeneity of the studies led to complexity in terms of interpretation of results. Studies examined differing interventions, delivered to different heterogeneous groups of subjects and using differing outcomes and timeframes. They did conclude however, that some programme factors were found consistently to significantly correlate with better outcome. These included treatment exposure (number of appointments) and methadone dose. The same research team subsequently used meta-analysis techniques to identify methodological factors which may be affecting outcome in 78 studies (Prendergast, Podus, Chang & Urada 2002). In this review, they concluded that treatment reduced illicit drug use

and criminal activity. The specific factors which predicted better drug use outcomes included: how consistently treatment approaches were implemented (e.g. manualised delivery of programmes by well-trained and supervised staff); programmes with less *"theoretical grounding"* – i.e. where the staff were less influenced by the background theories; those with strong *"researcher allegiance"*. Projects for younger adults were felt to deliver better crime outcomes. Other factors were not shown to be predictors of outcome in this review.

Does inclusion of additional therapies/service delivery elements affect outcome?

A Cochrane review of the added effect of psychosocial interventions to ORT was undertaken (Amato et al, 2011). The review included some 35 studies, incorporating 4319 subjects in 13 distinct intervention types. Duration of these studies was relatively short term, from 6-48 weeks with a mean of only 17 weeks. Researchers were unable to demonstrate any added effect from the introduction of any psychosocial intervention with regard to the outcomes of retention, abstinence, compliance with treatment or improvements in psychological symptoms. The researchers however did acknowledge that they *"did not evaluate the question of whether any ancillary psychosocial intervention is needed when (OST-M) is provided, but the narrower question of whether a specific more structured intervention provides any additional benefit".* They also acknowledged the issue of short timeframes – none of the studies cited assessed outcomes beyond one year.

Some other systematic reviews seem to challenge the conclusions of this Cochrane review – at least with regard to specific therapies.

Community Reinforcement Approach - in a review of Eleven RCTs (n=812), Roozen et al (2004) considered the effect of the so-called community reinforcement approach (CRA). This approach encompasses an holistic bio-psycho-social approach to treatment which acknowledges the effect of environmental factors on the care process and tries to incorporate these elements into an individual's care plan. Two of the RCTs addressed the effect on opioid treatment - one reporting a greater number of participants achieving at least 8 weeks' continuous abstinence with CRA and incentives than "usual care" in a detoxification programme. However, this trend was no longer statistically significant at 24

weeks post treatment. Another RCT - the only cited addressing OST-M - reported CRA as being statistically significantly better than usual care in a methadone maintenance programme (84% of urine samples opiate negative compared with 78%). With regard to opioid treatment, the authors' concluded that there is limited evidence that CRA with incentives is more effective in an opioid detoxification programme and more effective than a standard methadone maintenance programme.

Contingency Management Approach (CM) - Griffith , Rowan-Szal, Roark & Simpson (2000) - reviewed 30 studies (n=1,568) in a metanalysis of the effect of Contingency Management on outcome in OST-M. CM uses reinforcers – essentially rewards attained for achieving agreed goals during the programme. This behavioural approach aims to shape subjects behaviours towards normalised behaviour. Based on the type of reinforcer used (i.e. the reward being tested), there were: 4 studies of methadone increase or decrease; 1 of methadone increase; 2 of methadone decrease; 6 of allowing take-home methadone; 6 of receiving award vouchers; and 10 of using mixed interventions. The target behaviour (i.e. the expected change in response to the reward) was single-drug use in 9 studies and multi-drug use in 21 studies. The overall estimated effect size (all 30 studies) suggested that the CM interventions resulted in better outcomes. The hypothesis of an overall positive CM effect (reflected across the literature) was supported, although its magnitude varied considerably. The results were felt to confirm that CM was effective in reducing supplemental drug use while patients participated in OST-M treatment. Secondly, several parameters were shown to be effective in promoting drug-free urine samples while patients were in treatment. These included the following: the use of increases in methadone dose or take-home methadone as incentives; the use of immediate reinforcement; targeting a single drug; monitoring urine three-times a week.

In conclusion – systematic reviews

Quality of the evidence

Published systematic reviews have consistently commented on the poor quality of the research evidence. Studies often have small samples and short periods of follow up. Heterogeneous populations are commonly used. Research questions are often unclear and

outcomes neither objective nor compatible. The interventions being delivered (e.g. OST-M) may be delivered in a way which is unlike normal treatment in the community – for example using fixed doses of methadone, not allowing take home methadone or failing to also deliver counselling or psychosocial supports. In the context of the delivery of British services, little high quality research has emerged from the UK, with most RCTs from the USA making the generalizability of their findings to UK practice challenging.

Effectiveness of OST-M

Despite these concerns, systematic reviews have consistently concluded that OST-M is effective in a number of ways. In particular, OST-M has been shown to: improve treatment retention; reduce opioid use and injection–based risk–taking. It may also reduce sexual risk-taking. There is less consensus regarding its effects on death and criminal activity – some reviews supporting this effect, others not.

Factors affecting outcome

Effectiveness of OST-M seems to be affected by dose (higher doses are more effective). There is a question over the effectiveness of additional psychosocial interventions, reflecting poor quality or short term research. However, there is compelling support for the view that amount of treatment exposure – or treatment "dose" may positively affect outcome. A few reviews of specific psychotherapies – Contingency Management and Community Reinforcement Approach have reported some support from the research evidence base. Finally, one review suggested a number of factors which could predict less additional drug use. These included: high level of pre-treatment drug use; a history of prior treatment for opiate addiction; having a treatment history where there was no abstinence from opioids; abstinence from/light use of alcohol; depression; experiencing high levels of stress; having employment problems; association with substance abusing peers; a short treatment period or leaving treatment prior to completion.

Recovery or abstinence

Regarding recovery and abstinence – the evidence bases are not compelling and there is clearly a need for an approach to develop this research.

Table 4. Literature review – Summary of reviews and meta-analyses

Table 4a. Substance use outcomes		
Source	Details of review – summary of methods and conclusions	Notes
Marsch 1998	*Focus: GENERAL EFFECTIVENESS OF OST-M* *Methods:* 43 studies reviewed. 11 (2056 participants) considered ongoing illicit drug use; 24 (7173 participants) criminal activity; 8 studies (1,797) HIV risk behaviours *Conclusions:* being in receipt of OST-M reduces drug use, risk behaviours and criminal activity	
Simoens et al 2005	*Focus: GENERAL EFFECTIVENESS OF OST(methadone or buprenorphine)* *Methods:* 48 RCTs reviewed 14 OST- M, 20 BRT and 14 both. Issues of quality and consistency of review – criteria not clear. *Conclusions:* OST- M and BRT treatment positively predicts retention, and abstinence or reduction	
Connock et al 2007 NICE Technology Appraisal 2007 (TA114)	*Focus: RELATIVE EFFECTIVENESS OF OST (methadone or buprenorphine)* *Methods:* Guidelines for Clinicians in the UK (report produced to support update of UK National Treatment Guidance in 2007). Expert committee took evidence on both OST- M and BRT from a wide range of stakeholders. Reviewed 31 existing systematic reviews, 87 additional RCTs and 11 economic evaluations. No UK RCTs – 16 from USA. Most studies had fixed dosing, relatively restrictive delivery (supervised consumption etc.) no psychosocial interventions and short follow up (<1yr). *Conclusions (OST-M):* 1. OST-M supports retention;, reduced opiate use; reduced HIV risk behaviours and sero-conversions; reduced mortality (with 4x increased risk of death on discharge); reduced criminal activity. 2. Higher fixed doses more effective than lower fixed doses	***Issues:*** -fixed dose treatments do not reflect normal clinical practice -evidence not sufficient to draw conclusions regarding cost-effectiveness -recognising lack of UK evidence and heterogeneity of economic evaluations, states: "none used all of the appropriate parameters, effectiveness data, perspectives and comparators required to make their results generalisable to the NHS "
Mattick et al 2009	*Focus: GENERAL EFFECTIVENESS OF OST-M* *Methods:* Cochrane Systematic Review of all RCTs comparing OST- M with placebo or non-pharmacological therapy. Reviewed 11RCT - 2 double blind - covering 1969 participants. Outcomes assessed from 45 days to maximum of 2 years. *Conclusions:* Methadone increases retention and reduces heroin use. No effect on criminal activity.	***Issues:*** Authors acknowledge -lack of evidence in key outcomes (e.g. dose and deaths; social outcomes) -no research addressing relationship between medical treatment and psychosocial treatments -methodological concerns in many studies make generalising from research impossible

Veilleux et al 2010	*Focus: TREATMENT EFFECTIVENESS SUMMARY (ALL TREATMENTS)* Aim to "synthesize the current status of opioid dependence treatment". *Methods:* Systematic review article aiming to address OST- M and forms of detoxification and abstinence maintenance in a range of substances. For OST- M - reviewed existing systematic reviews plus additional meta-analyses or controlled trials published since the most recent update of each Cochrane review. Cited 10 publications, covering 155 studies involving 28,999 subjects. *Conclusions:* OST- M improves retention, reduces opiate use and withdrawal symptoms. There are dose effects. There is a need to broaden quality research to address a range of outcomes, including abstinence.	***Issues:*** Authors raise issues of -difficulty in executing meta-analyses due to range of methods and outcomes used -research questions not covering full treatment range
Lingford-Hughes et al 2012	*Focus: DELIVERY OF RANGE OF SUBSTANCE MISUSE OUTCOMES* Aim - guideline for clinicians – update of 2004 guideline by same organisation *Methods:* Three year process overseen by expert panel. Evidence for OST- M reviewed as part of comprehensive review of all addictions treatments. Systematic review of existing reviews from credible sources (e.g. Cochrane database) or RCTs when possible. Recognition of complexity of evidence base - categorization of evidence and strength of recommendation often reflects extrapolation from lower grade evidence. If evidence low grade but strong clinical consensus in place given "S" status – standard of care. *Conclusions:* 1. OST- M supports retention in treatment; reduced heroin use; trend regarding reduced mortality; reduced drug-related risk behaviours (NOT sexual risk) 2. Higher dose OST- M more effective at improving retention and reducing heroin and cocaine use 3. NO evidence for an added effect of psychosocial interventions 4. NO evidence of reduction in criminal justice activity.	***Issues:*** Little reference to potential confounders: -quality of primary evidence base – heterogeneity of subjects; clarity of research question; sample size and representativeness -timescales of effects –value in long term maintenance and "recovery" -largely USA-based evidence base – value in UK setting
Faggiano et al 2008	*Focus: METHADONE DOSE AND EFFECTIVENESS IN RANGE OF OUTCOMES* Aim was to evaluate the efficacy of different dosages of MMT in modifying health and social outcomes and in promoting patients' familiar, occupational and relational functioning. *Methods:* Randomised Controlled Trials and Controlled Prospective Studies evaluating methadone maintenance at different dosages in the management of opioid dependence. Non-randomised trials were included when proper adjustment for confounding factors was performed at the analysis stage. Reviewed 21 studies. 11 RCTs – all from USA (2279 subjects for 7-53 weeks) and 10 CPS (3715 subjects for 1-10 years). *Conclusions:* Higher dose OST- M (60-100mg) more effective at improving retention, reducing opiate and cocaine use.	***Issues:*** Authors raise issues of heterogeneity and inconsistency of sampling etc. affecting quality of studies RCTs all from USA and timeframes are <1 year only. Lack of sufficient evidence to assess certain outcomes – e.g. mortality, criminal activity and social outcomes

Table 4b. Harm reduction outcomes		
Source	Details of review – summary of methods and conclusions	Notes
Sorensen et al 2000	*Focus: HARM REDUCTION – RISK BEHAVIOUR AND HIV* *Methods:* 33 studies with over 17,000 participants reviewed. Numerous methodological issues raised. *Conclusions:* OST- M predicts reduced drug use, risk behaviour and criminal activity.	
Gowing et al 2011	*Focus: HARM REDUCTION – HIV RISK BEHAVIOURS AND SEROCONVERSION* Aim was to assess the effect of oral substitution treatment for opioid dependent injecting drug users on risk behaviours and rates of HIV infections *Methods:* Cochrane Systematic Review of Studies which considered the incidence of risk behaviours, or the incidence of HIV infection related to (any) substitution treatment of opioid dependence. All types of original studies were considered. 38 studies involving 12,400 subjects were included. Mainly descriptive studies, or studies in which randomisation processes did not relate to the data extracted. Most studies " at high risk of bias". *Conclusions:* ORT reduces opiate use, IV use, needle sharing and HIV seroconversion. May also affect sexual risk behaviours for HIV.	***Issues:*** Authors acknowledge that "The lack of data from randomised controlled studies limits the strength of the evidence presented in this review."
Turner et al 2011	*Focus: HARM REDUCTION - HEPATITIS C SEROCONVERSION* Aim to examine effect of harm reduction (needle exchange and ORT) availability and seroconversion. *Methods:* Meta-analysis and pooled analysis of data on 2986 subjects in six areas of the UK from 2001-9. Questionnaire survey to clarify availability of ORT and needle exchange. Primary outcome of new HCV infection. 919 subjects supplied information on interventions. 40 new HCV cases identified. *Conclusions:* Access to harm reduction interventions significantly reduced new HCV seroconversions.	

Table 4c. Delivering Recovery outcomes		
Source	Details of review – summary of methods and conclusions	Notes
Best et al 2010	*Focus: RECOVERY* Aim to "assess the current state of the evidence base" supporting recovery in the field of illicit drug use. *Methods:* Commissioned research by Scottish Government to support their national strategy. Systematic literature search and review resulted in 205 articles covering treatment (79 papers), children/families (62 papers), criminal justice (27 articles) and prevention/education (37 papers). Process of critical appraisal is not well defined and descriptive articles by recovery "experts" are widely cited. It is noted that much of the evidence on recovery is from overseas (USA) and is in other areas of addiction e.g. alcohol misuse. *Conclusions:* Sustained recovery is the norm but pathways are "individualistic"; "recovery capital" is "the best predictor" of recovery outcome; there are an identifiable range of "barriers" to recovery; structured treatment has a part to play but social support is also required.	***Issues:*** The authors acknowledge the lack of systematic, consistent and relevant research in this area – mainly foreign research from related care areas. Indeed they make a plea for a new approach to research – based on longer term outcomes.
De Maeyer et al 2010	*Focus: QUALITY OF LIFE* Aim to examine the relationship between treatment and QoL outcomes. *Method:* Systematic review of the literature. 38 studies identified of which 16 considered QoL changes with ORT treatment. They found that QoL was very low on entry, did improve significantly in the first few months of treatment but then declined – though not to pre-treatment levels. *Conclusions:* QoL is a measure of success in ORT – but services need to address more than the drug use to achieve sustained improvement.	
Bell 2012	*Focus: RECOVERY* Aim to "seeks to integrate, as far as is possible, the discourse of evidence-based practice (built on observation and measurement), with the humanitarian, recovery-based discourse based on values (such as responsibility, choice, and empowerment)". *Methods:* Part of government-funded expert advice group. Selective review of papers identified by sub-group of this national expert panel. Reiterated evidence base for harm reduction effects of OST. Also focused on: achieving abstinence; re-integration; quality of life. *Conclusions: Not optimistic about current state of evidence base. Stated:* "individuals need long-term social supports and personal psychological resources to sustain recovery. Formal treatment can be a powerful factor in building these social supports and psychological resources to facilitate positive change, but on its own it typically does not have a lasting influence."	***Issues:*** No search strategy defined and range of papers reviewed unclear. Highly personal selective review

Table 4d. Factors impacting on outcome		
Source	Details of review – summary of methods and conclusions	Notes
Brewer et al 1998	*Focus: REDUCING RELAPSE & IMPROVING OUTCOMES* Aim to identify factors which predict ongoing drug use in treatment *Methods:* Systematic review of 69 studies (43% OST- M). Correlations computed over time. 28 variables identified which may have impacted on substance use – these were from 8 categories: demographics; drug use history; non-opiate drug use; physical/mental health; criminal activity; employment; psychosocial variables; treatment length and completion. *Conclusions:* Factors associated with more continued use were: High levels of substance use pre-treatment; history of prior treatment; history of treatment without abstinence; light alcohol use depression; high stress levels; unemployed or employment problems; associating with substance using peers; short treatment period; leaving treatment before completion	
Griffith et al 2000	*Focus: TREATMENT DELIVERY – CONTINGENCY MANAGEMENT APPROACH (CMA)* Aim to assess the added effect of Contingency Management Approach to OST- M. *Methods:* Systematic review and meta-analysis of 30 studies involving 1562 patients (range 5-360). *Conclusions:* CMA has a significantly increased effect on outcome in OST- M. Moderators existed – relating to the targeting of CM/delivery of the intervention. These had impact on effect size	***Issues:*** Small numbers of studies and significant heterogeneity in terms of treatment delivery, OST- M dose ranges, follow up times etc. meant that further research is required
Amato et al 2011	*Focus: EFFECT OF PSYCHOSOCIAL INTERVENTIONS ON TREATMENT OUTCOME IN ARANGE OF INTERVENTIONS* *Methods:* Systematic review and metanalysis of 35 studies involving 4319 subjects in 13 distinct interventions. Studies short term (6-48 weeks duration, mean 17 weeks). *Conclusions:* Unable to demonstrate added effect regarding retention, abstinence, treatment compliance or improved psychological symptoms.	***Issues:*** Authors acknowledge - "the review, actually, did not evaluate the question of whether any ancillary psychosocial intervention is needed when methadone maintenance is provided, but the narrower question of whether a specific more structured intervention provides any additional benefit to a standard psychosocial support" -raises methodological questions -also issue of USA based evidence (relevance to UK practice) -issue of short timeframes

Table 4e. Patient characteristics impacting on outcome		
Source	Details of review – summary of methods and conclusions	Notes
Greenfield et al 2007	*Focus: GENDER* Aim to examine Factors affecting outcomes in women with substance use disorders. *Methods:* Literature search 1975-2005. 280 articles identified of which 11.8% were RCTs. *Conclusions:* Women less likely to enter treatment. Once in treatment, gender does not predict retention, completion or outcome. Gender specific services not necessarily of value but identify need for interventions focussed towards specific sub-groups.	***Issues:*** Authors acknowledge small sample sizes and lack of RCTs. Potential for positive bias from peer-reviewed research.
Ashley et al 2003	*Focus: GENDER* Aim to examine evidence for effectiveness of treatment programming for women and to summarize knowledge around effectiveness of different approaches for women. *Methods:* Systematic review of 38 studies (7 RCTs). The RCTs considered only 253 subjects for a timeframe of up to maximum 2 years. They considered specific gender-related treatment components: Child care; prenatal care; women only programmes; services addressing women's topics; mental health & comprehensive programming. *Conclusions:* They found evidence for these factors having an impact on outcomes including Illicit drug use reduction; Mental health symptom reduction; Improved birth outcomes; Employment; Health status and HIV risk reduction; treatment completion; length of stay	***Issues:*** Authors acknowledge the lack of research evidence from RCTs – most is cross-sectional and observational research

Factors influencing outcomes (Predictors)

The research papers identified in the literature search were critically appraised to identify potential predictors and suitable outcomes for scrutiny. Brief descriptions of the findings are included below. The results are summarized in Table 5. (p91).

Demographic factors

Age

A number of studies have assessed the potential impact of age on outcome in substance misuse treatment. The literature search identified 3 specific research papers which focussed on this issue in the OST-M population. Two of these studies included a follow up element, allowing researchers to comment on any effect on outcome. *In summary: Despite limited evidence (one paper) that retention is affected by age, there are no publications from this review which have found age to be a predictor of outcome in substance misuse treatment.*

Gender

Women often appear to be under-represented in drug treatment services. It has been hypothesised that gender may impact on clinical process – affecting how services are accessed, what treatment options are chosen, retention – or how services are experienced by women. This could affect treatment outcomes with the view often expressed that women would benefit from dedicated services to address their specific needs. The literature search identified 15 specific research papers which focussed on this issue in an OST population. Three were review papers. Unusually all but one of the remainder of these studies included a follow up element, ranging from 3 months to 30 years, thus allowing researchers to comment on any effect on outcome. One paper was excluded as it addressed only Buprenorphine (Back et al, 2011). *In summary: gender has been explored in the OST-M population – but often as part of other studies, with gender rarely the main research focus. Research questions have often been unclear. Unusually, however, much of the research does have follow up assessments. Despite this, gender has not been shown consistently to have any significant impact on outcome. Some researchers suggest there may be implications for*

treatment process/delivery but no research to date has explored this in any detail. NIDA has raised the need for gender issues to be better addressed in study design.

Personal & social factors

A number of studies have hypothesized that a range of personal and social factors may impact on the effectiveness of substance misuse treatments. The literature search identified 9 relevant papers of which 5 contained a follow up assessment from 35 weeks to 12 years after initial assessment. One paper was excluded as unavailable for review (Copenhaver et al, 2011). *In summary: there is some research evidence that social and inter-personal factors are important in terms of substance misuse treatment outcome. The body of evidence often reflects studies which have explored a broad range of factors with potential to influence outcome. Few studies address long term outcomes. More definitive, focused study of larger, more representative samples over longer, more relevant timeframes is required.*

Table 5. Literature review – Summary: Patient characteristics

Source	Independent Variables	Dependent variables	Study type	Findings
Burns et al 2009	Age	Retention	Longitudinal study (retrospective cohort study) using Australian national data on 42, 960 cases over 21 years	**Younger age had poorer retention**. Poorer retention not associated with poorer clinical outcomes
Rosen et al 2008	Age (>50s v <50)	Substance misuse outcomes	Retrospective cohort study with 24 month follow up	NSD
Johnston et al 2003; Najavits et al 2007	These studies simply described females accessing particular programmes – there was no specific research question and no control group for comparison			
Marsh & Simpson 1986	Gender	Behavioural differences Psychological status Reasons reported for stopping drug use	Retrospective cohort study – 12 years post DARP	NSD relating to IV **Positive gender differences found** **Positive gender differences found**
Karuntzos et al 1994	Gender	Service responses to employability requirements	Prospective descriptive study with 3 month follow up	**Positive gender differences found**
Grella & Lovinger 2012	Gender	Illicit drug use Chronic health problems Psychological distress	Retrospective cohort study with 30 year follow up	NSD **Positive gender differences found** **Positive gender differences found**
Eiroa-orosa et al 2010 , Jones et al 2005, Campbell et al 2009	Gender	Range of substance misuse outcomes including retention, treatment duration illicit drug use	RCT comparing ORT types 1 yr, Retrospective cohort study (4/12) Retrospective cohort study (6yr)	NSD NSD NSD
Burns et al 2010	Methadone/not [in women]	Range of reasons for hospital admissions	Retrospective cohort study of women on methadone with 4 year follow up	Identified significant differences in those on methadone/not

Havens et al 2009	Employment status; psychiatric distress; unstable housing; distance form treatment site	Retention	RCT of psychosocial interventions in needle exchange attenders	**Positive associations with retention found in all factors listed**
Flynn et al 2003	Patient characteristics: personal motivation at baseline; previous treatment; religion/spirituality; family relationships; employment	"Recovery" – drug free; reduced alcohol use; no illegal activity for 1 year	Retrospective cohort study using DATOS data -532 OST-M patients 5 year follow up	**Positive associations found with listed factors**
Skinner et al 2011	Patient characteristics: retention; education or employment; less relationship disruptions; depression; deviant friends; poor coping skills	Recovery and range of substance misuse outcomes	Retrospective cohort study of 144 patients 12 year follow up	**Positive associations found with listed factors**
Stewart et al 2007	With/without children	Substance use outcomes	Prospective cohort study as part of NTORS. 1 year follow up	NSD
Heinz et al 2009	Relationship closeness	Retention and substance use outcomes	9month follow up study of 635 new OST- M patients	**Positive associations found**

Common co-morbidities

Researchers have studied a number of common co-morbid conditions in substance misusers. The literature search identified studies relating to the co-morbid conditions which were relevant to the Tayside Methadone Cohort baseline assessment. The results are summarized in Table 6. (p96).

Pain

The management of pain in the context of substance misuse is challenging. This reflects a number of issues. Many pain medications carry addictive potential which means that in managing chronic pain syndromes, doctors must recognise the risk of developing substance use disorders, perhaps reflecting the development of hyperalgesia (Fishbain et al, 2009). The development of substance misuse issues may be further complicated by other, often psychiatric, co-morbidities (Manchikanti et al, 2007). This problem has the potential to be hazardous and may even predict overdose death in pain patients (Dunn et al, 2010). Primary substance misusers are a group who are prone to injury and may not utilize rehabilitative services effectively, resulting in long term pain management challenges. Also, methadone patients (or those on any opioid with a long half-life) have been shown to be more sensitive to pain (Compton, Charuvastra, Kintaudi & Ling, 2000). This could mean that they have increased needs for pain treatment when compared to the general population. Despite this, substance misusers are often treated outside normal guidance or are undertreated. Both chronic pain and substance misuse can be complex issues, requiring a coordinated approach to multi-disciplinary care delivery. This challenge has been recognised in the guidance available for doctors in the UK (Department of Health, 2007; British Pain Society, 2007).

Research in this field addresses the problem from both perspectives –the management of pain patients (researching the risk of developing a substance use disorder) or primarily from the perspective of the management of substance misusers who experience co-morbid pain. The literature review described considered the research evidence-base addressing the place of pain as a predictor of substance misuse outcome in substance misusers in receipt of OST-M. Seven studies were identified of which only one involved a follow up assessment of outcome. *In summary: Cross sectional studies have described many relationships between*

the presence of pain and substance misuse status. It has been suggested from these studies that substance misusers with chronic pain syndromes are less stable, more likely to use illicit drugs and require higher doses of methadone (if on OST-M) to achieve stability. Only one longitudinal study has been published to date, in the USA. This found that at 1 year follow up those on OST-M who also had chronic pain showed poorer measures of social functioning, but did not show any impact on substance use outcomes.

Psychiatric illness - general

Psychiatric illness is commonly found alongside substance misuse. The 2007 English Psychiatric Morbidity Study on adults living in their own home showed that 12% of males and 6% of females had some kind of substance dependence concurrent with a psychiatric illness (Adult psychiatric morbidity in England, [NHS Information Centre] 2007). The main substances misused by those with mental health problems are alcohol and cannabis. Half of those consulting a doctor for an alcohol problem present with mood or anxiety disorders. Some 50% of suicides in the UK since 1997 have had a history of alcohol misuse (NICE, 2011). Such problems are also common in the area of illicit drug dependency. In Scotland it was reported that 40% of new referrals to services (or those re-referred after a 6 month absence) did so for mental health reasons (Scottish Executive, 2006). The UK NTORS study found that one fifth of those presenting for a range of treatments for substance misuse had had previous treatment for psychiatric disorder (Marsden et al, 2000).

The literature review identified 26 studies which directly assessed the relationship between substance misuse treatment outcomes and psychiatric comorbidity. Twelve were cross-sectional studies, involving one off assessments of a sample while 14 were longitudinal studies which included a follow up component. These longitudinal studies had follow up periods of 6 months to 6 years. *In summary: the relationship between presence of co-morbid mental illness and substance misuse treatment outcomes for those on OST is complex. Even those studies which have shown a significant relationship with outcome have generally done so over relatively short timeframes. This could reflect the methodological difficulties in carrying out the diagnostic assessments required. However, the GHQ28 is a tool which has some merit in many clinical populations and has been shown to be valid and reliable in substance misusers. The screening of substance misusers for psychiatric "caseness" has not*

been well described in the literature but the limited research to date has linked "caseness" with short term outcomes.

Research which considers specific diagnoses was not found to be definitive in this literature review. Regarding ***depression*** *– only the ATOS study has brought forward compelling evidence regarding the impact on outcome in an OST-M sample. Regarding* ***PTSD -*** *Results are conflicting. Follow up studies have not consistently shown that PTSD impacts on process nor outcome in OST-M.* ***ADHD*** *seems to be highly prevalent in substance misusers yet little research has explored the impact on outcome. In this review, there was no published research which has explored impact on substance misuse outcomes in OST-M beyond 9 months.* ***Anxiety disorders*** *are commonly observed in OST-M populations but this review did not identify a definitive evidence base regarding the impact of any anxiety disorder on outcome.*

Many mental illnesses, like substance misuse are chronic relapsing conditions which fluctuate over time. Addressing issues of cause and effect is difficult. Longer term follow up and review is required to determine the true relationship with outcomes.

Table 6. Literature review – Summary: Impact of Comorbidities

Source	Independent Variables	Dependent variables	Study type	Findings
Ilgen et al 2006	Pain	Substance use outcomes	Prospective study of 200 new OST- M patients with 1yr follow up	**Impact on social functioning** but NSD with substance use
Cacciola et al 2001	Comorbid mental illness	Substance use outcomes	Retrospective cohort study of 278 OST- M patients with 7/12 follow up	NSD
Maremmani et al 2000	Axis 1 psychiatric diagnosis	Retention	Retrospective cohort study of 90 OST- M patients with 3 year follow up	NSD
Astals et al 2009	Axis 1 psychiatric diagnosis	Retention	Retrospective cohort study of 189 OST- M patients with 18/12 follow up	NSD (**but higher OST- M dose required for stability)**
Krausz et al 1999; Verthein et al 2005	Comorbid mental illness	Substance use outcomes	Prospective study of 219 OST- M patients with 5 year follow up	NSD
Pani 1997; Pani 2011	Severity of psychiatric symptoms	Substance use outcomes	Prospective study of 259 & 267 new OST- M patients with 1yr & 2 year follow up	NSD
Schafer et al 2010	Mental health symptoms	Substance use outcomes	RCT of different ORT types in 1015 new patients with 1yr follow up	NSD
Fernandez et al 2001	Psychiatric disorders/diagnosis	OST- M dose and substance use outcomes	6yr follow up study of 132 OST- M patients.	**Anxiety/affective disorders predicted heroin/benzodiazepine use.**
Schulte et al 2010	Unidentified/unaddressed mental health issues	Retention	Retrospective cohort study of 176 OST- M patients with 90/7 follow up	**If MH problems not addressed this impacted on retention**
Compton et al 2003	Baseline psychiatric disorders	Substance use outcomes	Prospective study of 401 new OST- M patients with 1 year follow up	**Positive association with outcome**

Broome et al 1999	Psychiatric symptoms and diagnosis	Substance use outcomes	Prospective study (DATOS) at 1 year	**Current symptoms better predictors than lifetime diagnosis**
Gelkopf et al 2006	Comorbid mental illness – symptoms, diagnosis and distress	Substance use disorders - SUD (type); Drugs misused; retention	Prospective study of 151 OST- M patients over 3 years	**Current comorbidity associated with SUD. Axis 1 diagnosis associated with better retention and outcomes; distress associated with poorer outcomes**
Musselman & Kell 1995	Severity of substance use disorder	Improvement in psychopathology	Prospective study of 71 new OST- M patients over 24 months	NSD
Gossop et al 2006	Mental health disorder	Substance use outcomes	Prospective study (NTORS) with 5 year follow up	**Association between improving mental health and SUD outcomes**
ATOS study - Havard et al 2006; Darke et al 2009	Major depression	A range of process measures and outcomes	Prospective study of 495 new patients in arrange of treatments with 1yr and 3yr follow up elements	**Complex association demonstrated between depression and substance use process and outcome.**
Fitzimmons et al 2007	Mood/anxiety disorders	Substance use outcomes	3/12 follow up of 106 pregnant drug users entering OST- M	**Mood disorder impacted on substance use outcome**
Chilcoat & Breslau	PTSD/Trauma	Development of substance use disorder	Prospective study of 1007 subjects screened for trauma. 5yr follow up	**PTSD had higher risk of SUD**
Trafton et al 2006	PTSD	OST- M treatment process; retention	Retrospective cohort study of 255 new OST- M patients – 28% PTSD. 1 year follow up	**PTSD cases worse at intake & longer history; also higher OST- M dose and better retention**
Hien et al 2000	PTSD	Retention and substance use outcomes	3/12 prospective study of 96 new OST- M patients	**PTSD associated with higher drug use.** Retention - NSD

Mills et al 2005 & 2007	PTSD	OST- M process, substance use outcomes	1 & 2 year follow up study of new OST- M patients	**PTSD – worse physical and mental disability and occupational functioning** Process NSD
Kolpe & Carlson 2007	ADHD	Substance use outcomes	9/12 follow up of 687 new OST- M patients	**58% had ADHD symptoms. ADHD associated with poorer outcomes**

Illicit drug use

The nature of substance misuse as a chronic relapsing condition associated with high risk – in particular relating to BBV infections through injecting - has resulted in the development of a hierarchy of "harm reduction" measures of progress in treatment. These measures are reflected in clinical practice across the world and most of the studies cited use validated tools which aim to demonstrate progress in a number of domains (Marsden et al 1998; McLellan et al 1992). Using such tools, substance misusers can often show improvement in their condition while failing to completely abstain from all illicit drug use. Indeed, in the clinical setting, improvements are often seen in areas of social functioning and physical and psychological health even while illicit drug use is ongoing. However, the extent of illicit drug use on OST-M treatment has consistently been seen to be an important outcome – as shown in the systematic reviews above. These systematic reviews have also shown that evidence of improvement in areas of social functioning is sparse.

Drug death data in the UK has shown that most deaths involve multiple substances (Zador et al 2005; Health & Social Care Information Centre, 2011; ISD, 2012). Over recent years, as more substance misusers in parts of the UK have entered OST-M, there seems to be an increase in the finding that methadone is a component in these deaths (ISD, 2012). Recovery has become a focus for treatment and, for many involved in this debate, moving towards objective abstinence is a key component of that recovery process, driving changes in guidance for clinicians in the UK (NTA, 2012). But this is inevitably a lengthy process. Research into long term abstinence from illicit drugs has suggested that the achievement of 5 years of abstinence is a strong indicator of success (Hser 2001).

In this context, it is important to consider the relevance of ongoing drug use in terms of the broader outcomes we are trying to achieve in OST-M. The results are summarized in Table 7. (p146).

Cannabis

In summary: all of the cannabis studies identified in the literature search had follow up components – though never longer than 1 year. Overall cannabis use seems to have little impact on these relatively short term treatment outcomes but there are hints that its use

may make recovery more challenging – in particular that the amounts used or the nature of that use may reduce success.

Benzodiazepines

At face value, use of benzodiazepines is a serious clinical challenge in OST-M services. Guidance is vague regarding how illicit benzodiazepine use should be addressed. In the context of recovery – at the very least improvement in social functioning is likely to be impacted on by ongoing sedative drug use. However, it is also clear that benzodiazepine use is a significant factor in drug death in the UK (Zador et al 2005; ISD, 2012; Health & Social Care Information Centre 2011). Eight relevant studies were identified exploring this issue, of which only 3 had any follow up assessment. *In summary: Benzodiazepine use is a common precursor to OST-M and, while on OST-M treatment, ongoing benzodiazepine use may affect participation in treatment and short term outcome – though the evidence identified is not conclusive.*

Prescribed opioids

The use of opioid drugs – either not prescribed for the individual, or prescribed (for pain for example) but used in a way that is not prescribed – is a long-standing problem in those traditionally presenting to addiction services. This problem however, has become an issue in people attending other medical services and potentially encroaches on new treatment populations, not previously seen as substance misusers. Consequently, misuse of prescribed opioids is now beginning to be seen as a significant public health issue in the USA and UK (Warner, Chen & Makuc, 2009; Volkow et al, 2011; Dhalla , Persaud & Juurlink, 2011). In this review, seven studies were found which considered the misuse of other opioid drugs (i.e. not illicit heroin) in substance misusers and their potential impact this could have on outcomes in OST-M. These studies were often in residential detoxification units. Other than the review, all were descriptive and none had a follow up component. *In summary – use of prescribed opioids/other opioid drugs is clearly extremely common in those presenting for substance misuse treatment. There is some evidence that certain factors may differentiate those who can be seen as having a "primary heroin" disorder or a "primary prescribed opioids" disorder – factors such as previous pain syndrome or mental health disorder.*

However, there is no research identified in this review into the potential effect of other opioid use on outcomes in OST-M.

Cocaine use

Many studies explore the effect of various treatments on cocaine use. Indeed improvements in use of cocaine is often a key outcome reported in systematic reviews of OST-M. Only one study was identified in this review, which addressed the specific impact of cocaine use on clinical outcomes in OST-M. *In summary: there is only one study identified. This showed that use of cocaine predicted more hospitalizations in an OST-M population over 2 years.*

Table 7. Literature review – Summary: Substance use

Source	Independent Variables	Dependent variables	Study type	Findings
Raffa et al 2007	Abstinence from illicit drugs	Programme adherence – process measures	Retrospective cohort study of 60 HIV positive OST- M patients with 3 year follow up	**Only 4/60 remained abstinent. Opiate users adhered less well while amphetamine and benzodiazepine users did better**
Budney et al 1998; Weizman et al 2004; Epstein & Preston 2003	Cannabis use	Substance use outcomes	Prospective study of 109; 283; 408 new OST- M patients. 1year follow up	NSD
Ghitza et al 2007	Reporting of cannabis use	Substance use outcomes	RCT of contingency management in 690 new cases for 6 months	**Under-reporters of cannabis more likely to use heroin and cocaine**
Brands et al 2008	Benzodiazepine use	Substance use outcomes	Retrospective cohort study of 172 new OST- M patients. 2year follow up	**Ongoing benzodiazepine users more likely to have +ve screens for opiates and cocaine. In this group cocaine use negatively affected retention**
Eroia-orosa 2010	Benzodiazepine use	Retention and outcomes	RCT of ORT types	**Baseline benzodiazepine use correlates with poorer retention (not outcome)** **Ongoing benzodiazepine use affects outcome (illicit use)**
Ghitza et al 2008	Benzodiazepine use	Substance use outcomes	12 week follow up study of 361 OST- M patients	**Baseline benzodiazepine use – even low dose associated with poorer outcomes –- in OST- M**
Bovasso & Cacciola	Baseline cocaine use/not	Hospitalization	Retrospective cohort study of 222 new OST- M patients. 2 year follow up	**Cocaine use predicted more hospitalizations**

Aspects of service delivery

Researchers have considered how the types of treatment available to substance misusers and how these treatments are delivered in practice may impact on outcomes. These issues were key aspects of the work progressed in the US prospective studies – especially DATOS. A number of studies and reviews have explored the literature relating to a number of these factors, including: patient characteristics and programme factors; attendance in services; patient satisfaction with the programme; patient motivation and commitment to treatment; locality and travel distance to services; treatment intensity; types of service delivery – including setting (specialist or primary care), high/low threshold programmes, with/without additional services, delivered within the main service or by an alternative provider. Results are summarized in Table 8. (p 104). *In conclusion: the way services are delivered has been exhaustively assessed in US studies but research has not shown definitively that the availability of additional counselling, therapy or practical support, focused on (for example) employment, consistently impacts on outcomes achieved. Indeed some studies into intensity of delivery give conflicting results. This could reflect the stage of recovery subjects are at when treated or assessed. None of the relevant research is UK-based and it must be recognise that the US systems for OST-M delivery differ considerably from those in the UK.*

Table 8. Literature review – Summary: Impact of aspects of service delivery

Source	Independent Variables	Dependent variables	Study type	Findings
Saxon et al 1996	Patient characteristics; Programme philosophy; ancillary services offered	Drug use (weekly urine) and ASI scores	Prospective controlled study of 353 new OST- M patients. 3 conditions. 18/12 follow up	**Complex relationships with multiple factors "predicting" outcomes. Enhanced services gave less cocaine +ves but more opiate +ves.**
Simpson et al 1995	Session attendance and assessment of quality of interactions	"Behavioural changes"	Prospective study of 557 new OST- M patients	**Session attendance and better patient/counsellor assessments of interaction improved outcome**
Crevecoeur-Macphail et al 2010	Attendance	Retention and Substance use outcomes	Prospective study of X new OST- M patients(20 programs) over 9 months	**Better attendance improved retention and outcomes**
Kelly et al 2010	Patient satisfaction	Substance use outcomes assessed by ASI	Prospective study of 283 new OST- M patients	**Patient satisfaction predicted outcome**
Morris et al 2008	Patient satisfaction (TPQ)	Substance use outcomes	Prospective study of 841 existing patients in arrange of treatments (including OST- M) 8 month follow up	**Patient satisfaction predicted outcome in all treatment types**
Broome et al 1999	Patient motivation and commitment	Process measures – maintaining motivation; establish rapport; attendance	Retrospective cohort study of DATOS patients with 3 month follow up	**Those scoring positively for commitment at outset maintained this and attended better**
Friedman et al 2001	Availability of transport provision	Retention	Retrospective cohort study of 3175 DATOS patients in various programmes (1144 in OST- M). Programmes asked about travel provision	**Retention better if provision in place**
Hubbard et al 1995	Sessions attended	Substance use outcomes	Retrospective cohort study of DATOS subjects	NSD

Avants et al 1995	Intensive day programme v standard care	Substance use outcomes	Prospective controlled study of 291 new OST- M patients in 2 treatment types – standard and intensive	NSD
King et al 2006	OST- M delivery types – degrees of intensity	Substance use outcomes	Prospective controlled study of three treatment types – own doc; doc + counsellor; specialist doc + counsellor	NSD
Teesson et al 2006	Treatment "dose"	Substance use outcomes	Prospective study of 745 patients in range of treatments (ATOS) with 1yr follow up	**"Dose" associated with improvements in drug use, criminality, psychopathology and injecting risk**
Corsi et al 2009	Treatment intensity & retention	Substance use outcomes	Retrospective cohort study of 160 new OST- M patients. 6/12 follow up	**Intensity and retention both impacted on drug use and injecting risk**
Rhoades et al 1998	Methadone dose; attendances	Retention and substance use outcomes	RCT of 150 new OST- M pts in 4 groups based on dose and intensity. 24/52 follow up	**Higher dropout in high intensity; lower drug use in higher dose. HIV risk reduced for all and older/experienced did best**
Kraft et al 1997	Support services available	Drug use; health; work; criminal activity; social functioning	RCT of 100 new OST- M patients. 6 month programme with 6 month follow up	**More intensity predicted better outcomes in programme – only abstinence maintained 6/12**
Mclellan et al 1993	Extra counselling; medical care; psychological services	Retention and outcomes	CT of 92 new OST- M patients to three trial conditions with 6/12 follow up	**Basic OST- M with no counselling ineffective. Counselling improved efficiency of OST- M**
Wu et al 2010	Additional external support	Reported drug use	Retrospective cohort study of 356 existing OST- M patients - 3x assessments 6/12 apart	**Extra support predicted less use**

Wasserman et al 2001	Focus of counselling – "abstinence specific" or "general"	Drug use	Prospective study of128 ORT patients (OST- M & LAAM). 3/12 follow up	**Abstinence-specific impacted on cocaine use NOT opiate**
Schwartz et al 2006	Interim OST- M v waiting list	Graduation to full OST- M; Substance use outcomes	RCT of 319 waiting list OST- M patients – allocated to 2 groups.	**Interim group showed considerable improvements**
Schwartz et al 2011	3 levels of OST- M intensity RCT	Substance use outcomes	4/12 follow up	NSD

Prediction of specific outcomes in OST-M

This section describes the results of the literature review regarding those papers considering prediction of specific outcomes in OST-M patients. These studies are summarized in Table 9. (p 108).

Research on the prediction of positive outcomes

A number of studies have explored prediction of a range of outcomes in OST-M patients. Substance use outcomes considered in focused studies have included: substance use (all substances); illicit opioid use; dose of methadone, retention or drug death. Blood borne virus infection or engagement in risk behaviours have also been specifically considered. Development of physical and psychiatric health problems and related use of health services have been explored. Limited research has attempted to predict social outcomes. However, much of the published literature has not assessed specific research questions or has considered the impact of a broad range of factors (predictors) and their potential impact on a range of outputs or outcomes. *In summary: This review has found that the identified predictive studies add little to the literature already identified. In some published papers, the prediction perspective of the work relates to a statistical exercise – usually a regression analysis, often examining data generated by a single cross sectional assessment of the data. While this may be valuable as preliminary research, it cannot replace a longitudinal assessment of relationships over time. There is often no identifiable research programme to take forward the findings of many of these preliminary descriptive studies. There is also a dearth of helpful information on some key outcome areas in OST-M treatment – such as employability and use of health services. This deficit makes assessment of many factors/processes potentially affecting recovery impossible.*

Table 9. Literature review – Prediction of clinical outcomes in OST-M patients

Source	Predictor variables	Clinical outcomes predicted	Study type	Findings
Mclellan et al 1994	Baseline: Severity of substance use; psychiatric, employment, family problems. At 6 months: Services received for substance use, psychiatric, employment and family problems	Substance use –by report and testing "Social adjustment"	6/12 follow up study of 649 substance users – mixed substances and programmes	Overall substance use outcomes predicted by same factors regardless of substance. Substance use predicted by severity of SUD and NOT by treatment received Social adjustment negatively predicted by psychiatric, employment and family problems and positively predicted by receipt of services for these issues
Peles et al 2008	OST- M (2 centres)	Retention and abstinence from opiates	302 US and 492 Israel, new OST-M patients. 1year follow up. Regression analysis.	Both: higher OST-M dose predicted positive outcomes. Israel: early abstinence from opiates/benzos +ve predictor US: not using stimulants and age (<30) +ve predictor
Marsch et al 2005	ORT – LAAM, OST- M,BRT	Retention and percentage of positive drug screens - opiates and cocaine	165 new OST-M patients. Follow up 119/7 (4/12).	NO PREDICTORS IDENTIFIED

Morral et al 1999	Early treatment characteristics	Retention and positive drug tests at 6 & 9/12 follow up	Retrospective cohort study of 59 new OST-M patients. Regression analyses.	Counselling attendance and opiate abstinence in first two weeks predicted +ve 6&9/12 outcomes in 80% of cases.
Friedman et al 2003	Patient characteristics at intake	Health status at 24/12 follow up	2966 new OST-M patients (DATOS) followed up for 24/12. Multivariate linear regression model used.	Poor physical health status; presence of comorbid conditions; severity of psychiatric symptoms at baseline strong predictors. Also age, public insurance cover and unemployment
Mancino et al 2010	Patient characteristics at intake	Retention at 3 year follow up	2363 US veterans – new OST-M patients	Younger age, serious mental illness, ethnicity (African American), race recorded as unknown strong predictors of negative outcome.
Peles et al 2010	Patient characteristics	Retention and survival over 15 years	613 patients ever on OST-M over 15 year period. 93 had died.	Survival predicted by: younger age (<40) at admission; living with partner; hep B negative; not using benzodiazepines; not referred directly from hospital or discharged from programme to hospital. Retention predicted by: not being referred from hospital or discharged to hospital; high OST- M dose; no opiate/benzo use at 1year; psychiatric diagnoses. NB Benzodiazepine use reduced both outcomes.

McCowan et al 2009	Patient characteristics	Mortality over 11 years	Retrospective cohort study. All 2378 OST- M patients prescribed in primary care in a UK region over 11 years. 181 dead (60 drug deaths). Data linkage and regression analyses used.	"All cause mortality" predicted by: overuse of Methadone; psychiatric admission history; increasing comorbidity Drug deaths predicted by: mental illness history; GP prescribing of benzodiazepines. Protective factors: retention and evidence of drug testing
Kimber et al 2010	Exposure to ORT	Injecting behaviour and mortality over 26 years	Follow up study of 655 injecting drug users from historical cohort. 577 had received OST- M. 277 had stopped injecting. 228 were dead.	ORT exposure did not predict reduced injecting but did reduce risk of mortality
Roszell & Calsyn 1986	Dose of OST- M: <35mg; 36-59mg; >60mg	Various outcomes – including emotional distress, hospitalization; drug use; retention at 1 yr.	1yr follow up of 106 OST- M patients. ASI at baseline. At 6/12 divided into 3 groups by dose range.	*High dose group*: high emotion and more psych treatments; also more use of barbiturates and stimulants. More drug use in treatment *Medium:* low 1 year retention *Low*: fewer friends
Donny et al 2005	OST- M dose & CM	Heroin use	Volunteers. Existing OST- M patients offered increased OST- M and CM. No controls.	Higher doses associated with less use and less need for CM
Gerra et al 2004	BRT v OST- M Range of patient factors	Retention	154 new OST- M/BRT patients. 12 week outcome	NSD between ORT types. Retention predicted by baseline psychosocial functioning and Rx dose

Kelly et al 2011	A range of baseline assessment factors – ASI scores	Retention at 3 months and 1yr	Longitudinal study of 351 new OST- M pts. Regression analysis. 248 of these reviewed 1yr	At 3/12: Female gender, treatment readiness predicted retention. At 1yr: ASI scores and MM dose
Joe et al 1995	Psychological difficulties	Engagement /attendance at 3 months	90 day follow up of 462 new OST- M patients	More psychological problems attended more
Joe et al 1999	A range of baseline factors	Engagement	6 month follow up of 396 new OST- M patients	Pre-treatment motivation impacted on engagement
Farre et al 2002	1.OST- M v placebo; 2.High v low dose 3.OST- M v BRT 4. OST- M v LAAM	Retention and reducing drug use	Review of 13 trials (1944 subjects – 1282 on OST- M)	1.High dose OST- M impacts on retention/drug use. Low dose OST- M predicts retention 2. NSD with retention. High dose reduces opiate use. 3. NSD in comparable doses 4.High dose OST- M> LAAM for retention. Low dose OST- M < LAAM for opiate use
Mattick et al 2009	OST- M v placebo	Retention, drug use and risk-taking	Review of 11 RCTs, 1969 subjects. Follow up <2years	OST- M improves retention, use
Gowing et al 2011	OST- M	HIV risk reduction	Review of 38 studes (35 with OST- M) – 12,400 subjects	OST- M reduces HIV IV risk behaviours.
Turner et al 2012	Harm reduction provision availability	Hepatitis C seroconversions	Metanalysis with pooled analysis; 6 UK cities; 2986 drug users.	Availability of BBV prevention activity reduced risk of Hep C conversion
Soyka et al 2008	BRT v OST- M	Retention and substance use	6 month follow up study – two treatment groups	Retention 52.8% NSD Drug use reduced NSD
Britton & Conner 2010[1]	Patient factors	Suicide attempts	1 year follow up of 2966 new SUD patients (mixed treatments). Multivariate logistic regression to identify predictors	*Risk factors*: Previous attempts; suicidal ideation; depressed; primary cocaine use; OP OST- M/short term in-patient *Protective:* Male; age

Britton et al 2010[2]	Patient factors	Suicide attempts	12 months follow up of SUDs after discharge from treatment	3.1% overdosed; Risk factors: O/D history; IV use; Male; Pain severity and H/O sexual abuse
Gibson et al 2008	Range of factors plus BRT v OST- M	Death	RCT of 450 ORT patients. 10 year follow up. Data linkage.	OST- M v BRT no difference. Increased ORT exposure by >7 days is protective. More dependent=lower risk & more exposure to treatment.
Hoffmann et al 2001	OST- M	Acute hospital admission	175 new OST- M patients. Hospital admissions recorded 3 years before and after OST- M started.	223 hospitalizations in 6.5yrs. NSD in before/after numbers but types changed - less to do with IV use
NGO et al 2008	OST- M v Naltrexone	Hospitalization	522 OST- M v 314 Naltrexone implant. Retrospective cohort study.	Both groups substantial reductions in admissions OST- M: less likely to be admitted for “non-opioid” or “any drug”. More likely to be admitted for “opioid”
NGO et al 2011	Psychiatric comorbidity	Hospitalization	Same cohort.	Psychiatric comorbidity increased admissions pre-treatment. Difference reduced after treatment
Bloor et al 2008	OST- M	Drug use	68 OST- M patients over 33 months	OST- M reduces “topping up” – greater effect than other treatments
Zanis et al 1994	Range of patient factors	Employment stages	340 existing OST- M patients. Cross sectional study and multiple regression	Low depression score, cocaine abstinence, education status, marital status predicted better employment status

Discussion – what do we know from the literature review?

This chapter has described the results of a structured review of the literature which aimed to scrutinize the published research considering the factors impacting on outcomes in patients receiving opioid substitution therapy using methadone (OST-M).

Outcomes assessed

The review has identified many papers describing primary research findings as well as a number of systematic reviews addressing the effectiveness of OST-M. Outcomes considered in much of the research are similar across the field. These include:

- *Retention:* Many studies and reviews consider treatment retention
- *Reduced drug use* - a measure of change in illicit drug use patterns – less drugs overall, impact on use of specific drugs (such as opiates, cocaine)
- *Reduced risk*-taking - less hazard, either injection-related or sexual activity. Deaths.
- *Criminal activity* – less theft, violence, drug dealing, arrests and imprisonments

How these outcomes are measured (objective assessments – for example by drug screening or "self-report") may make the validity of findings questionable and difficult to generalize.

There are few studies systematically addressing social outcomes, aspects of physical or psychiatric/psychological health or use of health services. This makes assessment of recovery progress difficult.

Factors affecting outcome

Many studies attempt to address the various external factors which may impact on treatment outcome. Examples include: demographic factors; previous histories of drug use; the nature of a wide range of problems which exist prior to entering treatment; psychological and physical health; social stability, housing and family support. Studies have also considered aspects of service delivery which may be important. Examples include the dose of prescribed methadone received, availability or quality of counselling support, practical aspects of service delivery (by whom, from where, how close to a person's home,

low or high threshold) as well as the drug user's own response – their engagement, attendance, therapeutic readiness or ongoing drug use.

Quality

The quality of the published research is variable. The systematic reviews published in recent years by Cochrane and NICE have all commented (with some surprise) the difficulty in drawing robust conclusions from the evidence. Citing small sample sizes, short follow up periods – often less than one year, poor study design – including the lack of a clear research question and a lack of controls – most reviews present their conclusions tempered with the view that more, better quality research is required. Specific areas of concern include:

- *Follow up period* - This review eventually identified some 180 articles for critical appraisal. Of these, 19 were authoritative systematic reviews which all raised issues around the quality of the original research from which they drew their conclusions. Of the 161 individual research papers reviewed, only 55% had any longitudinal follow up element with the majority of these describing findings at up to one year. Only 26 of the studies identified - representing 16% of all identified relevant studies in this review - had follow up periods of more than 1 year. Of these, the most common duration of follow up was only 2 years.
- *Study design* - One obvious area of concern is the fact that the research methods often eschew assessment of a condition which is realistic in terms of the clinical situation. This may be in an attempt to make research findings more robust. Examples include much of the cited OST-M research which uses fixed doses - a practice which is not relevant to modern practice and hasn't been for over 15 years. Similarly, longitudinal studies such as NTORS and DORIS were modelled on the US studies of the 1970s – and as such sampled subjects who were self-selecting to a range of treatment modalities. It is clear that this could reflect what was available locally or patient/family preference. This bias makes interpretation of, even high quality, studies difficult.

To address the effectiveness of OST-M and the factors which may impact on the outcomes it can achieve, research should focus on the relevant populations. Those presenting for detoxification in the real clinical world are as a rule very different from those presenting for

longer term harm-reduction interventions and future research must reflect this. The NTA report on treatment in recovery (NTA, 2012) with its emphasis on personalized treatment which is appropriately "phased" or "layered" illustrates this point as does the lack of available relevant research on achievement of recovery outcomes.

Generalizability

A clear issue from the published research is the fact that the vast majority is from large studies carried out in the USA. These studies may give important information regarding how American research subjects relate to medications or treatment approaches. But there is clearly a need to repeat such studies in the context of the UK health and social care system to allow the potential impact of local peculiarities to be fully assessed. As the NHS across the UK also starts to diversify this will require researchers to be ever more robust in their research methods and will make interpretation of results more complex –even in the UK.

The Tayside Methadone Cohort Study

The next chapter describes a naturalistic study which used existing clinical information from OST-M patients to create a dataset to allow close scrutiny of the relationship between a range of patient characteristics with service delivery (outputs) and treatment outcomes over 4-7 years.

This study therefore attempts to address many of the issues raised by the literature review above. As a proof of concept exercise the project uses everyday information, collected by clinical staff in front-line services, to describe those currently receiving OST-M for opiate dependency in a Scottish regional service. It has used standardised, validated tools in the context of a clinical service, improving the quality of assessment and review processes. Finally, the development effective data-linkage systems has facilitated use of a broad range of validated clinical information to give a better understanding of the true impact of treatment on OST-M patients' careers.

Chapter 4

Tayside Methadone Cohort Study

Materials and Methods

Chapter 4. Materials and methods

Introduction

This thesis describes a naturalistic study which aims to explore the relationship between a number of characteristics observed in a baseline (2005) sample of patients on prescribed Methadone as an Opioid Substitution Therapy and a range of clinical outcomes achieved in these cases 4-7 years later. The study utilizes information from various sources including: NHS clinical casenotes [2005 baseline data and 2009 casenote review] and linked patient-identifiable records held in the Tayside Health Informatics Centre (HIC) which describe use of NHS services – including admissions to hospital – as well as clinical outcomes, including drug use [NHS laboratory tests] and death records.

This chapter describes in detail the methods and procedures used in preparation of this thesis. Specifically, the chapter will address:

- the aims and objectives of the study
- identification and representativeness of the various study samples – including baseline (2005) and follow-up (casenote review - 2009; HIC dataset 2005-12) elements
- retrieval of clinical data and data inputting
- the use of data-linkage procedures
- study design and statistical methods applied.

Choice of baseline independent (predictor) variables and dependent (outcome) variables

1. Baseline data: Tayside Methadone Cohort (2005)

Background

In 2005 NHS Tayside Board agreed a plan to redesign its community treatment services for people experiencing problems with opioid dependency. Historically, as was the case across Scotland, Tayside's specialist treatment services had been developed rapidly in response to an HIV outbreak in Dundee in the 1980s (Scottish Home and Health Department, 1986).

While there had been some attempts to develop a strategic approach to the further development of these services in Tayside, issues of rapid increases in demand and historic low levels of investment had meant the services had been inconsistent in their delivery and performance. Issues to be addressed by the 2005 service redesign, therefore included:

- Some sectors in Tayside were experiencing long waits for access to treatment.
- Treatment options were limited – with the vast majority of patients offered only methadone OST with limited access to other treatment types. Few detoxification options were available and access to residential rehabilitation facilities - for which gatekeeping was a role of the three local authorities – was used sparingly and reflected local custom or funding issues rather than assessed need.
- Additional community nursing support or access to third sector agencies for counselling support was not accessible across the region.
- The services were also unable to demonstrate that existing patients were progressing from the OST programme and "flow" towards recovery – i.e. leaving specialist treatment services positively - was limited. A General Practitioner (GP) "shared care" programme – to take patients who had stabilized in the specialist service - was in place, but was under threat in the face of a new UK GP contract which had placed the treatment of substance use problems outside General Medical Services (GMS). Instead, GPs would be required to be contracted specifically to deliver OST or detoxification and this would be at a significantly increased cost to the NHS – based on a national proposed cost, a so-called "Nationally Enhanced Service" (NES). In Tayside, the OST programme was already under considerable financial pressure, considerably overspending its budget in the shared care element alone. At the time of the review, reflecting the national picture, it was threatened by local GP negotiators that they would withdraw from any involvement at all. In such circumstances all care would have to be delivered by specialist services and service gaps were likely.

There was therefore a need for NHS Tayside to address a number of issues:

- How to continue to meet the needs of existing methadone patients – many very long-term (i.e. in treatment/on methadone 10-20 years). An estimated 8 -1200 patients were thought to be in treatment at this point.
- How to improve quality of care and outcomes – by better matching patients to appropriate interventions – increasing choice and ensuring that the services were also addressing common co-morbid issues (such as chronic pain and a range of mental health issues) as well as managing specific substance use issues
- How to improve access for new patients in need of OST – by increasing capacity and improving "flow" – returning stable patients to their GP for ongoing care.

Service redesign 2005 – "Clean team"

In consultation with specialist and GP clinicians, NHS Tayside agreed a plan to address these issues. The first stage of this process was to assess all existing patients objectively and systematically. This assessment would aim to clarify:

1. Were patients objectively stable or not?
2. Did the patients have co-morbid problems requiring attention?

To achieve this it was important to ensure that the service had an understanding of:

1. *Their current status in terms of substance use*

This was assessed using the Maudsley Addiction Profile – MAP (Marsden et al 1998a) and its associated questionnaires relating to risk – taking - Injecting Risk Questionnaire (Stimson et al 1998) and patient satisfaction - Treatment Perception Questionnaire (Marsden et al 1998b) as well as recording physical examinations (specifically for evidence of injection sites) and taking supervised urine or oral fluid samples for biochemical testing and drug screening.

2. *Their current social/demographic situation*

This was assessed using an in-house demographics questionnaire

3. *The presence/absence/severity of a range of co-morbid health problems:*
    a. Pain – assessed using the Brief Pain Inventory – BPI (Keller et al 2004)
    b. Mental health "caseness" - assessed using the General Health Questionnaire - 28 item version - GHQ28 (Goldberg 1979)
    c. ADHD assessed using the Current Symptoms Scale – CSS (Barkley & Murphy 1998)

d. PTSD assessed using the Impact of Events Scale – IES (Horowitz, Wilner & Alavarez, 1979)
e. Social phobia assessed using the Social Phobia Diagnostic Questionnaire – SPDQ (Newman et al 2003)

The battery of tools applied reflected:

- service priorities – those issues or conditions which senior clinicians felt were affecting their ability to manage patients or were hindering a patient's progress
- advice from local specialists – e.g. Pain and mental health screens (GHQ28, SPDQ, CSS and IES assessments) were proposed by local clinical leads in those areas and often reflected the tools used in local services. [NB were not chosen with research in mind]
- senior clinicians' preferences and practical applicability/deliverability in the context of a busy working clinical service. Self-completion tools or shorter "screening" tools were therefore preferred.

The rationale for the use of these tools therefore reflected a pragmatic balance of their strengths and weaknesses. They were recommended by the relevant senior clinicians and then the practicality of their delivery measured against the time available for interviews. Copies of the tools used and associated references are contained in Appendix 1.

Process

Interviewers

A team of 5 full time experienced senior nursing staff was appointed over and above the existing service nursing complement and was made available for 1 year. This team was drawn from staff involved in local and national drug and alcohol services. It was managed by a newly appointed "team leader" – an experienced service manager from a third sector organisation in the substance misuse field – and was given dedicated administration for the project. The staff, however, worked in existing clinical facilities meaning there were some limitations in terms of availability of clinic space across Tayside for the review process. All review staff were trained in the administration of all the tools to be used in the review prior to commencing patient contact.

Subjects

All patients currently in receipt of OST- M in the NHS Tayside area at the inception of the project were identified from service databases by NHS administrators. Only methadone was used in as an opioid substitute in Tayside at this time – though Buprenorphine and dihydrocodeine were used in short-term detoxification episodes. Only those on a defined substitution therapy programme were included in the review. All had Tayside postcodes. This included patients in three main settings:

1. the NHS specialist service
2. patients within the criminal justice service – in particular two agencies:
    a. The Tayside Arrest Referral Scheme (TARS) – delivered by a third sector organization with access to NHS specialist nursing and prescribing support
    b. The Tayside Drug Treatment & Testing Order (DTTO) service - a partnership of the NHS specialist service with the three Tayside Local authority criminal justice services. This service had medical staff from the specialist agency embedded in the service and nursing staff support consisted of seconded specialist nurses
3. patients within the Tayside Shared Care Scheme – this group was prescribed methadone by their own GP, supported by specialist nurses who worked from the GP surgery.

The patients were given oral and written information about the review process by their keyworkers. They were then offered assessment appointments by post. The team concentrated its activity on a rotation of specific geographical areas, allowing reviews to be completed in an area so that thereafter normal services could resume as quickly as possible.

Interviews

The interviews took place in NHS facilities within the patients' own localities (Dundee city, Angus, Perthshire) during the calendar year 2005 - starting in February, with the last appointments occurring in December. If patients failed to attend they were offered a further appointment at their convenience. Failure to attend this second appointment resulted in a more assertive approach through their own locality team with contact made by their own

keyworker and communication delivered through the person's community pharmacy – the majority of subjects were attending daily to collect or consume their methadone.

Attendance

Poor attendance was a significant problem and delayed completion of assessments. This is thought to have reflected the fact that the NHS service keyworking staff had very high caseloads and were responding to high levels of demand. Consequently patients were often offered infrequent appointments (under one per month). The "Did not Attend" (DNA) rate was high at normal appointments and staff often asked community pharmacists to "hold" prescriptions until a patient was reviewed by the nursing staff if repeated failure to attend meant face to face contact had not occurred within one month. This situation unfortunately gave some patients the sense that their attendance was not required and this culture clearly impacted on the Tayside Methadone Cohort review –especially in its early stages. There was a real concern that the required reviews would not be completed in the year planned. In response, the project steering group was forced to reduce the amount of data to be collected on each case from July 2005, thus reducing the time demand of each interview and increasing the number of assessments which could be undertaken by a small team within the limited time available. This meant that a complete dataset was not available for all cases. As originally planned, the "clean team" was subsumed into the NHS treatment service from January 2006, ending the dedicated review process. At this point 649 of the 817 cases verified to have been in treatment at the inception of the project had been formally assessed. Any remaining cases were then reviewed as part of the normal clinical process in each locality.

The sample used in this thesis reflects those patients for whom a substantial dataset was obtained during February-December 2005 as part of the Tayside Methadone Cohort review process.

Data quality

A weekly *steering group* meeting involving senior clinical staff from the treatment services and the clean team manager collated, reviewed and quality assured the information returned by the interviewers. At this (clinical) meeting, patients were also broadly identified as "stable" or "unstable". This was based on a number of factors. These were:

- Evidence of ongoing regular illicit drug use - self report; observed behaviour during examination; testing; reports from other agencies
- Evidence of risk-taking - self report; examination; sequelae of injecting behavior – e.g. hospital admissions; overdoses
- Evidence of complex issues - self – report; examination; results of co-morbidity screens; reports from other agencies

As had been originally planned, depending on this clinical judgement, their future care was placed in a specific service element which focussed on stabilization/harm reduction (Assessment & Stabilization Service - ASS) or recovery/rehabilitation (Time Tay Change – a service designed to facilitate progress from the specialist services, delivered off-site, in collaboration with a third sector provider agency – the Scottish Association for Mental Health). This was intended to ensure that those in most need would receive the most intensive support while those ready to move on from specialist care were supported to achieve this.

Data entry

The clinical data were filed in a specific folder within the NHS casenotes and were referred to by clinicians in their care planning and delivery and other clinical interactions with their patients.

In 2006 a successful bid for a small NHS Research & Development (R&D) grant supported the development of a database which would contain all the clean team data and support the development of outcome measurement systems and audit tools in the service. Local Ethics Committee support was obtained. Full ethical committee approval was not required though agreement from the NHS Caldicott Guardian was. A bespoke database was built using SPSS 16 (SPSS 2003). The 2005 baseline data were input by dedicated and experienced

data-entry staff during 2006. The staff were accessed from the Health Informatics Centre – a dedicated data management centre jointly managed by NHS Tayside and the University of Dundee. Quality assurance was undertaken by a research assistant who checked 10% of database inputs against the hard copy information.

These data were then used by service managers and senior clinicians to report on the treatment population and to demonstrate progress in aspects of service delivery, quality and governance within the local accountability system. Local reports and presentations were delivered to the local NHS Tayside board as well as to partners including the local Drug and Alcohol Action Teams.

2. Follow up data – 2009 Casenote audit

In 2009 a further one year grant was obtained through NHS Tayside R&D to carry out a follow-up audit project, based on this 2005 baseline cohort.

Initially, it was planned that a sample of patients would be re-interviewed by dedicated researchers employed for this purpose. Unfortunately, as available funding was limited and this element of the study required full NHS Ethics Committee approval which took some months to acquire – delaying commencement of the data collection phase - data collection started very late in the agreed one year timeframe. Once the process for patient interviews was in place, attendance for interviews was again very poor with attendance rates below 10% in the first four weeks of the project.

Consequently, in consultation with the NHS Tayside Ethics Committee, it was agreed to modify the audit and instead carry out a casenote-based review. A proforma was created to capture a number of process-measures and outcomes from clinical records (Figure 5). These data were collected in 2009. An SPSS database was built and data entered for analysis. A service audit report was completed using these data. Further details of this process – including prioritization of data sources - are included in Chapter 5.

Figure 5 -*Data collection form used for 2009 casenote review*

Date of data collection	
Name	
Male/Female	
Date of Birth	
Age in 2005	
Locality (Dundee/Perth/Angus)	
Methadone dose in 2005	
Current Prescribed Medications **[TDPS Rx from methadone database.]**	
Key Stability indicators • **Biochemistry/oral fluid results** • **Results consistent with prescribed medications** • **Evidence of injecting/risk** • **Hospital admissions**	
Other: Any objective record of: Offending (+arrest+disposals), Employment/training/activity, Home stability (accommodation) Family/relationship stability Children/parenting responsibilities	

3. Follow-up data – Health Informatics Centre NHS datasets 2005-2012

In December 2010, the SUMIT (Substance Misuse Information – Tayside) project was launched. Funded by the three local Alcohol & Drugs Partnerships (ADPs – successor to Drug and Alcohol Action Teams,) and delivered by academic staff in the University of

Dundee, this was a multi-agency information-sharing project aiming to deliver linked data on outcomes in the substance misusing population in Tayside. The data would be collected electronically from all services and a new electronic record system in the NHS (MIDIS) would supply reports, facilitating clinical governance of care by local commissioning bodies and service managers.

Crucially, it was emphasised that the datasets created would also be available for academic research and the appropriate ethical approvals, Caldicott Guardian approval and data-sharing agreements were developed as part of this project. This multiple functionality would be achieved by managing all data in a "safe haven" – a virtual electronic environment where datasets are linked using unique identifiers and are then anonymised. This element of the project was delivered by the Health Informatics Centre (HIC) in Dundee. The SUMIT project is described in detail in the papers describing the project – contained in Appendix 2. Research governance paperwork is contained in Appendix 3.

The SUMIT project allowed the 2005 baseline data and 2009 follow up data (described above) to be linked with a range of other relevant existing datasets held by HIC. These data were then anonymised by HIC and these anonymised linked data given a unique identifier or "prochi". They could then only be accessed through the HIC "Safe Haven" – using a "virtual desktop" which is governed by strict Standard Operating Procedures. HIC processes and Standardised Operating Procedures are contained in Appendix 2.

This process supported creation of the comprehensive dataset used as the basis for the analyses described in this thesis.

Funding

Baseline data (2005/6)

The clinical assessments and record keeping were undertaken by a dedicated clinical assessment team - the "clean team" – funded as part of the service redesign by NHS Tayside Board. The staff to develop the baseline SPSS database and carry out data entry were funded by a small grant from EASTREN (the local NHS Tayside and Fife Research & Development office).

Casenote follow-up (2009)

The casenote review, including proforma development, data collection, SPSS database development, data inputting and cleaning were supported by a grant from NHS Tayside Research & Development.

HIC data-linkage process (2010-12)

This element of the study was funded as part of the SUMIT project, supported by dedicated funds from the three Tayside Alcohol & Drugs Partnerships.

Subjects & attrition

A schematic of all subjects' progress through the study and attrition through the various stages of the study is shown in Figure 6 (P129).

Baseline

The schematic shows that once data was cleaned and invalid Chi-identifiers were removed, 623 cases were ultimately reviewed as part of the Tayside Methadone Cohort study.

2009 casenote audit

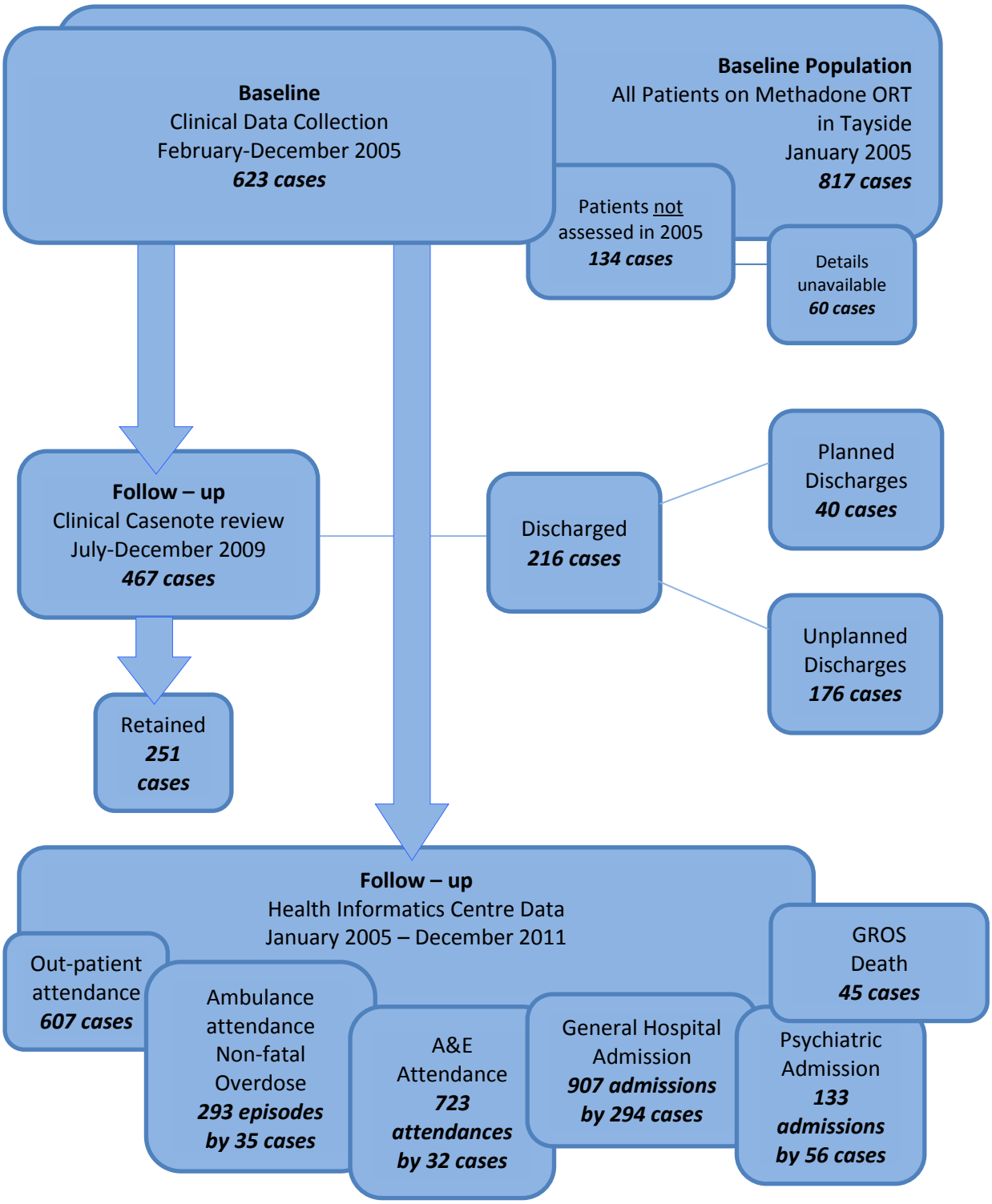
467 cases were reviewed as part of the casenote audit in 2009 – of whom 251 were active ongoing cases (54% of all follow ups) with 216 (46%) having been discharged and currently not in treatment. Of discharges, 40 (18.5% of discharges) were described as "planned" – representing positive discharges on completion of treatment (i.e. drug free – if in "shared care" they would have continued in the OST- M programme) or positive service transfers to another area or service. Some 176 cases (81.5% of those discharged, 38% of the casenotes available for follow- up) were described as "unplanned" – i.e. discharged before treatment completed. This group would include deaths – for whom clinical casenotes would not be available.

HIC linked datasets

HIC datasets contained differing sample sizes. Larger datasets were available for out-patient attendances in the drug service (giving a measure of "treatment dose") with data available on 607 (97%) of the original cases. Some 45 cases from the original TMC subjects had died in the period from 2005-12. This represents 7.2% of the baseline cohort. Data for other service involvement reflects these subjects' use of these services. For example, General Hospital admissions (from national Scottish Morbidity Record - SMR - data) were recorded for 294 cases (47% of the original cohort). This means that 294 of the TMC cases were admitted at any time in the 7 years to 2012. These 294 cases were admitted a total of 907 times. SMR01 contains details of diagnoses, days in hospital etc. The balance of cases were not admitted to a general hospital in that period – and therefore had no SMR01 completed.

It can be seen that, for some of the measures chosen – such as Ambulance Service call-outs or A&E attendances – there are only 35 cases (responsible for 293 events) and 32 cases (responsible for 723 episodes) recorded respectively. This reflects the fact that these data have only become available in recent years though the HIC process – i.e. they do not reflect the total follow up period.

Figure 6. Schematic of potential participants (numbers)



Ethical considerations & permissions

Baseline audit

In 2006 permission was obtained from the NHS Tayside Caldicott Guardian to access and organise the baseline clinical information for research purposes. Tayside Research Ethics Committee was approached regarding the need for ethical approval. They confirmed that no approval was required for this element of the study.

Follow-up casenote review

In 2009 permission was obtained from the Caldicott Guardian to carry out a follow up audit on the casenotes of the original 2005 cohort. Ethical approval was acquired from Tayside Research Ethics Committee to carry out follow up interviews. When this was found to be unfeasible, permission was formally obtained to proceed to a casenote-based audit.

Health Informatics Centre data-linkage

In 2010, permission was obtained from the Caldicott Guardian to include the 2005 Cohort and 2009 follow up data in the SUMIT project – a multi-agency information-sharing project aiming to deliver linked data on outcomes in the substance misusing population in Tayside. This allowed the TMC data to be linked with existing datasets held by the Tayside Health Informatics Centre (HIC). The total dataset was then anonymised by HIC and these anonymised linked datasets given a unique identifier or "prochi". They could then only be accessed by named staff, through the HIC "Safe Haven" – using a "virtual desktop" governed by strict Standard Operating Procedures. Tayside Research Ethics Committee confirmed no further ethical approval was required to allow the analyses to proceed. Confirmation of the approvals from the Tayside Caldicott Guardian and Ethics Committee is contained in Appendix 3 (TASC Ref: 2010PY01).

Statistical considerations

Data were analysed in the HIC safe haven environment and all outputs stored within that environment. All analyses used in this thesis were performed in 2012 using SPSS version 18 (IBM, 2010).

Baseline assessment of sample

Initial descriptive analyses were used to describe the key characteristics of the baseline sample. This included descriptions of: demographics and social circumstances; substance use and associated clinical problems (assessed by the MAP, IRQ and TPQ); co-morbid conditions – including pain (assessed by the BPI); GHQ caseness (assessed by GHQ28); ADHD (assessed by the CSS); PTSD (assessed by the IES); social phobia (assessed by the SPDQ).

Representativeness of baseline sample

Although the baseline study aimed to deliver a census of OST- M patients in Tayside, it was important to ensure that the Tayside Methadone Cohort sample was representative of all OST- M patients in Tayside.

A large proportion (76.2%) of the total Tayside OST- M population was assessed in 2005. However, in the early stages of the project it had proven difficult to be clear regarding the size of the baseline population, from which the sample was drawn. This may have reflected the rapid movement of patients into and out of the service. It was also impacted on by the poor quality of local administration systems in hard-pressed services which had been dispersed from a central base to localities up to 20 miles away. The original assessments were undertaken in a clinical setting and management of these clinical casenotes by medical records departments in three different NHS sectors meant that original patient lists were difficult to validate retrospectively. Any information at all on some 60 of the originally identified total of 817 active patients could not be retrieved for the study. Limited information from prescribing databases and service patient management systems were available for the 134 of the subjects who were not assessed by the clean team in 2005.

Means and standard deviations of a limited range of descriptive demographic variables were collected in order to assess representativeness. Variables available for testing were: gender, age, methadone dosage. Categorical variables were compared using the chi-squared test. Continuous variables were compared using the paired t-test. These results are shown graphically in Table 10.

Table 10. Representativeness of baseline sample

Continuous variables	***Population proportion Male***	***Sample proportion Male***	***Population mean (SD)***	***Sample Mean (SD)***	***Statistics***
Age			30.3 (6.7)	32.7yrs (7.8)	t-test; t=3.4; df=692; p=0.001
Methadone			55.3mg (21.5)	49.3mg (25.9)	t-test; t=2.3; df=752; p=0.022
Gender	57%	69%			Chi-squared test $\chi^2(1)=7.064$; p=0.008

As these figures show, significant differences were found for all three variables chosen, raising issues regarding the representativeness of the original sample. In the sample assessed, males were over-represented, mean age was older and methadone dose less than that in the treatment population as a whole. This may represent the fact that a harder-to-reach element of the treatment population (one which may have been on higher methadone doses) were the most resistant to being invited for review. Though they would have been reviewed by their own clinical team later, they were not included in the original cohort (or this study) as they were assessed outside the study period.

Selection of baseline (predictor) variables and follow-up (outcome) variables

The extensive literature review (Chapter 3 above) indicated a number of variables which previous research has indicated may be important in influencing outcome of treatment. Previous research also informed the outcomes which should be considered. Baseline and follow up datasets (2009 Casenote review and 2005-12 HIC datasets) were explored and a list of variables for assessment created. Quality of data and potential missing data were important factors in choosing the variables used for these analyses.

Representativeness of the 2009 follow -up sample

Although follow-up records were available for 75% of those assessed at baseline (467 of 623), it was important to determine whether this follow up sample was representative of the baseline sample. Categorical variables were compared using the chi-squared test and continuous variables using the paired t-test. The results are shown in Table 11.

Table 11. Representativeness of the follow – up sample

Categorical variables		% Baseline	% Follow-up	Statistic
Sex				
	Male	69	69	$\chi^2(1)=0.026$; p=0.873
	Female	31	31	
Geographical area				
	Dundee	62	63	$\chi^2(2)=3.864$; p=0.145
	Angus	23	18	
	Perth & Kinross	16	19	
Frequency of changing address				
	Never	22	22	$\chi^2(3)=0.065$; p=0.996
	Sometimes	58	58	
	Frequently	17	17	
	Very frequently	3	3	
Lives alone or with others				
	Alone	37	38	$\chi^2(5)=1.383$; p=0.926
	With partner	25	26	
	With family	31	29	
	With friends	5	5	
	Hostel	2	3	
Has children				
	Yes	75	74	$\chi^2(1)=0.098$; p=0.755
	No	25	26	
Has physical health problems				
	Yes	51	52	$\chi^2(1)=0.011$; p=0.915
	No	49	48	
Has mental health problems				
	Yes	50	47	$\chi^2(1)=0.596$; p=0.440
	No	50	53	
Has support from other agencies				
	Yes	30	30	$\chi^2(1)=0.011$; p=0.915
	No	70	70	
Literacy / numeracy skills				
	Not good	10	9	$\chi^2(2)=2.258$; p=0.879
	OK	38	38	
	Good	52	53	
Educational attainment				
	None	53	52	$\chi^2(4)=0.405$; p=0.982
	O' Grades	28	29	
	Apprentice/SVQ/City & Guilds	2	2	
	Highers	4	5	
	College / university	13	12	
Continuous variables		**Baseline mean(SD)**	**Follow-up mean(SD)**	
	Age	32.96 (7.746)	36.94 (7.603)	t-test t=-0.241; df=446; p=0.810

No significant differences were found for the variables assessed. The 2009 follow up sample is found to be representative of the baseline 2005 sample.

Follow – up assessment: Statistical tests

Normality of data and use of tests -parametric or non-parametric

It was important to establish whether the available data qualified as parametric or whether use of a nonparametric test would be appropriate. Parametric tests are seen as more precise, with greater statistical power but are not robust when there is non-adherence to the assumptions associated with parametric testing. To qualify for parametric testing, the data must meet the following assumptions:

- Data must be continuous (i.e. scalar data with the difference between any two points being the same as the difference between any other two points).
- Data must be normally distributed.

Normality was tested by visual inspecting of the standard histogram generated by SPSS with a superimposed normal curve. If there was some doubt further tests were undertaken. This included: a visual inspection of a Q-Q plot (approximation of the distribution of the variable in question to a straight line). If required it was also planned to apply further tests of normality – Kolmogorov-Smirnov and Shapiro-Wilk tests.

Longitudinal analyses of independent (baseline) and dependent (outcome) variables

Univariate associations were assessed. Categorical data were compared using the chi-squared test. Testing of continuous data was determined by normality. If data were normally distributed, parametric tests were favoured. In the initial analyses both independent variables (IVs) and dependent variables (DVs) were either categorical or continuous. Table 12. shows the tests undertaken, depending on the nature of the data.

Table 12. Statistical tests undertaken

Independent Variable	Dependent Variable	Statistical test undertaken
Categorical	Categorical	Chi square test
Categorical	Continuous	If data were parametric: **ANOVA** If data were non-parametric: **Mann Whitney U-test** (for 2 variables) **Kruskall-Wallis H-test** (for>2 variables)
Continuous	Categorical	linear (if data have a linear relationship) or quadratic (if not) **discriminant analysis**
Continuous	Continuous	linear (if data have a linear relationship) or quadratic (if not) **regression analysis**
Effect sizes were also assessed using a range of statistical tests: Phi; Cramer's V; Cohen's d and Partial η^2 Levels of effect are described, reflecting Cohen's "rule of thumb"		

Multiple testing

The effect of multiple testing is an issue with the proposed approach. If a true null hypothesis is tested, using (as planned) the 0.05 level as the critical significance level, then the probability of coming to a `not significant' (i.e. correct) conclusion is 0.95. If two independent true null hypotheses are tested, the probability that neither test will be significant is $0.95^2 = 0.90$. So, as the number of independent tests increases, the probability that none will be significant reduces to the power of the number of tests. Therefore, if twenty hypotheses were tested, the probability that none will be significant is $0.95^{20} = 0.36$. This gives a probability of 1 - 0.36 = 0.64 of getting at least one significant result meaning it is more likely to find a significant result than not. Multiple testing therefore increases the likelihood that a significant finding will appear spuriously by chance alone. This is an example of a Type 1 error – a false positive.

Bonferroni correction

There are a number of so-called *Post hoc* procedures which can be used to reduce the likelihood of a Type I error (Toothaker, 1993). One common example is the Bonferroni method. This method divides the significance value (α) by the number of tests undertaken. For example, if the proposed significance level (α) is 0.05 and ten tests have been undertaken, then using the Bonferroni method [α/10] the likelihood of Type 1 errors can be reduced if the proposed significance level is corrected to 0.005. It is, however, important to

be aware that this approach is statistically conservative and has the potentially negative effect of reducing statistical power. This phenomenon in turn brings an increased probability of rejecting a significant finding - a Type II error or false negative. Use of the Bonferroni correction in the analysis of these data will be discussed at the appropriate results section.

Effect sizes

In all cases the effect size was also assessed using appropriate tests. For data which used the Cohen's d and Partial η^2 tests, these statistics showed the level of the effect (small; medium; Large). In the case of Phi or Cramer's V, a score of >.10 was assessed as providing a minimum threshold for the presence of a substantive relationship between the variables. In some analyses (using the Kruskal -Wallis H test) the Monte Carlo estimate of significance was reported alongside its confidence intervals for significance. This test can give confidence that an apparently significant effect is genuine.

Tables containing the results of the univariate analyses are contained in Chapters 5 and 6. The results are reported as significance values (as described in Field 2005). Effect sizes are reported for those associations found to be statistically significant. These results generated a list of potential predictors which could then be used to develop and test a predictive model of relevance to the known evidence base and clinical experience.

Predictive modelling

This part of the project tested the prediction of 4-7 year outputs (process measures) and clinical outcomes using the 2005 baseline data.

A series of univariate analyses had assessed the associations between baseline (independent) and follow up (dependent) variables. The issue of multiple testing had been addressed using the Bonferroni Correction. Those associations then found to be significant were used to assess their value in predicting key outcomes for the TMC patients.

Reflecting the evidence base already discussed, a group of outcomes to be predicted was proposed. These were:

- alive/dead - recorded by Registrar General (Recorded in the GROS data available to the HIC dataset)
- ongoing illicit drug use – 1. by self-report and 2. +ve tests in 2009 (both from 2009 casenotes)

[NB It was planned that NHS Laboratory test results from HIC should be the basis of this analysis. However, these tests were were unavailable in HIC at the time of analysis making this analysis dependent on the quality of casenote recording/filing of results]

- indicator of family stability (as demonstrated in 2009 casenotes)
- physical health - acute hospital admissions (recorded in 2009 casenotes) and nights in acute hospital (SMR01)

Plans to consider other a number of potentially relevant outcomes such as overdoses from ambulance or A&E data) psychiatric admissions (casenotes and SMR04 data) and incarcerations (casenote data) were not progressed, as the number of cases involved in each were very small.

Method of regression analysis

Details of the analyses are contained in the relevant results section (Chapter 7). For those outcomes for which data were categorical, a logistic regression was undertaken. In the case of the data used in this analysis, all outcomes were binary meaning that a binary logistic regression analysis was required. For the one outcome which was continuous – hospital admissions – a multiple linear regression analysis was undertaken. The process involved:

1. *Initial selection of Independent variables*

The original group of predictor (independent) variables (IVs) were selected from all available variables in the 2005 baseline dataset as they had been identified - from the literature review - as having evidence to support their predictive value with regard to treatment outcomes.

2. *Associations with dependent variables*

The selected IVs were then tested individually and their impact on the selected DVs was assessed (Results are shown in Chapters 5, 6).

3. *Choice of variables for the multiple regression analysis*

Ideally, factors influencing recovery would have been assessed – but in 2012 the data available from the SUMIT dataset was in its early stages and information on social outcomes was unavailable in the HIC safe haven at this stage. Data-sharing agreements to access local authority and third sector data were in place but technical challenges meant that these data were not yet accessible. Variables relating to the broader recovery process had not therefore been prominent and more standard substance misuse outcomes relating to the extent or risk associated with illicit drug use along with indicators of health - such as hospital admission and death - were selected. Factors implying a high degree of family stability from casenotes were also used

4. *Method chosen*

These significant IVs were then placed in a multiple regression analysis in the SPSS statistics programme, using a Forced Entry method. A number of rules were followed whenever possible:

- The fewest variables with the best predictive value was the aim.
- Only variables with a good theoretical grounding were included.
- A process was undertaken to remove those variables found to be redundant

5. *Sample size*

Sample size was a key consideration (Green, 1991). To test best fit of the model (testing R^2) the minimum sample size follows the equation:

sample size = 50 + 8k (where k is number of predictors)

For a process to test the individual predictors then minimum sample size is calculated using the equation:

sample size = 104 +k (where k is number of predictors)

If overall fit and contribution of predictors is required, it is recommended that both tests are undertaken – in which case, the equation giving the highest number is used to calculate sample size required.

Cross – validation of predictive models

In order to validate any predictive models identified and ensure these models were generalizable - i.e. the model generated would predict outcomes in novel data - a process of cross-validation was undertaken. Cross-validation is a statistical technique for assessing

how the results of a statistical analysis on one set of data will generalize to another independent data set. It is mainly used in settings where the goal is prediction, and one wants to estimate how accurately a predictive model will perform in practice (Geisser, 1993; Devyver & Kittler, 1982).

Regression analysis can result in a model which displays so called *"over-fitting"* – with the regression analysis results incorrectly implying that the proposed model is a better fit to the data than it is, or has less *prediction error* - difference between the model predicted value and the actual observed value - than is the case. In a standard multiple regression, this *prediction error* refers to how well the regression equation predicts the outcome variable scores of new cases based on applying the original model coefficients to the novel cases' predictor variable scores. In the case of over-fitting, these errors will be biased - implying less prediction error - often due to the actual outcome variable values being used to create the prediction model – a process known as "double dipping" (Kriegeskorte, Simmons, Bellgowan & Baker, 2009). Cross validation techniques are one way which can be used to address this over-fitting bias by avoiding double dipping.

In the TMC example, the cross-validation process involved a number of steps:

- creating a complete dataset – removing all missing data
- randomly dividing the sample 50/50 into a *training* and *testing* dataset
- the appropriate regression analysis was undertaken in the first half of the dataset – *the training dataset* – generating a predictive model with β coefficients for each variable.
- these β values were then entered into the appropriate equation – this time using the novel *testing dataset* - to generate a predicted outcome in these novel data. The equation used reflected the type of regression being undertaken:
    - Linear regression: $Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots. \beta_n X_n + \varepsilon.$
      This was used when the DV was continuous
    - Binary logistic regression: $P(Y) = 1/1 + e^{-(\beta 0 + \beta 1 X1 + \beta 2 X2 + \ldots. \beta n Xn)}$
      This was used when the DV was binary

- the *predicted* outcome generated, was then compared to the actual *observed* outcome for the testing dataset, using a chi-squared test. A significant difference between the observed and predicted outcomes would imply that the proposed predictive model is NOT predictive in this novel dataset.

The results of this process are described in Chapter 7.

In conclusion

This chapter has described a process which aimed to develop a large and representative research database from existing identifiable clinical data accessed from a number of sources: a service review census (2005); a follow-up casenote review (2009) and linked data from national datasets (2005-12).

It has described the methods used to collate this database and the statistical plans developed for a number of analyses.

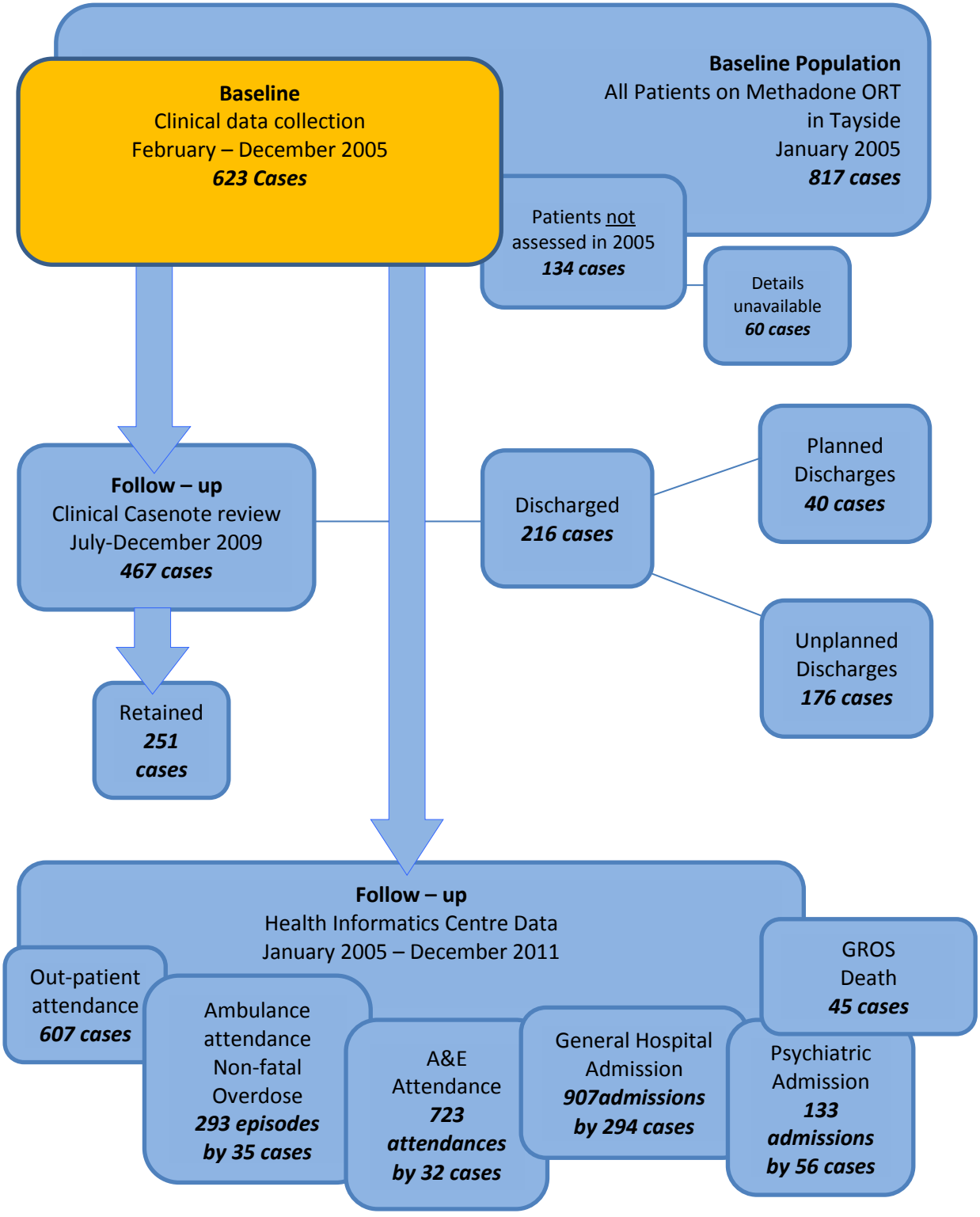
Reflecting key questions from the literature review, univariate analyses were then carried out using the 2005 baseline data as independent (predictor) variables and the 2009 casenote review and HIC linked-data as dependent (outcome) variables. These analyses generated associations which were then to be used as the basis to develop a testable predictive model.

The next section of the thesis – chapters 5-7 –describes the results.

Chapter 5

Results: baseline sample - descriptive statistics

Figure 7.Results: 2005 Baseline Sample - Descriptive statistics



Descriptive statistics

This section describes the characteristics of the 2005 baseline sample of the Tayside Methadone Cohort. Figure 7. illustrates the data sources used. The data were collected at their baseline assessment interview in 2005 using a variety of tools described above (Chapter 4). Additional data (e.g. regarding GP, postcodes and deprivation scores) were available retrospectively from HIC databases. The variables selected are later used as Independent variables/predictors. Demographic information was collected at baseline.

Table 13. Baseline Demographics (n=623)

	N	%	Mean	Median	Range	Min-max	SD
Age	**623**	**100**	**32.96**	**32**	**49**	**17-66**	**7.746**
Gender (n=620)							
Male	424	68.4					
Female	196	31.6					
M:F ratio	2.16:1						
Home (n=620)*							
Dundee	382	61.6					
Perth & Kinross	98	15.8					
Angus	140	22.6					
SIM-D Deprivation score (n=607)**							
Quintile 1	311	50.2					
Quintile 2	172	27.7					
Quintile 3	64	10.3					
Quintile 4	45	7.3					
Quintile 5 (most affluent)	15	2.4					
Time at current address (N=612)							
<1 month	37	6					
1-6 months	75	12.3					
6 months -1 yr	92	15					
1-3 yrs	165	27					
3-5 yrs	84	13.7					
>5yrs	159	26					
Frequency of changing address (n=500)							
never	109	21.8					
sometimes	294	58.8					
frequently	97	19.4					

**NHS Tayside board area contains three discrete local authority areas – Perth & Kinross, Angus and Dundee City. **Health board scores. 1=most deprived.*

Information regarding home circumstances, childcare/parenting responsibilities and the quality of relationships was collected (Table 14).

Table 14. – Family support and Childcare responsibilities

	N	%	Mean	Median	Range	Min-Max	SD
Children (n=585)							
Yes	443	75.7					
No	142	24.3					
If yes how many? (n=442)							
1	197	44.6					
2	135	30.5					
3	75	17					
4	22	5					
5	7	1.6					
6	6	1.3					
Living circumstances (n=616)							
Alone	232	37.7					
With partner	153	24.8					
With family	189	30.7					
With friends	28	4.5					
Days contact with partner (604)	266 no contact	44%	15.01 days		30 days	0-30	14.42
MAP Partner conflict score			6.06				18.64
Days contact with Family (606)	82 no contact	13.5%	18.54		30 days		12.42
MAP Family conflict score			5.09				17.59
Days contact with friends (606)	221 no contact		12.79		30 days		12.82
MAP Friends conflict score			0.67				6.33

The majority of subjects have at least one child though over one third live alone. The majority are living with a partner or family but the mean contact with partner family or friends is far less than daily.

Information regarding the subjects' educational attainment, self-assessment of their basic skills, and employment were collected (Table 15).

Table 15. Education, skills, training and employment

	N	%	Mean	Median	Range	Min-Max	SD
Self-rating of reading, writing and counting (601)							
Not good	61	10.1					
Okay	227	37.8					
Good	313	52.1					
Educational level achieved (593)							
No qualifications	312	52.6					
Standard grade or equivalent	164	27.7					
Higher	27	4.6					
College	78	13.1					
Days in paid work of 30 (607)			2.19		30	0-30	7.22
Days sickness absence from work of 30 (604)			0.26		30	0-30	2.519
Days unemployed of 30 (595)			23.58		30	0-30	12.264

The group self-assessed their basic reading writing and counting skills well though over 10% saw these skills as "not good". Educational attainment was poor with over 50% having no qualifications at all and over 61% of those with qualifications having only standard grades. Few were in paid work with those who were working a mean of only 2 days per month.

Information regarding physical and mental health problems was obtained. This included information regarding registration with a General Practitioner or support from another agency outside the NHS treatment service (Table 16).

Table 16. – Care & treatment status (general)

General	N	%	Mean	Median	Range	Min-Max	SD
Registered with a GP (n=620)							
Yes	580	93.5					
No	40	6.5					
Physical problems reported (n=567)							
Yes	293	51.7					
No	274	48.3					
Being treated	177	31.2					
MAP Physical health score (622)			14.2			0-37	7.98
Mental health problems reported (n=533)							
Yes	265	49.7					
No	268	50.3					
Being treated	184	34.6					
MAP psychological health score (620)			15.73			0-40	9.22
Support from other agencies (n=502)							
Yes	152	30.3					
No	300	69.7					

Only 87% were registered with a GP. 52% reported having physical health problems of which only 60% were receiving treatment. Mean MAP physical health score was 14.2 (SD 7.98) suggesting that in general physical health problems were mild/moderate. Some 49.7% reported mental health problems of which 69% were being treated. Mean MAP psychological health score was 15.73 (SD 9.22) suggesting that mental health problems were mild/moderate. Only 30% were receiving additional support from other (Non-NHS) agencies for themselves or their children.

Information regarding where they received their substance misuse treatment (i.e. which agency) and what prescribed treatments they were in receipt of were collected.

Table 17. – Care & treatment status (substance misuse)

Treatment specifically for substance misuse	**Number**	**%**	**Mean dose**	**Mode**	**Range**	**Min-max**	**SD**
Methadone prescribed (n=608)							
Yes	588	96.7	49.54mg	50mg	170mg	0-170	25.25
No	20	3.3					
Diazepam prescribed (n=619)							
Yes	178	29	6.84	20	85	0-85	13.65
No	441	71					
Treatment setting (n=547)							
GP shared care	156	24.8					
TDPS	298	47.4					
DTTO/TARS	93	14.8					

At the time of the assessment 97% of the subjects were in receipt of a methadone prescription from Tayside services. This may reflect that, having been identified from methadone databases, some patients had detoxified or had come off methadone for some other reason. Most commonly prescribed dose was 50mg with the mean dose 49.54mg (SD 25.25). Maximum dose was 170mg.

Some 29% of subjects were being prescribed diazepam. The most common dose was 20mg (range 0-85mg) with a mean dose of 6.84mg (SD 13.65).

Treatment was being delivered in three settings: NHS specialist service (TDPS) – 298 cases (47.4%); Criminal Justice services (DTTO and TARS) – 93 cases (14.8%); General Practice Shared Care – 156 cases (24.8%).

Details of their baseline drug and alcohol use were obtained (Table 18). This included information on injecting risk (Table 19).

Table 18. - Baseline substance use

	N	%	mean	median	range	Min-max	SD
Drug screens (n=582)							
Illicit Opiates positive (of 534)	289	54					
Benzodiazepines +ve (of 533)	314	58.9					
Methadone +ve (of 533)	508	95.3					
Alcohol days/30 (620)	387 no days	62.4	2.92 days	Mode 1 day	30	0-30	7.030
Alcohol amounts - units (616)			3.49 units	Median 8 units for drinkers	39	1-40	6.39
Cannabis days/30 (619)	186 no days	30%	15.11	Mode 1 or 16	30	0-30	13.72
Cannabis amounts	Not recorded in standardised way						
Heroin days/30 (619)	323 no days	52%	4.66	Mode 1 day	30	0-30	8.69
Heroin amounts (623)			0.14g	Mode 0.1g Median zero [or 0.1g if users]	4g	0-4	?
Heroin route (612)	324 none	52.9%					
Snort	7	1.1					
Smoke	190	31%					
IV	90	14.7					
IM	1						
Illicit Methadone days/30 (622)	416 no days	67.1	3.43	Mode 1 day	30	0-30	7.88
Methadone amounts (623)	Amounts poorly recorded in assessment records for methadone						
DHC days/30 (620)	536 no days	86.4	0.64	Mode 1 day	30	0-30	3.23
DHC amounts (619)			28.55	Mode 60mg Median 150mg	1200mg	0-1200mg	107.36
Morphine days/30 (621) (618 *no days* reported)	3 cases	0.5%	0.01		4 days	0-4	0.23
Morphine amounts (625)			0.78		400mg	0-400	16.256
MST days/30 (622)	572	92	0.30	Mode 1 day	30	0-30	1.946
MST amounts (616)			14.71mg	Mode 100mg Median 100mg	1000mg	0-1g	75.06
Diconal days/30 (622) (620 *no days* reported)	2 cases	0.3%	0.00	Mode 1 or 2 days	2 days	0-2	0.09
Diconal amounts (629)			0.00			0-2mg	0.09
Diazepam days/30 (620) (409 *no days* reported)	211	34	2.96 days	Mode 1 day	30	0-30	7.21
Diazepam amounts (620)			13.39mg		450	0-450	32.99
Temazepam days/30 (607) 495 *no days* reported	112	18.5	3.48 days	Mode 1 day	30	0-30	9.23
Temazepam amounts (621)			6.28mg		400	0-400	32.47

At baseline 54% of patients tested positive for heroin at their review appointment. Some 58.9% tested positive for diazepam (29% were prescribed diazepam).

Table 19. – Injecting risks (from MAP and IRQ)

	N	%	Mean	Median	Range	Min-max	SD
IRQ - Any injecting/28 days (537)							
yes	87	16.2					
never	450	83.8					
Days injected/30 (616)			1.86 days		30	0-30	6.14
Times/day injected (613)			0.26 times		5 times	0-5	0.70
IRQ – sharing/28 days (82)							
Never	67	81.7					
Sometimes	11	13.4					
Frequently	4	4.9					
Days shared/30 (613)			0.08 days		30	0-30	1.24

Only 87 cases (16.2%) reported any injecting at all. Of those who injected, most injected rarely with mean injecting days of 1.86 days of the last 30 (SD 6.14). Range was 0-30 days meaning that daily injecting was occurring in a minority. Mean frequency of daily injecting was 0.26 injections/day (range 0-5 times; SD 0.70). Over 80% stated they never shared with only 4.9% stating they shared frequently.

2. Comorbidity assessment at 2005 baseline

Assessments were undertaken regarding a number of common comorbidities. Tool used were selected by clinical lead staff or were recommended by local experts.

Table 20. Pain – Brief Pain Inventory

	N	%	mean	Median	Mode	Min-max	SD
Pain problem (522)							
Yes	300	57.5					
No	222	42.5					
Duration–months (295)			77.82	48	120	0-384	77.07
Chronic @ 6/12 (296)							
yes	258	87.2					
no	38	12.8					
Chronic @ 12/12 (296)							
Yes	238	80.4					
no	58	19.6					
Intensity score (624)			76.78	60	50	0-100	21.865
Severity quintiles (296)							
1st	13	4.4					
2nd	41	13.9					
3rd	97	32.8					
4th	97	32.8					
5th	48	16.2					
Location (299)							
Multiple sites	64						
Back	78						
Head/neck/shoulders	26						
Chest	15						
Abdomen/liver	32						
Arms/hands	9						
Legs/feet	73						
Characteristics							
Pain before SUD?	Yes 51	18					
SUD before Pain?	Yes 58	20.6					
Affects sleep	233	77.9					
Affects ADL	207	72.1					
Medical treatment							
Saw doctor for pain	227	76.7					
Type of doctor							
GP	134	62.3					
Pain specialist	17	7.9					
Other	64	29.8					
Taken seriously	138	61.1					
Prescribed opiate for pain	41	16.4					
Prescribed benzodiazepine	3	1.2					

Pain was common in the baseline population with 57.5% of those asked reporting a problem with pain (Table 20). Pain was reported as long lasting with mean duration of pain reported as 77.82 months (range 0-384 months; SD 77.07). Of those experiencing pain, 80.4% would be defined as "chronic" using the commonly-used 12 month cut-off. Pain was reported as severe. In the BPI intensity score (ranges from 0-100) the mean score was 76.78 (range 0-

100; median 60; SD 21.87). Pain affected many areas of the body with the back, lower limbs and multiple sites the most common. Pain was reported as preceding substance misuse in 18% with 20.6% reporting substance misuse before onset of their pain. Pain affected many activities with 77.9% reporting it affected sleep and 72.1% reporting an effect on basic activities of daily living. Some 62.3% reported seeing a doctor to address their pain problem but only 7.9% had ever seen a pain specialist. Some 61% of those seen by a doctor felt their pain was taken seriously but only 16.4% had been prescribed an opiate for their pain.

Some 300 cases (58.4% of 514 interviewed) scored above the likert threshold for "caseness" in the GHQ28 (Table 21).

Table 21. Psychiatric "caseness" - General Health Questionnaire (GHQ28)

	N	%	Mean	median	Mode	Min-max	SD
Total score (514)			28.11	26	21	1-78	13.609
Likert threshold for caseness: 23/24 (514)							
Yes - caseness	300	58.4					
No - caseness	214	41.6					

Some 215 (40% of 539 interviewed) received a diagnosis of Social Phobia based on the threshold of 21/22 (Table 22).

Table 22. Social Phobia – Social Phobia Diagnostic Questionnaire (SPDQ)

	N	%	Mean	median	Mode	Min-max	SD
Total score (539)			6.88	0	0	0-27	8.587
Likert threshold for social phobia: 21/22							
Yes - caseness	215	40%					
No - caseness	323	60%					

Using this version of the Impact of Events Scale, 280 cases (48% of the 601 assessed at baseline) have a high likelihood of having a form of Post -Traumatic Stress Disorder, based on the likert threshold of 26 for caseness (Table 23).

Table 23. PTSD - Impact of Events Scale (IES)

	N	%	Mean	median	Mode	Min-max	SD
Total score (601)			23.90	19	0	0-75	24.981
Likert threshold for caseness: 26							
Yes - caseness	280	48%					
No - caseness	299	52%					
Avoidance score			14.04	14.00	0	0-65	13.390
Intrusion score			13.06	13.00	0	0-35	12.383

ADHD screening was one of the areas lost due to time pressures. Consequently, only 368 cases were interviewed using the Current Symptoms scale. Of these, only 59 cases (16%) were felt to have symptoms of ADHD with the majority in the "inattentive" group (Table 24).

Table 24. ADHD – Current Symptoms Scale (CSS)

Presence/type of ADHD	N	%
Any ADHD? (n=368)		
No ADHD	309	
ADHD present	59	16%
Type of ADHD (59)		
Inattentive	31	52.5%
Hyperactive/impulsive	8	13.6%
Combined	20	33.9%

Discussion and conclusions – descriptive data

The Tayside Methadone Cohort consists of 623 existing cases in OST- M treatment for the management of opiate dependency across a Scottish region – Tayside - comprising one city (Dundee) and two counties – Angus and Perth and Kinross. The sample represents some 76% of those in receipt of OST- M in the region. The cases were included if interviewed in the calendar year 2005 (February to December). Tests show the sample to differ from those not assessed in terms of methadone dose, age and gender distribution. This may reflect that those who were difficult to engage differed significantly from the sample.

Demographics

The sample is 68.4% male with a mean age of 32.96 (SD 7.746). 61.6% of the sample lives in Dundee City, 22.6% in Angus and 15.8% Perth & Kinross. The sample is exposed to high levels of deprivation with 77.7% living in the two most deprived health board area quintiles. Some 39.7% have lived at their current address for over 3 years while 33.3% have lived there for less than 1 year. Some 443 (75.7%) are parents of 851 children while 232 (37.7%) report that they live alone. Some 44% had no contact with their partner in the previous 30 days.

Educational attainment was poor with over 50% having no qualifications at all and over 60% of those with any qualifications having only achieved standard grades. Few were in paid work with those who were working reporting a mean of only 2 days per month in active employment.

Healthcare

Only 87% were registered with a GP. Despite this, 52% reported having physical health problems of which only 60% were receiving treatment. Mean MAP physical health score was 14.2 (SD 7.98) suggesting that in general physical health problems were mild/moderate. Some 49.7% reported mental health problems of which 69% were being treated. Only 30% were receiving support from other agencies (for themselves or their children) outside the NHS specialist treatment agencies.

Treatment for substance misuse

Though the cohort was identified via methadone prescribing information systems, only 97% of the cohort was currently prescribed methadone when assessed. This is likely to reflect a natural fluctuation of those on prescriptions – either though successful detoxification or loss of a community prescription for some clinical reason (e.g. imprisonment; hospital admission; failure to attend to access a script etc.). The most commonly prescribed dose of methadone was relatively low at 50mg with the mean dose of 49.54mg (SD 25.25). The maximum dose was 170mg. Some 29% of subjects were also being prescribed diazepam – often as a detoxification agent but some would be “maintenance” prescriptions. The information contained within the database could not determine which group an individual

patient would be in. Treatment was being delivered in three settings: NHS specialist service (TDPS) – 47.4%; Criminal Justice services (DTTO and TARS) – 14.8%; General Practice Shared Care – 24.8%. At baseline 54% of patients tested positive for heroin at their review appointment. Some 58.9% also tested positive for diazepam (only 29% were prescribed). However, only 16% of subjects reported any injecting. Of those, over 80% stated they never shared injecting equipment, with only 4.9% stating they shared frequently.

Comorbidities

Chronic pain: This was a common complaint with 57.5% stating they had a pain issue. Pain was long lasting. Mean duration of pain was 77.8 months (SD 77.07) and 80.4% would be described as "chronic" at the 1 year cut-off. Pain was severe. In the BPI intensity score, mean score was 76.68/100 (SD 21.87). Pain affected many activities of daily living. Over 60% had seen a doctor about their pain but only 7.9% had seen a pain specialist. Only 16.4% had been prescribed an opiate for their pain.

Mental health "caseness" and other issues: of the 514 assessed using the GHQ28, 300 (58.4%) scored above the Likert scale threshold for "caseness".

Social Phobia: Of 539 interviewed, 215 (40%) scored above the SPDQ diagnostic threshold.

PTSD: 601 were interviewed using the IES scale. Of these some 280 (48%) scored higher than the threshold of 26 for "caseness". Mean score was 23.9 (SD 24.981).

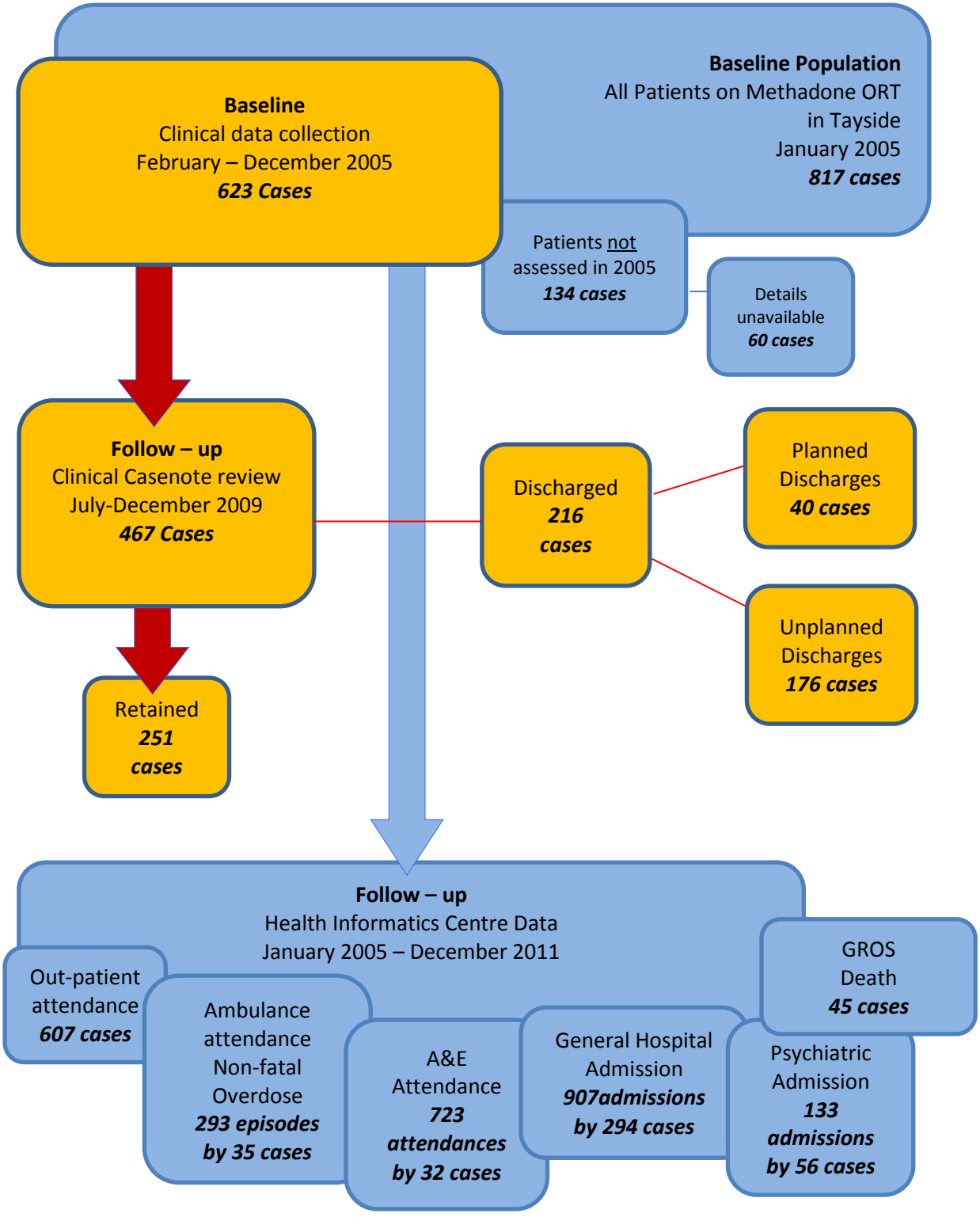
ADHD: The current symptoms scale assessed 368 subjects. Only 16% had symptoms suggestive of ADHD. Using this tool, the majority would be classed as "inattentive".

Chapter 6

Results: Follow – up 1.

Clinical casenote review, 2009

Figure 8. Follow up – Clinical casenote review - 2009



Process - Follow up analyses 1. Clinical casenote review 2009

Introduction

This chapter describes the first follow up element of the study. Figure 8. illustrates the data sources of data used in these analyses.

In 2008, NHS Tayside research & Development (R&D) office offered an opportunity to bid for small grants to support the development of information systems in specific clinical areas seen as NHS priorities. These were generally areas which were experiencing waiting time delays or quality concerns. The researchers successfully bid for an R&D grant to deliver a follow-up study of the sample described as the "Tayside Methadone Cohort" from 2005.

Process

The original Tayside Methadone Cohort sample from 2005 was used as the basis of the study. It was first planned to use follow up interviews using the Maudsley Addiction Profile (MAP), Injection Risk Questionnaire (IRQ) and Treatment Perception Questionnaire (TPQ) to demonstrate objective changes in the baseline sample regarding their illicit drug use, risk taking and associated sequelae. The study received Ethics Committee and Caldicott Guardian approval and proceeded in the autumn of 2009. Unfortunately, attendance at the follow up assessments was extremely poor and this issue threatened the value of the study. Consequently, the researchers obtained permissions to alter the data collection process and, instead, collected data from the NHS clinical casenotes.

Data collection

The medical records were made available to the researcher in the clinical service bases. This reduced the likelihood of the research obstructing clinical practice and also increased accessibility of as much information as was available. The clinical information was collected using a data-collection pro-forma (Figure 5 – p125). Clinical notes recorded in the calendar year 2009 were examined.

Data quality and validity

The quality of clinical casenote recording was found to be inconsistent in many clinical services. Some records to be accessed were also from non-NHS services (e.g. Drug Treatment & Testing Order and Arrest Referral Schemes) making quality assurance an issue. It was recognised that this raised a potential risk to the study. In response, 3 priority levels for data collection were created – reflecting the likely quality of data available. The researcher was advised to use the highest level of information available for completion of the data collection tool. If conflicting or confusing information was found this was discussed with the project lead clinician. If the true nature of the status of a case could not be agreed and this was unresolvable, information was defined as "missing".

The priority levels used were as follows:

- **Level 1**: The highest level included any validated assessment tools completed by staff. Examples included the MAP and associated forms; Treatment Outcome Profile (TOP). This tool had been introduced as a follow up measure of outcome in the service. It was preferred by clinicians because of its brevity (compared to the MAP). New cases (or those returning after an absence of 6 months) would also have a Scottish Morbidity Record (SMR) 25 completed. A copy is often held in the casenotes. Completion of this document is mandatory across Scotland and is the basis of national statistics - making it a likely source of valid information from the casenote.
- **Level 2**: The next level included formal reports /correspondence relating to hospital admissions, the criminal justice system (often a source of background reports) and child protection. Included in this level were care plans – completed by keyworkers at regular case reviews or on discharge. These were only included if the service proforma – which objectively assessed a number of areas of progress in a case - was completed.
- **Level 3**: The lowest level accepted was contemporaneous handwritten notes.

Data entry and cleaning

The information collected on the proforma, which had unique identifiers, allowing matching with the Tayside Methadone Cohort baseline data, was input into a bespoke database built in SPSS version 18 (IBM 2010). The data was initially held in an encrypted form on a secure hard drive which was password protected and stored in a locked cupboard in the Department of Psychiatry, University of Dundee Medical School.

Data – linkage: SUMIT project and HIC Safe Haven

In Autumn of 2010, the SUMIT project was launched. The project is described in detail in Chapter 7. Associated papers are contained in Appendix 3. SUMIT engaged the support of the Health Informatics Centre (HIC) and, as part of this project, data were migrated into the HIC "Safe Haven" – a virtual environment where data is held securely with a new, unique identifier or "Prochi". The data can then be linked with other relevant clinical data. The Tayside Methadone Cohort (2005) data and 2009 casenote follow up data were migrated into the HIC Safe Haven in Spring 2011. All subsequent data handling took place in that secure environment.

Analyses

The data used in these analyses were:

- Data collected at the baseline assessment interview in 2005
- Data collected at the casenote review of 2009

The literature review described in Chapter 3, informed the development of an analysis plan, using data available in the linked dataset to assess the individual impact of a range of predictor variables (independent variables) on a range of process measures or outcomes (dependent variables). The variables chosen for this analysis are shown in Tables 25 and 26.

The generic research question being addressed in this case is:

Does (baseline - independent variable) impact on (follow up - dependent variable)?

From this, a null hypothesis can be generated:

Baseline (independent variable) does not impact on follow up (dependent variable)

Table 25.–independent and dependent variables – patient characteristics (casenote review)

Predictor Variable (Independent) at baseline	Dependent variable (2009 casenote review)
Demographics	***Process measures***
Age	Retained on treatment - 4 years
Gender	If discharged positive or negative discharge
Home District	Methadone dose
Deprivation score (NHS Board SIM-D)	Diazepam dose
Social stability	Regular drug screen done
Time at address	***Outcome measures***
Lives alone	Employment status
Has children	Family stability
Lives with children	Any illicit drug use
MAP Conflict scores –partner; family; friends	Heroin use reported
Educational level achieved	Heroin use (days)
Days in paid work	Heroin use (route)
Treatment status	Diazepam use
Provider (Specialist; GP; CJS)	Diazepam days
Registered with GP	Illicit methadone use
Support from other agency	Illicit methadone days
MAP Physical health score	Illicit painkiller (opiate) use
MAP Psychological health score	Illicit painkiller days
Prescribed methadone dose	Test positive opiates
Prescribed diazepam dose	Test positive benzodiazepines
TPQ patient satisfaction score	Acute hospital admissions reported
Illicit drug use	Psychiatric hospital admissions reported
Any heroin use	Incarceration reported
Extent of use (“Days used”)	
Route	
Risk taking (IRQ score)	
Illicit benzodiazepine use	

Table 26. –independent and dependent variables - comorbidities (casenote review)

Predictor Variable (Independent) at baseline	Process (Dependent variable)
Co-morbidities	***Process measures***
Psychiatric caseness	Retained on treatment - 4 years
GHQ 28 Caseness	If discharged – positive or negative
GHQ 28 Total score	Methadone dose
Chronic Pain	Diazepam dose
BPI-Pain presence	Regular drug screen done
BPI-Pain duration	***Outcome measures***
BPI-Pain chronicity (12/12 cut off)	Employment status
BPI-Pain intensity (score)	Family stability
BPI-Pain intensity (quintiles)	Any illicit drug use
Anxiety disorders	Heroin use reported
Social phobia diagnosis (as SPDQ)	Heroin use (days)
PTSD caseness (IES cut off 26)	Heroin use (route)
PTSD severity (IES total score)	Diazepam use
ADHD	Diazepam days
ADHD Symptoms (CSS)	Illicit methadone use
ADHD type (CSS)	Illicit methadone days
ADHD impairment (CSS)	Illicit painkiller (opiate) use
	Illicit painkiller days
	Test positive opiates
	Test positive benzodiazepines
	Acute hospital admissions reported
	Psychiatric hospital admissions reported
	Incarceration reported

Statistics

When both independent and dependent variables were categorical - Chi-squared tests were undertaken. For categorical independent and continuous dependent variables, an ANOVA was used (if data were parametric). If not, the Kruskall-Wallis H-test or Mann-Whitney U-test (for binary data) were used.

For continuous independent variables with categorical dependent variables, discriminant analyses were used. If the DV/IV relationship was linear, linear discriminant analyses were used. If not, quadratic discriminant analyses were used.

When both independent and dependent variables were continuous – linear regression analyses were undertaken.

Addressing Multiple Testing

The issue of multiple testing has been discussed in Chapter 4. There is a risk of overestimating the significance of results when large numbers of tests are being undertaken. There are a number of ways a Bonferroni Correction could be applied (Toothaker 1993).

As has been described in Chapter 4, the Bonferroni Correction involves dividing the accepted significance level (p-value) by the number of repeat tests. In these datasets, there are 22 individual analyses being undertaken using each Independent Variable. Statistical significance is being defined at the p= 0.05 level. Using the Bonferroni Correction, involving all of the analyses, this would require statistical significance to be accepted only at the p=0.002 level for all analyses.

Alternatively, however, it could be argued that a number of discrete groups of tests are being undertaken and using the Bonferroni Correction as described above would reduce the statistical power of the tests – increasing the likelihood of a false negative result (Type 2 error). In fact only 5 tests per Independent Variable relate to a Dependent Variable (DV) regarding measures of the treatment process; 2 tests relate to a social functioning (DV); 12 relate to any drug use [4 – heroin; 3 diazepam; 2 methadone; 2 other opiates]; 3 relate to the outcomes of admissions or incarcerations. If this approach were applied, more appropriate significance levels can be determined which reduce the likelihood of Type 2 error. The significance levels are shown in Table 27.

These corrections were applied when considering the relevance of any associations demonstrated.

Table 27. Bonferroni Correction – significance by Dependent Variable

Dependent Variable	Number of analyses	Significance level
Process Measures		
Retained on treatment - 4 years	**5**	**0.01**
If discharged – positive or negative		
Methadone dose		
Diazepam dose		
Drug screen done		
Social functioning		
Employment status	**2**	**0.025**
Family stability		
Drug use		
All drugs	**12**	**0.0041**
Heroin	**4**	**0.0125**
Diazepam	**3**	**0.0167**
Methadone (Illicit)	**2**	**0.025**
Other opiates	**2**	**0.025**
Admissions		
General Hospital	**3**	**0.0167**
Psychiatric Hospital		
Prison		

Results – Clinical casenote review 2009

This section describes the results of the analyses undertaken using data collected from clinical casenotes (n= 467) in 2009. Significant associations are shown in a series of tables – Tables 28-42. Tables of negative results (where no significant associations were demonstrated in the univariate analyses) are contained in Appendix 5.

Demographic factors

Neither gender nor deprivation score at baseline was shown to be associated with 4 year outcomes.

Age and gender (Table 28)

Age was found to have a significant association with the treatment process reported in casenotes in 2009. Younger subjects were more likely to have a drug screen undertaken than older subjects. Age was also associated with the recorded state of family stability.

Again being younger was associated with poorer family stability recorded in the casenotes. Complete results are shown in table 28.

Table 28. Associations: age/process & 4 year outcomes

Independent Variable	Dependent (Process) variable	Statistics	Effect size
Age **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	Retained in treatment **Younger = better retention**	LDA **$X^2(1)=4.412$; p=0.036**	
	If NOT retained, +ve or –ve discharge (n=198)	LDA $X^2(1)=0.001$; p=0.977	
	Drug screen done **Younger = more tests done**	LDA **$X^2(1)=7.628$; p=0.006**	Cohen's d=-.211 r = -0.105 *small effect size*
	Methadone dose	QRA t(1)=1.063; p=0.288	
	Diazepam dose	QRA t(1)=0.845; p=0.399	
	Dependent (Outcome) variable		
	Employment status	LDA $X^2(1)=0.927$; p=0.336	
	Family stability **Younger = less stable family**	LDA **$X^2(1)=11.321$; p=0.001**	Cohen's d = .63 r = 0.301 *medium effect size*
	Any illicit drug use reported	LDA $X^2(1)=1.853$; p=0.173	
	Heroin use reported **Younger = more likely to use**	LDA **$X^2(1)=5.429$; p=0.020**	
	Heroin days	LDA$X^2(5)=4.285$; p=0.509	
	Heroin route	LDA $X^2(1)=0.092$; p=0.762	
	Illicit Diazepam use **Younger = more likely to use**	LDA **$X^2(1)=5.301$; p=0.021**	
	Illicit diazepam days	LDA $X^2(1)=7.549$; p=0.183	
	Ill meth use	LDA $X^2(1)=0.010$; p=0.920	
	Illicit methadone days	LDA $X^2(3)=3.322$; p=0.345	
	Illicit painkillers	LDA $X^2(1)=1.458$; p=0.227	
	+ve opiates recorded	LDA $X^2(1)=3.639$; p=0.056	
	+ve benzos recorded	LDA $X^2(1)=0.439$; p=0.507	
	Acute admissions reported	LDA $X^2(1)=1.175$; p=0.278	
	Psych admissions reported	LDA $X^2(2)=0.144$; p=0.931	
	Prison reported	LDA $X^2(3)=1.331$; p=0.722	

Place of residence (Table 29)

Place of residence was strongly associated with a number of process measures and outcomes. Regarding *process* – Dundee residents were retained in treatment best with those residing in Angus retained least well. Prescribed Diazepam dose also differentiated the area (despite the whole region using the same prescribing protocols). Angus subjects had the highest prescribed diazepam doses, Dundee the lowest. Regarding *outcomes* – Dundee subjects reported less illicit drug use overall (P&K was poorest) and had better

recorded family stability (Angus was poorest). Subjects from Dundee & Angus showed more illicit diazepam use (through recorded drug testing) than those from P&K.

Table 29. Associations: place of residence/process and 4 year outcomes

Independent (Predictor) Variable	Dependent (Process) variable	Statistics	Effect size
Residence **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	Retention (Yes 156) **Dundee>P&K>angus= retained**	**Chi square $X^2(2)=11.352$; p=0.003**	Cramer's v=.164 p=0.003 *Substantial relationship*
	If NOT= +ve or –ve discharge **Negative P&K>Angus>Dundee**	**Chi square $X^2(6)=14.435$; p=0.025**	
	Drug screen done (D>P>A)	**Chi square $X^2(4)=11.342$; p=0.023**	
	Methadone dose (A>D>P)	**KWH $X^2(2)=8.409$; p=0.015**	
	Diazepam dose **Higher dose= Angus>P&K>Dundee**	**KWH $X^2(2)=9.660$; p=0.008**	Partial η^2 = .014 *Small effect size*
	Dependent (Outcome) variable		
	Employment status	Chi square $X^2(2)=0.820$; p=0.664	
	Family stability **Dundee>P&K>Angus**	**Chi square $X^2(4)=20.796$; p<0.001**	Cramer's v = .157 P=.004 *Substantial relationship*
	Any illicit drug use reported **P&K>Angus>Dundee**	**Chi square $X^2(6)=18.917$; p=0.004**	Cramer's v = .149 P=.004 *Substantial relationship*
	Heroin use reported (A>P>D)	**Chi square $X^2(6)=14.102$; p=0.029**	
	Heroin days (A>P>D)	**Chi square$X^2(16)=30.946$; p=0.014**	
	Heroin route	Chi square $X^2(8)=14.266$; p=0.075	
	Illicit Diazepam use **Dundee=Angus>P&K**	**Chi square $X^2(6)=21.583$; p=0.001**	Cramer's v = .160 p=0.001 *Substantial relationship*
	Illicit Diazepam days	Chi square $X^2(16)=24.491$; p=0.079	
	Illicit Methadone use (D=A>P)	**Chi square $X^2(6)=12.763$; p=0.047**	
	Illicit Methadone days	Chi square $X^2(12)=18.697$; p=0.096	
	Illicit painkillers **25 cases **Angus>Dundee>P&K**	**Chi square $X^2(6)=16.932$; p=0.010**	Cramer's v=.141 P=0.010 *Substantial relationship*
	+ve opiates tests	Chi square $X^2(8)=14.531$; p=0.069	
	+ve benzodiazepine tests **Dundee>Angus>P&K**	**Chi square $X^2(6)=35.621$; p<0.001**	Cramer's v = .160 P=.004 *Substantial relationship*
	Acute admissions reported **Angus>P&K>Dundee**	**KWH $X^2(2)=2.842$; p=0.241**	
	Psych admissions reported **Angus>P&K>Dundee**	**KWH $X^2(2)=0.776$; p=0.678**	
	Prison reported **Angus>P&K>Dundee**	**KWH $X^2(2)=0.449$; p=0.799**	

Social stability at baseline

Most factors describing baseline social stability showed no associations with outcomes. These factors included: time at current address; living status (alone/not); living with their children; educational level attained; days in paid work. Some factors did show significant associations.

Children (Table 30) **-** Having children recorded at baseline was found to have negative associations with 2009 status. Having children was associated with negative discharge being recorded and with notes recording poor family stability.

Table 30. Associations: having children/process and 4 year outcomes

Independent Variable	Dependent (Process) variable	Statistics	Effect size
Has children **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention**	Chi square $X^2(1)=0.442$; p=0.506	
	Pos/neg discharge **Kids predict negative discharge**	**Chi square$X^2(1)=11.194$; p=0.001**	Cramer's v=.167 P=0.011 *Substantial relationship*
	Drug screen done	Chi square $X^2(2)=3.466$; p=0.177	
	Methadone dose	KWH $X^2(1)=1.946$; p=0.163	
	Diazepam dose	KWH $X^2(1)=1.407$; p=0.236	
	Dependent (outcome) variable		
	Employment status	Chi square $X^2(5)=7.520$; p=0.185	
	Family stability **Kids negative predictor of stability**	Chi square **$X^2(2)=7.723$; p=0.021**	Cramers v=.136 P=0.025 *Substantial relationship*
	Any illicit drug use reported	Chi square $X^2(3)=3.812$; p=0.283	
	Heroin use reported; days; route	Chi square $X^2(3)=1.634$; p=0.652 Chi square $X^2(8)=12.531$; p=0.129 Chi square $X^2(4)=1.063$; p=0.900	
	Ill Diazepam use; days;	Chi square $X^2(3)=0.856$; p=0.836 Chi square $X^2(8)=14.243$; p=0.076	
	Ill meth use; days;	Chi square $X^2(3)=0.805$; p=0.848 Chi square $X^2(6)=4.027$; p=0.673	
	Illicit painkillers days	Chi square $X^2(3)=0.864$; p=0.834 Chi square $X^2(4)=1.070$; p=0.899	
	+ve opiates	Chi square $X^2(4)=1.240$; p=0.871	
	+ve benzos	Chi square $X^2(3)=1.1085$; p=0.781	
	Acute admissions reported	KWH $X^2(1)=0.590$; p=0.443	
	Psych admissions reported	KWH $X^2(1)=0.208$; p=0.648	
	Prison reported	KWH $X^2(1)=0.539$; p=0.463	

MAP Partner, relative and friend conflict scores (Table 31) **-** Having higher conflict scores recorded at baseline was associated with 4 year outcomes. A higher Friends conflict score

was associated with more illicit diazepam and illicit methadone use. A higher partner conflict score was associated with more illicit methadone days used recorded at follow up.

Table 31. Associations: MAP conflict scores/process and 4 year outcomes

Independent (Predictor) Variable	Dependent variable	Statistics	Effect size
MAP conflict scores: **1. Partner** **2. Relative** **3. Friends** **Significant impact set at the p<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention**	1.LDA $X^2(1)=0.146$; p=0.702 2.LDA $X^2(1)=0.532$; p=0.466 3.LDA $X^2(1)=0.711$; p=0.399	
	Positive/negative discharge	1. LDA $X^2(1)=1.814$; p=0.178 2. LDA $X^2(1)=2.015$; p=0.156 3. LDA $X^2(1)=0.400$; p=0.527	
	Drug screen done	1.LDA $X^2(1)=0.345$; p=0.557 2.LDA $X^2(1)=0.610$; p=0.435 3.LDA $X^2(1)=1.667$; p=0.197	
	Methadone dose	1.LRA t(1)=-1.384; p=0.167 2.LRA t(1)=-0.387; p=0.699 3.LRA t(1)=0.798; p=0.425	
	Diazepam dose	1.LRA t(1)=-0.597; p=0.551 2.LRA t(1)=-0.738; p=0.461 3.LRA t(1)=0.669; p=0.504	
	Employment status	1.LDA $X^2(1)=0.030$; p=0.862 2.LDA $X^2(1)=0.932$; p=0.334 3.LDA $X^2(1)=0.249$; p=0.618	
	Family stability	1.LDA $X^2(1)=2.884$; p=0.089 2.LDA $X^2(1)=0.648$; p=0.421 3.LDA $X^2(1)=0.040$; p=0.841	
	Any illicit drug use reported	1.LDA $X^2(1)=0.039$; p=0.844 2.LDA $X^2(1)=0.002$; p=0.967 3.LDA $X^2(1)=0.443$; p=0.506	
	Heroin use reported	1.LDA $X^2(1)=0.960$; p=0.327 2.LDA $X^2(1)=0.006$; p=0.936 3.LDA $X^2(1)=0.277$; p=0.598	
	Heroin days	1.LDA $X^2(5)=8.281$; p=0.141 2.LDA $X^2(5)=2.798$; p=0.731 3.LDA $X^2(5)=0.649$; p=0.986	
	Heroin route	1.LDA $X^2(1)=0.017$; p=0.895 2.LDA $X^2(1)=1.315$; p=0.252 3.LDA $X^2(1)=0.897$; p=0.344	
	Ill Diazepam use; days (of 90);	1.LDA $X^2(1)=0.049$; p=0.825 2.LDA $X^2(1)=1.279$; p=0.258 3.LDA $X^2(1)=2.094$; p=0.148	
	Illicit diazepam days **Higher PCS score predicts less days use** **Higher FCS predicts more days used**	**1.LDA $X^2(5)=11.547$; p=0.042** 2.LDA $X^2(5)=4.904$; p=0.428 **3.LDA $X^2(5)=22.927$; p<0.001**	Partial η^2 = .019 *Small effect size*
	Illicit methadone use **Higher FCS predicts illicit use**	1.LDA $X^2(1)=0.001$; p=0.975 2.LDA $X^2(1)=2.684$; p=0.101 **3.LDA $X^2(1)=11.903$; p=0.001**	Partial η^2 = .017 *Small effect size*
	Illicit methadone days **Higher PC score predicts more days used**	**1.LDA $X^2(3)=11.096$; p=0.011** 2.LDA $X^2(3)=7.266$; p=0.064 3.LDA $X^2(3)=3.461$; p=0.326	Partial η^2 = .092 *Medium effect size*
	+ve opiates	1.LDA $X^2(1)=0.415$; p=0.519; 2.LDA $X^2(1)=0.112$; p=0.738; 3.LDA $X^2(1)=0.064$; p=0.800	
	+ve benzos	1.LDA $X^2(1)=0.053$; p=0.818; 2.LDA $X^2(1)=0.036$; p=0.850; 3.LDA $X^2(1)=0.000$; p=0.999	
	Acute admissions reported	1.LRA t(1)=-0.419; p=0.676; 2.LRA t(1)=-0.727; p=0.468; 3.LRA t(1)=0.831; p=0.406	
	Psych admissions reported	1.LRA t(1)=-0.417; p=0.677; 2.LRA t(1)=-0.724; p=0.469; 3.LRA t(1)=0.833; p=0.405	
	Prison reported	1.LRA t(1)=-0.392; p=0.695; 2.LRA t(1)=-0.704; p=0.482; 3.LRA t(1)=0.850; p=0.396	

Educational attainment (Table 32) **-** The level of educational attainment achieved was recorded at baseline. It was found that this was associated with recording of acute and psychiatric admissions in casenotes. Perhaps surprisingly, those who had attained a level of education/training which was an apprenticeship or higher were more likely to have hospital admissions recorded in their casenotes.

Table 32. Associations: Educational level achieved/process and 4 year outcomes

Independent Variable	Dependent (Process) variable	Statistics	Effect size
Educational level achieved **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention**	Chi square **$X^2(4)=11.870;p=0.018$** **More s =less retention**	
	Positive/negative discharge	Chi square $X^2(4)=3.133$; p=0.536	
	Drug screen done	Chi square $X^2(8)=9.298$; p=0.318	
	Methadone dose	KWH $X^2(4)=8.631$; p=0.0.071	
	Diazepam dose	KWH $X^2(4)=9.212$; p=0.056	
	Dependent (outcome) variable		
	Employment status	Chi square $X^2(4)=2.316$; p=0.678	
	Family stability	Chi square $X^2(8)=12.395$; p=0.134	
	Any illicit drug use reported	Chi square $X^2(12)=17.052$; p=0.148	
	Heroin use reported	Chi square $X^2(12)=18.321$; p=0.106	
	Heroin days	Chi square $X^2(32)=37.535$; p=0.230	
	Heroin route	Chi square $X^2(16)=20.460$; p=0.200	
	Ill Diazepam use	Chi square $X^2(12)=14.883$; p=0.248	
	Illicit diazepam days	Chi square $X^2(32)=22.167$; p=0.903	
	Illicit methadone use	Chi square $X^2(12)=17.233$; p=0.141	
	Illicit methadone days	Chi square $X^2(24)=17.659$; p=0.819	
	Illicit painkillers	Chi square $X^2(12)=15.212$; p=0.230	
	Illict painkillers days	Chi square $X^2(16)=19.781$; p=0.230	
	+ve opiates	Chi square $X^2(16)=14.454$; p=0.565	
	+ve benzos	Chi square $X^2(12)=12.245$; p=0.426	
	Acute admissions reported **Apprentice= >admissions**	**KWH (4)=15.447; p=0.004**	Monte carlo sig test =.003 99% CI .002-.005 *Likely effect*
	Psych admissions reported **Apprentice= >admissions**	**KWH(4)=14.782; p=0.005**	Monte carlo sig test =.004 99%ci=.002-.005 *Likely effect*
	Prison reported	**KWH(4)=10.638; p=0.31** **Apprentice= >incarcerations**	

Treatment status (Services received at baseline)

Factors relating to the service received at baseline were found to be associated with outcome at 4 years.

Treatment setting (Table 33) Regarding *Process*: specialist services (NHS and Criminal Justice) were more likely to retain patients in treatment than GPs. Criminal Justice services

(CJS) recorded more drug screens. Regarding *outcomes*: specialist services recorded more evidence of family stability. GP patients were considerably more likely to have injecting and any admissions recorded (including incarcerations). CJS patients were most likely to report heroin and illicit diazepam use but least likely to report injecting. Illicit methadone use was most likely to be recorded in specialist NHS service whose cases were least likely to test positive for opiates or benzodiazepines.

Table 33. Associations: treatment setting/process and 4 year outcomes

Independent (Predictor) Variable	Dependent (Process) variable	Statistics	
GP or specialist setting (+CJS) **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention Specialist>GP**	**Chi square $X^2(2)=10.902$; p=0.004**	Cramer's v=.163 p=0.004 *Relevant Effect*
	Pos/neg discharge	Chi square $X^2(2)=3.593$; p=0.166	
	Drug screen done CJS>TDPS>GP	**Chi square $X^2(4)=14.019$; p=0.007**	Cramer's V=.131 p=0.007 *Small effect*
	Methadone dose	**Anova F(2,8)=3.093; p=0.046**	
	Diazepam dose	Anova F(2,8)=0.927; p=0.397	
	Dependent (outcome) variable		
	Employment status	Chi square $X^2(12)=20.024$; p=0.067	
	Family stability Specialist>GP	**Chi square $X^2(4)=12.301$; p=0.015**	Cramer's v=.123 p=0.015 *Relevant Effect*
	Any illicit drug use reported	Chi square $X^2(6)=12.093$; p=0.060	
	Heroin use reported CJS>GP>TDPS	**Chi square $X^2(6)=20.392$; p=0.002**	Cramer's v=.158 p=0.002 *Relevant Effect*
	Heroin days	Chi square $X^2(16)=26.067$; p=0.053	
	Heroin route GP IV ++>TDPS>CJS	**Chi square $X^2(8)=26.233$; p=0.001**	Cramer's V=.179 p=0.001 *Relevant Effect*
	Illicit Diazepam use CJS>GP>TDPS	**Chi square $X^2(6)=17.906$; p=0.006**	Cramer's V=.148 p=0.006 *Relevant Effect*
	Illicit diazepam days	Chi square $X^2(16)=25.021$; p=0.069	
	Illicit methadone use TDPS<GP+CJS	**Chi square $X^2(6)=21.325$; p=0.002**	Cramer's v=.162 p=0.002 *Relevant Effect*
	Illicit methadone days TDPS <GP/CJS	**Chi square $X^2(10)=22.283$; p=0.014**	Cramer's V=.165 p=0.014 *Relevant Effect*
	Illicit painkillers	**Chi square $X^2(6)=13.621$; p=0.034**	
	Illicit painkillers days	Chi square $X^2(8)=12.559$; p=0.128	
	+ve opiates CJS>GP>TDPS	**Chi square $X^2(6)=19.642$; p=0.003**	Cramer's V=.155 p=0.003 *Relevant Effect*
	+ve benzos CJS>GP>TDPS	**Chi square $X^2(6)=22.884$; p=0.001**	Cramer's v =.167 p=0.001 *Relevant Effect*
	Acute admissions reported GP>TDPS>CJS	**ANOVA F(2,8)=5.619; p=0.004**	Partial η^2 = .027 *Small effect*
	Psych admissions reported GP>TDPS>CJS	**ANOVA F(2,8)=5.368; p=0.005**	Partial η^2 = .026 *Small effect*
	Prison reported GP>TDPS>CJS	**ANOVA F(2,8)=4.888; p=0.008**	Partial η^2 = .024 *Small effect*

Registration with a General Practitioner (Table 34) - Being registered with a GP at baseline showed consistent associations with some markers of stability at 4 year follow up. Those registered with a GP in 2005 were more likely to be employed, had more evidence of family stability recorded in their casenotes and also had less opiate positive drug tests recorded.

Table 34. Associations: GP registration at baseline/process and 4 year outcomes

Independent Variable	Dependent variable	Statistics	Effect size
Registered with GP **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention**	**Chi square $X^2(1)=5.353$; p=0.021**	
	Pos/neg discharge	Chi square $X^2(1)=0.115$; p=0.735	
	Drug screen done	Chi square $X^2(2)=3.594$; p=0.166	
	Methadone dose	KWH $X^2(1)=0.268$; p=0.605	
	Diazepam dose	**KWH $X^2(1)=4.668$; p=0.031** **GP predicts lower dose**	
	Dependent (outcome) variable		
	Employment status **GP predicts better employment**	**Chi square $X^2(6)=17.800$; p=0.007**	Cramer's V=.195 p=0.007 *Relevant effect*
	Family stability **GP predicts family stability**	**Chi square $X^2(2)=8.973$; p=0.011**	Cramer's V=.139 p=0.011 *Relevant effect*
	Any illicit drug use reported	Chi square $X^2(3)=6.792$; p=0.079	
	Heroin use reported; days; route	Chi square $X^2(3)=7.459$; p=0.059	
	Heroin days	Chi square $X^2(8)=9.956$; p=0.268	
	Heroin route	**Chi square $X^2(4)=10.551$; p=0.032** **GP predicts less injecting**	
	Illicit Diazepam use	Chi square $X^2(3)=5.638$; p=0.131	
	Illicit diazepam days	Chi square $X^2(8)=7.089$; p=0.527	
	Illicit methadone use	Chi square $X^2(3)=7.344$; p=0.062	
	Illicit methadone days	Chi square $X^2(6)=7.863$; p=0.248	
	Illicit painkillers use	Chi square $X^2(3)=5.604$; p=0.133	
	Illicit painkillers days	Chi square $X^2(4)=9.063$; p=0.060	
	+ve opiates **GP predicts less +ve tests**	**Chi square $X^2(4)=11.411$; p=0.022**	Cramer's V=.156 p=0.022 *Relevant effect*
	+ve benzos	Chi square $X^2(3)=4.750$; p=0.191	
	Acute admissions reported	**KWH $X^2(1)=4.657$; p=0.031** **GP predicts more admissions**	
	Psych admissions reported	**KWH $X^2(1)=4.822$; p=0.028** **GP predicts more admissions**	
	Prison reported	**KWH $X^2(1)=5.661$; p=0.017** **GP predicts more incarcerations**	

Support from other agencies (Table 35) - Subjects reported if they or their children were in receipt of additional support from external agencies in the third sector or from the local authority at baseline. The records of those who reported they were being supported showed more recorded evidence of family stability at 4 year follow up.

Table 35. Associations: agency support at baseline/process and 4 year outcomes

Independent (Predictor) Variable	Dependent (Process) variable	Statistics	Effect size
Support from other agencies **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention**	Chi square $X^2(1)=1.414$; p=0.234	
	Pos/neg discharge	Chi square $X^2(1)=0.186$; p=0.667	
	Drug screen done	Chi square $X^2(2)=1.101$; p=0.577	
	Methadone dose	KWH $X^2(1)=0.185$; p=0.667	
	Diazepam dose	KWH $X^2(1)=3.057$; p=0.080	
	Dependent (outcome) variable		
	Employment status	Chi square $X^2(5)=7.083$; p=0.215	
	Family stability >support predicts stability	**Chi square $X^2(2)=7.712$; p=0.021**	Cramer's V=.149 p=0.021 *Relevant effect*
	Any illicit drug use reported	Chi square $X^2(3)=1.973$; p=0.578	
	Heroin use reported	Chi square $X^2(3)=2.306$; p=0.511	
	Heroin days	Chi square $X^2(8)=5.209$; p=0.735	
	Heroin route	Chi square $X^2(4)=2.944$; p=0.567	
	Illicit Diazepam use	Chi square $X^2(3)=2.886$; p=0.410	
	Illicit diazepam days	Chi square $X^2(8)=11.402$; p=0.180	
	Illicit methadone use	Chi square $X^2(3)=2.170$; p=0.538	
	Illicit methadone days	Chi square $X^2(6)=10.476$; p=0.106	
	Illicit painkillers use	Chi square $X^2(3)=1.959$; p=0.581	
	Illicit painkillers days	Chi square $X^2(4)=2.636$; p=0.620	
	+ve opiates	Chi square $X^2(4)=4.059$; p=0.398	
	+ve benzos	Chi square $X^2(3)=1.791$; p=0.615	
	Acute admissions reported	KWH $X^2(1)=1.743$; p=0.187	
	Psych admissions reported	KWH $X^2(1)=1.726$; p=0.189	
	Prison reported	KWH $X^2(1)=2.669$; p=0.102	

Treatment status (Prescribed opiates and benzodiazepines at baseline)

Doses of methadone and diazepam were associated with 4 year outcomes. Patients on higher doses of methadone were more likely to be retained and had more drug screens recorded. They were also less likely to screen positive for non-prescribed opioids or to be admitted or incarcerated (Table 36).

Table 36. Associations: baseline methadone dose/process and 4 year outcomes

Independent (Predictor) Variable	Dependent (Process) variable	Statistics	Effect size
Methadone dose **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention** **↑ dose predicts retention**	**LDA** **$X^2(1)=10.643$; p=0.001**	Cohen's d = 0.307 R=0.152 *Small effect size*
	Pos/neg discharge	LDA $X^2(1)=0.760$; p=0.383	
	Drug screen done **↑baseline dose=↑tests**	**LDA** **$X^2(1)=14.916$; p<0.001**	Cohen's d = 0.365 R=0.179 *Small effect size*
	Methadone dose	**LRA t(1)=2.521; p=0.012** **Baselinedose = ↑2009 dose**	
	Diazepam dose	**LRA t(1)=-2.119; p=0.035** **Baselinedose = ↓2009 dose**	
	Dependent (outcome) variable		
	Employment status	LDA $X^2(1)=0.074$; p=0.785	
	Family stability	LDA $X^2(1)=0.009$; p=0.924	
	Any illicit drug use reported	LDA $X^2(1)=2.307$; p=0.129	
	Heroin use reported	**LDA $X^2(1)=5.360$; p=0.021** **Baselinedose = ↓use**	
	Heroin days	LDA $X^2(5)=1.806$; p=0.875	
	Heroin route	LDA $X^2(1)=0.256$; p=0.613	
	Illicit Diazepam use	LDA $X^2(3)=1.013$; p=0.314	
	Illicit diazepam days	LDA $X^2(5)=5.500$; p=0.358	
	Illicit methadone use	LDA $X^2(1)=0.266$; p=0.606	
	Illicit methadone days	LDA $X^2(3)=0.278$; p=0.964	
	Illicit painkillers use	LDA $X^2(1)=0.125$; p=0.723	
	Illicit painkiller days	**LDA $X^2(1)=4.751$; p=0.029** **↑baseline dose=↓days**	
	+ve opiates **↑baselinedose=less +ve**	**LDA** **$X^2(1)=5.569$; p=0.018**	Cohen's d=-.321 R=-0.158 *Small effect size*
	+ve benzos	LDA $X^2(1)=0.035$; p=0.852	
	Acute admissions reported **Higher dose less admissions**	**LRA t(1)=-3.448; p=0.001**	Partial η^2 = .100 *Medium effect*
	Psych admissions reported **Higher dose less admissions**	**LRA t(1)=-3.466; p=0.001**	Partial η^2 = .100 *Medium effect*
	Prison reported **Higher dose less prison**	**LRA t(1)=-3.432; p=0.001**	Partial η^2 = .101 *Medium effect*

The reverse was generally true for diazepam prescribing. Higher diazepam doses were associated with poorer retention and less evidence of drug screening having been undertaken. However, for those screens undertaken, a higher dose was associated with less positive screens for illicit opioids. Higher baseline diazepam dose was associated with a higher follow up methadone dose, with poorer family stability, and increased likelihood of admission or incarceration (Table 37).

Table 37. Associations: baseline diazepam prescribed dose/process and 4 year outcomes

Independent Variable	Dependent (Process) variable	Statistics	Effect size
Diazepam dose **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention** **Lower dose predicts retention**	**LDA $X^2(1)=14.522$; p<0.001**	Cohen's d=-1.246 R=-0.529 *Large effect size*
	Pos/neg discharge	**LDA $X^2(1)=5.344$; p=0.021** **Lower dose predicts +ve discharge**	
	Drug screen done **Higher dose predicts no test done**	**LDA $X^2(1)=16.418$; p<0.001**	Cohen's d= -1.067 R=-0.471 *Large effect size*
	Methadone dose **Higher dose predicts higher dose**	**LRA t(1)=3.986; p<0.001**	Partial η^2 = .076 *Medium effect*
	Diazepam dose	LRA t(1)=-0.763; p=0.446	
	Dependent (outcome) variable		
	Employment status	LDA $X^2(1)=1.437$; p=0.231	
	Family stability **Higher dose predicts less stability**	**LDA $X^2(1)=4.993$; p=0.025**	Cohen's d = 0.081 R=0.041 *Small effect size*
	Any illicit drug use reported	LDA $X^2(1)=0.210$; p=0.647	
	Heroin use reported; days; route	LDA $X^2(1)=3.045$; p=0.081	
	Heroin days	LDA $X^2(5)=0.633$; p=0.986	
	Heroin route	LDA $X^2(1)=2.203$; p=0.138	
	Illicit Diazepam use	LDA $X^2(3)=0.000$; p=0.985	
	Illicit diazepam days	LDA $X^2(5)=4.410$; p=0.492	
	Illicit methadone use	LDA $X^2(1)=0.887$; p=0.346	
	Illicit methadone days	LDA $X^2(3)=0.236$; p=0.972	
	Illicit painkillers use	LDA $X^2(1)=0.583$; p=0.445	
	Illicit painkillers days	LDA $X^2(1)=0.131$; p=0.717	
	+ve opiates **Higher dose –ve test**	**LDA $X^2(1)=5.220$; p=0.022**	Cohen's d = 0.060 R=0.030 *Small effect size*
	+ve benzos	**LDA $X^2(1)=5.216$; p=0.022** **Higher dose +ve test**	
	Acute admissions reported **Higher dose =more admiss**	**LRA t(1)=4.183; p<0.001**	Partial η^2 = .974 *Large effect size*
	Psych admissions reported **Higher dose=more admiss**	**LRA t(1)=3.963; p<0.001**	Partial η^2 = .974 *Large effect size*
	Prison reported **Higher dose= more incarc**	**LRA t(1)=3.990; p<0.001**	Partial η^2 = .966 *Large effect size*

Treatment status (Perception of treatment (TPQ) on outcomes (Table 38)

A baseline cross-sectional analysis found a strong association between where main care was received and the degree of "satisfaction" as measured by the TPQ total score (ANOVA F(2,8)=6.291; p=0.002). Those in the specialist services had higher TPQ scores than those in GP shared care. At follow up a higher TPQ total score was associated with more illicit methadone use.

Table 38. Associations: Perception of treatment (TPQ)/process and 4 year outcomes

Independent Variable	Dependent (Process) variable	Statistics	Effect size
Satisfaction at baseline (TPQ total score) **Significant impact set at the p<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	Retention	LDA $X^2(1)=0.199$; p=0.655	
	Pos v neg discharge	LDA $X^2(1)=0.000$; p=0.998	
	Drug screen done	LDA $X^2(1)=0.114$; p=0.736	
	Methadone dose	LRA t(1)=-1.927; p=0.055	
	Diazepam dose	LRA t(1)=-1.106; p=0.269	
	Dependent (outcome) variable		
	Employment status	LDA $X^2(1)=1.002$; p=0.317	
	Family stability	LDA $X^2(1)=1.788$; p=0.181	
	Any illicit drug use reported	LDA $X^2(1)=0.490$; p=0.484	
	Heroin use reported; days; route	LDA $X^2(1)=1.396$; p=0.237	
	Heroin days	LDA $X^2(5)=1.606$; p=0.901	
	Heroin route	LDA $X^2(1)=1.667$; p=0.197	
	Illicit Diazepam use	LDA $X^2(1)=2.013$; p=0.156	
	Illicit diazepam days	LDA $X^2(5)=2.279$; p=0.809	
	Illicit methadone use	**LDA $X^2(1)=4.848$; p=0.028**	
	Illicit methadone days	**LDA $X^2(1)=12.002$; p=0.007**	Partial η^2 = .118 *Medium effect*
	Illicit painkillers *use	LDA $X^2(1)=1.111$; p=0.292	
	Illicit painkiller days	LDA $X^2(1)=1.153$; p=0.215	
	+ve opiates	LDA $X^2(1)=1.555$; p=0.212	
	+ve benzos	LDA $X^2(1)=1.170$; p=0.279	
	Acute admissions reported	LRA t(1)=-0.428; p=0.669	
	Psych admissions reported	LRA t(1)=-0.403; p=0.687	
	Prison reported	LRA t(1)=-0.441; p=0.660	

Illicit drug use at baseline

Heroin use reported at baseline was strongly associated with a number of outcomes – predicting any drug use in 2009 (Table 39). Route of use was also relevant with baseline injecting predicting more heroin use and more injecting in 2009 (Table 40).

Table 39. Associations: baseline heroin use/ process and 4 year outcomes

Independent Variable	Dependent (Process) variable	Statistics	Effect size
Heroin use (baseline test) **Significant impact set at the p<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention**	Chi square $X^2(2)=5.507$; p=0.064	
	Pos/neg discharge	Chi square $X^2(2)=0.877$; p=0.645	
	Drug screen done	Chi square $X^2(4)=6.389$; p=0.172	
	Methadone dose	**ANOVA F(2,8)=3.618; p=0.028 +ve predicts higher dose**	
	Diazepam dose	**ANOVA F(2,8)=3.490; p=0.031 +ve predicts higher dose**	
	Dependent (outcome) variable		
	Employment status	Chi square $X^2(12)=14.637$; p=0.262	
	Family stability	Chi square $X^2(4)=7.849$; p=0.097	
	Baselin heroin use predicts any illicit drug use reported in 2009	**Chi square $X^2(6)=20.892$ p=0.002**	Cramer's V=.154 p=0.002 *Relevant effect*
	Heroin use reported; +ve predicts use	**Chi square $X^2(6)=13.867$p=0.031**	
	Heroin days used	KWH $X^2(1)=0.140$; p=0.904	
	Heroin route	Chi square $X^2(8)=8.736$; p=0.365	
	Ill Diazepam use +ve predicts use	**Chi square $X^2(6)=13.789$p=0.032**	
	Illicit diazepam days	Chi square $X^2(16)=21.456$; p=0.162	
	Illicit methadone use	Chi square $X^2(6)=5.450$; p=0.488	
	Illicit methadone days	Chi square $X^2(12)=12.143$; p=0.434	
	Illicit painkillers use	Chi square $X^2(8)=8.559$; p=0.200	
	Illicit painkillers days	Chi square $X^2(8)=11.554$; p=0.172	
	+ve opiates	Chi square $X^2(8)=11.926$; p=0.155	
	+ve benzos	Chi square $X^2(8)=11.043$; p=0.087	
	Acute admissions reported	ANOVA F(2,8)=2.421; p=0.090	
	Psych admissions reported	ANOVA F(2,8)=2.336; p=0.098	
	Prison reported	ANOVA F(2,8)=2.126; p=0.121	

Table 40. Associations: baseline heroin route / process and 4 year outcomes

Independent Variable	Dependent (Process) variable	Statistics	Effect size
Heroin use - route **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention**	Chi square $X^2(4)=1.782$; p=0.776	
	Pos neg discharge	Chi square $X^2(2)=2.707$; p=0.258	
	Drug screen done	Chi square $X^2(8)=3.107$; p=0.927	
	Methadone dose	ANOVA F(2,6)=0.415; p=0.798	
	Diazepam dose	ANOVA F(4,6)=1.235; p=0.295	
	Dependent (outcome) variables		
	Employment status	Chi square $X^2(24)=17.751$; p=0.815	
	Family stability	Chi square $X^2(8)=5.462$; p=0.707	
	Any illicit drug use reported	**Chi square $X^2(6)=14.207$; p=0.027** **Injecting predicts less use**	
	Heroin use reported **Injecting 05 = use 09**	**Chi square $X^2(6)=30.699$; p<0.001**	Cramer's V=.158 p=0.001 *Relevant effect*
	Heroin days	**KWH $X^2(4)=1.240$; p=0.872**	
	Heroin route **Injecting 05 = injecting 09**	**Chi square $X^2(8)=49.851$; p<0.001**	Cramer's v =.173 p<0.001 *Relevant effect*
	Illicit Diazepam use	Chi square $X^2(12)=10.626$; p=0.561	
	Illicit Diazepam days	Chi square $X^2(32)=20.972$; p=0.932	
	Illicit methadone use	Chi square $X^2(12)=7.546$; p=0.820	
	Illicit methadone days	Chi square $X^2(24)=13.679$; p=0.954	
	Illicit painkillers use	Chi square $X^2(12)=3.608$; p=0.990	
	Illicit painkillers days	Chi square $X^2(16)=5.876$; p=0.989	
	+ve opiates	Chi square $X^2(16)=22.582$; p=0.125	
	+ve benzos	Chi square $X^2(12)=7.287$; p=0.838	
	Acute admissions reported	ANOVA F(4,6)=0.339; p=0.851	
	Psych admissions reported	ANOVA F(4,6)=0.344; p=0.848	
	Prison reported	ANOVA F(4,6)=0.372; p=0.829	

Comorbidity screening at baseline

Few associations were found between comorbidity findings and 4 year recorded outcomes. GHQ28 total score was associated with more illicit diazepam use and more illicit methadone

days used (Table 41). PTSD "caseness" was associated with methadone dose and family stability while severity of PTSD symptoms was associated with methadone dose (Table 42).

Table 41. Associations: GHQ28 scores and caseness / process and 4 year outcomes

Independent (Predictor) Variable	Dependent variable	Statistics	Effect size
1. GHQ caseness 2. GHQ total score **Significant impact set at the p<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention** **Higher score=lower retention**	1.Chi square $X^2(1)=0.711$; p=0.399 **2.LDA $X^2(1)=4.683$; p=0.030**	
	Pos/neg discharge	1.Chi square $X^2(1)=2.077$; p=0.150 2.LDA $X^2(1)=0.042$; p=0.837	
	Drug screen done **Higher score=less likely screened**	1.Chi square $X^2(2)=1.652$; p=0.438 **2.LDA $X^2(1)=5.218$; p=0.022**	
	Methadone dose	1.KWH $X^2(1)=0.466$; p=0.495 2.QLR t(1)=1.871; p=0.062	
	Diazepam dose	1.KWH $X^2(1)=0.007$; p=0.931 2.QLR t(1)=-0.090; p=0.928	
	Employment status	1.Chi square $X^2(6)=7.890$; p=0.246 2.LDA $X^2(1)=2.965$; p=0.085	
	Family stability	1.Chi square $X^2(2)=1.478$; p=0.478 2. LDA $X^2(1)=1.562$; p=0.211	
	Any illicit drug use reported	1.Chi square $X^2(2)=1.296$; p=0.523 2.LDA $X^2(1)=1.009$; p=0.315	
	Heroin use reported	1.Chi square $X^2(3)=2.115$; p=0.549 2.LDA $X^2(1)=0.096$; p=0.756	
	Heroin days	1.Chi square $X^2(7)=8.756$; p=0.195 2.LDA $X^2(4)=3.973$; p=0.410	
	Heroin route	1.Chi square $X^2(4)=1.710$; p=0.789 2.LDA $X^2(1)=0.062$; p=0.804	
	Illicit Diazepam use **Higher score=more diazepam use**	1.Chi square $X^2(3)=4.789$; p=0.188 **2. LDA $X^2(1)=6.686$; p=0.010**	Cohen's d = 0.367 R=0.180 *Small effect size*
	Illicit diazepam days	1.Chi square $X^2(8)=9.140$; p=0.331 2.LDA $X^2(5)=4.119$; p=0.532	
	Ill meth use	1.Chi square $X^2(3)=4.508$; p=0.212 2.LDA $X^2(1)=1.643$; p=0.200	
	Illicit methadone days **Higher score=more mm days**	1.Chi square $X^2(6)=7.756$; p=0.256 **2.LRA $X^2(3)=13.755$; p=0.003**	Partial η^2 = .118 *Medium effect*
	Illicit painkillers	1.Chi square $X^2(3)=2.331$; p=0.507 2.LDA $X^2(1)=1.720$; p=0.190	
	Illicit painkiller days	1.Chi square $X^2(4)=2.338$; p=0.674 2.LDA $X^2(1)=0.083$; p=0.773	
	+ve opiates	1.Chi square $X^2(4)=3.869$; p=0.424 2.LDA $X^2(1)=0.538$; p=0.463	
	+ve benzos	1.Chi square $X^2(3)=2.380$; p=0.497 2.LDA $X^2(1)=1.734$; p=0.188	
	Acute admissions reported **Higher score=more admissions**	1.KWH $X^2(1)=1.74$ 3; p=0.187 **2. LRA t(1)=2.159; p=0.032**	
	Psych admissions reported **Higher score=more admissions**	1.KWH $X^2(1)=1.726$; p=0.189 **2.LRA t(1)=2.123; p=0.034**	
	Prison reported **Higher score=more admissions**	1.KWH $X^2(1)=2.669$; p=0.102 **2.LRA t(1)=2.216; p=0.027**	

Table 42. Associations: PTSD (Impact of Events scale) / process and 4 year outcomes

623 screened. 601 total scores of whom 271 scored zero. 280 show PTSD "caseness" based on cut off of 26 on scale. 321 no PTSD. Severity scale shows 175 "severe" and 105 "moderate"

Independent (Predictor) Variable	Dependent (Process) variable	Statistics	Effect size
PTSD (IES) 1. **Caseness (>26)** 2. **Severity** **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention : PTSD = better** **Severity of PTSD=better retention**	**1.Chi square $X^2(1)=6.862$; p=0.009** **2.LDA $X^2(1)=5.112$; p=0.024**	
	Pos/neg discharge	1.Chi square $X^2(1)=0.218$; p=0.641 2. LDA $X^2(1)=0.311$; p=0.577	
	Drug screen done	1.Chi square $X^2(2)=3.657$; p=0.161 2.LDA $X^2(1)=2.322$; p=0.128	
	Methadone dose **Caseness and score = higher dose**	**1.KWH $X^2(1)=5.009$; p=0.025**	Partial η^2 = .001 *Small effect*
		2.QRA t(1)=-2.674; p=0.008	Partial η^2 = .003 *Small effect*
	Diazepam dose	1.KWH $X^2(1)=2.395$; p=0.122 2.QRA t(1)=-1.673; p=0.095	
	Dependent (outcome) variable		
	Employment status	1.Chi square $X^2(6)=11.589$; p=0.072 2.LDA $X^2(1)=0.315$; p=0.575	
	Family stability **PTSD caseness = less family stability**	**1.Chi square $X^2(2)=6.648$; p=0.036**	Cramer's V=.122 p=0.036 *Relevant effect*
		2.LDA $X^2(1)=1.357$; p=0.244	
	Any illicit drug use reported	1.Chi square $X^2(3)=3.153$; p=0.369 2. LDA $X^2(1)=0.869$; p=0.351	
	Heroin use reported; days; route	1.Chi square $X^2(3)=5.781$; p=0.123 2.LDA $X^2(1)=0.129$; p=0.720	
	Heroin days	1.Chi square $X^2(8)=12.703$; p=0.122 2.LDA $X^2(5)=7.302$; p=0.199	
	Heroin route	1.Chi square $X^2(4)=5.397$; p=0.249 2.LDA $X^2(1)=0.109$; p=0.741	
	Illicit Diazepam use	Chi square $X^2(3)=6.407$; p=0.093 LDA $X^2(1)=0.269$; p=0.604	
	Illicit diazepam days	Chi square $X^2(8)=13.398$; p=0.099 LDA $X^2(5)=8.039$; p=0.154	
	Illicit methadone use **PTSD=illicit use**	**1.Chi square $X^2(3)=8.429$; p=0.038** **2.LDA $X^2(1)=4.248$; p=0.039**	
	Illicit methadone days	1.Chi square $X^2(6)=9.911$; p=0.128 2.LDA $X^2(3)=1.713$; p=0.634	
	Illicit painkillers use **PTSD=illicit painkiller use**	**1.Chi square $X^2(3)=8.750$; p=0.033** **2.LDA $X^2(1)=1.966$; p=0.161**	
	+ve opiates	1.Chi square $X^2(4)=3.162$; p=0.531 2.LDA $X^2(1)=0.009$; p=0.925	
	+ve benzos	1.Chi square $X^2(3)=3.020$; p=0.389 2.LDA $X^2(1)=0.004$; p=0.950	
	Acute admissions reported	**1.KWH $X^2(1)=3.498$; p=0.061** **2.LRA t(1)=-2.312; p=0.021**	
	Psych admissions reported	**1.KWH $X^2(1)=5.167$; p=0.023** **2.LRA t(1)=-2.328; p=0.020**	
	Prison reported	**1.KWH $X^2(1)=3.890$; p=0.049** **2.LRA t(1)=-2.364; p=0.019**	

Other analyses

Following application of the Bonferroni Correction, no statistically significant associations were demonstrated between a number of the selected independent baseline variables and dependent variables at 4 year follow up.

Factors showing no associations included: Gender; SIMD-local quintile (deprivation score); time at current address; lives alone/not; lives with children/not; days in paid work in last 30 days; MAP Physical Health Score; MAP Psychological Health Score; Heroin days used; Positive benzodiazepine tests; Injection risk taking (IRQ); comorbidities – pain, social phobia and ADHD.

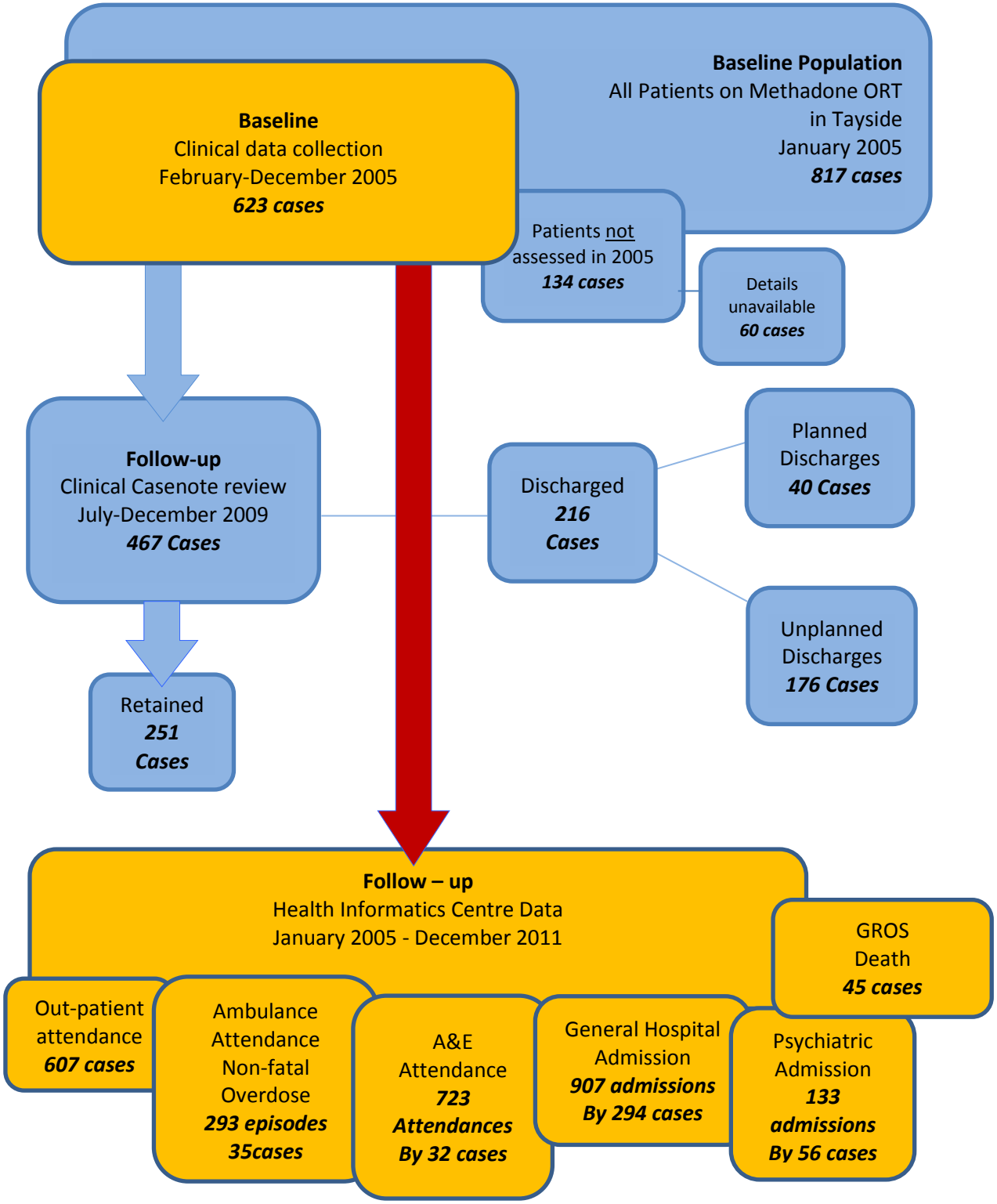
Full results tables for these negative results are shown in Appendix 5.

Chapter 7

Results: Follow up 2.

HIC Linked datasets 2005-2011

Figure 9. Follow up – HIC Linked datasets 2005-2011



Results - Follow up analyses 2. HIC Linked datasets – 2005-11

This section describes the findings of the follow up review utilizing the linked datasets available through HIC. The data used in the analysis were:

- Data collected at the baseline assessment interview in 2005
- HIC linked datasets

The literature review informed the development of a model, using data available in the linked dataset, to assess the associations a range of independent variables had with a range of process measures or outcomes (dependent variables). The variables chosen are shown in Table 43.

Table 43. Additional dependent variables

Dependent Variables (HIC linked datasets)
SMR00 (out-patient) sessions (number)
SAS (Ambulance) attendances
Naloxone administrations
A&E attendances
SMR01 admissions (acute) - All
SMR01 duration (acute nights) - All
SMR04 admissions (psychiatric)
SMR04 (psych) emergency/routine
SMR04 admissions - total days
SMR04 admissions - longest stay
GROS dead/alive

Statistics

As before, for analyses when both independent and dependent variables were categorical - Chi-squared tests were undertaken. For categorical independent and continuous dependent variables, an ANOVA was used (if data were parametric). If not, the Kruskall-Wallis H-test or Mann-Whitney U-test (for binary data) were used. For continuous independent variables with categorical dependent variables, discriminant analyses were used. If the DV/IV relationship was linear, linear discriminant analyses were used. If not, quadratic discriminant analyses were used. When both independent and dependent variables were continuous – linear regression analyses were undertaken.

Multiple testing and the Bonferroni Correction

This process did not involve significant multiple testing - making it unlikely that there will be false positives as a result. No Bonferroni Correction was applied.

Results – Clinical HIC Linked datasets 2005-12

This section describes the results of the analyses undertaken using data collected from the HIC datasets from 2005-12. Positive results are shown in a series of tables – Tables 44-59 below. Tables of negative results (where no associations were demonstrated in the univariate analyses) are contained in Appendix 5.

Demographic factors

Younger age was associated with having more out-patient appointments with the drug treatment services and younger subjects were less likely to have died in the 7 year follow up period (Table 44).

Table 44. Associations: Age / HIC outcomes (7 year follow up)

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics	Effect size
Age **Significant impact at the p<0.05 level**	***Out-patient appointments*** SMR00 sessions (number) **Younger= more appointments**	**LRA t(1)=-4.096; p<0.001**	Partial η^2 = .657 Large effect size
	Acute services contacts		
	Ambulance Service call-outs SAS attendances	LRA t(1)=-0.008; p=0.994	
	Naloxone administrations	LRA t(1)=-0.201; p=0.843	
	A&E attendances	LRA t(1)=1.647; p=0.112	
	General Hospital Admissions		
	SMR01 admissions (acute) - All	LRA t(1)=1.753; p=0.081	
	SMR01 duration (nights) -All	LRA t(1)-0.966; p=0.335	
	Psychiatric Admisisons		
	SMR04 admissions (psych)	LRA t(1)=-0.924; p=0.363	
	SMR04 total days	LRA t(1)=-1.059; p=0.298	
	Registrar General Death data GROS dead/alive **Younger = less likely dead**	**LDA $X^2(1)=19.567$; p<0.001**	Cohen's d =.585 R=0.281 *Medium effect*

Gender was associated with a number of 7 year process measures and outcomes (Table 45). Females attended significantly more appointments than males. Males were more likely to be admitted to a psychiatric unit and if admitted, spent more time as an in-patient than females. Males were also more likely to have died in the 7 year follow up period.

Table 45. Associations: Gender / HIC outcomes

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics	Effect size
Gender **Significant impact at the p<0.05 level**	***Out-patient appointments*** SMR00 sessions 2005/10 **Females more attendances**	**KWH $X^2(1)=11.225$; p=0.001**	Monte Carlo sig test=.002 99% CI .001-003 *Likely effect*
	Acute services contacts		
	Ambulance service call-outs SAS attendances 2008/11	KWH $X^2(1)=0.010$; p=0.921	
	Naloxone administrations 2008/11	KWH $X^2(1)=1.721$; p=0.190	
	A&E attendances <2008	KWH $X^2(1)=0.254$; p=0.614	
	General Hospital Admissions		
	SMR01 admissions (acute) - ALL	KWH $X^2(1)=0.614$; p=0.433	
	SMR01 duration(nights) - ALL	KWH $X^2(1)=0.126$; p=0.723	
	Psychiatric Admissions		
	SMR04 admissions(psych) 2005/11 **Males more admissions**	**KWH $X^2(1)=5.046$; p=0.025**	Monte Carlo sig test =.038 99% CI .033-042 *Likely effect*
	SMR04 total days **Males = more time as IP**	**KWH $X^2(1)=5.499$; p=0.019**	Monte Carlo sig test =0.017 99%CI=.013-020 *Likely effect*
	Registrar general Death Data GROS dead/alive **M>F**	**Chi square $X^2(2)=17.287$; p<0.001**	Cramer's v=.184 p<0.001 *Relevant effect*

Markers of social stability

A number of factors, reflecting a degree of social stability, were assessed.

MAP conflict scores were assessed. The score recording conflict with friends at baseline was associated with death – higher conflict score predicting an increased likelihood of dying in the 7 year follow up period (Table 46).

Table 46. Associations: MAP conflict scores / HIC outcomes

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics	Effect size
MAP conflict scores: **1. Partner** **2. Relative** **3. Friends** **Significant impact at the p<0.05 level**	***Out-patient Attendances*** SMR00 sessions 2005/10	1.LRA t(1)=-0.213; p=0.832 2.LRA t(1)=1.196; p=0.232 3.LRA t(1)=-0.554; p=0.580	
	Acute Services Contacts		
	Ambulance Service Call-outs SAS call outs	1.LRA t(1)=-1.181; p=0.242 2.LRA t(1)=0.398; p=0.692 3.LRA t(1)=-0.404; p=0.688	
	Naloxone administrations 2008-11	1.LRA t(1)=-0.831; p=0.413 2.LRA t(1)=0.227; p=0.822 3.LRA t(1)=0.548; p=0.589	
	A&E attendances <2008	1.LRA t(1)=0.016; p=0.987 2.LRA t(1)=1.287; p=0.208 3.LRA t(1)=-0.142; p=0.888	
	Acute Hospital Admissions		
	SMR01 admissions (acute) - ALL	1.LRA t(1)=0.876; p=0.382 2.LRA t(1)=-0.953; p=0.342 3.LRA t(1)=-0.917; p=0.360	
	SMR01 duration(nights) - ALL	1.LRA t(1)=0.517; p=0.606 2.LRA t(1)=-0.656; p=0.513 3.LRA t(1)=-0.562; p=0.575	
	Psychiatric Admissions		
	SMR04 admissions(psych) 2005/11	1.LRA t(1)=-0.791; p=0.434 2.LRA t(1)=0.580; p=0.566 3.LRA t(1)=0.184; p=0.855	
	SMR04 total days	1.LRA t(1)=-0.456; p=0.651 2.LRA t(1)=0.294; p=0.770 3.LRA t(1)=-0.291; p=0.773	
	Registrar General Death Data GROS death	1.LDA $X^2(1)=0.566$; p=0.452 2. LDA $X^2(1)=2.590$; p=0.108 **3. LDA $X^2(1)=4.007$; p=0.045**	Cohen's d=0.164 R=0.082 *Small effect size*

Days in paid work were found to be associated with psychiatric admission – with more days associated with more and longer admissions (Table 47).

Table 47. Associations: days in work at baseline assessment / HIC outcomes

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics	Effect size
Days in paid work **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10	LRA t(1)=-1.339; p=0.181	
	Acute Services Contacts		
	Ambulance Service Call-outs SAS attendances 2008/11	LRA t(1)=-0.502; p=0.617	
	Naloxone administrations 2008-11	LRA t(1)=-0.514; p=0.611	
	A&E attendances <2008	LRA t(1)=0.195; p=0.847	
	Acute Hospital Admissions		
	SMR01 admissions (acute) -	LRA t(1)=-1.490; p=0.137	
	SMR01 duration(nights) -	LRA t(1)=-1.449; p=0.149	
	Psychiatric Admissions		
	SMR04 admissions(psych) 2005/11 **More predicts > admissions**	**LRA t(1)=2.730; p=0.009**	Partial η^2 = .024 *Small effect size*
	SMR04 total days **More work predicts >days IP**	**LRA t(1)=5.984; p<0.001**	Partial η^2 = .001 *Small effect size*
	Registrar General death Data GROS death	LDA $X^2(1)=1.007$; p=0.316	

Treatment status

A number of factors relating to the delivery of treatment and care were considered.

The treatment setting (NHS specialist, Criminal Justice or GP) was found to be relevant with specialist NHS services seeing patients more frequently in the 7 year follow up period. Criminal Justice Services saw patients more often than GP shared-care services (Table 48). Registration with a GP (not drug treatment delivery by a GP) was associated with increased acute hospital admissions (Table 49).

Table 48. Associations: treatment setting / HIC outcome

Independent Variable	Dependent Variable	Statistics	Effect size
Treatment setting **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10 **TDPS>CJS>GP**	**ANOVA F(2,8)=5.305; p=0.005**	Partial η^2 = .021 *Small effect size*
	Emergency Services Contacts		
	Ambulance Service Call-outs SAS attendances 2008/11	ANOVA F(2,8)=0.608; p=0.548	
	Naloxone administrations 2008/11	ANOVA F(2,8)=0.951; p=0.400	
	A&E attendances <2008	ANOVA F(2,8)=0.181; p=0.835	
	Acute Hospital Admissions		
	SMR01 admissions (acute)	ANOVA F(2,8)=1.404; p=0.247	
	SMR01 duration(nights)	ANOVA F(2,8)=1.563; p=0.212	
	Psychiatric Admissions		
	SMR04 admissions(psych) 2005/11	ANOVA F(2,8)=0.117; p=0.890	
	SMR04 total days	ANOVA F(2,8)=0.335; p=0.717	
	Registrar General Death Data GROS death	Chi square $X^2(2)$=1.753; p=0.416	

Table 49. Associations: registration with a GP at baseline / HIC outcomes

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics	Effect size
Registered with GP **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10	MWU=16739.0; p=0.069	
	Acute Services Contacts		
	Ambulance service Call-outs SAS attendances 2008/11	MWU=100.0; p=0.488	
	Naloxone administrations 2008-11	MWU=33.0; p=0.449	
	A&E attendances <2008	MWU=45.0; p=0.672	
	Acute Hospital Admission		
	SMR01 admissions (acute) - ALL **GP predicts more**	**MWU=4096.5; p=0.024**	Partial η^2 = .017 *Small effect size*
	SMR01 duration(nights)	MWU=4490.0; p=0.175	
	Psychiatric admission		
	SMR04 admissions(psych) 2005/11	MWU=232.5; p=0.325	
	SMR04 total days	MWU=246.0; p=0.515	
	Registrar General Death Data	Chi square $X^2(1)$=0.236; p=0.627	

Support services delivered by another (non-NHS) agency increased the likelihood of attendance at substance misuse out-patient clinic appointments (Table 50). Satisfaction

with treatment – shown by higher Treatment Perception Questionnaire scores at baseline - was associated with a reduced likelihood of acute hospital admission during the follow up period (Table 51).

Table 50. Associations: support from other (non-NHS) agencies / HIC outcome

Independent Variable	Dependent Variable	Statistics	Effect size
Support from other agencies **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10 **Support predicts attendance**	**MWU=16441.5; p=0.021**	Cohen's d= -0.307 R=-0.152 *Small effect size*
	Emergency Service Contacts		
	Ambulance Service Call-outs SAS attendances 2008/11	MWU=249.0; p=0.127	
	Naloxone administrations 2008-11	MWU=70.5; p=0.746	
	A&E attendances <2008	MWU=93.0; p=0.090	
	Acute Hospital Admissions		
	SMR01 admissions (acute)	MWU=4680.0; p=0.911	
	SMR01 duration(nights)	MWU=4452.0; p=0.503	
	Psychiatric Admissions		
	SMR04 admissions(psych) 2005/11	MWU=200.0; p=0.844	
	SMR04 total days	MWU=177.5; p=0.437	
	Registrar General Death Data GROS death	Chi square $X^2(1)=0.233$; p=0.630	

Table 51. Associations: baseline TPQ total score / HIC outcome

Independent Variable	Dependent Variable	Statistics	Effect size
TPQ total score **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10	LRA t(1)=-0.916; p=0.360	
	Emergency Service Contacts		
	Ambulance service Call-outs SAS attendances 2008/11	LRA t(1)=-0.642; p=0.523	
	Naloxone administrations 2008-11	LRA t(1)=-0753; p=0.457	
	A&E attendances <2008	LRA t(1)=-0.784; p=0.438	
	Acute Hospital Admissions		
	SMR01 admissions (acute) **Higher score =less admission**	**LRA t(1)=-2.247; p=0.025**	Partial η^2 = .069 *Medium effect*
	SMR01 duration(nights)	LRA t(1)=-1.394; p=0.164	
	Psychiatric Admissions		
	SMR04 admissions 2005/11	LRA t(1)=-1.107; p=0.273	
	SMR04 total days	LRA t(1)=-1.563; p=0.124	
	Registrar General Deaths	LDA $X^2(1)=0.130$; p=0.719	

A higher MAP Physical Health Score was associated with acute admissions and increased deaths (Table 52). A higher prescribed methadone dose was associated with an increased likelihood of acute hospital admission and longer admissions (Table 53). Though higher methadone dosage was not associated with increased psychiatric admissions, those who were admitted had longer in-patient stays.

Table 52. Associations: baseline MAP Physical Health Score / HIC outcomes

Independent Variable	Dependent Variable	Statistics	Effect size
Map Physical Health Score **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10	LRA t(1)=0.734; p=0.463	
	Acute Services Contacts		
	Ambulance Service Call-outs	LRA t(1)=0.996; p=0.323	
	Naloxone administrations	LRA t(1)=0.477; p=0.637	
	A&E attendances <2008	LRA t(1)=-0.976; p=0.335	
	Acute Hospital Admissions		
	SMR01 admissions (acute)	**LRA t(1)=2.291; p=0.023**	Partial η^2 = .145 *Large effect size*
	SMR01 duration(nights)	LRA t(1)=1.434; p=0.153	
	Psychiatric Admissions		
	SMR04 admissions(psych) 2005/11	LRA t(1)=0.633; p=0.529	
	SMR04 total days	LRA t(1)=1.349; p=0.183	
	GROS death	**LDA X^2(1)=4.226; p=0.040**	Cohen's d=.248 R=0.123 *Small effect size*

Table 53. Associations: baseline methadone dosage / HIC outcomes

Independent Variable	Dependent Variable	Statistics	Effect size
Methadone dose **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10	LRA t(1)=1.796; p=0.073	
	Emergency service Contacts		
	Ambulance Service Call-outs SAS attendances 2008/11	LRA t(1)=-0.267; p=0.790	
	Naloxone administrations 2008-11	LRA t(1)=-1.246; p=0.223	
	A&E attendances <2008	LRA t(1)=0.084; p=0.934	
	Acute Hospital Admissions		
	SMR01 admissions (acute)	**LRA t(1)=2.125; p=0.035**	Partial η^2 = .951 *Large effect size*
	SMR01 duration(nights)	**LRA t(1)=2.187; p=0.030**	Partial η^2 = .997 *Large effect size*
	Psychiatric Admissions		
	SMR04 admissions(psych) 2005/11	LRA t(1)=-1.614; p=0.112	
	SMR04 total days	**LRA t(1)=-2.125; p=0.038**	Partial η^2 = .122 *Medium effect*
	GROS death	LDA X^2(1)=0.172; p=0.679	

Illicit drug use

Illicit drug use was associated with a number of outcomes. Those using more heroin at baseline were seen less frequently over the follow up period (Table 54). Those using more frequently at baseline experienced longer periods of in-patient psychiatric care (Table 55).

Table 54. Associations: heroin use at baseline / HIC outcomes

Independent Variable	Dependent Variable	Statistics	Effect size
Heroin use **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10 **More use predicts less**	**ANOVA F(2,8)=4.050; p=0.018**	Partial η^2 = .171 *Large effect size*
	Emergency Services Contacts		
	Ambulance Service Call-outs	ANOVA F(2,8)=2.762; p=0.071	
	Naloxone 2008-11	ANOVA F(2,8)=1.121; p=0.339	
	A&E attendances <2008	ANOVA F(2,8)=0.035; p=0.966	
	Acute Hospital Admissions		
	SMR01 admissions (acute)	ANOVA F(2,8)=1.993; p=0.138	
	SMR01 duration(nights)	ANOVA F(2,8)=0.754; p=0.471	
	Psychiatric Admissions		
	SMR04 admissions(psych) 2005/11	ANOVA F(2,8)=1.311; p=0.279	
	SMR04 total days	ANOVA F(2,8)=0.551; p=0.580	
	GROS death	Chi square $X^2(2)$=2.707; p=0.258	

Table 55. Associations: extent of baseline heroin use (heroin days) / HIC outcomes

Independent Variable	Dependent Variable	Statistics	Effect size
Heroin days used **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10	LRA t(1)=-0.477; p=0.655	
	Emergency service Contacts		
	Ambulance service call-outs SAS attendances 2008/11	LRA t(1)=-0.193; p=0.847	
	Naloxone administrations 2008-11	LRA t(1)=1.152; p=0.258	
	A&E attendances <2008	LRA t(1)=-0.102; p=0.919	
	Acute Hospital Admissions		
	SMR01 admissions (acute) - ALL	LRA t(1)=1.700; p=0.090	
	SMR01 duration(nights) - ALL	LRA t(1)=1.630; p=0.104	
	Psychiatric Admissions		
	SMR04 admissions(psych) 2005/11	LRA t(1)=-1.897; p=0.063	
	SMR04 total days **More days= longer stays**	**LRA t(1)=2.940; p=0.005**	Partial η^2 = .018 *Small effect size*
	GROS death	LDA $X^2(1)$=0.160; p=0.689	

Comorbidities

A number of common comorbidities were assessed at baseline and positive associations were found with 7 year HIC outcomes.

Comorbid Pain – the presence of any pain was associated with increased stays in acute hospital admissions. Increased intensity of pain was associated with an increased likelihood of death in the 7 year follow up period (Table 56). ***Psychiatric caseness (GHQ28) –*** Caseness had no associations. However, a higher total GHQ28 score was associated with longer psychiatric admissions (Table 57).

Table 56. Associations: pain and its characteristics at baseline / HIC outcomes

Independent Variable	Dependent Variable	Statistics	Effect size
Pain **1. Pain present** **2. Duration** **3. Chronic (12/12)** **4. Severity score** **5. Severity quintiles** **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10	1.MWU=28032.0; p=0.567 2.LRA t(1)=-0.603; p=0.547 3. MWU=5243.000; p=0.251 4. LRA t(1)=-1.839; p=0.066 5.KWH(4)=8.012; p=0.091	
	Emergency Service Contacts		
	Ambulance Service Call-outs SAS attendances 2008/11	1.MWU=416.500; p=0.784 2.LRA t(1)=-0.307; p=0.761 3.MWU=82.000; p=0.945 4.LRA t(1)=1.607; p=0.113 5. KWH(3)=1.468; p=0.690	
	Naloxone administrations 2008-11	1.MWU=97.500; p=0.379 2.LRA t(1)=0.181; p=0.859 3.MWU=19.000; p=0.599 4.LRA t(1)=1.274; p=0.212 5.KWH(2)=0.638; p=0.727	
	A&E attendances <2008	1.MWU=95.500; p=0.307 2.LRA t(1)=1.238; p=0.232 3. MWU=6.500; p=0.700 4.LRA t(1)=0.961; p=0.343 5. KWH(4)=6.736; p=0.150	
	Acute Hospital Admissions		
	SMR01 admissions (acute) - ALL	1.MWU=6068.500; p=0.414 2.LRA t(1)=-0.957; p=0.340 3.MWU=1530.500; p=0.299 4.LRA t(1)=0.155; p=0.877 5. KWH(4)=4.125; p=0.389	
	SMR01 duration(nights) - ALL **Pain predicts longer stays**	**1.MWU=5349.000; p=0.035**	Partial η^2 = .032 *Small effect size*
		2.LRA t(1)=-1.667; p=0.098 3.MWU=1347.500; p=0.054 4.LRA t(1)=-0.611; p=0.541 5. KWH(4)=2.448; p=0.654	
	Psychiatric Admissions		
	SMR04 admissions(psych) 2005/11	1.MWU=235.000; p=0.712 2.LRA t(1)=-1.452; p=0.160 3.MWU=23.500; p=0.071 4.LRA t(1)=0.499; p=0.620 5. KWH(3)=0.879; p=0.831	
	SMR04 total days	1.MWU=214.500; p=0.416 2.LRA t(1)=-1.462; p=0.157 3. MWU=22.000; p=0.060 4.LRA t(1)=0.284; p=0.777 5. KWH(3)=0.539; p=0.910	
	Registrar general Death Data GROS death **Pain severity predicts death**	1.Chi square $X^2(1)=1.160$; p=0.281 2.LDA $X^2(1)=0.000$; p=0.988 3.Chi square $X^2(1)=2.330$; p=0.127 4. LDA $X^2(1)=1.495$; p=0.221	
		5. Chi square $X^2(4)=12.815$; p=0.012	Cramer's V=.208 *Relevant effect*

Table 57. Associations: baseline GHQ28 scores and caseness / HIC outcomes

IndependentVariable	Dependent Variable	Statistics	Effect size
1. GHQ caseness **2. GHQ total score** **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10	MWU=25312.5; p=0.160 LRA t(1)=1.705; p=0.089	
	Acute Services Contacts		
	Ambulance Service Call-outs SAS attendances 2008/11	MWU=350.0; p=0.422 LRA t(1)=0.759; p=0.451	
	Naloxone administrations 2008-11	MWU=63.5; p=0.077 LRA t(1)=1.563; p=0.129	
	A&E attendances <2008	MWU=97.5; p=0.662 LRA t(1)=1.452; p=0.158	
	Acute Hospital Admissions		
	SMR01 admissions (acute) - ALL	MWU=6052.0; p=0.736 LRA t(1)=1.705; p=0.089	
	SMR01 duration(nights)	MWU=5689.0; p=0.325 LRA t(1)=1.705; p=0.089	
	Psychiatric Admissions		
	SMR04 admissions(psych) 2005/11	MWU=199.0; p=0.634 LRA t(1)=1.926; p=0.061	
	SMR04 total days **Higher score predicts >days**	MWU=210.0; p=0.863 **LRA t(1)=2.643; p=0.011**	Partial η^2 = .995 *Large effect size*
	Registrar general Death Data GROS death	1.Chi square $X^2(1)=0.181$; p=0.670 2.LDA $X^2(1)=1.566$; p=0.211	

Table 58. Associations: baseline PTSD (IES) / HIC outcomes

Independent Variable	Dependent Variable	Statistics	Effect size
PTSD (IES) **Caseness (>26)** **Severity score** **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10	1.MWU=36142.000; p=0.181 2. LRA t(1)=2.022; p=0.155	
	Emergency Service Contacts		
	Ambulance Service Call-outs SAS attendances 2008-11 **PTSD predicts more attendances**	**1.MWU=349.500; p=0.050** 2. LRA t(1)=1.069; p=0.289	Partial η^2 = .021 *Small effect size*
	Naloxone administrations 2008-11	1.MWU=124.500; p=0.683 2. LRA t(1)=-0.395; p=0.696	
	A&E attendances <2008	1.MWU=157.500; p=0.685 2. LRA t(1)=0.922; p=0.363	
	Acute Hospital Admissions		
	SMR01 admissions (acute)	1.MWU=8987.000; p=0.529 2. LRA t(1)=-1.511; p=0.132	
	SMR01 duration(nights)	1.MWU=9111.000; p=0.754 2. LRA t(1)=-0.926; p=0.355	
	Psychiatric Hospital Admissions		
	SMR04 admissions(psych)	1.MWU=362.500; p=0.791 2. LRA t(1)=-0.756; p=0.453	
	SMR04 total days	1.MWU=368.000; p=0.879 2. LRA t(1)=-1.054 p=0.297	
	Registrar General Death Data GROS death	1.Chi square $X^2(1)=0.253$; p=0.615 2. LDA $X^2(1)=0.575$; p=0.448	

Post Traumatic Stress Disorder (PTSD) – a score of greater than 26 on the Impact of Events Scale – indicating "caseness" was associated with an increased likelihood of emergency ambulance call outs (Table 58).

Attention Deficit Hyperactivity Disorder - ADHD – Presence of any type of ADHD (assessed using the current symptoms scale - CSS) is associated with administration of naloxone to treat overdose during an emergency ambulance call out. The *hyperactive* type is more likely to be offered more appointments (Table 59).

Table 59. Associations: ADHD symptoms, type and impairment (CSS) / HIC outcomes

Independent Variable	Dependent Variable	Statistics	Effect size
ADHD (CSS) **1.symptoms** **2.types** **3.impairment** **Significant impact at the p<0.05 level**	***Out-patient attendances*** SMR00 sessions 2005/10 **H>I>C type predicts appts**	1.MWU=7232.000; p=0.204	
		2.KWH(2)=7.009; p=0.030	Partial η^2 = .070 *Medium effect*
		3.MWU=3235.000; p=0.400	
	Emergency Service Contacts		
	Ambulance Service Call-outs SAS attendances 2008-11	1. MWU=127.500; p=0.114 2. KWH(2)=0.478; p=0.787 3.MWU=67.000; p=0.783	
	Naloxone administrations 2008-11	**1. MWU=20.500; p=0.031**	Partial η^2 = .235 *Large effect size*
		2.KWH(2)=1.900; p=0.387 3.MWU=20.500; p=0.877	
	A&E attendances <2008	1.MWU=28.000; p=0.538 2. KWH(2)=1.000; p=0.607 3.Not computed (numbers)	
	Acute Hospital Admissions		
	SMR01 admissions (acute) - ALL	1.MWU=1708.500; p=0.679 2.KWH(2)=0.323; p=0.851 3.MWU=8987.000; p=0.529	
	SMR01 duration(nights) - ALL	1.MWU=1538.500; p=0.374 2.KWH(2)=1.407; p=0.495 3.MWU=401.000; p=0.170	
	Psychiatric Admissions		
	SMR04 admissions(psych) 2005/11	1.MWU=118.000; p=0.850 2.KWH(2)=0.114; p=0.944 3.MWU=341.500; p=0.070	
	SMR04 total days	1.MWU=110.500; p=0.623 2.KWH(2)=1.311; p=0.519 3.MWU=23.000; p=0.253	
	GROS death	1.Chi square $X^2(2)=0.032$; p=0.858 2. Chi square $X^2(2)=4.922$; p=0.085 3. Chi square $X^2(1)=0.021$; p=0.884	

Other analyses

Following application of the Bonferroni Correction, no statistically significant associations were demonstrated between the selected independent baseline variables and dependent variables at 4 year follow up.

Factors showing no associations included: home district; SIMD-local quintile (deprivation score); time at current address; lives alone/not; has children; lives with children/not; educational level attained; MAP Psychological Health Score; Prescribed diazepam dose; Heroin route; Positive benzodiazepine tests; Injection risk taking (IRQ); comorbidities – social phobia.

Full results tables are shown in Appendix 5.

Chapter 8

Discussion: Univariate analyses

Introduction

This chapter summarises and discusses the positive findings from the univariate analyses described in Chapters 6 and 7. Once the Bonferroni corrections were applied, there remained a number of highly statistically significant associations over the 4-7 year follow up period. This chapter will collate these findings and discuss the implications.

Demographics (Table 60)

Basic demographics

Age had an impact on the *process* of care experienced over the follow up period – with younger subjects attending services more frequently and being tested more. The published evidence suggests these younger patients would be more likely to be showing clinical progress, but no significant differences in terms of specific clinical *outcomes* were observed in this cohort. It was observed that younger subjects were less likely to have died during the follow up period, however. Regarding family stability, records of younger patients suggested they were less stable. Gender also showed some associations. Females were better attenders at clinics but males were more likely to have been admitted to psychiatric hospital, had longer admissions when they were admitted and were more likely to have died during the follow up period.

Family and supportive relationships

Perhaps surprisingly, having childcare responsibilities was associated with negative clinical outcomes. Parents were found to be more likely to be discharged negatively from services [i.e. poorly retained] and also scored lower for measures indicating family stability. MAP conflict scores with friends were associated with a range of poorer outcomes including more illicit methadone and diazepam use as well as an increased likelihood of death during the follow up period.

Educational attainment and employment status

Higher educational attainment was associated with more hospital admissions – both acute and psychiatric. The small number of subjects who were in work were more likely to be admitted to psychiatric hospitals and remained in-patients for more days when they were

admitted to psychiatric hospitals. This finding raises questions beyond the scope of this study. Recent reports on stigma have highlighted the difficulty experienced by active substance misusers who try to access generic healthcare (UKDPC, 2010). Also, studies of comorbid substance misuse and mental illness have reported that this patient group are treated differently by mental health services, when compared to those without a substance use disorder (e.g. Scottish Executive 2003; Scottish Executive 2006). The findings of the current study could reflect a stigma effect and could illustrate the fact that subjects who are more able to demonstrate "normal" (or acceptable) behaviours were more likely to be admitted to hospital – i.e. not "excluded" when experiencing psychiatric distress. However, further research is required to explore the significance of these initial findings.

Home – residence and deprivation

Where people lived and who looked after them was of considerable relevance regarding clinical outcomes – though these univariate analyses seemed to reveal some inconsistencies.

Angus is a very rural and relatively prosperous district in the NHS Tayside area. Yet it showed a higher rate of diazepam prescribing to OST- M patients. Angus patients were also the poorest retained in treatment and were most likely to have an admission to hospital or incarceration recorded in their casenotes. Paradoxically, Dundee City – the most deprived area in Tayside - had the best retained subjects who were the least likely to be using any drugs at follow up. They were also prescribed diazepam less and were least likely to have admissions or incarcerations recorded in their casenotes. The district of Perth & Kinross was the area where subjects were most likely to use any illicit drugs at follow up. It is notable that deprivation scores (using national SIM-D data) were found to have associations with these outcomes – a surprising finding.

There may be an issue regarding clinical processes although all the services managing OST-M patients in Tayside are governed by a single set of clinical standards and guidelines which define clearly how OST-M patients should be assessed and treated. It must also be acknowledged that the observed differences could have been impacted on by variation in the quality of clinical casenotes across a large area service.

Table 60. Univariate analyses results: Demographics

Independent variable	Dependent variable	Statistics
Age	Family stability	(p=0.001) Younger less stable
	Death	(p<0.001) Older>Younger
	Drug tests done	(p=0.006) Young more
	OP attendances	(p<0.001) Young more
Gender	Psychiatric admissions	(p=0.025) Male>Female
	Psychiatric days admitted	(p=0.019) Male>Female
	death	(p<0.001) Male>Female
	Out-patient attendance	(p=0.001) Female> Male
District D=Dundee P=Perthshire A=Angus	Family stability	(p<0.001) D>P>A
	Any drug use	(p=0.004; P>A>D)
	Diazepam use	(p=0.001; D=A>P
	Illicit painkillers	(p=0.010; A>D>P)
	Morphine specific +ves	(p<0.001; A>P>D)
	Benzo +ves	(p<0.001; D>A>P)
	Acute admissions	(p=0.013; A>P>D)
	Psychiatric admissions	(p=0.006; A>P>D)
	Incarcerations	(p=0.003; A>P>D)
	Retention	(p=0.003; D>P>A)
	Diazepam dose Rx	(p=0.008; A>P>D)
Has children	Nature of discharge	(p=0.001) Children= -ve d/c
	Family stability	(p=0.025; Children=less stable
Conflict scores (Partner)	Methadone (days)	(p=0.011) High score=more
	Diazepam (days)	(p<0.001) High score=more
Conflict score (Family)	Methadone use	(p=0.001) High score=use
	Death	(p=0.045) Higher score=death
Educational level	Acute admissions	(p=0.004)↑qualifications= more
	Psychiatric admissions	(p=0.005)↑qualifications= more
Days in paid work	Psychiatric admission	(p=0.009) ↑days= ↑admissions
	Psychiatric admission days	(p<0.001) ↑days= ↑days work

Treatment - providers and additional support (Table 61)

The nature of the medical treatment provider for delivery of OST- M – person's own GP, Criminal Justice (CJS) or NHS specialist service – raised conflicting associations. Specialist services (both CJS and NHS) saw patients more frequently, tested them more often and retained patients in treatment better than GPs. There were no consistent differences between CJS and NHS – which suggests that more intensive support by a service with low caseloads (the DTTO has average caseloads for nursing staff of 10 cases at any one time – the NHS has average caseloads of over 40 cases) had little effect on outcome. This is perhaps even more surprising as the DTTO is an "alternative to custody" scheme and therefore has an added incentive to demonstrate improvement. Comparing the outcomes achieved in all three elements, the specialist CJS element demonstrated more illicit

diazepam use than specialist NHS – supported by positive tests for these drugs. The NHS patients did, however, show more illicit Methadone use – "topping up" - while in OST- M. Regarding clinical outcomes, both of these specialist services, compared to primary care, were associated with more family stability. The GP – treated group showed more injecting, and had more admissions – both psychiatric and acute - and more incarcerations recorded in their casenotes. Additional support from external agencies was associated with better clinic attendance and more evidence of family stability. Regardless of the methadone provider, GP registration (for general medical services) showed a strongly positive association with better employment status, improved family stability and reduced likelihood of positive drug tests. GP registration was, however, also associated with more acute admissions – potentially a positive finding in light of the many health problems prevalent in this population. The MAP physical health score predicted both acute admissions and death in the follow up period.

Table 61. Univariate analysis results: Healthcare support

Independent variable	Dependent variable	Statistics
Non NHS support	Family stability	(p=0.021) support=stability
	Out-patient attendance	(p=0.021) support=attendance
Registered with GP (GMS)	Employment status	(p=0.007) GP=better
	Family stability	(p=0.011) GP=stable
	Opiate positive tests	(p=0.022) GP=less +ve
	Acute admissions (SMR)	(p=0.024) GP=more
Treatment provider	Family stability	(p=0.015; Specialist>GP)
	Heroin use	(p=0.002; CJS>GP>TDPS)
	Heroin route	(p=0.001; GP IV++)
	Diazepam use	(p=0.006; CJS>GP>TDPS)
	Methadone use	(p=0.002 TDPS↑)
	Methadone days	(p=0.014 TDPS↑)
	DF118 use	(p=0.038; CJS>TDPS>GP)
	Opiate positive tests	(p=0.003; CJS>>GP>TDPS)
	Benzodiazepine +ve tests	(p=0.038; CJS>GP>TDPS)
	Acute admissions	(p=0.004) GP>TDPS>CJS
	Psychiatric admissions	(p=0.005) GP>TDPS>CJS
	Incarcerations	(p=0.008) GP>TDPS>CJS
	Retention	(p=0.004) Specialist>GP
	Screens done	(p=0.007; CJS>TDPS>GP)
	Out-patient attendance	(p=0.005; TDPS>CJS>GP)
MAP Physical	Acute admissions (SMR)	(p=0.023) >score=admissions
	Death	(p=0.040) >score=death

Substance use and treatment (Table 62.)

Substance use at baseline shows strong associations with treatment outcome. Previous reports have found that the nature and extent of illicit use and injecting/risk-taking on commencing treatment is a strong predictor of outcomes. In this cohort of existing OST- M patients, higher levels of heroin use at 2005 baseline were associated with poorer attendance at services and more illicit drug use at follow up as well as more psychiatric admissions during the follow up period. More injecting at baseline was associated with ongoing injecting during the follow up period and more heroin use at follow up.

Medical treatments for substance misuse

Also as expected and reflecting the evidence base, higher prescribed methadone doses at baseline were associated with positive effects in terms of treatment processes. The current study found higher doses were associated with better treatment retention, more frequent testing - and better (harm reduction) outcomes, in terms of less drug use (fewer positive drug tests) and fewer incarcerations. It is notable that acute admissions reported in SMR data and those recorded in casenotes show a difference here, implying that admissions are not reported/recorded consistently through the patient self-report process.

Higher diazepam doses (recorded in MAP) had almost universally negative associations. These included: poorer retention in treatment with fewer drug screens performed and, though this group were often prescribed higher methadone doses (often viewed by service providers as positive process measures of treatment quality) they were also found to have more opiate positive drug screens on follow-up. Higher diazepam doses also correlated with poorer measures of family stability along with more recorded admissions and incarcerations.

Patient satisfaction with the treatment they received (measured by the TPQ) was associated with fewer recorded admissions but more illicit methadone use by self-report. This could reflect that those with a more positive (or less challenging) relationship with the services are more likely to admit to illicit use of methadone (which is impossible to detect unless patients are using heavily and are seen to be over-sedated).

Table 62. Univariate analysis results: Substance use and treatment

Independent variable	Dependent variable	Statistics
Methadone dose at baseline	Opiate positive tests	(p=0.018) ↑baseline=↓+ves
	Acute admissions (notes)	(p=0.001) ↑baseline=↓admiss
	Acute admissions (SMR)	(p=0.035) ↑baseline=↑admiss
	Acute nights (SMR)	(p=0.030) ↑baseline=↑nights
	Psychiatric admission (notes)	(p=0.001) ↑baseline=↓admiss
	Psychiatric days (SMR)	(p=0.038) ↑baseline=↓days
	Incarcerations (notes)	(p=0.001) ↑baseline=↓admiss
	Retention	(p=0.001) ↑baseline=retention
	Screens done	(p<0.001) ↑baseline=↑tests
Baseline diazepam dose	Family stability	(p=0.025) ↑baseline =less stable
	Opiate positive drug screens	(p=0.022) ↑baseline=neg tests
	Acute admissions	(p<0.001) ↑baseline=more
	Psychiatric admissions	(p<0.001) ↑baseline=more
	Incarcerations	(p<0.001) ↑baseline=more
	Retention	(p<0.001) ↓predicts retention
	Methadone dose	(p<0.001) ↑baseline=↑dose
	Drug screen done	(p<0.001) ↑baseline=less tests
Patient satisfaction (TPQ)	Illicit methadone days	(p=0.007) satisfaction=less
	Acute admission (SMR)	(p=0.025) ↑score=less
Heroin use	Any illicit use	(p=0.002) +ve test predicts use
	Heroin days	(p=0.005) +ve test predicts use
	Out-patient attendance	(p=0.018) +ve predicts less
Heroin use (days used)	Psychiatric admission (days)	(p=0.005) ↑use predicts ↑days
Heroin route	Heroin use	(p=0.001) injecting predicts use
	Heroin days	(p=0.014) injecting =more
	Heroin route	(p=0.001) injecting persists

Co-morbidities (Table 63.)

The total GHQ score at baseline (n.b. but not *"caseness"* status) was associated with diazepam use, illicit methadone days used and psychiatric days admitted during follow up. Presence of any Pain was associated with longer acute hospital stays while Pain Intensity was associated with death. PTSD "caseness" was associated with lower family stability, more ambulance callouts and higher prescribed methadone doses. PTSD score (severity) was associated with a higher prescribed methadone dose and better retention. The presence of ADHD symptoms was associated with more episodes of naloxone requirements following overdose (though numbers were very small). ADHD type was associated with out-patient attendances with the hyperactive type reviewed more frequently.

Though they are commonly observed in clinical practice, this study has not found these common comorbidities (as assessed in clinical services) to be strongly associated with the longer term outcomes measured in this cohort.

Table 63. Univariate analyses results: Comorbidity

Independent variable	Dependent variable	Statistics
GHQ score	Illicit diazepam use	(p=0.010) ↑score=more use
	Illicit methadone days	(p=0.003) ↑score=more days
	Psychiatric admissions (days)	(p=0.011) ↑score=more days
Pain presence	Acute admission nights (SMR)	(p=0.035) pain=longer stays
Pain intensity quintiles	Death	(p=0.012) ↑intense=↑deaths
PTSD Caseness	Family stability	(p=0.036; PTSD=less)
	Ambulance callouts	(p=0.050) PTSD=more
	Methadone dose	(p=0.025) PTSD=higher
PTSD severity score	Retention	(p=0.010) ↑severity=retention
	Methadone dose	(p=0.008) PTSD=higher
ADHD symptoms	Naloxone administrations	(p=0.031) ADHD predicts use
ADHD type	Out patient attendance	(p=0.030) H>I/C predicts number of attendances

In conclusion

These univariate analyses have revealed a number of strong associations between the selected independent and dependent variables measured at 4-7 years .

Some of the associations replicate previous research findings. Examples include:

- higher baseline heroin use and risk-taking was associated with poorer outcomes
- higher prescribed methadone dose was associated with better outcomes
- more diazepam use was associated with poorer outcomes
- more external support and GP registration was associated with better outcomes

Some of these associations challenge the published evidence base or have shown conflicting results. Examples include:

- being a parent was actually associated with poorer clinical outcomes
- the comorbidities chosen did not show many strong or consistent associations
- the “area” effect was unexpected. The most affluent Tayside area (Angus), is associated with poor process measures and outcomes while the most deprived

(Dundee City) shows the reverse. Meanwhile, the SIM-D deprivation scores showed no significant associations at all. Tayside is a diverse region and many factors may have been important. Issues relating to local services and consistency of practice may also be relevant – though Tayside-wide standards were in place to ensure consistency of all elements of the OST- M prescribing programme. Further study is required to explore the many factors which may be influencing these results.

It is important to recognise that data quality may be important here – with recorded admissions and incarcerations, for example, seeming to be discrepant from the findings of analyses using validated SMR data on admissions.

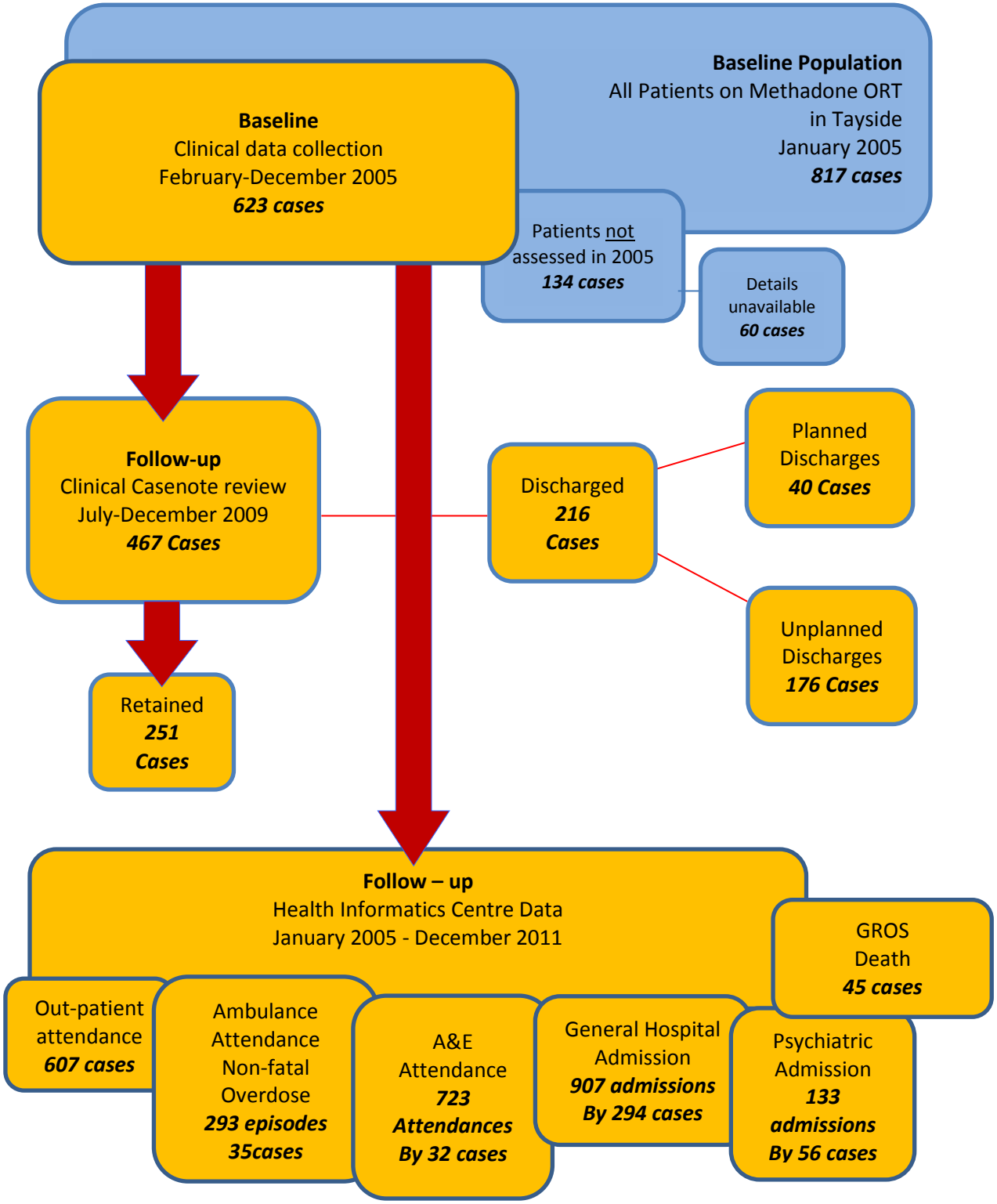
The next chapter describes a series of multiple regression analyses and cross-validation exercises, undertaken to determine whether these data could successfully predict clinical outcomes and whether the predictive models developed were generalisable – i.e. effectively predict outcomes in novel datasets.

Chapter 9

Results:

Prediction of Outcomes

Figure 13. Results: Prediction of outcomes



Introduction

This chapter describes attempts to test the ability of the Tayside Methadone Cohort clinical data to *predict* clinical outcomes. It also describes a process of cross-validation, which aimed to test the ability of any predictive models generated to predict clinical outcomes in a novel dataset.

Univariate analyses

A series of univariate analyses have been described. Using a group of baseline (independent) variables and outcome (dependent) variables, identified from the literature, it was shown that there are significant associations between some variables over time.

Multiple testing – the Bonferroni correction

The issue of multiple testing had been addressed by using the Bonferroni method as described in the methods chapter.

The next phase was to introduce these variables into a model which could be tested in terms of its ability to predict specific outcomes. A multiple regression analysis would be undertaken to achieve this.

Process

Choosing variables to test

Again using the literature review, a series of relevant outcomes of clinical significance were identified. The outcome variables chosen are shown in Table 64.

Table 64. Outcome variables for multiple regression

Outcomes	Data source
Death (2005-2009)	HIC data - GROS
Opiate positive drug screens	2009 casenotes
Self-report of opiate use	2009 casenotes
Family stability	2009 casenotes
Acute admissions 2005-9	HIC data – SMR01

The relevant independent variables, found to have a highly significant association with these outcomes were identified. These are shown in Table 65.

Table 65. Predictive model – variables for multiple regression analysis

DV (outcome)	IV (Predictor)	Statistics (Chapters 6,7)
Death (2005-2009) GROS (HIC)	No of medical admissions	LDA $X^2(1)=41.053$; p<0.001
	Age	LDA $X^2(1)=19.567$; p<0.001
	Gender	Chi square $X^2(2)=17.287$; p<0.001
	Retention (2009)	Chi square $X^2(1)=19.224$; p<0.001
	Drug screen done 2009	Chi square $X^2(2)=20.620$; p<0.001
	Number of SAS attendances	LDA $X^2(1)=9.985$; p=0.002
	Number of SU OP attendances	LDA $X^2(1)=7.659$; p=0.006
	BPI Pain severity (quintile)	Chi square $X^2(4)=12.815$; p=0.012
	MAP friends conflict score	LDA $X^2(1)=4.007$; p=0.045
	MAP physical health score	LDA $X^2(1)=4.226$; p=0.040
Opiate positive drug screens in 2009 casenotes	Treatment setting	Chi square $X^2(6)=19.642$; p=0.003
	Baseline Methadone dose	LDA $X^2(1)=5.569$; p=0.018
	Registered with GP	Chi square $X^2(4)=11.411$; p=0.022
	Baseline Diazepam dose	LDA $X^2(1)=5.220$; p=0.022
Self - report of opiate use in 2009 casenotes	Route of heroin use - baseline	Chi square$X^2(6)=30.699$; p<0.001
	Treatment setting	Chi square $X^2(6)=20.392$; p=0.002
	Age	LDA $X^2(1)=5.429$; p=0.020
	Baseline Methadone dose	LDA $X^2(1)=5.360$; p=0.021
	Days heroin use at baseline	LDA $X^2(1)=5.231$; p=0.022
	Area lives in	Chi square $X^2(6)=14.102$; p=0.029
	Any heroin use at baseline	Chi square $X^2(6)=13.867$; p=0.031
Family stability recorded in 2009 casnotes	Age	LDA $X^2(1)=11.321$; p=0.001
	Area lives in	Chi square $X^2(4)=20.796$; p<0.001
	Registered with GP	Chi square $X^2(2)=8.973$; p=0.011
	Treatment setting	Chi square $X^2(4)=12.301$; p=0.015
	Has children	Chi square $X^2(2)=7.723$; p=0.0.021
	Support from other agencies	Chi square $X^2(2)=7.712$; p=0.021
	Baseline prescribed diazepam dose	LDA $X^2(1)=4.993$; p=0.025
	Illicit diazepam use	Chi square $X^2(4)=10.699$; p=0.030
	PTSD caseness	Chi square $X^2(2)=6.648$; p=0.036
Acute admissions 2005-9 SMR01 (HIC)	Presence of pain	MWU=5349.000; p=0.035
	Methadone dose	LRA t(1)=2.187; p=0.030

Key: from univariate analysis (following Bonferroni Correction) P<0.001

from univariate analysis (following Bonferroni Correction) P<0.005

from univariate analysis (following Bonferroni Correction) P<0.05

Multiple regression analysis.

Where the outcome to be assessed was categorical, a multiple logistic regression was undertaken. Where the outcome was continuous – in this case, only the number of acute admissions – a multiple linear regression was undertaken.

Independent variables were placed in the appropriate multiple regression analysis in the SPSS18 computer programme (IBM, 2010), using a Forced Entry (ENTER) method. Stepwise methods were avoided as it has been argued that these computer-based approaches rely on the computer selecting variables statistically - i.e. not based on their theoretical importance – and are more likely to result in over/under fitting - a process of including variables with little effect or excluding some which are clinically relevant (Field, 2009). A number of rules were considered when developing the model:

- Finding a model with the fewest variables but with the best predictive value was the aim.
- Only variables with a good theoretical grounding were included – the variables chosen reflected the evidence base explored in the literature review and the results of the univariate analyses.
- A process was undertaken to remove variables found to be redundant – provided this did not reduce the predictive power of the model.

Sample size

Sample size was another important consideration (Green, 1991). The sample size recommended depends on the size of the effect (i.e. how well a variable predicts an outcome). It is generally felt that the larger the sample the more generalizable is the predictive model. Simple rules are often applied suggesting 10 or 15 cases are required for each predictor in the model (Field, 2009). However, more specific approaches to agreeing sample size in a multiple regression analysis can be used, depending on the purpose of the analysis.

- To test *best fit* of the model to the data (testing R^2) the minimum sample size is calculated by using the following equation:

  sample size = 50 + 8k (where k is number of predictors included)

- For a process intended to test the role of the *individual predictors* within a model then minimum sample size is calculated using the equation:

sample size = 104 +k (where k is number of predictors)

Green states that, if both a measure of overall fit to the data and a test of the contribution of all predictors are required, it is recommended that both tests are undertaken – in which case, the equation giving the highest number is used to calculate sample size required for the regression to be successful.

Multicollinearity

The purpose of the regression analysis is to be able to draw conclusions about the population of interest based on the sample. For this to be accurate (or unbiased) it is important that a number of assumptions are true. One key assumption is that there should be no perfect linear relationship (correlation) between two or more predictors. Though perfect collinearity is rare, a degree of correlation is very common. As the degree of correlation increases, there are a number of potential impacts:

- the standard error of the β coefficient rises (i.e. is more variable and therefore less representative of the population as a whole)
- the size of R (degree of correlation between predicted and observed outcome) is limited
- the importance of specific predictors is difficult to assess

In this analysis plan, should a strong predictive model be identified, it was planned that the degree of multicollinearity would be assessed using the SPSS collinearity diagnostic function as described by Field (2009). Two characteristics would be examined:

1. The tolerance value. Menard (1995) suggests a tolerance value of less than 1 indicates a significant collinearity problem.
2. The Variance Inflation Factor (VIF). A value of 10 would be taken to indicate a high level of collinearity (Myers 1990).

Outputs from the multicollinearity process undertaken are contained in Appendix 7.

Cross – validation of the predictive models

A process of cross-validation was also undertaken to determine whether the findings of the regression analysis would produce a valid predictive model when applied to an unrelated dataset.

The process undertaken is described in Chapter 4 (Materials and methods). To summarize, the following steps were planned:

- a complete dataset was created - all subjects with any missing data in the relevant fields were removed from the analysis
- dividing the sample 50/50 into a *training* and *testing* dataset
- a test of sample size was applied
- the appropriate regression analysis was undertaken in the first half of the dataset – *the training dataset* – generating a model with β coefficients for each variable.
- these β values were then applied to the novel *testing dataset* - to generate a predicted outcome in these novel data. The equation used reflected the type of regression being undertaken:
    - Linear regression: $Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots. \beta_n X_n + \varepsilon.$

      This was used when the Dependent Variable was continuous
    - Binary logistic regression: $P(Y) = 1/1 + e^{-(\beta 0 + \beta 1 X1 + \beta 2 X2 + \ldots. \beta n Xn)}$

      This was used when the Dependent Variable was binary
- the *predicted* outcome generated, was then compared to the actual *observed* outcome for the testing dataset. A significant difference between the observed and predicted outcomes would imply that the proposed predictive model is NOT predictive in this novel dataset.

The next section describes the results of these multiple regression analyses.

Regression 1: Death 2005-2009 (from HIC GROS death data)

The initial analysis had found a number of associations between independent (predictor) variables and the outcome variable, DEATH. Many of these associations were significant at the p<0.001 level. These are summarized in Table 66.

Table 66. Statistically significant associations – dependent variable DEATH

DV (outcome)	IV (Predictor)	Statistics
Death (2005-2009)	No of medical admissions	LDA $X^2(1)=41.053$; p<0.001
	Age	LDA $X^2(1)=19.567$; p<0.001
	Gender	Chi square $X^2(2)=17.287$; p<0.001
	Retention (2009)	Chi square $X^2(1)=19.224$; p<0.001
	Drug screen done 2009	Chi square $X^2(2)=20.620$; p<0.001
	Number of SAS attendances	LDA $X^2(1)=9.985$; p=0.002
	Number of SU OP attendances	LDA $X^2(1)=7.659$; p=0.006
	BPI Pain severity (quintile)	Chi square $X^2(4)=12.815$; p=0.012
	MAP friends conflict score	LDA $X^2(1)=4.007$; p=0.045
	MAP physical health score	LDA $X^2(1)=4.226$; p=0.040

Methods

As outcome variable is dichotomous (Dead v not dead) a binary logistic regression was carried out.

Developing a predictive model - Binary Regression Analysis

First a complete dataset was created by removing all missing data. The complete dataset contained 184 cases of which 15 had died between 2005 and 2009.

Initial sample size was assessed. The two equations proposed by Green (1991) would suggest:

- Best fit equation - *sample size = 104 +k (where k is number of predictors = 10)* – sample size of 114 was required
- Individual variables equation - *sample size = 50 + 8k (where k is number of predictors)* – sample size of 130 is required. The complete dataset of 184 cases was, theoretically, sufficient.

Using the complete dataset, a series of binary logistic regressions were undertaken to identify the relevant IVs to include in the most powerful predictive model.

Results

Table 67. shows the results of the first multiple binary regression undertaken. In this analysis only the 6 highly significant (P<0.001) associations were included. This would also reduce the required sample size to 110 (Best fit) or 98 (Variables).

Table 67. Death: Complete dataset - all highly significant predictors

Predictor	B (SE)	Significance
Constant	6.581 (56841.828)	
No of medical admissions	-0.175 (0.104)	P=0.093
Age	-0.145 (0.042)	P=0.001
Gender	19.881 (40193.110)	P=1.000
Retention (2009)	-0.725 (1.050)	P=0.490
Drug screen done 2009	-15.308 (40193.887)	P=0.052

R^2 = 0.585 (Hosmer&Lemeshow), 0.209 (Cox & Snell), 0.484 Nagelkerke. Model $X^2(7)=43.121$; p<0.001. Model classifies 94% correctly [40% of deaths v 0 before model applied; 98.8% of living v 100% before. Before model, prediction 91.8% correct]

It is clear that in this regression, some variables are not contributing to the predictive power of the model. The variables *Gender* and *Retention* were excluded and the analysis repeated. The results are shown in table 68.

Table 68. Death: Complete dataset – selected highly significant predictors

Predictor	B (SE)	Significance
Constant	26.125 (40192.968)	
No of medical admissions	-0.227 (0.096)	P=0.018
Age	-0.134 (0.040)	P=0.001
Drug screen done 2009	-15.453 (40192.968)	P=0.036

R^2 = 0.630 (Hosmer&Lemeshow), 0.189 (Cox & Snell), 0.437 Nagelkerke. Model $X^2(4)=38.492$; p<0.001. Model classifies 93.5% correctly. Before model, prediction 91.8% correctly.

The small number of cases of death make the overall prediction level - 93.5% - seem high. However, the "before" model (i.e. the prediction before a model is applied) predicts 91.8% of the variance. This apparent high level of prediction, reflects the high correlation with the the state "not dead". Death is a rare event and even though the TMC dataset is large – if all deaths were included there would only be 45 events in 623 cases. The creation of a complete dataset has reduced the number of cases even further – making accurate

prediction impossible. There is little improvement achieved by adding the proposed model as less than 2% of the variance would be explained by the model.

Multicollinearity was not found to be a concern with tolerance levels ranging from .973 to .999 and VIF close to 1 for all factors.

Conclusion: The model has therefore not been demonstrated to be useful at predicting death in this sample. As the model was not a useful predictor of outcome, no cross-validation was undertaken.

Regression 2: Drug use – record of positive opiate screens recorded in casenotes - 2009

The significant variables identified from the longitudinal analyses are shown in table 69.

Table 69. Statistically significant associations – DV positive drug screens 2009

DV (outcome)	IV (Predictor)	Statistics
Opiate positive drug screens in 2009 casenotes	Treatment setting	Chi square $X^2(6)=19.642$; p=0.003
	Baseline Methadone dose	LDA $X^2(1)=5.569$; p=0.018
	Registered with GP	Chi square $X^2(4)=11.411$; p=0.022
	Baseline Diazepam dose	LDA $X^2(1)=5.220$; p=0.022

Developing a predictive model - Binary Regression Analysis

First a complete dataset was created by removing all missing data. The complete dataset contained 200 cases of which 66 had positive tests recorded in their casenotes in 2009. As the number of predictors was small, rather than use the whole dataset to develop the model to be tested, it was decided to use all of the predictors in the regression and cross validation process. This complete dataset was therefore divided into two elements each with 100 cases.

Sample size an issue. According to Green (1991) – sample sizes of 90 (best fit) or 108 (variables) cases would be required. Small sample size is therefore a potential weakness.

A Binary Logistic regression was undertaken using the first half of the dataset – ML=1. This is the *training* dataset. The results are shown in Table 70. In this case, we can see that the model is a good fit to the data, the model chi-squared test is highly significant (p<0.001) but the proposed model predicts only 13% of the variance. Two variables - *being registered with a GP* and *the baseline methadone dose* in 2005 are the stronger predictors in the model. Multicollinearity was not a concern with tolerance levels of .982- to .990 and VIF close to 1 for all factors (details can be found in Appendix 7).

Table 70. Positive drug screens: Complete dataset –highly significant predictors

Predictor	β (SE)	Significance
Constant	-1.785 (0.784)	
Treatment setting	0.837 (0.534)	P=0.117
Baseline Methadone dose	0.046 (0.020)	P=0.020
Registered with GP	-3.303 (1.268)	P=0.009
Baseline Diazepam dose	0.096 (0.050)	P=0.056

R^2 = 0.824 (Hosmer&Lemeshow), 0.215 (Cox & Snell), 0.287 Nagelkerke. Model $X^2(5)=24.164$; p<0.001. Model classifies 67% correctly [54% of +ve& 78% of –ve]. Before model, classifies 54% correctly.

Cross validation

The β values from this first regression were inserted into the following equation:

$$P(Y)= 1/1+e^{-(b0+b1X1+b2X2+....+bnXn)}$$

When applied to the dataset ML=2 - *the testing dataset,* this generates a series of predicted outcomes for that dataset. The predicted outcomes and observed outcomes in this novel dataset – ML=2 - can then be compared using a Chi-squared test, using the predictive model generated using the original dataset ML=1. The results are shown in Table 71.

Table 71. Cross validation: Observed and predicted outcomes – opiate +ve drug tests

	Observed positives	Observed negatives
Predicted positives	29	28
Predicted negatives	18	25

Chi squared test: $X^2(1)=0.800$; p=0.371.

Though the chi-squared test has produced a non-significant result, observation of Table 100 shows that this comes about because there is no discrimination between predicted/observed positive and predicted/observed negative outcomes. There is no relationship between observed and predicted outcomes.

Conclusion: Despite the univariate analyses suggesting these factors were strong predictors of illicit drug use (measured by positive tests recorded in casenotes), multiple regression analysis found the model to be a weak predictor of this outcome. When this weak model was applied to a novel dataset there was no relationship between observed and predicted outcomes, showing that the model was not generalisable.

Regression 3: Drug use – DV *self-report* of opiate use recorded in casenotes

The significant variables identified from the longitudinal analyses are shown in table72.

Table 72. Statistically significant associations – DV self-report of opiate use

DV (outcome)	IV (Predictor)	Statistics
Self - report of opiate use in 2009 casenotes	Route of heroin use - baseline	Chi square$X^2(6)=30.699$; $p<0.001$
	Treatment setting	Chi square $X^2(6)=20.392$; $p=0.002$
	Age	LDA $X^2(1)=5.429$; $p=0.020$
	Baseline Methadone dose	LDA $X^2(1)=5.360$; $p=0.021$
	Days heroin use at baseline	LDA $X^2(1)=5.231$; $p=0.022$
	Area lives in	Chi square $X^2(6)=14.102$; $p=0.029$
	Any heroin use at baseline	Chi square $X^2(6)=13.867$; $p=0.031$

Developing a predictive model - Binary Regression Analysis

In this case, as there were 7 potential variables to be included in the model – making sample size a significant issue if attempting to create a valid predictive model - the whole sample was used initially to develop a predictive model.

First a complete dataset was created by removing all missing data. The complete dataset contained 193 cases of which 91(47.2%) had reported opiate use recorded in their casenotes in 2009. Some 102 (52.8%) did not have a self-report of illicit heroin use recorded. Sample size was adequate -106 (variables) or 111 (best fit) cases would be required.

Step 1 Regression analysis – whole dataset with selected predictors

An initial binary regression analysis was undertaken using the two most significant predictors ($p<0.005$) – these were: *route of heroin use at baseline* and *treatment setting.* The resulting model predicted 16.2% of the variance observed, was a good fit to the data (R^2 of 0.868) and the model Chi-squared test was highly significant ($p<0.001$) (Table 73).

Table 73. Self – report: Complete dataset – selected highly significant predictors

Predictor	β (SE)	Significance
Constant	19.941 (40192.587)	
Treatment setting	1.319 (0.417)	P=0.002
Baseline route of heroin use	-20.153 (40192.587)	P<0.001

R^2 = 0.868 (Hosmer&Lemeshow), 0.167 (Cox & Snell), 0.223Nagelkerke. Model $X^2(6)=35.009$; $p<0.001$. Model classifies 69.3% correctly [77.8% of +ves& 61.8% of –ves]. Before model, classifies 53.1% correctly.

Step 2 Regression analysis – whole dataset with remaining predictors introduced

All remaining predictors were then introduced to determine whether any improvement in the model was achieved.

When all significant predictors (from the univariate analyses) were included this new model predicted only 68.6% correctly (65.6% of positives and 71.3% of negatives). The baseline model predicted 52.9% correctly – 15.7% of the variance is accounted for by the model. Also, R^2 reduced to 0.835 (Hosmer & Lemeshow). The model Chi-square remained significant ($X^2(8)=43.526$; $p<0.001$). Three factors were found to be significant contributors to the predictive model: Treatment setting ($p=0.011$); Baseline route of heroin use ($p=0.012$) and Age ($p=0.042$).

Step 3 Regression analysis – whole dataset with only significant predictors

These three significant predictors were then included in a new model. This only predicted 67.2% correctly (67.8% of positives and 66.7% of negatives). R^2 increased to 0.852 (Hosmer & Lemeshow). The model Chi-square remained significant ($X^2(7)=39.322$; $p<0.001$). Though it had only predicted some 16.2% of the variance, it was felt that the original model was a more powerful predictor of self-reported opiate use, and showed better goodness of fit to the data. It also used only variables which objectively contributed to the model- reducing the number of predictors and increasing compliance with the rules set initially. This

model was therefore used as the basis for the cross validation process. Multicollinearity was not found to be a concern as tolerance levels were low and VIF 1.000 for all factors.

Cross validation

The complete dataset was divided into two elements ML=1 and ML=2 with 97 and 96 cases respectively.

Sample size: this may not be adequate – Green's equation for best fit would imply a sample of 108 is required. For assessment of variables' contribution it would be 74.

Training dataset (ML=1)

A Binary Regression Analysis was performed using the preferred predictive model. The results are shown in Table 74. The model predicts 17.5% of the variance observed.

Table 74. Training dataset (ML=1) – self-report of opiate use

Predictor	β (SE)	Significance
Constant	21.068 (40192.789)	
Treatment setting	0.868 (0.596)	P=0.251
Baseline route of heroin use	-19.993 (40192.789)	P=0.002

R^2 = 0.819 (Hosmer&Lemeshow), 0.221 (Cox & Snell), 0.295 Nagelkerke. Model $X^2(6)=24.181$; $p<0.001$. Model classifies 71.1% correctly [75.6% of +ves& 67.3% of –ves]. Before model, classifies 53.6% correctly.

Cross validation

The β values from this first regression were applied to the dataset ML=2 - *the testing dataset,* generating a series of predicted outcomes for that dataset. The predicted outcomes and observed outcomes in this novel dataset – ML=2 - were then be compared with the original dataset ML=1. The results are shown in Table 75.

Table 75. Cross validation: Observed and predicted outcomes – self-reported drug use

	Observed positives	Observed negatives
Predicted positives	26	42
Predicted negatives	19	8

Chi squared test: $X^2(1)=8.005$; $p=0.005$

Again, observation of the table shows that there is no relationship between predicted and observed outcomes. The model was found not to be generalisable when applied to these novel data.

Regression 4: Positive record in casenotes indicating family stability

The significant variables identified from the longitudinal analyses are shown in table 76.

Table 76. Statistically significant associations – DV family stability

DV (outcome)	IV (Predictor)	Statistics
Family stability recorded in casenotes 2009	Age	LDA $X^2(1)=11.321$; p=0.001
	Area lives in	Chi square $X^2(4)=20.796$; p<0.001
	Registered with GP	Chi square $X^2(2)=8.973$; p=0.011
	Treatment setting	Chi square $X^2(4)=12.301$; p=0.015
	Has children	Chi square $X^2(2)=7.723$; p=0.0.021
	Support from other agencies	Chi square $X^2(2)=7.712$; p=0.021
	Baseline prescribed diazepam dose	LDA $X^2(1)=4.993$; p=0.025
	Illicit diazepam use	Chi square $X^2(4)=10.699$; p=0.030
	PTSD caseness	Chi square $X^2(2)=6.648$; p=0.036

Developing a predictive model - Binary Regression Analysis

First a complete dataset was created. This complete dataset contained 189 cases of which 114 (60.3%) had a positive report of factors indicating family stability recorded in their casenotes in 2009. 75 (39.7%) contained data suggesting poor family stability. Sample size is adequate. If all predictors were included, sample size should be between 113 and 122.

Step 1 Regression analysis – whole dataset with selected predictors

Using this complete dataset (n=189) an initial regression analysis was undertaken using the four most significant predictors– these were *age, area lived in, registered with GP and treatment setting.* The results are shown in Table 77. While it appears to be a reasonable fit

to the data, with the model Chi-squared test significant (p=0.002), the proposed model only predicted 7.4% of the variance observed.

Table 77. Family stability Complete dataset – selected most significant predictors

Predictor	β (SE)	Significance
Constant	3.900 (1.289)	
Age	-0.067 (0.024)	P=0.005
Area lives in	0.930 (0.654)	P=0.012
Registered with GP	-0.118 (1.722)	P=0.946
Treatment setting	0.073 (0.403)	P=0.631

R^2 = 0.917 (Hosmer&Lemeshow), 0.105 (Cox & Snell), 0.143Nagelkerke. Model $X^2(6)=21.038$; p=0.002. Model classifies 67.7% correctly. Before model, classifies 60.3% correctly.

Step 2 Regression analysis – whole dataset with all significant predictors

All 9 predictors from the univariate analyses were then entered into the model to determine whether any improvement was achieved. Results are shown in table 78.

Table 78. Family stability Complete dataset – all significant predictors

Predictor	β (SE)	Significance
Constant	3.391 (1.293)	
Age	-0.067 (0.024)	P=0.005
Area lives in	0.930 (0.654)	P=0.012
Registered with GP	-0.118 (1.722)	P=0.946
Treatment setting	0.073 (0.403)	P=0.631
Has children	-1.257 (0.539)	P=0.020
Support from other agencies	-0.395 (0.455)	P=0.385
Baseline diazepam dose	0.032 (0.022)	P=0.146
Illicit diazepam use	-1.447 (1.037)	P=0.015
PTSD caseness	-0.013 (0.408)	P=0.975

R^2 = 0.806 (Hosmer&Lemeshow). Model $X^2(12)=39.131$; p<0.001. Model classifies 72.8% correctly. Before model, classifies 60.3% correctly.

When all significant predictors were included the new model showed some improvement. It predicted 72.8% correctly, representing 11.9% of the variance observed. Also, R^2 reduced to 0.806 (Hosmer&Lemeshow). The model Chi-squared test was highly significant ($X^2(12)=39.191$; p<0.001). Two of the factors included, however, were found to be highly insignificant contributors to the model. These were *registered with a GP* (p=1.000) and *PTSD caseness at baseline* (p=0.975). These factors were then excluded for step 3.

Step 3 Regression analysis – whole dataset with insignificant predictors removed

All remaining significant predictors were then included in a new model. This new model predicted 72.4% - explaining 12.1% of the variance observed. R^2 was unchanged from step 2 = 0.805 (Hosmer & Lemeshow) and the model Chi-square remained highly significant ($X^2(10)=40.926$; $p<0.001$). The next two factors which were least significant were then removed from the model. These were *treatment setting* (p=0.610) and *support from other agencies* (p=0.385).

Step 4 Regression analysis – whole dataset with further insignificant predictors removed

Only significant predictors were then included in a new model. This model predicted only 10.5% of variance observed. R^2 increased to 0.841 (Hosmer & Lemeshow) while the model Chi-square remained highly significant ($X^2(7)=38.148$; $p<0.001$).

As model 3 predicted the highest proportion of the variation (albeit only 12.1%) with the least number of factors and acceptable goodness of fit, this model was used as the basis for the cross validation process. Multicollinearity was again not found to be a concern with tolerance levels ranging from .697 to .956 and VIF from 1.067 to 1.435.

Cross-validation process

The complete dataset was divided into two elements ML=1 (94 cases) and ML=2 (95 cases). Sample size is lower than required. For best fit sample sizes of 111 would be required while for variables, 106.

A Binary Regression Analysis was performed using the preferred predictive Model 3. The results are shown in Table 79. In this subset, the proposed model is less of a good fit with R^2 reducing to 0.630. Model Chi-squared remains highly significant ($p<0.001$). The model however, predicts an increased 20.8% of the variance observed.

Table 79. Family Stability: training dataset ML=1 (n=94 cases)

Predictor	β (SE)	Significance
Constant	6.057 (1.962)	
Age	-0.093 (0.052)	P=0.072
Area lives in	-20.594 (27710.084)	P=0.335
Has children	-2.333 (0.962)	P=0.012
Baseline diazepam dose	0.014 (0.036)	P=0.704
Illicit diazepam use	-4.027 (1.770)	P=0.015
Treatment setting	-1.023 (0.761)	P=0.179
Support from other agencies	-0.444 (0.687)	P=0.518

R^2 = 0.630 (Hosmer&Lemeshow), 0.394 (Cox & Snell), 0.531 Nagelkerke. Model $X^2(10)=41.135$; $p<0.001$. Model classifies 79.3% correctlyBefore model, classifies 58.5% correctly.

The β values from ML=1 were then used to generate a series of predicted outcomes in ML=2 using this predictive model. A Chi-squared test was then undertaken to compare the predicted and observed outcomes in the novel dataset ML=2, using the predictive model generated using the original dataset ML=1. Results are shown in Table 80.

Table 80. Cross validation: Observed and predicted outcomes – family stability

	Observed stable	Observed unstable
Predicted stable	46	25
Predicted unstable	0	3

Chi squared test: $X^2(3)=5.137$; p=0.162.

Though the chi-squared test has produced a non-significant result, observation of Table 80 shows that this comes about because there is no discrimination between predicted and observed outcomes. The proposed model is found not to be generalizable when applied to novel data.

Regression 5: Measures of Health status – NHS service use (Acute hospital admissions)

Two proxy measures of "health status" were available in the database and were considered. These were:

1. admissions to hospital (recorded in casenotes in 2009 – either contemporaneous notes or discharge letters)
2. SMR01 records of number of nights in the acute hospital.

Recorded admissions to acute hospital (casenotes)

The variables to be used in developing this predictive model are shown in Table 81.

Table 81. Statistically significant associations – DV Admissions recorded in casenotes

DV (outcome)	IV (Predictor)	Statistics
Recorded acute admissions 2009	RX methadone dose	LRA t(1)=-3.448; p=0.001
	Rx diazepam dose	LRA t(1)=4.183; p<0.001
	Educational level achieved	KWH(4)=15.447; p=0.004
	Treatment setting	ANOVA F(2,8)=5.619; p=0.004
	Area	KWH X^2(2)=8.696; p=0.013
	Pain intensity	LRA t(1)=2.366; p=0.018
	PTSD severity	LRA t(1)=-2.312; p=0.021
	Registered with GP	KWH X^2(1)=4.657; p=0.031
	GHQ total score	LRAt(1)=2.159; p=0.032

As the outcome variable was continuous a linear regression analysis was planned.

First, a complete dataset was created. All subjects with missing data relating to the relevant variables were removed. The resulting complete dataset contained only 17 cases. It was felt that no generalizable findings could be generated in this case. No further analysis was therefore undertaken using this outcome variable.

SMR01 Acute hospital nights

The two variables to be used in developing this predictive model are shown in Table 82.

Table 82. Statistically significant associations – DV SMR01 Acute admissions

DV (outcome)	**IV (Predictor)**	**Statistics**
SMR01 – acute admissions 2005-9	Presence of pain	MWU=5349.000; p=0.035
	Methadone dose	LRA t(1)=2.187; p=0.030

As the outcome variable was continuous a linear regression analysis was planned.

First, a complete dataset was created - all subjects with missing data relating to the relevant variables were removed. The resulting complete dataset contained 96 cases with an SMR01 record of admissions and no missing data. Sample size recommended would range from 66 cases to 106.

A multiple linear regression was undertaken on the complete dataset. The predictor *presence of pain* is categorical. In order to include this in the analysis it was recoded to zero and one as a "dummy variable". The results of the regression analysis are shown in Table 83.

Table 83. SMR01 admission nights: Complete dataset

Predictor	β (SE)	Significance
Constant	-3.442 (16.550)	
Methadone dose	0.100 (0.133)	P=0.455
Presence of pain (BPI)	11.751 (7.055)	P=0.099

The fit of the regression model was assessed. R^2 was 0.036 – showing that only 3.6% of the variance is explained by the model. ANOVA gave a result of F(2,8)=1.740; p=0.181. This shows that the model is not a significant fit of the data overall. There is an assumption that any errors in the regression are independent. This is tested using the Durbin-Watson statistic which in this case this was 1.406. This statistic should be close to 2 (and between 1 and 3). This assumption is therefore met. Multicollinearity was not a concern as VIF was 1.003.

Conclusion: It was concluded that the model proposed by these data is not a good predictive model of nights in an acute hospital ward as recorded by SMR01 returns. In such circumstances, no cross validation was undertaken.

Discussion

The multiple regression analyses have shown that, despite apparently strong associations found in the univariate analyses, it has not been possible to create strong predictive models for the selected outcomes. This could reflect a number of issues.

Data quality and sample size

The quality of available data - in particular the amount of missing data - meant that the creation of a complete dataset removed a large proportion of certain variables. For example, in the regression attempting to predict deaths, the complete dataset contained only 15 of the 45 deaths on the database. Death is a rare event – and prediction is difficult -

but clearly, this level of missing data is likely to have influenced the result. The loss of subjects could also have affected the sample size which, especially as the dataset was split into training and testing groups, fell below the recommended levels.

Multicollinearity of predictors

One effect of multicollinearity is to reduce the potential size of R. It was possible that this could have reduced the overall predictive value of the models generated. In order to determine whether this was an issue, the degree of multicollinearity was assessed for all models using the Variance Inflation Factor output from SPSS and the associated tolerance levels. This assessment found no evidence of a significant influence from multicollinearity. SPSS diagnostic outputs are shown in Appendix 7.

Cross-validation

The process of cross-validation adds more rigour to the regression analysis process. However, by splitting the dataset in half any statistically significant findings become more difficult to achieve. If they are achieved – and a valid predictive model is found – the process of cross-validation could demonstrate more robustly the predictive value of the model by testing the model on observed outcomes in a novel (untested) dataset.

In this project, however, none of the models generated were found to be strongly predictive – even when univariate analyses had shown individual predictors to have highly significant relationships with outcomes over time. Those models generated, which were found to have some limited predictive value, were further assessed using a cross-validation exercise. But in none of these three outcomes – drug use (self - report); drug use (positive tests filed); family stability – was the model found to be generalisable to a novel dataset.

Testing the cross-validation approach

It is important to determine whether there has been any error in executing the cross-validation exercise. If it is clear that the method used would have been successful if a strong predictive model were tested then the failure to positively discriminate outcomes reflects the weakness of the model - i.e. the lack of predictive value - and not some methodological failing in the study.

In order to determine whether the cross-validation exercise was appropriate (i.e. was likely to demonstrate generalisability) a multiple regression and cross-validation exercise was undertaken using a correlated novel dataset. A comprehensive description of this test is contained in Appendix 6.

This test demonstrated that the approach taken was valid.

In conclusion

The multiple regression analysis has shown that even in relatively large samples of OST-M patients (compared to many in the published literature), highly statistically significant findings from univariate analyses may not form the basis of a strong predictive model. Even when a reasonable degree of prediction can be demonstrated by the multiple regression, this model may not be capable of predicting outcomes in novel datasets. The cross-validation exercise has demonstrated that more rigorous testing is a valuable addition when testing the predictive value of these models.

Chapter 10. Discussion

All that is gold does not glitter, Not all those who wander are lost.

J.R.R. Tolkien

It is good to have an end to journey toward; but it is the journey that matters, in the end.

Ernest Hemingway

Introduction

This chapter will discuss the strengths and weaknesses of the research described in this thesis. It will also consider the clinical relevance of the project – in terms of the process (using clinical data to assess longer term outcomes in a large, UK – based clinical sample) and implications for future research and development.

The thesis describes a series of separate studies in the same treatment sample. The initial baseline review was stand-alone work, undertaken for clinical reasons, but developed to be more systematic by the introduction of validated tools. This was then used as the basis for identification of the follow up study cohort in 2009. Finally, the SUMIT project delivered access to additional validated datasets and also an environment – the HIC Safe haven – within which the separate datasets could be linked and anonymised, with appropriate governance and security in place – delivering the complete Tayside Methadone Cohort database.

This naturalistic approach brings strengths and weaknesses.

Strengths of the study

Setting

This study is set in NHS treatment services in the UK. The services involved in the project represent a common example of the treatment approach/environment in Scotland and across the UK as a whole. Specialist NHS services deliver medical treatments and specialist counselling or psychological interventions, supported by a General Practice “shared care” scheme (for those less complex patients who are in no need of specialist care). Additional

dedicated Criminal Justice Services are available to some patients involved with the justice system as a result of their drug problem. All of these services are supported by a range of local authority and third sector services offering specific interventions to address a broad range of relevant issues including childcare, family stability, employability and homelessness. As in many parts of the country, the services being accessed by the subjects of this study are not located in one discreet locality – instead being delivered in a range of urban, rural and semi-rural settings in three very different local authority areas. However, the protocols overseeing service delivery (e.g. prescribing practice) are standardised across the NHS Board area – meaning observed variation should reflect more specific patient differences and be less affected by variation in practice by locality services. The geographical area of "Tayside" is often seen in Scottish terms as "representative" of many of the Scottish NHS Board regions – encompassing inner city areas of high deprivation, small and large towns and a considerable rural hinterland with patchy levels of social exclusion. The Tayside Methadone Cohort sample is therefore likely to be more representative of "standard" UK service users than those seen in some studies.

In the Scottish context, the research and service-evaluation evidence available to plan services has been dominated by work done in the two large cities – Edinburgh and Glasgow. The services in which that work is set, has reflected local history, however. For example, the HIV epidemic in Edinburgh in the 1980s generated the opportunity for very long term follow-up of a specific cohort of individuals in one deprived area of the city (e.g. Kimber et al, 2010). Simultaneously, Glasgow specialists and GPs resisted harm reduction approaches, only launching a GP-led methadone service in 1994. This has grown into one of the largest in Europe and its standards are often described as being of the highest level. Despite this apparent success in terms of the care process – access and retention - Glasgow still sees the highest levels of drug death in the UK (ISD, 2012). It seems likely that this reflects local phenomena. It is important to consider the degree of generalisability of research findings.

Over 70% of substance misusers in Scotland are not found in Edinburgh or Glasgow. There is an urgent need for research which is more relevant to those services outside the major conurbations where service delivery is less concentrated and the controls available in the inner city (easy access to 7 day dispensing, for example) may be unachievable.

This study is one of the first large studies of long-term outcomes in substance misusers in treatment delivered in Scotland.

International relevance

This study has been based in a UK treatment system and has emphasised the need for longitudinal research with relevance to UK practice. As well as being important in terms of the Scottish and UK treatment system, however, the study also has international relevance. There is a strong, long-standing international consensus regarding the place of OST-M in the treatment of opioid dependency and any challenge to this view has historically been perceived to be hostile (e.g. Newman 2005). However, on reviewing the international evidence, it is clear that significant gaps remain in our understanding of the strengths and weaknesses of this treatment – especially when the existing evidence-base is challenged regarding the delivery of Recovery outcomes and progress from OST-M (NTA, 2012). Consolidation and development of the evidence base is required to ensure that the use of OST-M is scrutinised objectively, its potential risks reduced and its effectiveness maximised. The current study addresses some of the weaknesses in the international evidence, identified by previous systematic reviews (e.g. Lingford-Hughes, Welch, Peters & Nutt, (2012).

Sample size & cases available for follow up

One of the main strengths of this study is the size of the sample. Initially 647 of a total treatment population of 817 patients in a Scottish regional service were assessed using a validated assessment tool (the Maudsley Addiction Profile). When data were cleaned and invalid identifiers removed this still left a large baseline sample of 623 cases. This represents more subjects than most long term studies carried out in the UK. A high proportion of cases were also available for the follow up study. Some 467 of Tayside OST-M cases were followed up at 4 years – 75% of the baseline sample. NTORS - a good comparison as a longitudinal UK study following patients up for 5 years – had a baseline population in *Methadone Maintenance* [OST-M] of 458 cases (plus a further 209 described as being in *Methadone reduction*) of which 46% were followed up at 5 years. DORIS, the main comparable Scottish study recruited less than 300 cases in OST-M with some 47% followed up at 33 months.

Other recent UK studies have examined large samples over longer periods. McCowan, Kidd & Fahey (an earlier study using the data held in the Dundee Health Informatics Centre) had tested the use of linked datasets to examine a sample of 2378 Tayside GP-prescribed OST-M patients who were followed up over 11 years using SMR-linked data to imply outcomes. No rich in-depth clinical information was collected in that study, however. The researchers simply utilized data available in standard NHS databases – but the size of the sample and the long follow up period gave valuable information regarding potential future research to better understand risk/protective factors for death in these patients (McCowan, Kidd & Fahey, 2009). Another large Scottish sample was reported by Kimber et al (2010). This sample consisted of injecting drug users initially recruited in the 1980s and followed up in depth for over 30 years. Some 557 of that sample were reported to have had some OST at some stage in that period (Kimber et al 2010).

The approach described in this thesis offers a potential model to further develop rich datasets, describing large representative samples which could be tracked over long time periods, allowing more consistent and relevant outcomes to be measured in these populations than is often the case in the international literature. This would also create the environment within which original research could flourish – allowing assessment of the impact of a range of factors on development of addictive behaviours, associated risks and long term clinical outcomes.

Length of follow up with a representative sample

The follow up period of 4 years (for clinical data from casenotes) and up to 7 years (for the HIC linked datasets) is a real strength of this study. Many research studies in this field are descriptive, with no longitudinal element. Those that do tend to report on short term outcomes – often less than one year – and this has been cited as a weakness for even the more well-constructed and more rigorous research studies, cited in recent systematic reviews (e.g. Lingford-Hughes et al 2012; Gowing et al 2011; Faggiano et al 2008; Mattick et al 2009). In the context of a chronic relapsing condition in which 5 years' stability is seen as a reasonable indicator of success (Hser, 2007) it is valuable to take a long view of progress to allow an understanding of the natural history of the condition as well as progress through treatment. Indeed the early US longitudinal studies acknowledged that the effectiveness of

individual treatments is difficult to discern in the context of patients in the clinical setting moving through different treatments over time.

While research into short term outcomes give an indication of the challenges experienced in the early stages of treatment, it is clear that those in treatment for longer periods - years or even decades - face different challenges. As clinicians are challenged to evidence the recovery outcomes delivered by OST-M, these deficits in supporting evidence have become a vulnerability. Developing research programmes based on the type of approach used in this thesis would allow the impact of treatment to be more comprehensively and meaningfully assessed.

Outcomes not process

The study has taken care to collect data on a range of treatment outcomes – as well as some process measures. Many studies in the published literature focus simply on treatment processes. On occasion aspects of process can be seen as helpful proxy measures of treatment success – for example retention in treatment has been described as an outcome by many in original research. However, it is important that meaningful valid clinical outcomes are reported if the effectiveness of treatment is to be demonstrated. This study has, for example, shown a disparity between different outcome measures which would be expected to show a high degree of correlation - with self-report of heroin use not consistent with the laboratory findings on drug screens. Previous reviewers have commented on this weakness – and it may be important that researchers – at the very least acknowledge that some of the outcomes measured (perhaps adopted as they are more readily available in the research setting) require closer scrutiny. The outcomes chosen also need to include more socially-orientated measures of success to better inform the developing recovery aspirations of those in treatment across the world.

Ultimately, political and social concern about these programmes reflects, to some extent, an inability to demonstrate measureable change in substance misusers in those aspects of their condition in which society expects to see progress. Academics should consider how best to address these information deficits – by constructing high quality research projects which address specific testable hypotheses in representative samples.

Co-morbidities – novel research

This thesis addresses some common co-morbidities and presents initial findings. Pain and substance misuse are common bedfellows and are problematic clinical syndromes to manage, even when they present in isolation (BPS, 2007). Yet no longitudinal studies in the UK have to date, reported on the relationship between co-morbid pain and substance misuse outcomes. The most recent UK national treatment guidance could only cite cross-sectional descriptive research from the USA (Department of Health et al, 2007). Little longitudinal research exists in the international literature with regard to the relationship between pain and outcomes on OST-M. Although one US study has assessed 1 year outcomes in small sample of OST patients (Ilgen et al 2006), there is a need to duplicate and develop this work in the UK health system.

Other co-morbidities also require more in-depth investigation if their role in the development, maintenance of and recovery from substance misuse is to be understood. A range of mental health problems are common in the substance misuse population – but it is unclear what relevance they have in affecting an individual's ability to recover and progress. Mental disorders could drive the development of substance misuse. Alternately, substance misuse might lead to development of a mental disorder or both conditions could develop in the context of common vulnerabilities. Managing mental disorder in substance misusers could be a crucial area of work required to maximise recovery outcomes for those in OST-M.

The Tayside Methadone Cohort has demonstrated that the routine assessment of these co-morbid conditions can be achieved in standard NHS services and has delivered initial research into their associated outcomes.

Casenote process

The rigour of the casenote follow-up process managed to collect a valuable dataset which was quality assured and only recorded those findings which could be validated. If there were discrepancies or conflicting information in the casenotes, a "missing" status was given in this case. The main disadvantage in this element of the study was the poor quality of the casenotes themselves. Missing information or poor filing meant that in some fields, missing data were recorded. Though a challenge during this project, this issue could be addressed

when the SUMIT project systems are fully operational – as access to higher quality data from SMR forms as well as more use of standardised data collection "forms" in the clinical casenotes would reduce the gaps in data.

SUMIT and data-linkage

The data-linkage process, brought to the study by the SUMIT project and supported by the Health Informatics Centre, has shown that it is possible to develop operational data management systems which have multiple uses but maintain data security. SUMIT was in development during the data collection and analysis phase of this project and early difficulties – such as the lack of availability of key data due to slow development of the NHS MIDIS system – meant that validated data from the Treatment Outcome Profile or SMR25b as well as comprehensive laboratory data and virology information (HIV and Hepatitis C status) could not be included in the analysis.

In future there is an expectation that local authority and third sector data will also be available to make our understanding of each case richer and more complete. Data-sharing agreements are in place to allow this within SUMIT and local authority data from two of the three areas is currently being fed into the HIC safe-haven where it will be available for future analysis. Such an approach will remove the need to use self-report data on housing, criminal justice, parenting/child protection, employability and other key outcome areas potentially impacted on by OST-M treatment.

Comprehensiveness of the analysis – use of multiple regression and cross-validation

Many studies proposing predictive models in the published literature describe less rigorous approaches than that undertaken in this study. Some do perform multiple regression analyses, but often in datasets collected in a single cross-sectional study at one time point, drawing conclusions about the ability of these models to predict future outcome despite no follow up component. Others describe a series of univiariate analyses, essentially mining large datasets to find a range of associations over time. Both approaches are valuable *initial* steps but cannot demonstrate the ability of any predictive model to predict true outcomes in novel data. These pilots should be followed by more systematic research projects, which scrutinize the true predictive value of any associations demonstrated.

This study has adopted a more rigorous method. A systematic literature review informed the selection of independent and dependent variables and testing was underpinned by a series of hypotheses relating to the current understanding of relationships between predictors and outcomes. The findings of these univariate analyses were then used to inform multiple regression analyses which aimed to produce models to predict key, clinically relevant outcomes. This process was in turn exposed to a cross-validation exercise which demonstrated which models were potentially generalisable and which were not. Essentially, the predictive value of the model was tested against the actual outcomes observed in a different/novel sample.

It is an important finding of this study that strong, statistically significant, associations over time, demonstrated in the univariate analyses, did not result in useful strong predictive models. The few weak models developed did not generalise to novel datasets. Using generated data it has been possible to show that the approach taken is valid and would be expected to demonstrate predictive power if it were present.

This is an approach which would greatly improve the evidence base in these complex cases and help us to understand the relative importance of the many factors which may affect outcomes in OST- M patients.

Weaknesses of the study

Study design - Retrospective cohort study

Study design has reflected the way data became available during the study process. Consequently the study design reflected data which had emerged from clinical processes and did not reflect a standard hypothesis – driven prospective study. However, the study did generate testable hypotheses regarding the relationships between factors identified in the evidence base as being influential regarding outcome and undertook initial testing of these hypotheses. These effects were then included in regression analyses. While it could be assumed that some of the factors tested – such as gender or age – may be confounding variables – confounding “by indication” – it is likely that this would have resulted in unacceptable levels of multicollinearity during the regression analyses. Tests did not show

this to be the case. Alternative statistical approaches - such as causal modelling - could be considered which would reduce the likelihood of bias in future studies, allowing identification of confounders and specific hypotheses to be tested.

Clearly the retrospective nature of the study is a weakness. The ideal approach would have been to identify new treatment-naïve patients and follow them-up over time in a prospective longitudinal study. However, it could be argued that one of the key current issues to be addressed in this field is how best to adjust the approach to treatment for those who have been on OST-M for many years. It is this very population – longer term opioid prescribed patients [often described as "parked on methadone"] who are the basis of much of the socio-political debate of the present day. In the recovery literature, it is clear that the current research evidence base is of little value in understanding how best to improve outcomes for this group. The current study would have been strengthened if data on previous treatment or length of time in treatment data were available. Neither of the recent reviews of the recovery literature in substance misusers (Best et al 2010; Bell, 2012) could cite rigorous and convincing research to inform the development of services more likely to deliver progress in treatment beyond the standard harm-reduction outcomes.

Research into how best to improve patient outcomes and progress towards recovery is urgently required. The basic infrastructure in place from this project could be used to generate hypotheses which will be the subject of prospective longitudinal follow up studies in the future to address these issues.

In a future study using similar linked datasets it would be valuable to include other datasets which would offer a richer understanding of each individual's progress through the treatment process.

Baseline sample

There are a number of specific weaknesses in the baseline element of the study.

Representativeness – it was disappointing and surprising that the large baseline sample was found not to be representative of the treatment population as a whole using the demographic variables chosen. This may have reflected the data collection process

during the 2005 review, meaning that a particular group, who were '*hard to reach'* or resistant to attending, were only seen late in the process – by which time the database used in this study was already completed. It is, however, important to recognise that this remains one of the largest OST-M samples described in the UK and world literature. It has been the case in the international literature that sample size or representativeness is difficult to determine. Many publications citing large samples may have a similar issue of selection bias. Indeed, studies such as NTORS and DORIS have clear selection bias as subjects were self-selecting to a particular treatment intervention. In future studies it would be useful, if time was available, to carry out an additional data collection process to access more detailed information on the cases unavailable at baseline.

Missing information – The study was limited by being based on existing data collected in the clinical setting. There was no opportunity in this study to return to collect data on subjects not included in the original clinical exercise- though some data on demographic characteristics was available from HIC linked datasets – allowing tests of representativeness. Some information which would have been very valuable, therefore, was not available without a further data collection exercise which was not feasable. For example: richer data on the duration and outcomes of previous treatment episodes or experiences would have been extremely useful and clearly has relevance; the duration of the current OST-M episode; valid data on criminal justice outcomes; more detailed information on other service involvement – including mental health services. This information clearly has the potential to strongly influence outcome and mechanisms to reduce this deficit would be included in any future study design. If missing data remained a challenge – a common problem with large datasets using routine data – statistical approaches such as a form of imputation of data could be used to resolve these issues. This may be unsuitable for some variables where a large proportion of data were missing. Indeed, since the completion of this pilot, as SUMIT has become the basis for clinical information management in Tayside, much of these data are now available routinely on new cases, if requested and missing data may be less of an issue.

Tools used - Not all the data-collection tools used were ideal. This reflected the "clinical" nature of the initial data collection and the local opinions regarding the tools best suited to the task. For example, a range of screening tools for ADHD in adults were not available in 2004 when the study was being developed. The Current Symptoms Scale

(Barklay & Murphy 1998) – a screening tool for symptoms suggestive of ADHD in children – was recommended by local Child & family Psychiatrists with expertise in the ADHD field as the most useful and adaptable tool available for use with adults at the time which was also quick and easy to use. Since then, new, rapid, adult screening tools have become available – such as the WHO screener (WHO, 2003). The Impact of Events Scale (Horowitz, Wilner & Alvarez, 1979) was recommended by local clinical psychologists, who regularly screened individuals for trauma using this tool in the NHS addiction services. This tool is regularly used to screen for PTSD in a range of populations. It was at the database development and data entry stages of the study that it became apparent that the tool used in the Tayside study had been superseded by an extended version, not used in the local services (Weiss & Marmar, 1997) – making the findings for this work less valuable in the research field.

Process of baseline data collection – lack of complete data - The time pressures during the original review reflected the fact that the process was a clinical one and had clinical drivers and timescales. This meant that the *"clean team"* was forced to reduce the information collected on some subjects. This inevitably reduced available data for some variables.

2009 follow up data – casenote information issues

Though the process of data collection was rigorous and quality assured, the quality of casenotes meant that follow up clinical information was sub-optimal. This meant that the researcher recorded data as "missing" – for example when there was conflicting information in different casenotes on a particular subject. This becomes clear when "hard" data from (for example) laboratory tests is at odds with "self-report" data on illicit drug use.

SUMIT – timing – delays in delivery of key reports: TOP, SMR25b and MIDIS forms

The planning of this study coincided with the creation of the SUMIT system. This system has great promise – but its early stages coincided with the development of the NHS MIDIS electronic casenote system. MIDIS allows clinicians to complete validated forms - such as the *Treatment Outcome Profile* – TOP (NTA, 2007) or *Assessment of Recovery Capital* – ARC (Groshkova, Best & White 2012) - as part of their normal clinical work. It was planned that such data would be collected in 2011 as part of standard clinical processes – making patient identifiable outcome data, collected using validated tools, an element available for the

current thesis. However, the MIDIS data system took much longer to deliver than anticipated – meaning that these data were not available as the research project reached key milestones.

If these data had been available then the 2009 casenote review data would have been seen as a pilot – with the stronger data in place for the final analysis, alongside the already-validated HIC data. It is likely that this would have removed some of the need to interpret ambiguity in the recordings in casenotes and would have ensured more complete datasets. Crucially, it would also have allowed assessment of more recovery-orientated data than was available in normal clinical recording.

HIC late delivery of laboratory results

As well as the MIDIS issues described above, HIC were also challenged by this project regarding availability of data. Project timeframes coincided with key HIC technical staff leaving their posts and delays were experienced in accessing some of the datasets and linking them with TMC. In particular, two datasets planned to be part of the linked dataset were not available when required – GP prescribing data (data is available on all GP prescriptions in Tayside – as was used in McCowan, Kidd & Fahey, 2009) and laboratory tests (which would have included all drug screens undertaken in any setting as well as HIV and Hepatitis C test results). It is clear that use of hard valid measures of outcome would provide stronger evidence of the effectiveness or otherwise of treatment and BBV sero-conversion would be a valuable addition.

Proof of Concept

Clearly the strength of these analyses and the ability to scrutinize more comprehensive and recovery-orientated data would have made the final study outputs more powerful. However, the sample size, length of follow up and strength of much of the data used make this study an important proof-of-concept which may be developed further as a research tool as the clinical systems become more reliable and the data more valid.

Clinical significance of this research

This research has used data from standard NHS clinical systems to develop a comprehensive dataset which has allowed hypotheses to be tested and outcomes to be validated. It has

given access to a large sample of OST-M patients and has followed them up over a long period. The failings of the study, described above, perhaps make the conclusions of this work of less relevance than the implications of the process which has been piloted for the first time here.

Substance misuse is a chronic relapsing condition which can take a lifetime to overcome (Hser, 2007). It is a hazardous activity associated with high levels of morbidity and mortality and is a high profile area of clinical work, often raising political and social debates about how best to manage the problem. Harm reduction has altered the course of substance misuse, and in-particular the impact of injecting heroin use in the UK. This has not been associated with a coordinated drive to consolidate the evidence base, however. Now, as political concerns drive the direction of treatment, yet again, it is more important than ever that good quality research underpins the evolution of clinical practice. This can only occur in the presence of UK-relevant, long-term prospective studies of representative samples in treatment. The process piloted here has the potential to deliver this.

Recommendations for future research

Process

The study has given a proof-of-concept regarding the use of the SUMIT system to bring together relevant data to allow longer term research, addressing a wide range of outcomes, in large representative samples. The deficits reflect the available data and it is clear that, now the SUMIT project has the ability to deliver more consistent data in a range of fields – many more relevant to the recovery agenda – a prospective, longitudinal follow-up study should be planned and delivered.

Hypothesis-driven research

The hypothesis – driven element of this study has re-iterated some of the facts already known from the international literature. The univariate analyses have shown that previous drug history (in this case illicit heroin use at baseline) was associated with 4-7 year substance use outcomes. Higher methadone dose at baseline was associated with better clinical outcomes and certain aspects of service delivery - such as having support from

external agencies or being registered with a GP for General Medical Services – were also associated with positive treatment outcomes. Use of illicit diazepam was associated with poorer outcomes. It is striking that the nature of the service delivery – e.g. primary care or specialist care - and, to some extent, the locality in which a person resided - were associated with considerable variation in outcomes. This inconsistency is a finding which has been commented on by previous researchers (Gossop, Marsden & Stewart, 1998). The longitudinal US studies commented on the importance of the nature of therapeutic delivery. Further study of this factor would be an important element in improving the ability of services to deliver recovery.

Unfortunately, as a result of deficits in the final dataset, the study has not been able to explore in depth the relationship with a number of outcomes, including social outcomes - relating to family life or work. These are areas in which further high quality longitudinal research is required if recovery is to be realised.

Choosing alternative statistical approaches – such as causal modelling – and, where appropriate, considering development of clinical trials (for example in those areas where specific treatment interventions can be tested) would be useful developments of these data-collection systems. Trials could focus on aspects of treatment delivery – setting, therapies offered, etc.

The recovery agenda in the UK requires that research should focus on long term recovery outcomes. This does not mean that harm reduction outcomes are irrelevant. Indeed, some opponents of the move towards recovery seem to see it as, in some way, a challenge to harm reduction and therefore a backward step. It is clear, however, that one important measure of success in the area of recovery would be an ability to demonstrate that new treatment approaches were not associated with deterioration in harm reduction outcomes and achievements.

In Conclusion

The treatment of substance misusers in the UK continues to be in need of a convincing evidence base which can demonstrate that patients in the UK are receiving treatments

which deliver the progress they are seeking and secure socio-political support for the treatments that work.

The Tayside Methadone Cohort study, described in this thesis, has demonstrated that it is possible to use standard clinical data to generate hypotheses, test these using univariate analyses and then use these results to develop a testable predictive model for clinical outcomes in an OST-M sample.

Future research using a similar system – such as the SUMIT system in Tayside – would ensure that research addressed long term outcomes in large representative UK samples. This, in turn, could generate evidence around the recovery agenda and would influence the debate regarding the future balance of substance misuse treatment services in the UK.

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Appendices

List of Appendices

The Appendices section contains:

1. **Rating scales used – plus examples and coding information**
2. **SUMIT project scoping document**
3. **Documents regarding governance of the research process and data management**
4. **Tables from univariate analyses – no significant findings (Chapter 6 – casenote follow up)**
5. **Tables from univariate analyses – no significant findings (Chapter 7 – HIC linked datasets)**
6. **Test cross validation exercise and associated dataset**
7. **Screenshots from online articles on Methadone in Scotland 2012**

Appendix 1 Rating scales used and coding process

Choice of instruments/tools

The project uses data collected using instruments which were chosen by the clinical team for reasons of applicability in the original baseline data-collection exercise. Issues which influenced choice of instrument included its brevity or ease of use, availability for self-completion, familiarity with front line clinicians and evidence of validity and specificity.

Demographic and substance misuse information

The baseline assessment by the "clean team" included elements of the assessment which used standardised instruments with some applicability in research. The tools used, however, primarily reflected standard clinical practice in the clinical service (e.g. the use of the Maudsley Adiction Profile, Injecting Risk Questionnaire and Treatment Perception Questionnaire). A tool was also created to collect basic demographic information in a standardised way during the interviews – as at the time basic information on family circumstances etc. was lacking in the clinical records.

Co-morbidities

Psychiatry and psychology staff requested that specific tools be used to assess common co-morbidities. These included:

- the Impact of Events Scale – IES - (to assess trauma and PTSD and help to direct treatment of trauma issues);
- the Social Phobia Diagnostic Questionnaire – SPDQ - (to assess presence of Social Phobia with a view to offering Cognitive Behavioural Therapy interventions)

Psychiatrists within services were concerned about diagnosis of ADHD in some patients. No routinely – used brief screening tools were available for use with adults in 2005. It was unlikely that staff would have time to administer larger diagnostic tools. The team consulted a local child/adolescent psychiatrist with special expertise in the diagnosis and treatment of ADHD in children and adolescents. The Current Symptoms Scale (CSS) was recommended for the exercise.

Specialist services/professionals, also involved in jointly managing opiate dependent patients with the clinical teams, requested specific assessments. Examples include the Chronic pain questionnaire. This is based on the Brief Pain Inventory (BPI) but also includes specific fields used by local pain services).

The main instruments used are discussed briefly below. Examples/illustrations of the data collection tools are included.

Maudsley Addiction Profile (MAP) Plus Injection Risk (IRQ) and Satisfaction (TPQ)

Introduction

The MAP is a brief, interviewer administered questionnaire which is useful in treatment outcome research. It measures problems in four domains: substance use, health risk behaviour, physical &psychological health, and personal/social functioning. It was developed in the UK for assessing people with drug and alcohol problems and was designed as a core research instrument and to be a resource for treatment services wishing to undertake outcome studies (Marsden et al 1998).

Key advantages of the MAP:

- Developed in the UK - relevant to UK practice
- Brief to administer – when compared to other research tools (e.g. Addiction Severity Index – ASI (McLellan et al. 1980; 1992) and Opiate Treatment Index - OTI (Darke, Ross & Teesson, 1992).
- Can be used repeatedly for outcomes research. All measures can be repeatedly administered at points after an index treatment episode. allowing observation of changes while in treatment
- Previously used in UK research – allowing comparison with existing findings

Domains assessed

Three problem domains are assessed in the MAP:

- drug and alcohol consumption
- injecting and other health risk behaviours (Strang, 1992).
- health problems
- personal/social functioning (Including relationships, employment and crime)

Practical applications

The authors recommend a "modular approach" is taken to allow comparison of data between services and over time. They also endorse use of additional tools to measure needle/syringe sharing - Injecting Risk Questionnaire (Stimson, et al., 1998) and patient satisfaction - Treatment Perceptions Questionnaire - TPQ (Marsden et al., 1998).

Use of the instrument

Detailed information on the use of the MAP, its scoring and analysis is contained within: **Marsden J, Gossop M, Stewart D, Best D, Farrell M, Strang J (1998)** The Maudsley Addiction Profile. A brief instrument for treatment outcome research. Development and User manual. London. National Addiction Centre/Institute of Psychiatry

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MAUDSLEY ADDICTION PROFILE (MAP)

SECTION A: MANAGEMENT INFORMATION

Include the study specific information as required (e.g. participant identification, programme codes; interview point

SECTION B: SUBSTANCE USE

CARD 1

None	1 day only	2 days only	3 days only	1 day a week	2 days a week	3 days a week	4 days a week	5 days a week	6 days a week	Every day	Some other number
0	1	2	3	4	9	13	17	21	26	30	

CARD 2

Oral	Snort/sniff	Smoke/chase	Intravenous	Intramuscular
1	2	3	4	9

a. Enter number of days used in past 30 days [Card 1] – enter "0" for no use:
b. Enter amount used on a typical day in the past 30 days [verbatim]
c. Record route(s) of administration [Card 2]

SUBSTANCE	DAYS USED	AMOUNT USED ON TYPICAL DAY	ROUTE(S)
B1. Alcohol			
B2. Heroin			
B3. Illicit methadone			
B4. Illicit benzodiazepine		Drug:	
B4. Cocaine powder			
B5. Crack cocaine			
B6. Amphetamine			
B7. Cannabis			
B8. Other:			
_____			
_____			

SECTION C: HEALTH RISK BEHAVIOUR

If no illicit drugs injected in the past 30 days, skip to sexual behaviour questions

C1. Days injected drugs in the past 30 days [card 1] _____ Days

C2. Times injected on a typical day in the past 30 days _____ Times

C3. Times injected with a needle/syringe already used by someone else _____ Times

If no penetrative sex in the past 30 days, skip to Section D

C4. Number of people had sex with and not used condom _____ People

C5. Total number of times had sex with and not used condom _____ Times

---

SECTION D: HEALTH SYMPTOMS

CARD 3

Never	Rarely	Sometimes	Often	Always
0	1	2	3	4

D1. How often experienced the following physical health symptoms

	Never (0)	Rarely (1)	Sometimes (2)	Often (3)	Always (4)
a. Poor appetite	☐	☐	☐	☐	☐
b. Tiredness/fatigue	☐	☐	☐	☐	☐
c. Nausea (feeling sick)	☐	☐	☐	☐	☐
d. Stomach pains	☐	☐	☐	☐	☐
e. Difficulty breathing	☐	☐	☐	☐	☐
f. Chest pains	☐	☐	☐	☐	☐
g. Joint/bone pains	☐	☐	☐	☐	☐
h. Muscle pains	☐	☐	☐	☐	☐
I. Numbness/tingling	☐	☐	☐	☐	☐
J. Tremors/shakes	☐	☐	☐	☐	☐

D2. How often experienced the following emotional or psychological symptoms [card 3]

	Never (0)	Rarely (1)	Sometimes (2)	Often (3)	Always (4)
a. Feeling tense	❒	❒	❒	❒	❒
b. Suddenly scared for no reason	❒	❒	❒	❒	❒
c. Feeling fearful	❒	❒	❒	❒	❒
d. Nervousness of shakiness inside	❒	❒	❒	❒	❒
e. Spells of terror or panic	❒	❒	❒	❒	❒
f. Feeling hopeless about the future	❒	❒	❒	❒	❒
g. Feelings of worthlessness	❒	❒	❒	❒	❒
h. Feeling no interest in things	❒	❒	❒	❒	❒
I. Feeling lonely	❒	❒	❒	❒	❒
j. Thoughts of ending your life	❒	❒	❒	❒	❒

SECTION E: PERSONAL/SOCIAL FUNCTIONING

If not in a relationship in the past 30 days, skip to relatives questions

E1. Days had contact with partner in the past 30 days [card 1] Days
(ie. say them or talked on the telephone)

E2. Number of these days were there was conflict with partner Days
(ie. had major arguments)

If not relatives or any contact with relatives in past 30 days, skip to friends questions

E3. Days had contact with relatives in the past 30 days [card 1] Days
(ie. say them or talked on the telephone)

E4. Number of these days were there was conflict with relatives Days
(ie. had major arguments)

If not friends or any contact with friends in past 30 days, skip to Section E7

E5. Days had contact with friends in the past 30 days [card 1] Days
(ie. say them or talked on the telephone)

E6. Number of these days were there was conflict with friends Days
(ie. had major arguments)

E7. Number of days of paid work in past 30 days [card 1] _____ Days

E8. Days missed from work because of sickness or unauthorised absence in the past 30 days _____ Days

E9. Days formally unemployed in the past 30 days _____ Days

CARD 4

Selling drugs	Fraud/forgery	Shoplifting	Theft from a property	Theft from a vehicle	Theft of a vehicle	Other crimes

E10. Crimes committed in the past 30 days [card 4 and card 1]

	Days committed [card 1]	Number of times committed on a typical day [card 2]
a. Selling drugs		
b. Fraud/forgery		
c. Shoplifting		
d. Theft from a property		
e. Theft from a vehicle		
f. Theft of a vehicle		
Other crimes: _____		
_____		
_____		

END OF INTERVIEW

NHS Pain Services Chronic Pain Questionnaire (includes the Brief Pain Inventory – BPI)

Introduction

The Brief Pain Inventory (BPI) is a brief, self-administered questionnaire to assess pain severity. It was developed for use in cancer patients but had been used in published studies of patients with both cancer pain and non-cancer pain. The BPI was shown to be reliable and valid when used in non-cancer pain patients (Keller et al 2004). Cronbach alpha reliability ranges from 0.77 to 0.91

Key advantages of the BPI/NHS data collection tool

The BPI was available in two formats: the BPI short form (used for clinical trials) and the BPI long form, which contains additional detailed descriptive items - e.g. pain descriptors. For brevity's sake and for the patient's ease of use, the short form was recommended as used in local pain services.

Domains assessed

The BPI tool collects information on the severity of pain, location of pain, impact of pain on daily function, pain medications received and amount of pain relief in the past 24 hours or the past week .

Practical applications/Use of the instrument

The BPI can be used in any patients with pain from chronic diseases or conditions such as cancer, osteoarthritis and low back pain, or with pain from acute conditions such as postoperative pain. The questionnaire is completed by either self-report or interview and takes five minutes (short form) or 10 minutes (long form) to complete. There is no scoring algorithm, but "worst pain" or the arithmetic mean of the four *severity items* can be used as measures of pain **severity**. The arithmetic mean of the seven *interference items* can be used as a measure of pain **interference.**

References

Keller S., Bann C.M., Dodd S.L., Schein J., Mendoza T.R. & Cleeland C.S. (2004) Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain *Clinical Journal of Pain,* **20(5)** 309-18.

Cleeland C.S. (1989) Measurement of pain by subjective report. In: Chapman C.R. & Loeser J.D. editors. *Advances in Pain Research and Therapy*, Volume 12: Issues in Pain Measurement. New York: Raven Press

Atkinson T.M., Rosenfeld B.D., Sit L., Mendoza T.R., Fruscione M., Lavene D., Shaw M., Li Y., Hay J., Cleeland C.S., Scher H.I., Breitbart W.S. & Basch E. (2011) Using confirmatory factor analysis to evaluate construct validity of the Brief Pain Inventory (BPI). *Journal of Pain Symptom Management,* **41(3),** 558-565

STUDY ID# _____ HOSPITAL # _____

DO NOT WRITE ABOVE THIS LINE

Brief Pain Inventory (Short Form)

Date: _____/_____/_____ **Time:** _____

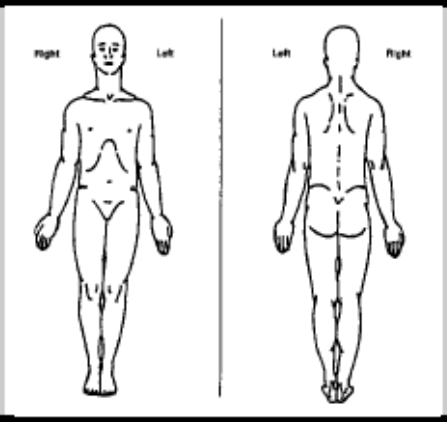
Name: _____ _____ _____

Last First Middle Initial

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these every-day kinds of pain today?

1. Yes 2. No

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3. Please rate your pain by circling the one number that best describes your pain at its worst in the last 24 hours.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

4. Please rate your pain by circling the one nuimber that best describes your pain at its least in the last 24 hours.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

5. Please rate your pain by circling the one number that best describes your pain on the average.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

6. Please rate your pain by circling the one number that tells how much pain you have right now.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

7. What treatments or medications are you receiving for your pain?

8. In the last 24 hours, how much relief have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
No Relief										Complete Relief

9. Circle the one number that describes how, during the past 24 hours, pain has interfered with your:

A. General Activity

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

B. Mood

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

C. Walking Ability

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

D. Normal Work (includes both work outside the home and housework)

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

E. Relations with other people

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

F. Sleep

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

G. Enjoyment of life

0	1	2	3	4	5	6	7	8	9	10
Does not Interfere										Completely Interferes

General health Questionnaire – 28 item (GHQ28)

Introduction

The GHQ is a self-administration screening tool designed to detect probable psychiatric disorder in primary care settings (Goldberg, 1972). The tool has evolved in response to demand from researchers as well as greater understanding of the role of its components - resulting in the development of the Scaled GHQ (GHQ28) which has become a popular screening tool in a range of settings (Goldberg & Hillier, 1979).

Key advantages of the GHQ28

The GHQ 28 is a shorter version of the original 60 item GHQ questionnaire but has also been shown to more clearly address the 4 main components.

Domains assessed

Depression; anxiety; social performance; somatic complaints

Practical applications/use of the instrument

Self -completion questionnaire – used in a wide range of clinical settings and well tolerated by patient groups. In drug users potential issue of literacy. Short questionnaire allows time to support completion.

References

Goldberg D.P. (1972) *The Detection of Psychiatric Illness by Questionnaire*. London: Oxford University Press.

Goldberg D.P. & Hillier V.F. (1979) A scaled version of the General health Questionnaire. *Psychological Medicine ,* **9:** 139-145

Goldberg D. & Williams P. (1991) *A User's Guide to the General Health Questionnaire***.** Windsor: NFER-Nelson

General Health Questionnaire (GHQ-28)

Please read this carefully:We would like to know if you have had any medical complaints and how your health has been in general, over the last few weeks. Please answer ALL the questions by ticking the answer which best applies to you. Remember that we want to know about PRESENT and RECENT complaints, not those that you have had in the past. It is important that you try to answer ALL questions.

Have you recently…..

A1.	**Been feeling well and in good health?**	Better than usual	Same as usual	Worse than usual	Much worse than usual
A2.	**Been feeling in need of a good tonic?**	Not at all	No more than usual	Rather more than usual	Much more than usual
A3.	**Been feeling run down and out of sorts?**	Not at all	No more than usual	Rather more than usual	Much more than usual
A4.	**Felt that you are ill?**	Not at all	No more than usual	Rather more than usual	Much more than usual
A5.	**Been getting pains in your head?**	Not at all	No more than usual	Rather more than usual	Much more than usual
A6.	**Been getting a feeling of tightness or pressure in the head?**	Not at all	No more than usual	Rather more than usual	Much more than usual
A7.	**Been having hot or cold spells?**	Not at all	No more than usual	Rather more than usual	Much more than usual
B1.	**Lost much sleep over worry?**	Not at all	No more than usual	Rather more than usual	Much more than usual
B2.	**Having difficulty staying asleep once you are off?**	Not at all	No more than usual	Rather more than usual	Much more than usual
B3.	**Felt constantly under strain?**	Not at all	No more than usual	Rather more than usual	Much more than usual
B4.	**Been edgy and bad tempered?**	Not at all	No more than usual	Rather more than usual	Much more than usual
B5.	**Been getting scared and panicky for no good reason?**	Not at all	No more than usual	Rather more than usual	Much more than usual
B6.	**Found everything getting on top of you?**	Not at all	No more than usual	Rather more than usual	Much more than usual
B7.	**Been feeling nervous and strung-up all the time?**	Not at all	No more than usual	Rather more than usual	Much more than usual

PLEASE TURN OVER

Have you recently…..

C1.	**Been managing to keep yourself busy and occupied?**	More so than usual	Same as usual	Rather less than usual	Much less than usual
C2.	**Been taking longer you over things you do?**	Quicker than usual	Same as usual	Longer than usual	Much longer than usual
C3.	**Felt on the whole you were doing things well?**	Better than usual	About the same	Less well than usual	Much Less Well
C4.	**Been satisfied with the way you carry out a task?**	More satisfied	About the same as usual	Less satisfied than usual	Much less capable
C5.	**Felt that you are playing a useful part in things?**	More so than usual	Same as usual	Less so than usual	Much less useful
C6.	**Felt capable of making decisions about things?**	More so than usual	Same as usual	Less so than usual	Much less capable
C7.	**Been able to enjoy your normal day-to -day activities?**	More so than usual	Same as usual	Less so than usual	Much less than usual
D1.	**Been thinking of your self as a worthless person?**	Not at all	No more than usual	Rather more than usual	Much more than usual
D2.	**Felt that life is entirely hopeless?**	Not at all	No more than usual	Rather more than usual	Much more than usual
D3.	**Felt that life is not worth living?**	Not at all	No more than usual	Rather more than usual	Much more than usual
D4.	**Thought of the possibility that you might do away with yourself?**	Definitely not	I don't think so	Has crossed my mind	Definitely have
D5.	**Found at times you couldn't do anything because your nerves were so bad?**	Not at all	No more than usual	Rather more than usual	Much more than usual
D6.	**Found yourself wishing you were dead and away from it all?**	Not at all	No more than usual	Rather more than usual	Much more than usual
D7.	**Found that the idea of taking your own life kept coming into your mind?**	Definitely not	I don't think so	Has crossed my mind	Definitely has

Social Phobia Diagnostic Questionnaire (SPDQ)

Introduction

Social phobia is an intense, irrational fear of social situations. Most sufferers fear only specific social situations, though those with generalized social phobia fear most social encounters. The DSM-IV (Diagnostic and Statistical Manual; 4th Ed.) provides a specific list of diagnostic criteria for social phobia. These are listed as:

- Marked and Persistent Fear: A persistent, intense fear of social situations, due to a fear of showing anxiety symptoms or acting in an embarrassing way.
- Anxiety Response: Exposure to the situation results in an intense anxiety reaction
- Recognition That Fear is Irrational: Adults with social phobias recognize that their fear is out of proportion.
- Avoidance or Distress: The sufferer goes out of his or her way to avoid the situation which can only be endured with great distress.
- Life-Limiting: The phobia severely impacts the sufferer's life.
- Six Months Duration: In children and teens, the phobia has lasted at least six months.
- Not Caused by Another Disorder: Many anxiety disorders and physical illnesses cause similar symptoms.
- Not Related to a specific *Physical Disorder*: If the sufferer also has a physical condition, the phobic response is not limited to anxiety about displaying the effects of that condition in public.

Key advantages of the SPDQ

The SPDQ is a brief self-report questionnaire which takes only a few minutes to complete and can help diagnose social phobia. It has been shown to be reliable and valid in a number of populations (Newman et al, 2003)

Domains assessed

The SPDQ addresses questions relating to the DSM1V criteria above. The scores are collated to give a Fear score, avoidance score and a total score of overall severity

Practical applications/Use of the instrument

Can be completed by the subject or at interview.

References

Newman M.G., Kachin K.E., Zuellig A.R., Constantino M.J. & Cashman-McGrath L (2003) The social phobia diagnostic questionnaire: preliminary validation of a new self-report diagnostic measure of social phobia. *Psychological Medicine,* **33(4),** 623-635

SPDQ

1. In social situations where it is possible that you will be noticed or evaluated by other people, do you feel excessively nervous, fearful or uncomfortable? Yes___ No___

2. Do you tend to be overly worried that you may act in a way that might embarrass or humiliate yourself in front of other people, or that others may not think well of you? Yes___ No___

3. Do you try to avoid social situations? Yes___ No___

Below is a list of some situations that are fear provoking for some people. Rate the severity of your anxiety and avoidance on the following scales:

	0=No fear 1=Mild fear 2=Moderate fear 3=Severe fear 4=Very severe fear (a) fear	0=Never avoid 1=Rarely avoid 2=Sometimes avoid 3=Often avoid 4=Always avoid (b) avoidance
4. Parties	0 1 2 3 4	0 1 2 3 4
5. Meetings	0 1 2 3 4	0 1 2 3 4
6. Becoming the focus of attention	0 1 2 3 4	0 1 2 3 4
7. Dating circumstances	0 1 2 3 4	0 1 2 3 4
8. Meeting people in authority	0 1 2 3 4	0 1 2 3 4
9. Speaking with people in authority	0 1 2 3 4	0 1 2 3 4
10. Saying 'no' to unreasonable requests	0 1 2 3 4	0 1 2 3 4
11. A first date	0 1 2 3 4	0 1 2 3 4
12. Asking others to do something differently	0 1 2 3 4	0 1 2 3 4
13. Being introduced	0 1 2 3 4	0 1 2 3 4
14. Initiating a conversation	0 1 2 3 4	0 1 2 3 4
15. Keeping a conversation going	0 1 2 3 4	0 1 2 3 4
16. Giving a speech	0 1 2 3 4	0 1 2 3 4
17. Others judging you	0 1 2 3 4	0 1 2 3 4
18. Being under observation by others	0 1 2 3 4	0 1 2 3 4
19. Being teased	0 1 2 3 4	0 1 2 3 4

20. Do you tend to experience fear each time you are in feared social situations? Yes___ No___

21. Does the fear come on as soon as you encounter feared social situations? Yes___ No___

22. Would you say that you social fear is excessive or unreasonable? Yes___ No___

23. Circle the degree to which your social fear interferes with your life, work, social activities, family, etc.?

0	1	2	3	4
No Interference	Mild	Moderate	Severe	Very Severe/Disabling

24. How distressing do you find social fear? (Circle one)

0	1	2	3	4
Not Distressing	Mild	Moderately	Severely	Very Severely

25. Has what you have been able to achieve in your job or in school been negatively effected by your social fear? Yes___ No___

Current Symptoms Scale (CSS)

Introduction

This diagnosis of attention-deficit/hyperactivity disorder (ADHD) in adults can be a challenging process because it includes making judgments based on clinical interviews, rating scale results, informant ratings, and objective supporting. Patient evaluation should gather information on: 1. severity /frequency of symptoms; 2. establishment of childhood onset of symptoms; 3. chronicity and pervasiveness of symptoms; 4. the impact of symptoms on major life activities (Barklay & Murphy 1998).

Many rating scales may be helpful, including: the Conners' Adult ADHD Rating Scale; the Brown Attention-Deficit Disorder Scale for Adults; the Wender Utah Rating Scale, the ADHD Rating Scale and ADHD Rating Scale-IV; the Current Symptoms Scale, and the recently-developed Adult ADHD Self-Report Scale-v 1.1 Symptom Checklist. However, specialists agree that more research is needed to establish the usefulness of self-administered rating scales compared with investigator-administered scales (Murphy & Adler 2004).

Key advantages of the CSS

The CSS was included in the battery of tests as it was (in 2004) one of only a few self-completion questionnaires seen as a useful screener - which could be completed rapidly by patients and was free to use in the public domain.

Domains assessed

There are 3 sections in the questionnaire – assessing inattention and hyperactivity as well as the degree of impairment. There are 4 possible answers - Never/Rarely=0; Sometimes=1; Often=2; Very Often=3. There is an assessment of when problems began (though clearly there is no possibility of recording collateral history).

Practical applications

This tool has been used a s a useful screening tool in a range of populations in the past.

Use of the instrument

“A” scores (relating to symptoms experienced) are calculated into A-odd (inattentive – 9 questions) and A- even (hyperactive/impulsive – 9 questions). High scores in these areas indicate that type of ADHD may be present. An A-total score adds these two components. If there are 6/9 questions answered and high scores chosen for both odd/even questions, then the individual likely to have combined ADHD. The “B” score (relating to impairment) is given as a total. If an individual is scoring 3 points (very often) on at least 2 questions there is impairment in at least 2 areas of life

References

Barkley R.A. & Murphy K.R. (1998) Attention-Deficit Hyperactivity Disorder: A Clinical Workbook, 2nd ed. New York: Guilford Publications.

Murphy K.R. & Adler L.A. (2004) Assessing attention-deficit/hyperactivity disorder in adults: Focus on rating scales. *Journal of Clinical Psychiatry*, **65 (Suppl 3),** 8-11.

CURRENT SYMPTOMS SCALE—SELF-REPORT FORM

Name_____ Date_____

Instructions: Please circle the number next to each item that best describes your behavior *during the past 6 months.*

Items:	Never or rarely	Sometimes	Often	Very often
1. Fail to give close attention to details or make careless mistakes in my work	0	1	2	3
2. Fidget with hands or feet or squirm in seat	0	1	2	3
3. Have difficulty sustaining my attention in tasks or fun activities	0	1	2	3
4. Leave my seat in situations in which seating is expected	0	1	2	3
5. Don't listen when spoken to directly	0	1	2	3
6. Feel restless	0	1	2	3
7. Don't follow through on instructions and fail to finish work	0	1	2	3
8. Have difficulty engaging in leisure activities or doing fun things quietly	0	1	2	3
9. Have difficulty organizing tasks and activities	0	1	2	3
10. Feel "on the go" or "driven by a motor"	0	1	2	3
11. Avoid, dislike, or am reluctant to engage in work that requires sustained mental effort	0	1	2	3
12. Talk excessively	0	1	2	3
13. Lose things necessary for tasks or activities	0	1	2	3
14. Blurt out answers before questions have been completed	0	1	2	3
15. Am easily distracted	0	1	2	3
16. Have difficulty awaiting turn	0	1	2	3
17. Am forgetful in daily activities	0	1	2	3
18. Interrupt or intrude on others	0	1	2	3

[cont.]

How old were you when these problems with attention, impulsiveness, or hyperactivity first began to occur? _____years old

To what extent do the problems you may have circled on the previous page interfere with your ability to function in each of these areas of life activities?

Areas:	Never or rarely	Sometimes	Often	Very often
In my home life with my immediate family	0	1	2	3
In my work or occupation	0	1	2	3
In my social interactions with others	0	1	2	3
In my activities or dealings in the community	0	1	2	3
In any educational activities	0	1	2	3
In my dating or marital relationship	0	1	2	3
In my management of my money	0	1	2	3
In my driving of a motor vehicle	0	1	2	3
In my leisure or recreational activities	0	1	2	3
In my management of my daily responsibilities	0	1	2	3

Instructions: Again, please circle the number next to each item that best describes your behavior *during the past 6 months.*

Items:	Never or rarely	Sometimes	Often	Very often
1. Lose temper	0	1	2	3
2. Argue	0	1	2	3
3. Actively defy or refuse to comply with requests or rules	0	1	2	3
4. Deliberately annoy people	0	1	2	3
5. Blame others for my mistakes or misbehavior	0	1	2	3
6. Am touchy or easily annoyed by others	0	1	2	3
7. Am angry or resentful	0	1	2	3
8. Am spiteful or vindictive	0	1	2	3

Impact of Events Scale (IES)

Introduction

The Impact of Event Scale (IES) is a 15 item questionnaire that measures the amount of distress a person associates with a specific event. It was developed 1979 (Horowitz, Wilner & Alavarez, 1979). In 1997, the scale was revised by adding seven additional questions (Weiss & Marmar 1997). The earlier version (used and proposed by the clinical psychology staff in the substance misuse services locally) was used in this study.

Key advantages of the IES

The test is used to measure the impact experienced following a traumatic event. Studies show the IES can be valuable in spotting both trauma and less intense forms of stress and is capable of detecting Post Traumatic Stress Disorder (PTSD). It is recommended for use in a clinical setting as a measure of symptom severity or symptom change. It is a descriptive rather than a diagnostic tool. It is well tolerated by patients and has been used as a screening tool in a range of general populations.

Practical applications & Use of the instrument

The IES is a self-completion questionnaire. It consists of 15 questions and has two subscales which look separately at *intrusion* and *avoidance*. Together these scales give a total impact of event score and serve as a useful indicator of the extent to which a traumatic event is reverberating in the mind.

There are 4 possible responses to this questionnaire- not at all, rarely, sometimes, often. Intrusion, avoidance and total scores are recorded. A *total score* cut-off of 24 can be a valuable indicator of PTSD "caseness".

References

Horowitz, M. Wilner, N. & Alvarez, W. (1979) Impact of Event Scale: A measure of subjective stress. *Psychosomatic Medicine,* **41,** 209-218.

Weiss, D.S., & Marmar, C.R. (1997). The Impact of Event Scale-Revised. In J.P. Wilson & T.M. Keane (Eds.), Assessing Psychological Trauma and PTSD (pp.399-411). New York: Guilford.

Creamer, M. Bell, R. & Falilla, S. (2002). Psychometric properties of the Impact of Event Scale-Revised. *Behaviour Research and Therapy*, **41,** 1489-1496.

IMPACT OF EVENTS SCALE

On (date) _____ you experienced a motor vehicle accident.
Below is a list of comments made by people after stressful life events. Please check each item, indicating how frequently these comments were true for you DURING THE PAST SEVEN DAYS. If they did not occur during that time, please mark the "not at all" column.

1. I thought about it when I didn't mean to.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

2. I avoided letting myself get upset when I thought about it or was reminded of it.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

3. I tried to remove it from memory
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

4. I had trouble falling asleep or staying asleep, because pictures or thoughts about it came into my mind.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

5. I had waves of strong feelings about it.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

6. I had dreams about it.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

7. I stayed away from reminders of it.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

8. I felt as if it hadn't happened or it wasn't real.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

9. I tried not to talk about it.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

10. Pictures about it popped into my mind.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

11. Other things kept making me think about it.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

12. I was aware that I still had a lot of feeling about it, but I didn't deal with them.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

13. I tried not to think about it.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

14. Any reminder brought back feelings about it.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

15. My feelings about it were kind of numb.
- ❑ Not at all
- ❑ Rarely
- ❑ Sometimes
- ❑ Often

Appendix 1.2 Tayside Methadone Cohort - Coding for Databases

Data entry staff were given the following coding guidance to ensure consistency of data entry

---

General scores
0 = No
1 = Yes
88 = Not known/not applicable
99 = Missing information (if no information has been given and it ought to have been
IDCODE = for each database- enter 10 digit chi number [converted to prochi]
Date refers to date of assessment – enter as dd.mm.yy only

Demographic information form

Id code (chi)	10 digits
Date (date of assessment)	dd.mm.yy
Dob (date of birth)	dd.mm.yy
Age put in age (work out from date of assessment and DOB)	
Sex (sex)	1 = male2 = female

Q1. How long have you lived at your present address?
1 = less than 1 month; 2 = less than 6 months; 3 = less than 1 year; 4 = less than 3 years
5 = less than 5 years; 6 = 5 or more years; 88 = not known

Q2. How often do you usually change address?
0 = never; 1 = sometimes; 2 = frequently; 3 = very frequently; 88 = not known

Q3. Do you live:0 = alone; 1 = with partner; 2 = with family; 3 = with friends; 4 = hostel
88 = not known

Q4a. Do you have any children?
0 = no; 1 = yes; 88 = not known
Q4b. If yes, how many? Write in number e.g 3
Q4c. Male or Female? Write in (e.g 2 males and 1 female)
Q4d. Age of children. Write in e.g 8, 16, 20
Q4e – 4j Put in age ranges of children for each child
0-4 years=0; 5 -12 years=1; 13 – 18years=2; 18 + years=3; Not applicable 88
(e.g if 3 children aged 1, 8 and 19 then - 4e = 0, 4f = 1 and 4g = 3. 4h and 4i = 88)

Q5a. Do your children live with you? 0 = no; 1 = yes; 88 = not known
Q5b.If your children don't live with you, do you have access?0 = no; 1 = yes
88-not known/not applicable

Q6a. Do you have any physical problems? 0 = no; 1 = yes; 88 = not known

Q6b. If yes, what are these? Write in response(s) e.g back pain
Q6c. Do you currently have any mental health problem? 0=no; 1=yes; 88 = not known
Q6d. If yes, what are these? Write in response(s)e.g PTSD

Q7a. Are you receiving any treatment for physical condition?0=no; 1=yes; 88 = not known
Q7b. If yes, please detail treatments Write in response(s) e.g physio
Q7c. Are you receiving any treatment for MH problems? 0 = no; 1 = yes; 88 = not known
Q7d. If yes, please detail treatments Write in response(s) e.g anti-depressants

Q8a. Do you or your children receive support from any other agency? 0=no; 1=yes; 88 = NK
Q8b. If yes, which agency? Write in response(s) e.g SW

Q9. How do you rate your writing, reading and numeracy skills? 0=not good; 1=OK; 2 = good
Q10. If answered 'not good' are you interested in improving? 0=no;1=yes;2=don't know; 88=Not known/not applicable

Q11. What level of education have you reached? 0=none; 1= O'Grade; 2=apprentice/C&G/SVQ; 3 = Higher; 4 = College/University

Q12a. Have you ever had a head injury?0 = no; 1 = yes; 88 = not known
Q12b. If yes, did you attend hospital? 0 = no; 1 = yes; 88 = not known

Q13a. Have you ever been unconscious?0 = no; 1 = yes; 88 = not known
Q13b. Did you receive medical attention?0 = no; 1 = yes; 88 = not known

Maudsley Addiction Profile (MAP)

Id code
Date of assessment

4 columns added to account for certificate of analysis screening tests. (These are stapled on the front of assessment pack).

Benzodiazepines/ Methadone/ Opiates/ Morphine- Specific.
Codes- 0 = No, 1 = Yes 2 = Not screened for substance.
If screen has not been done e.g individual only screened for 2/4 use code 2 for not screened.

Section B: Substance Use

Codes are as follows:

Card 1

None	1 day only	2 days only	3 days only	1 day a week	2 days a week	3 days a week	4 days a week	5 days a week	6 days a week	Every day	Other number
0	1	2	3	4	9	13	17	21	26	30	

Card 2

Oral	Snort/Sniff	Smoke/Chase	Intravenous	Intramuscular
1	2	3	4	9

Enter number of dates used in past 30 days. Enter '0' for none (Card 1) . Enter amount used on a typical day in the past 30 days (verbatim). Record routes of administration (Card 2)

SUBSTANCE	DAYS USED	AMOUNT USED ON TYPICAL DAY	ROUTE(S)
B1. Alcohol			
B2. Heroin			
B3. Illicit Methadone			
B4. Cocaine Powder			
B5. Crack Cocaine			
B6. Amphetamine			
B7. Cannabis			
B8. Prescribed methadone			
B9. Prescribed DF118's			
B10. Illicit DF118's			
B11. Morphine			
B12. MST			
B13. Diconal			
B14. Amphetamine Base			
B15. Ecstasy			
B16. Prescribed diazepam			
B17. Illicit Diazepam			
B18. Prescribed Temazepam			
B19. Illicit Diazepam			
Other:			

Review team have not consistently used Card 1 for scoring, therefore this section cannot be scored according to MAP instructions.

Section C: Health Risk Behaviour

If no illicit drugs injected in past 30 days enter '0' in C1- C3. Use response from card 1 to complete C1 (see above).If some answers have not been completed e.g if C1 has been answered but C2, C3 have not, enter 88 for 'not known.'

If no penetrative sex in past 30 days enter '0' in C4 and C5.If some answers have not been completed enter 88 for 'not known'

Section D: Health Symptoms

Card 3

Never	Rarely	Sometimes	Often	Always
0	1	2	3	4

D1: How often experienced the following physical health symptoms. (total score 0-40)
D1score. Total scores from D1a- D1j and add to get total.

A-J has 5 possible responses (Card 3). Each should be completed with one of the 5 choices. If not completed enter '99' for missing response.

D2: How often experienced the following emotional or psychological symptoms.(total score 0-40). D2scrore. Total score from D1a – D1j and add to get total.

A-J has 5 possible responses (Card 3). Each should be completed with one of the 5 choices. If not completed enter '99' for missing response.

Section E: Personal/Social Functioning

Card 1

None	**1 day only**	**2 days only**	**3 days only**	**1 day a week**	**2 days a week**	**3 days a week**	**4 days a week**	**5 days a week**	**6 days a week**	**Every day**	**Other number**
0	**1**	**2**	**3**	**4**	**9**	**13**	**17**	**21**	**26**	**30**	

If not in a relationship enter '0' in E1 and E2.

Use Card 1 responses to complete responses for E1-E7.

E8 and E9 should be written in verbatim e.g days formally unemployed (E9) write 30.

E10: Crimes committed in past 30 days.

Card 1

None	1 day only	2 days only	3 days only	1 day a week	2 days a week	3 days a week	4 days a week	5 days a week	6 days a week	Every day	Other number
0	**1**	**2**	**3**	**4**	**9**	**13**	**17**	**21**	**26**	**30**	

Responses for this question should use Card 1 for 'days committed' from A-F and other crimes.
Responses for 'number of times committed on a typical day' should be written in verbatim.

Total score for E1-E6 are totalled by calculating conflict days/contact days x100 = % time in contact. Add score to columns partnerc (E1-E2), relationc (E3- E4) and friendco (E5-E6).

General health Questionnaire (GHQ28)

The GHQ scores can be interpreted in 3 ways:

1. Severity of psychological disorder
2. Estimate prevalence of psychiatric illness
3. Indicator of morbidity.

Complete: Idcode; Date

There are 4 sections in the GHQ: A 1-7, B1-7, C 1-7 and D 1-7.
Total of 28 questions in this version. There are 4 possible answers per question.

e.g A1 ' been feeling perfectly well and in good health? esponses :- better than usual, same as usual, worse than usual , much worse than usual.

All responses in all sections should be score 0, 1, 2, 3 (Likert scale) from left to right.
Better than usual=0; Same as usual=1;Worse than usual=2;Much worse than usual=3
Total score for each section will be between 0 and 21.
Each section score should be totalled and added to variable ascore, bscore, cscore, dscore and total score.

ADHD (current symptoms scale- self report - CSS)

Id code
Date of assessment

On database there are 3 sections. There are 4 possible answers. Each response should be circles and coded in the database as follows:

Never/Rarely=**0;** Sometimes=**1;** Often=**2;** Very Often=**3If no response is indicated enter '99' for missing.**

A1-18- This section asks individual to circle the number next to each item that best describes your behaviour.

B 0- this refers to when problems began. ' I was approximately ____ years old' Complete this by entering age, if given. If not, enter 99 for missing information.

B1- 10 – To what extent do the problems you may have circled on the previous page interfere with your ability to function in each of these areas of life activities

C1-9 – List of items that describes people. Please tick the boxes that best applies to you.

SCORING

A scores are calculated into A-odd (inattentive) and A- even (hyperactive/impulsive)

So in A-odd column add up all odd scores and total. There are 9 odd questions
In A-even column add up all even scores and total. There are 9 even questions
In A-total column add scores for both odd and even. If there are 6/9 questions answered and high scores chosen for both odd/even questions, individual likely to have combined ADHD.

B-total (impairment) are all scores from b1- 10. Total all scores given. If individual is scoring 3 points (very often) on at least 2 questions there is impairment in at least 2 areas of life.

Injecting Risk Questionnaire (IRQ)

Idcode
Date of assessment

There are 18 questions in this questionnaire. Apart from Q1 and Q18 all questions have 4 possible responses and are coded as set out below e.g (Q2).

If Q1 is answered 'no' which is 0, complete all other questions by inputting '88' – not known/not applicable.

Q1. Have you injected a drug during the last 4 weeks? No=0; Yes=1
e.g Q2. During the last 4 weeks, how often have you shared Injecting equipment?

Answer all other questions Q2-Q17 using same codes:
Never=0; Rarely=1; Sometimes=2; Frequently=3; Not known/not applicable=88

Q18. During last 4 weeks, with how many *different* people have youd one any of the things on this page? Complete this by inputting verbatim response e.g . 2.

Total score. Calculate the scores from questions 2, 4 – 17. Total will be from 0 –45. High score = greater injecting risk.

Id code
Date of assessment

CHRONIC PAIN ESTABLISHED FROM Q2 IF LONGER THAN ONE YEAR.

Q1. Do you have a problem with pain? No=0; Yes=1; Not known=88
Q2. For how long have you had this pain? Enter response e.g months/years
Q3. Where is your body do you have this pain?
Head=0; Neck=1; Shoulders=2; Upper back=3; Lower back=4; Chest=5; Abdomen=6; Liver=7; Arms=8; Hand(s)=9; Legs=10; Feet=11; Not known/not stated=88
Q4. What do you think caused this pain? Trauma=0; Disease=1; Drug Use=2; other=3; NK=88
Q5. Have you ever seen/are you seeing a doctor for this pain? No=0; Yes=1; Not known=88
Q6. Which doctor did you see? GP=0; Pain specialist=1; Other consultant =2; NK=88
* The name of the doctor is likely to be given Therefore to code appropriately is a question of Interpretation – check with BK.
Q6b. When was this? Type in date e.g. mmm.yy (APR 02)
Q7. Do you feel your pain problem was taken seriously?No=0; Yes =1; Not known=88
Q8a. What are you taking for this pain? PRESCRIBED
Opiates=0; Benzo's=1; NSAID's=2; Anti-inflammatories=3; Other=4 (list)
No prescribed drugs= 5; 2 prescribed drugs =6; 3 or more prescribed drugs=7
Not known=88
Q8b. Non-prescribed drugs: Opiates=0; Benzo's=1; NSAID's=2; Anti-inflammatories=3;
Other= 4; No non- prescribed drugs= 5; 2 non prescribed drugs=6;
3 or more non- prescribed drugs=7; Not known=88
Q8c. Over the counter (OTC) drugs : Opiates=0; Benzo's=1; NSAID's=2;
Anti-inflammatories=3; Other=4; No OTC drugs=5; 2 OTC drugs=6
3 or more OTC drugs=7; Not known= 88
Q9. Is any of this pain due to withdrawal from drugs?No=0; yes=1; Not known=88
Q10a. Did you first have a pain problem which lead you to use drugs/medication?
No=0; Yes=1; Not known=88
Q10b. Did you have a problem with drug/medication use, then developed pain?
No=0; Yes=1; Not known=88
Q10c. Do you feel that your drug/medication use and pain are unrelated?
No=0; Yes=1; Not known=88
Q11. Does your pain problem cause you disturbed sleep? No=0; Yes=1; NK=88
Q12a. Does your pain problem affect your ability to go about daily activities?
No=0; Yes=1; Not known=88
Q12b. If yes, how does it affect you? Work= 0; Shopping=1; Walking=2; Standing =3
Self care=4; Social activities=5; multiple activities=6; Not known=88
Q13. Please indicate pain intensity (0-100) Input as a number e.g 60

Treatment Perceptions Questionnaire (TPQ)

ID codeDate of assessment
Specify where the patient receives his/her main treatment: TDPS= ;1; GP=2; other=3

	Strongly Agree	**Agree**	**Disagree**	**Strongly Disagree**
Question 1	0	1	2	3
Question 2	0	1	2	3
Question 3	3	2	1	0
Question 4	3	2	1	0
Question 5	3	2	1	0
Question 6	0	1	2	3
Question 7	3	2	1	0
Question 8	3	2	1	0
Question 9	0	1	2	3
Question 10	0	1	2	3
Question 11	0	1	2	3
Question 12	0	1	2	3
Question 13	3	2	1	0
Question 14	3	2	1	0

Total scores 0-42.
HIGHER TOTAL SCORE REFLECTs GREATER SATISFACTION WITH TREATMENT.

Stress/ PTSD (Impact of Events Scale - IES)

IdcodeDate of assessment
88 – not known (i.e if some answers are missing)

The IES used here consists of 15 questions and has two subscales which look separately at *intrusion* and *avoidance*. Together these scales give a total impact of event score and serve as a useful indicator of the extent to which a traumatic event is reverberating in the mind. Recommended for use in a clinical setting as a measure of symptom severity or symptom change. It is a descriptive rather than a diagnostic tool.

In a general stress clinic population, the intrusion subscale mean was 21.4 (SD 9.6) and avoidance subscale mean was 18.2 (SD 10.8) N.B this can be taken as a guide.

There are 4 possible responses to this questionnaire- not at all, rarely, sometimes, often.

Intrusion questions are Q1, Q4, Q5, Q6, Q10, Q11, Q14
Avoidance questions are Q2, Q3, Q7, Q8, Q9, Q12, Q13, Q15

The responses for all questions are: Not at all= 0; Rarely=1; Sometimes= 3; Often= 5

There are 3 stand alone questions 1,2, 3 (labelled a,b,c) on the database. No = 0, yes= 1

Total score for intrusion (questions Q1, Q4, Q5, Q6, Q10, Q11, Q14) put in INTSCOR column
Total score for avoidance (questions Q2, Q3, Q7, Q8, Q9, Q12, Q13, Q15) put in AVOSCOR
Total score to be inputted into TOTALSCO column all at end of database.

Social Phobia Diagnostic Questionnaire (SPDQ)

Id codeDate of assessment

There are 3 primary questions to be completed. If 'yes' is answered to any of these first 3 questions, continue and input particular choices for the rest of questionnaire. If 'no' to first 3 questions input '88' for not known/not applicable for all remaining questions.

The database is numbered A, B and C for initial questions. Followed by q1- 23. There are parts A and B for questions 1-17 inclusive as demonstrated on questionnaire form.

Responses are **part A (Fear)**	**part B (avoidance)**
0 – no fear	0 – never avoid
1 – mild fear	1 – rarely avoid
2 – moderate fear	2 – sometimes avoid
3 – severe fear	3 – often avoid
4 – very severe fear	4 – always avoid

However, the numbering is odd. It jumps from 10 to 12. Therefore database has followed same numbering and omitted number 11 **(be careful)!!**

Q18- 20 and Q23 have yes/no/ not known/N.A choice
Q21 and Q22 have 5 possible answers (and also 88- not known/NA)

SCORING

The SPDQ is scored using a sum total response. This scoring system was devised in an attempt to create a score that would best enable detection of the presence of social phobia.

To create total score all 'yes' answers (A, B, C and q 18, 19, 20) to be computed in TOTALYN column

A – in social situations where it is possible that you will be noticed or evaluated by others do you feel excessively nervous, fearful or uncomfortable?

B – Do you tend to be overtly worried that you may act in a way that night embarrass or humiliate yourself in front of other people or that others may not think well of you?

C – Do you try to avoid social situations?

Q18 Do you tend to experience fear each time you are in feared social situations?
Q19 Does the fear come on as soon as you encounter feared social situations?

Q20 Would you say that your social fear is excessive or unreasonable?

Additional items e.g. fear responses (q1a- 17a) only are each divided by four and total scores for these are to be computed in FEARTOT column.

Q21 and 22 (interference and distress) are divided by two.

All yes/no, fear responses and q21 and 22 totals are added to make final total. (total column)

Total scores range from 0 –27.

Appendix 2. – SUMIT Scoping Document

SUbstance Misuse Information – Tayside: "*SUMIT*"
A 2 year, Time-Limited Project to Deliver a Functioning Care, Treatment & Recovery Information System for Substance Misuse in Tayside.

Background

Organisational support

In 2008 NHS Tayside Board and the three Tayside DAATs agreed to prioritise funding the purchase of an information system to support delivery of the substance misuse care and treatment pathway. Funds were identified and committed from ring-fenced care & treatment resources for drugs and alcohol. Tayside Substance Misuse Services are leading on this project and have support from key partners to progress the deployment of a system based on the new *MIDIS* system.

HAF Information Working Group

On 14th October 2009, the NHST Health Advisory Forum (HAF) discussed the need to ensure that any new information systems must support effective commissioning. A working group was formed - the Information Working Group (IWG) – and a process commenced to develop an options paper for consideration. At a meeting on 18th February 2010, the IWG considered the paper *"Tayside Substance Misuse Information Systems. Opportunities to maximize performance: an Options Paper – draft 4"* and supported "Option 3" which proposed that "the HAF sets up a working group to develop a proposal in partnership with NHST/ADPs/ and University of Dundee (UoD) to maximize the potential value of the new system using resources already committed for this purpose." The membership of the IWG and Executive Summary of the options paper are included in Appendix 1.

Delivery plans

Following the decision of the IWG, this paper describes an initial plan for delivery of a fit-for-purpose substance misuse information system for Tayside's care treatment & recovery pathway. In line with the aspirations described by the HAF IWG, the system is required to address a number of key areas. These include:

1. *Services* delivering care, treatment & recovery (Statutory & voluntary sectors) – ensuring valid real time information is available to inform clinical governance, clinical decision making and care planning as well as revalidation of staff
2. *Commissioners* of services (ADPs, NHS & Local Authority commissioners) – ensuring commissioners have access to meaningful information flows to allow adequate planning and commissioning of services [monitoring of SOAs & HEAT] and demonstration of effectiveness (including cost-effectiveness).

Any system should also aim to supply valid information to improve potential for active involvement in academic research and audit activity, building on existing achievements.

An essential element of the proposal is the development of *local capacity* to deliver the required elements in a sustainable way.

In March 2010, NHS Tayside Strategic Plan 2010-2015 was published. It states: "The first financial challenge is to assess the relative cost effectiveness of our services. Once this information is available an even greater challenge will be to change long established practices in order to increase overall efficiency, improve productivity and maximise health gain. This may involve reducing services which are shown to be the least cost effective and redirecting resources into services which achieve greater health gain. This process will be facilitated through the use of appropriate economic analysis techniques." The message is clear that any information development project must ensure that some form of health economic evaluation is integral to the delivery plan.

The current proposal describes a *time-limited delivery project* which has been developed through a process of meetings with key partners including ADP and Local Authority leads, NHS clinical and IT staff as well as academics from relevant departments in the University of Dundee – the Centre for Addiction research & Education, Scotland (CARES), the Health Informatics Centre (HIC) and the Dundee Health Economics Group (DHEG). List of participants to date is included in Appendix 2.

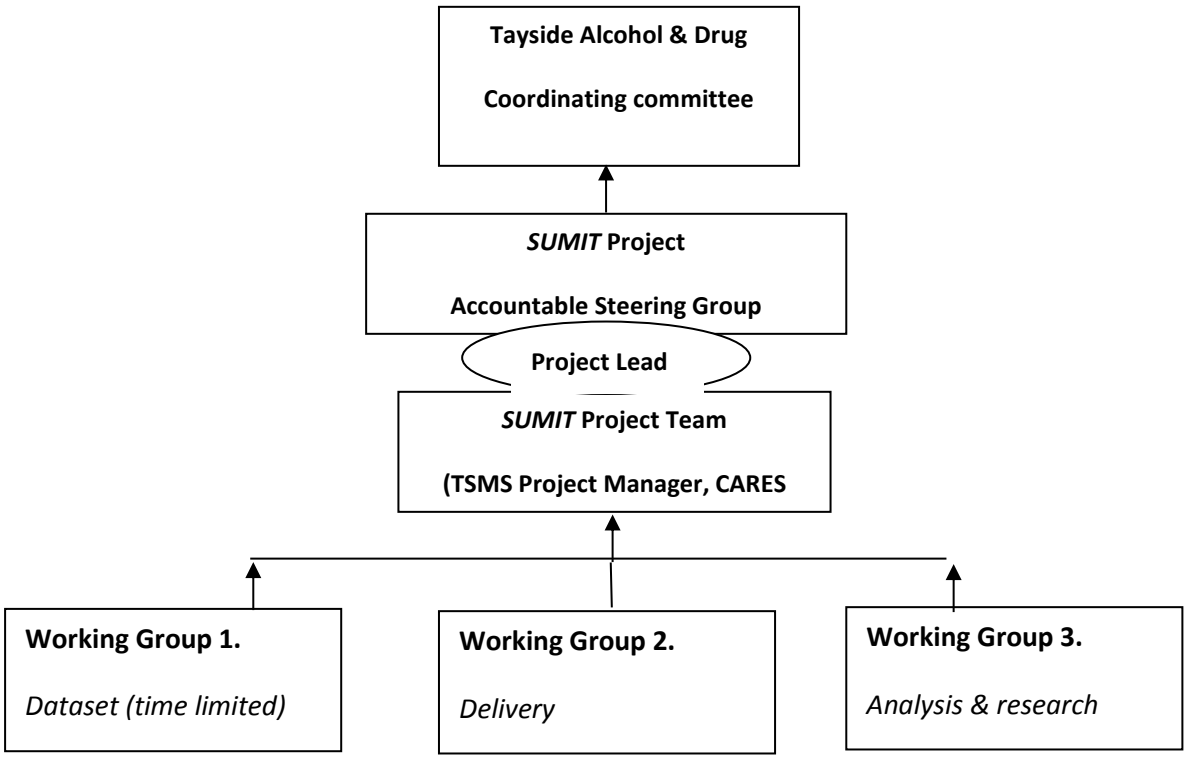
Issues to be addressed

This proposal aims to achieve agreement for key components of the ***SUMIT*** Project which are designed to ensure the project delivers the desired result. These components are: a governance process; clear deliverables; realistic timelines.

Governance process

This project has the potential to be complex and it is therefore essential that a focus on delivering clear objectives on behalf of the key partners responsible for delivering care treatment and recovery in Tayside is maintained. To this end, an accountability/reporting framework is proposed (Fig. 1)

Figure 1. – Governance process.



Tayside Alcohol & Drug Coordinating Committee

The project is commissioned by the NHST HAF. This group has close links with the Tayside Coordinating Committee ensuring stakeholder input is maximised. *ThisCommittee will receive project update reports at agreed intervals.*

Project Steering (Accountable) Group

It is essential that the project is overseen by an appropriate group of stakeholders who carry relevant accountability to their respective organisations. From the discussions to date this *should include* the budget holder (NF); ADP/LA reps from all three areas [requirement will be judged by ADPs and depend on degree of CPP integration of ADPs]; TSMS lead (BK); IT lead (JB). UoD lead (KM/BG). *A Project Lead will be agreed. NHST will appoint a project coordinator (Band 6 clinician) to oversee delivery of the clinical systems. The project coordinator will be managed by TSMS Clinical Governance Lead. UoD (CARES) will appoint & manage a lead researcher to coordinate delivery. Their work plans will be set by the* ***SUMIT*** *steering group.*

Working groups

Specific areas of work are required to deliver the optimal system. These include:

Working Group 1. – Dataset workstream (time limited)

A group to ensure the data collection tools and linkages proposed are capable of responding to the needs of ongoing clinical governance (staff & team performance; impact of interventions); monitoring of service performance (HEAT & SOA etc); commissioning of services (needs assessment, cost effectiveness & best value etc). The group will be very active in the early stages (<3/12) to ensure project is appropriately focussed. If required this group could be reconvened at a later stage to consider issues raised in the delivery phase including any refinement of data collection tools to ensure data are useful and of high quality. This group could also address sustainability.

Key output will be that the project agrees a *clearly defined valid dataset.*

Inputs required will include those setting strategic objectives (NHST; ADPs; LA SOA leads); those leading clinical delivery (service delivery leads); academics (CARES); technical advisers with experience in managing data or systems development (ADP Info officer; HIC; DHEG; NHST Lead Pharmacist).

Working Group 2. – Delivery workstream

A group to ensure the system functions optimally. This group will address such issues as agreeing systems (technical or manual); delivering training and support for clinical staff; putting data management systems in place (quality assurance; security; data entry). The group will initially set up systems and will then govern their delivery and effectiveness.

Key output will be that the project *collects high quality data timeously*

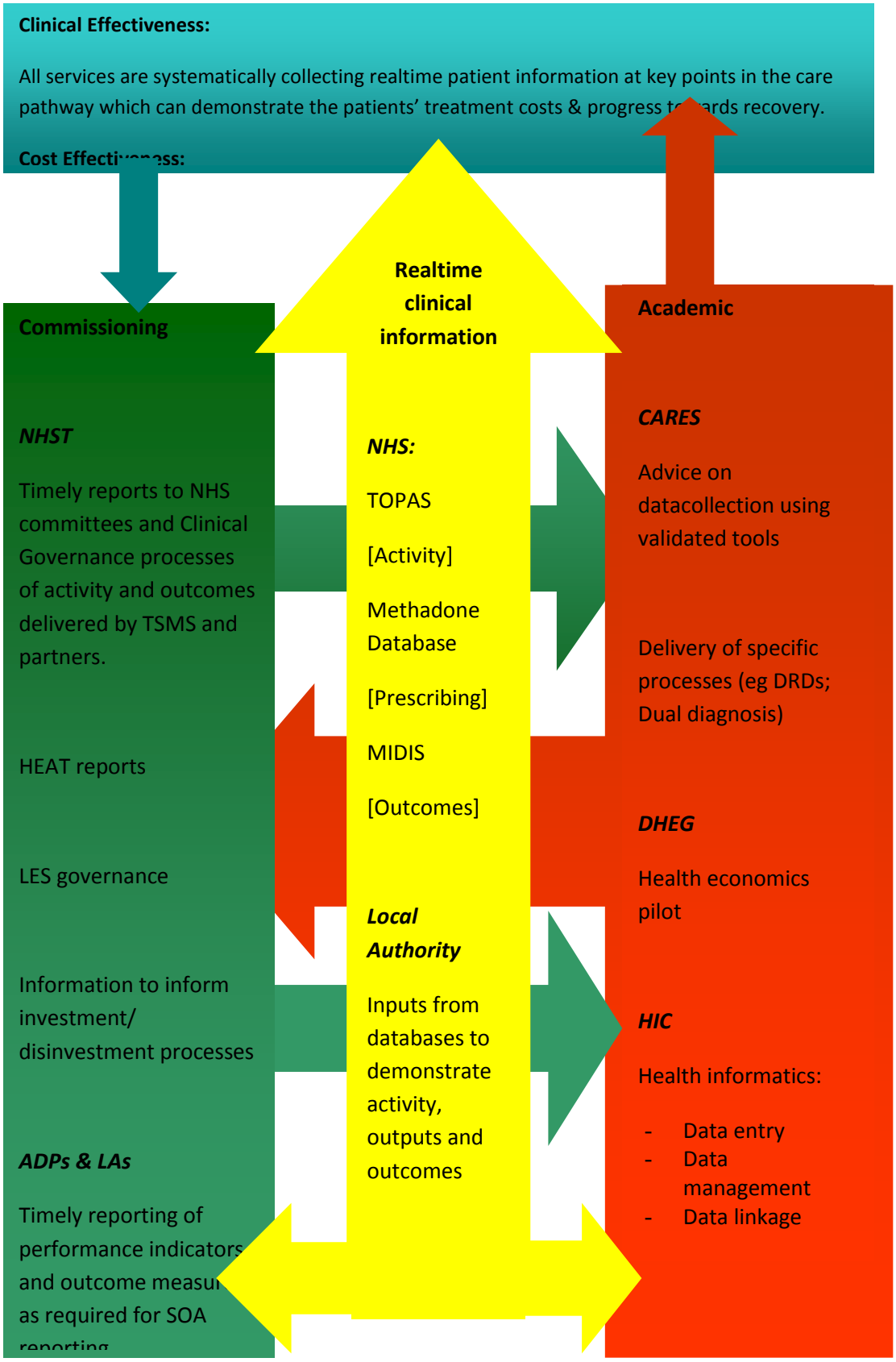
Inputs required will include operational managers/clinical leads; technical support staff; administration managers & those with data handling expertise.

Working Group 3. – Analytical & research workstream

This group has two areas of focus. One is to ensure that the data collected is available for reporting as required by commissioners (NHST, ADPs, SOAs – including cost-effectiveness); clinical services (clinical governance; revalidation). A second is that it works to maximise value of these data for audit and research purposes. This work may be directed by existing activities (eg Drug Death data – on behalf of DRD Group; Outcomes data – such as the Tayside Methadone Cohort etc). Specific datasets will allow objective assessment of the cost effectiveness of new service delivery models – eg new HITS service post RIE. This group will also bring forward proposals to maximise academic use of these data within acceptable ethical constraints. Examples will include data linkage to NHS datasets (hospital admissions; labs; death; GP prescribing) and potentially to others (eg child development; criminal justice) depending on data sharing agreements. This linkage would allow additional outcomes to be taken into consideration within the cost-effectiveness analysis and also ensure that the long term cost effectiveness of activities (changes in long-term outcomes) can be assessed.

Key output will be that the project's data handling *can answer key strategic questions*

Inputs required will include ADPs (through information officer), Local Authority SOA development, NHS data handling (HIC) and academics (CARES, DHEG etc).



Deliverables

Figure 2. contains a schematic of the proposed ***SUMIT*** system.

When completed, the SUMIT project will deliver:

- A fully functioning information system which collects high quality activity & outcomes data from the care, treatment and rehabilitation pathway across Tayside.
- Data sets will have been designed to meet the needs of key stakeholders
- Data will be analysed to allow reporting on various aspects of service delivery including commissioning, performance management and clinical governance as well as revalidation of clinicians.
- Tailored/bespoke reports will be available in a timely way for stakeholders

In addition, the system will aim to build local capacity to excel in this work by forming a link with existing local academic partnerships, allowing it to:

- Address questions of cost-effectiveness and health economic analyses
- Develop data linkage processes – allowing relationships to be explored and long term cost-effectiveness and performance to be evaluated (eg links with hospital admissions, deaths).
- Bid for additional resources through academic channels to test and evaluate treatment strategies with potential for improved cost-effectiveness. This will support exit strategy.

Effective local clinical/academic partnerships are already in place in substance misuse. Examples include: active support from NHS Boards to support development of UoD CARES – which has delivered the drug deaths collaboration with ADPs and the Tayside Methadone Cohort Project; Development of a health economics project by Dundee City ADP in collaboration with DHEG. Processes are underway to secure funding to further develop research capacity (eg ESRC/MRC studentship application). Academic outputs have included a recent high impact publication on drug deaths in the BMJ (McCowan, Kidd & Fahey 2009).

Finally, the project will deliver an exit strategy, clearly outlining options for the established system to be progressed once the delivery project has been completed. This exit strategy will aim to engage ongoing processes within partner agencies (e.g. ADP support; NHS Business Support Unit etc.). Opportunities to access research/matched funds are an untapped option to increase support for the analytical elements. The aim is to deliver a cost neutral exit strategy.

Timelines

The project will be delivered in a coordinated way and is divided into key time periods which aim to ensure that the project delivers the required outcome and concludes with an acceptable exit strategy. Milestones are identified.

Phase 1: Immediate actions and objectives (<3/12 from initiation)

Initial investment will put basic infrastructure in place and focus on the completion of an agreed set of data collection tools to meet stakeholders' needs. This early stage will be completed in 3 months.

Key inputs will be:

- Agree funding & governance arrangements
- Appoint NHS Band 6 project manager to lead delivery of clinical information system
    - Ensure hardware & software in place (?gradual/phased roll out)
    - Staff training plans
- Appoint NHS/UoD researcher coordinating development of academic activities/process
- Set up working groups and agree workplans
- Put immediate "quick win" processes in place – eg HIC baseline data entry
- Develop detailed plans for full project

Key outputs will be:

- Infrastructure in place and functioning within 3 months of commencing project
- Working groups in place and workplans agreed
- "Quick wins" delivered or progressing – eg. Baseline TOP data report; Follow-up Methadone Cohort Data; data linkage process developed; Health economics processes agreed.

Phase 2: Main body of project – 3/12-18/12

From this stage the working groups will bring forward a prioritised programme of work to

- Refine and develop a quality-assured data handling process
- Ensure the system meets the reporting needs of all stakeholders
- Maximise the audit, research & clinical governance potential of the system
- Evaluate the system

Key inputs and outputs will be developed during Phase 1.

Phase 3: Exit strategy18-24/12

Evaluation report will inform appropriate options for exit strategy. This will ensure system is sustainable beyond the timeframes for the delivery project.

In conclusion

It is proposed that the Tayside Substance Misuse partners agree to the plans outlined above.

If agreed this will allow the immediate phase to progress - launching the project, putting in place key staff and progressing detailed plans.

Appendix 3 Research Governance

This Appendix contains copies of documentation associated with the process of research governance for the three elements of the project. This includes:

- **Correspondence with the NHS Tayside Research Ethics Committee**
- **Correspondence with the Caldicott Guardian**
- **Data management documentation relating to the Health Informatics Centre (HIC)**

NHS Tayside Research Ethics Committee

From: Coote Liz (NHS Tayside) [liz.coote@nhs.net]
Sent: 25 November 2010 13:40
To: Cassie Higgins
Cc: Kidd Brian (NHS Tayside); Baldacchino Alexander (NHS Fife); c.w.crawford@dundee.ac.uk; McKenzie Peter (NHS Tayside); Hunter Stewart (NHS Tayside); Fenton Ian (NHS Tayside); Ackland Caroline (NHS Tayside)
Subject: SUMIT and R&D Approval situation

Dr Kidd

SUMIT and R&D Approval situation (TASC Ref: 2010PY01)

I have now reviewed the documentation submitted to TASC R&D on the above study. I note that this study relates to the Development of a system that can receive, manage and process information across the alcohol and drug care, treatment and recovery agenda. SUMIT aims to ensure delivery of high quality clinical information to support services, reporting of service performance, economic assessment of service, data linkage and further academic collaboration. It has been agreed that the SUMIT proposal does NOT therefore require TASC R&D approval as the development of the system is not research per se. The proposal should be reviewed and approved by the Data protection officers and Caldicott guardians whom I have copied in on this email for information.

Please note however that all research proposals utilising patient data from the system is required to be notified to TASC R&D office for review and approval.

Please find below guidance from IRAS website on NHS management permissions for Databases. This supports our decision that R&D approval for the development of the system itself is not required.

NHS management permission

Under the Research Governance Framework (RGF), there is no requirement for NHS research permission for the establishment of research databases in the NHS. Applications to NHS R&D offices through IRAS are not required as all NHS organisations are expected to have included management review in the process of establishing the database.

Research permission is also not required by collaborators at data collection centres (DCCs) who provide data under the terms of a supply agreement between the organisation and the database. DCCs are not research

sites for the purposes of the RGF.

Database managers are advised to provide R&D offices at all DCCs with a copy of the REC application for information, together with a copy of the favourable opinion letter when available. All DCCs should be listed in Part C of the REC application.

NHS researchers undertaking specific research projects using data supplied by a database must apply for permission to R&D offices at all organisations where the research is conducted, whether or not the database has ethical approval. Where the data is received in non-identifiable form and the research is covered by the terms of generic ethical approval for the database, no further REC application is required but the database should list the project in its annual report to the REC.

I hope this clarifies matters with respect to R&D/NHS management approval. Please feel free to contact me should you wish to discuss this further.

Liz Coote

R&D Manager
Tayside Medical Sciences Centre,
Ninewells Hospital & Medical School
TASC Research & Development Office
Residency Block, Level 3, George Pirie Way,
Dundee, United Kingdom
DD1 9SY

Caldicott Guardian Approval

User Details	
Name:	Dr Brian Kidd
Position:	Consultant Psychiatrist / Senior Lecturer
Organisation:	NHS Tayside
Address:	Constitution House 55 Constitution House Dundee DD1LB
Tel:	01382 424512

Sponsor Details	
Name:	Dr Andrew Russell
Position:	Medical Director
Organisation:	NHS Tayside
Address:	Kings Cross Clepington Road Dundee DD3 8EA
Tel:	01382 424176

Data Protection Reg. No.	Z8537226
Data Requested :	Pilot Update to Tayside Methadone Cohort – Audit & Research Plans.
A Data Processing Specification must also be completed.	Original approval Dr Mutch July 2005
Co-Users of the Data :	1. Data will be used by NHS Tayside Substance Misuse Lead Clinician – Dr Brian Kidd - to support process of performance improvement. 2. Data may also be used by clinical governance staff under supervision of Dr Kidd (eg administrative/research staff associated with the clinical governance office TSMS/CARES UoD). 3. Anonymised data [supplied by TSMS] may be used by attached medical students to support their requirement to undertake research projects under supervision of Dr Kidd
Intended use of data (inc. publications) :	Initial project will support reports addressing changes in patient outcomes from original audit in 2005. It will be the intention to disperse relevant research papers more widely through peer-reviewed journals.If students use anonymised data these will be included in their UoD research reports

User's Declaration

I declare that I understand and undertake to abide by the rules for confidentiality, security and release of data received from NHS Tayside.

Signature

Date 12th February 2010

Sponsor's Declaration (to be signed by a consultant if patient data is requested and the applicant is not of that status or is not medically qualified)

I declare that the above named user of the data is a bona fide worker engaged in a reputable project and that the data requested can be entrusted to this person in the knowledge that they will conscientiously discharge their obligations in regard to confidentiality of the data.

Signature

Date

RULES ON CONFIDENTIALITY, SECURITY AND RELEASE OF INFORMATION

FOR USERS OF NHS PATIENT DATA

1) If the data received from NHS Tayside are to be held on computer, the signatory of this request, or the organisation (s)he represents, should have an appropriate registration with the Office of the Data Protection Registrar. Details of the registration number should be entered on this document.

2) Data received from NHS Tayside must not be used for any purpose other than for the intended use specified on this document.

3) Data received from NHS Tayside must not be divulged to any person who is not specified as a 'co-user of the data' on this document.

4) Proper safeguards should be applied in keeping the data and destroying it on completion of the work/project declared to prevent any breach of confidentiality.

5) Any misuse or loss of these data should be notified immediately to the Information Governance Officer for NHS Tayside at AshludieHospital, Monifieth (01382-527920).

6) Recipients of information supplied by NHS Tayside are reminded that the data has been supplied for the purposes stated in the approved study only. Further submission for approval will be required for any other uses of that data.

7) Any statistics or results of research based on data received from NHS Tayside should not be made available in a form which:
   a) directly identifies individual data subjects
   b) is not covered by the 'intended use of data' specified

Information Governance
AshludieHospital

Monifieth

DD5 4HQ

Telephone : 01382 527920

Fax : 01382 527808

CALDICOTT APPROVAL - DATA PROCESSING SPECIFICATION

To be submitted with application for Caldicott Approval

For **each separate source** of patient identifiable data that you intend to access in support of your study please provide the following information.

Data Source: (*Medical Records/System Name)*
Medical records

Data Items: (list the data items that you will require from the named data source)			
Outcome data (TOP)	Maudesley Addiction Profile (MAP)	Urine/oral fluid drug screens	Information from contemporaneous clinical record indicating progress in treatment – listed below 1-3
1. Evidence of drug use and risk behaviours eg overdose etc.	2. Evidence of housing & family stability	3. Evidence of criminal justice involvement	

Data Source Contact Details: (who have you agreed access to the source data with?)	
Name: Dina Ajeda	Designation: TSMS Clinical Governance Lead
Base: Constitution House	Tel No: 07803671870
Email address: dinaajeda@nhs.net	

Data Storage Arrangements: (where arrangements are described in a supplied study protocol then reference to the relevant sections of the protocol can be used)	
Location: (NHS Tayside, University, etc.) Data will be stored in a bespoke computer database The computer is password protected and the data is encrypted (process supervised by HIC technical staff). When not in use the computer will be stored in a locked drawer in a filing cabinet in the CARES office, Dept of Psychiatry, UoD, Ninewells.	Device to be held on(desktop, laptop, network storage, etc.) Laptop computer. Password protected. Data encrypted.
Access Controls (how will the data be protected from unauthorised access?) Password protected computer. Encrypted data	Encryption: (will encryption be used to protect the data?) Yes
Anonymisation: (how will the identity of individuals be protected) Data will be identifiable in the main database by Chi number. Names will not be retained	Format (spreadsheet, database, etc.) SPSS version 12

If you intend to make contact with patients identified through the processing of this data, indicate how this will be done and how you will ensure that it is appropriate to contact them. It is recommended that contact with patients is through correspondence signed by the patient's GP/Clinician or Head of Clinical Service.
At this stage it is NOT intended to contact patients for this follow up audit. Future processes which are dependent on available resources may require patient interviews. In such circumstance Dr Kidd will require a further Caldicott approval.

HIC Data User Agreement

Approved Data User- is the project Principal Investigator (PI) or a person who is authorised by the PI to also have access tothe Project Dataset at an approved location. The Approved Data User must be an employee of NHS Tayside, NHS Fife or the University of Dundee. All project collaborators must sign and agree to abide by the terms of the HIC Data User Agreement.

Where a data user is not such an employee but is an external project collaborator, then they will be logged on the HIC Project Management System as an Approved Data User subject to the following:

a) The HIC Data User Agreementmust also be signed by an authorised signatory from their organisation.

HIC may choose to make the project data available to the Approved Data User by hosting the data on a HIC server, within HIC's Safe Haven environment and providing secure remote access to the server, rather than releasing the data externally.

Data User Responsibilities

All Approved Data Users are expected to maintain the security and confidentiality of their project datasets in accordance with this agreement and the Data Protection Principles (see **Appendix A**). HIC expectsApproved Data Users to report significant events that are in breach of the terms of the HIC Data User Agreement. Contact the HIC Operations Manager in the first instance to report the incident, who will initiate a Significant Event Report.

1) Approved Data Users will not reuse the data for purposes outside the scope of each project; share it with colleagues who are not named project Approved Data Users; attempt to link it to other datasets; or to de-anonymise it.
2) Approved Data Users will only keep the data on a secure password-protected and encrypted hard drive partition or remotely access their centrally-held data within the HIC Safe Haven. Data is not permitted to be stored or transferred on unencrypted removable devices, e.g. unencrypted USB keys. HIC can offer advice and install encrypted partitions to researcher's hardware, if required.
3) Further transfer of data between named project Approved Data Userswill only be of encrypted data, usually directly from an access controlled FTP server to the FTP client but data may also be sent via email using encrypted data files. HIC can offer advice and provide encryption tools, to help meet this requirement.

4) Approved Data Userswill notify HIC when the project is complete and arrange for the return of the data and the analysis syntax used for archiving, deleting all local copies. HIC will require written confirmation that all locally-held data has been deleted.

5) Approved Data Users will ensure that HIC and the Health Board responsible for initially providing data are acknowledged as data sources in all resulting reports and publications. Eg. "We acknowledge the support of the Health Informatics Centre, University of Dundee for managing and supplying the anonymised data and NHS 'XXX', the original data source"

Signatures

a) Approved Data User

By signing and dating below you confirm that you have read, understood and will abide by this HIC Data User Agreement and the Data Protection Principles in relation to data being provided to you from HIC.Any breach of this agreement will result in your access to HIC data being reviewed by the HIC Executive Committee

Name: _____

Position: _____

Signature _____

Date signed: _____

b) Student Supervisor

(Note: Where the Approved Data User is a student, this Declaration must be signed by the student's supervisor.)

By signing and dating below you confirm that you will ensure the above named ApprovedData User has read, understood and will abide by this HIC Data User Agreement and the Data Protection Principles in relation to data being provided to him/her by HIC.

Name: _____

Position: _____

Signature _____

Date signed: _____

c) Project Collaborators/External Organisations

External project collaborators (Approved Data Users who are not employees of University of Dundee, Tayside Health Board or Fife Health Board) must have this section signed by an authorised signatory from their organisation.

Authorised Signatory for Project Collaborator's Institution to sign the following declaration:

"We declare that the above named researcher is a bona fide employee of this Institution engaged in a reputable project for which all relevant required permissions have been granted, and that the data requested can be entrusted to this person in the knowledge that they will conscientiously discharge their obligations in regard to the confidentiality of the data. This Institutionagrees to abide by the terms of this agreement and takes responsibility for ensuring that researchers are knowledgeable of, and compliant with required statutory and regulatory permissions and Data Protection requirements, and will provide a secure working environment and suitable technical resources to meet this obligation."

We declare that we understand that any breach of this agreement will lead to the withdrawal of access to HIC data for this Institution and its staff, and that HIC has a duty to report serious legal or regulatory breaches to the appropriate authorities (such as the Data Protection Commissioner and professional regulatory bodies)."

Name: _____

Position: _____

Signature _____

Date signed: _____

For and On behalf of:_____

(Name of Institution)

Appendix A: The 8 Data Protection Principles

1. Personal data shall be processed fairly and lawfully
   - must not deceive or mislead
   - must state the purpose of the processing
   - must provide your identity
   - must have consent of the data subject – cannot infer this from a lack of response
   - must specify time period of consent
   - must have appropriate safeguards for data
   - must obtain consent from data subjects for processing if data provided by a third party

2. Personal data shall be obtained only for one or more specified and lawful purposes, and shall not be further processed in any manner incompatible with that purpose or purposes
   - Must identify purposes for which data is being processed
   - Must ensure purposes are compatible with information given to data subjects and to the Office of the Information Commissioner (www.ico.gov.uk)
   - Must not further process if purposes are not compatible with consent or notification to OIC without resolving conflicts

3. Personal data shall be adequate, relevant, and not excessive in relation to the purpose or purposes for which they are processed
   - Must establish what is collected and why
   - Must audit data holding against need – minimum information must be collected – do not collect 'just in case'
   - Must establish effective data retention and disposal policies
   - Must establish policies and procedures to test new and modified data collection against the principles

4. Personal data shall be accurate and, where necessary, kept up to date
   - Must establish methods to validate the source of data
   - Must establish policies and procedures to keep data up–to-date
   - Must establish policies and procedures to correct or mark as incorrect any disputed data

5. Personal data processed for any purpose or purposes shall not be kept for longer than is necessary for that purpose or those purposes
   - Must establish policies and procedures review why you are retaining data – eg current use, audit/ legal purposes, research purposes
   - Must delete data that is no longer needed

6. Personal data shall be processed in accordance with the rights of data subjects under this Act
   - Rights of data subjects include:
     - Right to be told that their personal data is being processed and for what purpose
     - Right to obtain a copy of their personal data

- Right to prevent the use of their data for direct marketing purposes
- Right to be told to whom the data will be disclosed
- Right to prevent processing which may cause substantial damage or distress to he data subject
- Right to have explained the logic behind any decision taken on the basis of the processing of the data

- Must manage operations to ensure that data subjects can exercise their rights properly and fully

7. Appropriate technical and organisational measures shall be taken against unauthorised or unlawful processing of personal data and against accidental loss or destruction of, or damage to, personal data
   - practical steps to compliance include:
     - do not allow staff to share password
     - site PCs where the screen cannot be seen by unauthorised staff or the public and do not leave information on the screen when you are not there
     - when using external agencies ensure processing is carried out under written contracts
     - block access to systems by former staff
     - vet all prospective employees
     - react to allegations of access to unauthorised data
     - do no leave files unattended in the open
     - shred personal data rather than bin it
     - do not design documents/ write papers in ways that reveal personal data
     - physical and electronic security
     - staff training
     - measures to prevent accidental loss, damage or destruction of data

8. Personal data shall not be transferred to a country or territory outside the European Economic Area (25 EU Member States + Iceland, Lichtenstein & Norway) unless that country or territory ensures an adequate level of protection for the rights and freedoms of data subjects in relation to the processing of personal data
   - must not transfer data by any means (including electronic) if in doubt

Data release agreement -HIC

Project 1013 – Substance Misuse in Tayside (SUMIT)

Data User: Brian Kidd/ Cassie Higgins / Colin McCowan

Anonymised:	Yes
PROCHI:	bmz

Date Released: 8th June 2011

SQL tables:

Work..tt_1013_presc	Prescribing imported from PSD_Flow on ATHENA
ATHENA.SUMIT..tt_1013_cohort	Cohort on Athena to allow extraction of ATOPs

Data Requirement	Filename	Notes	No. of records extracted
Demography	Demog.txt	Demography including anon date of birth, and date of death. Note that 20 patients were lost from the original methadone baseline dataset due to invalid CHI numbers.	731 (627 unique)
ATOPS	ATOPS_Alcohol Liason.txt ATOPS_AlcoholServiceCommunity.txt ATOPS_DrugService_AISS.txt ATOPS_DrugService_DTTO.txt ATOPS_DrugService_ISP.txt ATOPS_DrugService_TARS.txt	ATOPs data for the cohort. Refer to supplied metadata files for lookups. **Note**: HIC does not have paper copies of the Alcohol Liason or DrugService_ISP forms so unsure what each columns are (ie no metadata for these files)	No results. 6 157 23 2 39

	ATOPS_TimeTayChange.txt		271
SMR00	SMR00.txt	All outpatient records for the cohort from 2005 to 31/Mar/2010 **Note: seems to be missing SMR00 data 01/Jan/2009 – 30/06/2009, HIC to request from ISD, was never received.**	23,057
SMR01	SMR01.txt	All hospital admissions for the cohort from 2005 to 30/Sep/2010	907
Ward Data	TOPAS_Ward.txt	Ward data from 01/Oct/2010 to 31/Dec/2010 to supplement SMR01 above	44
SMR04	SMR04.txt	All psychiatric admissions for the cohort from 2005 to 31/Mar/2010	133
Methadone	Methadone_baseline.txt Methadone_followup.txt	Anonymous Methadone baseline and follow-up database supplied by Cassie.	627 467
GRO	GRO.txt	GRO deaths for the cohort	45
Biochemistry	Biochem.txt	Biochemistry from 2005 for the codes: BENZ : BENZODIAZEPINES (URINE) METH : METHADONE (URINE) OPIA : OPIATES (URINE) AMPH : AMFETAMINES (URINE) BARB : BARBITURATES (URINE) COCN : COCAINE (URINE) UCAN : CANNABINOIDS (URINE) OTOX : OPIATE CONFIRMATION (URINE)	84,634

		UTOX : TOXICOLOGY (URINE) UALC : ALCOHOL (URINE) CRU : URINE CREATININE	
Prescribing	Presc.txt Presc_items.txt	HIC Prescribing for the cohort, plus directions entered for certain drug groupings. Note that (additional methadone ones to be done separately to capture information such as quantity, days, total, supervised, frequency). Use res_seqno to link between the 2 files.	117,746 2,318
A&E	AandE.txt AandE_accompany.txt AandE_diag.txt AandE_drugs.txt	Accident and Emergency data for the cohort. The file AandE.txt represents the actual admission to the A&E department. Accompany links to this via CHI and Attendance_Number and shows who was with the patient at their attendance (ie mother, police, prison officer, teacher etc). There can be more than one person accompanying the patient. The diag and drugs files show what decision was made on the diagnosis and any treatment given.	710 714 723 118

Date Released: 28th June 2011

SQL tables: ATHENA.SUMIT..tt_1013_cohort Cohort on Athena to allow extraction of ATOPs

Work..baseline_xxxxx, (11 files)

Data Requirement	Filename	Notes	No. of records extracted
Baseline data	baseline_ADHD.txt		623
Methadone cohort	baseline_CORE.txt		620
	baseline_Chronic_Pain.txt		625
	baseline_Demographic.txt		623
	baseline_GHQ.txt		626
	baseline_Injecting_Risk_Behaviour.txt		625
	baseline_MAP.txt		625
	baseline_PTSD.txt		623
	baseline_Social_Phobia.txt		621
	baseline_Sweating.txt		624
	baseline_TPQ.txt		621

University of Dundee Research and Innovation Services

Research and Innovation Services

Project Registration Form - Costing

SECTION 3 - Project Approval by Applicants, Heads of Divisions, Deans and Heads of Colleges

TITLE: Substance Misuse Information - Tayside (SUMIT)
PI: Dr Brian Kidd

Budget Summary

	Dundee Costs fEC	Dundee Costs Applied for	Total Project Costs (all institutions) if joint submission
Directly Incurred costs			
Salaries	£ 166,060	£ 166,060	
Travel	£ -		
Consumables	£ -		
Equipment	£ -		
Other DI	£ 56,247	£ 56,247	
PhD Stipend	£ -		
PhD Fees	£ -		
Directly Allocated Costs			
Directly Allocated salary costs	£ 27,334		
Other DA costs	£ -		
Estates costs	£ 49,025	£ -	
Indirect costs	£ 115,802	£ -	
TOTAL	£ 414,468	£ 222,307	£ -
Difference between fEC and amount applied for		-£ 192,161	

Additional Information for noting by RFO (free text)

Declarations

1. For research rating purposes "Research" shall be as defined in the Frascati Guidelines (available from RIS).
2. Costs shown fully reflect the costs of carrying out the proposed work.
3. There are no implications for University costs (alterations, equipment, space requirements, etc) other than those detailed.
4. All projects shall be carried out in accordance with normal standards of safety, ethical and other legal and regulatory provisions in force.
5. Staff participation in this project is compliant with the University's policy on Conflict of Interest: www.somis.dundee.ac.uk/court/policy/conflict_of_interest.htm
6. The directly allocated academic time detailed in section 1 can be met through the normal research allocation. If any additional research time is required this has been separately agreed with the Head of School.
7. Institutional Consultancy : Any surplus generated is normally split equally between academic, College and the University as detailed at University Court Guidelines

ANY variation from this must be agreed by the Dean and Head of College. and the agreed split detailed here.

Academic ..... %
College ..... %
University ..... %

Applicant Name(s)	Signature(s)	Date	Dean's Signature	HoD Signature	Date
Dr Brian Kidd					
Dr Alex Baldacchino					
Mark McGilchrist	M. McGilchrist	21/7/10			
Dennis Petrie					
Keith Matthews					
Colin McCowan	Colin McCowan	21/7/10			
Professor Catia Montagna					
Professor Bruce Guthrie		21/7/10			

Head of College(s)

(Necessary if the project involves more than one College, if the cost of an industry funded project falls below Full Economic Cost, if Institutional Consultancy split differs from University standard, or if required by College policy)

Name(s)	College(s)	Signature(s)	Date

Research and Innovation Services

Project Registration Form - Costing

SECTION 3 - Project Approval by Applicants, Heads of Divisions, Deans and Heads of Colleges

TITLE: Substance Misuse Information - Tayside (SUMIT)
PI: Dr Brian Kidd

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Travel	£ -		
Consumables	£ -		
Equipment	£ -		
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PhD Stipend	£ -		
PhD Fees	£ -		
Directly Allocated Costs			
Directly Allocated salary costs	£ 27,334		
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TOTAL	£ 414,468	£ 222,307	£ -
Difference between fEC and amount applied for		-£ 192,161	

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4. All projects shall be carried out in accordance with normal standards of safety, ethical and other legal and regulatory provisions in force.
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   www.somis.dundee.ac.uk/court/policy/conflict_of_interest.htm
6. The directly allocated academic time detailed in section 1 can be met through the normal research allocation. If any additional research time is required this has been separately agreed with the Head of School.
7. Institutional Consultancy : Any surplus generated is normally split equally between academic, College and the University as detailed at University Court Guidelines
   ANY variation from this must be agreed by the Dean and Head of College. and the agreed split detailed here.

Academic	%
College	%
University	%

Applicant Name(s)	Signature(s)	Date	Dean's Signature	HoD Signature	Date
Dr Brian Kidd					
Dr Alex Baldacchino					
Mark McGilchrist	M. McGilchrist	21/7/10			
Dennis Petrie					
Keith Matthews					
Colin McCowan	Colin McCowan	21/7/10			
Professor Catia Montagna					
Professor Bruce Guthrie		21/7/10			

Head of College(s)

(Necessary if the project involves more than one College, if the cost of an industry funded project falls below Full Economic Cost, if Institutional Consultancy split differs from University standard, or if required by College policy)

Name(s)	College(s)	Signature(s)	Date

Appendix 4 – Additional tables of results – Chapter 6

This Appendix contains the additional results tables for which no significant associations were demonstrated once the Bonferroni correction was applied – 2009 casenote follow up

Table A1. Impact of gender on process and 4 year outcomes

Independent (Predictor) Variable	Dependent (Process) variable	Statistics
Gender **No significant impacts demonstrated**	Retention (Yes 156)	Chi square $X^2(1)=0.168$; p=0.682
	If NOT= +ve or –ve discharge (n=139)	Chi square $X^2(6)=7.220$; p=0.301
	Drug screen done	Chi square $X^2(2)=0.890$; p=0.641
	Methadone dose	KWH $X^2(1)=0.317$; p=0.574
	Diazepam dose	KWH $X^2(1)=0.606$; p=0.436
	Dependent (Outcome) variable	
	Employment status	Chi square $X^2(1)=0.057$; p=0.812
	Family stability	Chi square $X^2(2)=1.147$; p=0.564
	Any illicit drug use reported	Chi square $X^2(3)=1.728$; p=0.631
	Heroin use reported	Chi square $X^2(3)=0.720$; p=0.868
	Heroin days	Chi square $X^2(8)=8.526$; p=0.384
	Heroin route	Chi square $X^2(4)=0.618$; p=0.961
	Illicit Diazepam use	Chi square $X^2(3)=2.591$; p=0.459
	Illicit Diazepam days	Chi square $X^2(8)=8.959$; p=0.346
	Illicit Methadone use	Chi square $X^2(3)=2.672$; p=0.445
	Illicit Methadone days	Chi square $X^2(6)=4.774$; p=0.573
	Illicit painkillers **25 cases	Chi square $X^2(3)=2.558$; p=0.564
	+ve opiates tests	Chi square $X^2(4)=2.946$; p=0.567
	+ve benzodiazepine tests	Chi square $X^2(3)=1.159$; p=0.763
	Acute admissions reported (18)	KWH $X^2(1)=0.007$; p=0.932
	Psych admissions reported (14)	KWH $X^2(1)=0.274$; p=0.600
	Prison reported (48)	KWH $X^2(1)=1.055$; p=0.304

Table A2. Impact of NHS Deprivation score (SIM-D) on process and 4 year outcomes

Independent (predictor) Variable	Dependent (process) Variable	Statistics
SIM-D quintile (local) **NO significant impacts identified**	Retention	Chi square $X^2(4)=5.516$; p=0.238
	Pos/neg discharge	Chi square $X^2(12)=10.760$; p=0.550
	Drug screen done	Chi square $X^2(8)=3.592$; p=0.892
	Methadone dose	KWH $X^2(4)=2.981$; p=0.561
	Diazepam dose	KWH $X^2(4)=5.901$; p=0.207
	Dependent (Outcome) variable	
	Employment status	Chi square $X^2(4)=7.188$; p=0.126
	Family stability	Chi square $X^2(8)=8.357$; p=0.399
	Any drug use reported	??
	Heroin use	Chi square $X^2(12)=11.842$; p=0.458
	Heroin days	Chi square $X^2(32)=26.819$; p=0.726
	Heroin route	Chi square $X^2(16)=9.363$; p=0.898
	Illicit Diazepam use	Chi square $X^2(12)=8.271$; p=0.764
	Illicit diazepam days	Chi square $X^2(32)=24.497$; p=826
	Illicit methadone use	Chi square $X^2(12)=8.905$; p=0.711
	Illicit methadone days	Chi square $X^2(24)=16.290$; p=0.877
	Illicit painkillers	Chi square $X^2(12)=10.039$; p=0.613
	Illicit painkiller days	Chi square $X^2(16)=12.767$; p=0.690
	+ve opiate	Chi square $X^2(16)=7.592$; p=0.960
	+ve benzos	Chi square $X^2(12)=8.720$; p=0.727
	Acute admissions reported (18)	KWH $X^2(4)=5.641$; p=0.228
	Psych admissions reported (14)	KWH $X^2(4)=5.885$; p=0.208
	Prison reported (48)	KWH $X^2(4)=3.296$; p=0.510

Table A3. Impact of social stability – time at address - at baseline on process and 4 year outcomes

Independent Variable	Dependent (process) Variable	Statistics
Time at address **No significant impacts identified**	Retention	Chi square $X^2(5)=2.772$; p=0.735
	Pos/neg discharge	Chi square $X^2(5)=6.878$; p=0.230
	Drug screen done	Chi square $X^2(10)=7.625$; p=0.665
	Methadone dose	KWH $X^2(5)=2.055$; p=0.841
	Diazepam dose	KWH $X^2(5)=2.182$; p=0.823
	Dependent (outcome) variable	
	Employment status	Chi square $X^2(25)=16.319$; p=0.905
	Family stability	Chi square $X^2(10)=8.270$; p=0.603
	Any illicit drug use reported	Chi square $X^2(15)=18.521$; p=0.236
	Heroin use reported; days; route	Chi square $X^2(15)=18.168$; p=0.254
	Heroin days	Chi square $X^2(15)=31.601$; p=0.826
	Heroin route	Chi square $X^2(20)=21.416$; p=0.373
	Illicit Diazepam use	Chi square $X^2(15)=12.447$; p=0.645
	Illicit diazepam days	Chi square $X^2(40)=31.353$; p=0.834
	Illicit methadone use	Chi square $X^2(15)=11.979$; p=0.681
	Illicit methadone days	Chi square $X^2(25)=18.525$; p=0.819
	Illicit painkillers use	Chi square $X^2(15)=13.556$; p=0.559
	Illicit painkillers days	Chi square $X^2(20)=17.854$; p=0.597
	+ve opiates;	Chi square $X^2(15)=8.168$; p=0.917
	+ve benzos	Chi square $X^2(15)=6.641$; p=0.967
	Acute admissions reported	KWH $X^2(5)=2.870$; p=0.720
	Psych admissions reported	KWH $X^2(5)=2.349$; p=0.799
	Prison reported	KWH $X^2(5)=4.074$; p=0.539

Table A4. Impact of Social stability – living circumstances - on process and 4 year outcomes

Independent Variable	Dependent (process) Variable	Statistics
Lives alone or not **No significant impacts identified**	**Retention**	Chi square $X^2(5)=6.491$; p=0.261
	Pos/negative discharge	Chi square $X^2(5)=5.873$; p=0.319
	Drug screen done	Chi square $X^2(10)=6.875$; p=0.737
	Methadone dose	KWH $X^2(1)=0.819$; p=0.365
	Diazepam dose	KWH $X^2(4)=4.982$; p=0.289
	Dependent (outcome) variable	
	Employment status	Chi square $X^2(25)=14.071$; p=0.960
	Family stability	Chi square $X^2(10)=13.430$; p=0.201
	Any illicit drug use reported	Chi square $X^2(15)=16.142$; p=0.373
	Heroin use reported; days; route	Chi square $X^2(15)=12.430$; p=0.646
	Heroin days	Chi square $X^2(40)=28.477$; p=0.913
	Heroin route	Chi square $X^2(20)=23.698$; p=0.256
	Illicit Diazepam use	Chi square $X^2(15)=21.012$; p=0.136
	Illicit diazepam days	Chi square $X^2(40)=30.383$; p=0.864
	Illicit methadone use	Chi square $X^2(15)=15.264$; p=0.433
	Illicit methadone days	Chi square $X^2(30)=20.278$; p=0.909
	Illicit painkillers use	Chi square $X^2(15)=13.336$; p=0.576
	Illicit painkillers days	Chi square $X^2(20)=17.043$; p=0.650
	+ve opiates	Chi square $X^2(20)=15.828$; p=727
	+ve benzos	Chi square $X^2(15)=13.186$; p=0.588
	Acute admissions reported	KWH (4)=5.810; p=0.214
	Psych admissions reported	KWH $X^2(4)=6.168$; p=0.187
	Prison reported	KWH $X^2(4)=4.039$; p=0.401

Table A5. Impact of Social stability – living with children - on process and 4 year outcomes

Independent (Predictor) Variable	Dependent (Process) variable	Statistics
Lives with kids **No significant impacts identified**	**Retention**	Chi square $X^2(1)=0.143$; p=0.706
	Pos/neg discharge	Chi square $X^2(1)=0.053$; p=0.819
	Drug screen done	Chi square $X^2(1)=0.477$; p=0.490
	Methadone dose	KWH $X^2(1)=0.807$; p=0.369
	Diazepam dose	KWH $X^2(1)=0.641$; p=0.423
	Dependent (outcome) variable	
	Employment status	Chi square $X^2(5)=2.620$; p=0.758
	Family stability	Chi square $X^2(2)=1.147$; p=0.563
	Any illicit drug use reported	Chi square $X^2(2)=0.077$; p=0.962
	Heroin use reported	Chi square $X^2(3)=1.281$; p=0.734
	Heroin days	Chi square $X^2(8)=7.014$; p=0.535
	Heroin route	Chi square $X^2(4)=2.487$; p=0.647
	Illicit Diazepam use	Chi square $X^2(3)=1.710$; p=0.635
	Illicit diazepam days	Chi square $X^2(7)=5.654$; p=0.581
	Illicit methadone use	Chi square $X^2(3)=4.545$; p=0.208
	Illicit methadone days	Chi square $X^2(6)=4.671$; p=0.587
	Illicit painkillers	Chi square $X^2(3)=1.898$; p=0.594
	Illicit painkillers days	Chi square $X^2(4)=1.223$; p=0.874
	+ve opiates	Chi square $X^2(4)=6.219$; p=0.183
	+ve benzos	Chi square $X^2(3)=0.669$; p=0.880
	Acute admissions reported	KWH $X^2(1)=0.015$; p=0.902
	Psych admissions reported	KWH $X^2(1)=0.275$; p=0.600
	Prison reported	KWH $X^2(1)=0.163$; p=0.686

Table A6. Impact of employment on process and 4 year outcomes

Independent (Predictor) Variable	Dependent (Process) variable	Statistics
Days in paid work/30 **No significant impact identified**	**Retention**	LDA $X^2(1)=1.153$; p=0.283
	Pos/neg discharge	LDA $X^2(1)=0.838$; p=0.360
	Drug screen done	LDA $X^2(1)=0.757$; p=0.384
	Methadone dose	QRA t(1)=0.147; p=0.883
	Diazepam dose	QRA t(1)=0.865; p=0.387
	Dependent (outcome) variable	
	Employment status	LDA $X^2(1)=2.404$; p=0.121
	Family stability	LDA $X^2(1)=1.463$; p=0.226
	Any illicit drug use reported	LDA $X^2(1)=1.210$; p=0.271
	Heroin use reported	LDA $X^2(1)=0.000$; p=0.995
	Heroin days	QDA $X^2(6)=2.520$; p=0.866
	Heroin route	LDA $X^2(1)=0.069$; p=0.793
	Ill Diazepam use	LDA $X^2(1)=1.506$; p=0.220
	Ill meth use	LDA $X^2(1)=1.688$; p=0.194
	Illicit painkillers used	LDA $X^2(1)=0.068$; p=0.795
	+ve opiates	LDA $X^2(1)=0.011$; p=0.918
	+ve benzos	LDA $X^2(1)=2.141$; p=0.143
	Acute admissions reported	LRA t(1)=1.043; p=0.298
	Psych admissions reported	LRA t(1)=1.044; p=0.297
	Prison reported	LRA t(1)=1.068 p=0.280

Table A7. Impact of MAP physical health score on process and 4 year outcomes

Independent (Predictor) Variable	Dependent (Process) variable	Statistics
Baseline MAP physical health score **No significant impact identified**	**Retention**	LDA $X^2(1)=0.000$; p=0.995
	Pos/neg discharge	LDA $X^2(1)=1.243$; p=0.265
	Drug screen done	LDA $X^2(1)=0.176$; p=0.675
	Methadone dose	LRA t(1)=0.212; p=0.832
	Diazepam dose	LRA t(1)=-0.098; p=0.922
	Dependent (outcome) variable	
	Employment status	LDA $X^2(1)=2.092$; p=0.148
	Family stability	LDA $X^2(1)=0.560$; p=0.454
	Any illicit drug use reported	LDA $X^2(1)=0.438$; p=0.508
	Heroin use reported; days; route	LDA $X^2(1)=0.593$; p=0.441
	Heroin days	LDA $X^2(6)=7.330$; p=0.291
	Heroin route	LDA $X^2(1)=2.271$; p=0.132
	Illicit Diazepam use	LDA $X^2(1)=0.002$; p=0.968
	Illicit diazepam days	QDA $X^2(6)=9.237$; p=0.161
	Illicit methadone use	LDA $X^2(1)=0.894$; p=0.344
	Illicit methadone days	QDA $X^2(4)=5.132$; p=0.274
	Illicit painkillers use	LDA $X^2(1)=1.959$; p=0.581
	Illicit painkillers days	QDA $X^2(2)=4.049$; p=0.132
	+ve opiates	LDA $X^2(1)=1.033$; p=0.310
	+ve benzos	LDA $X^2(1)=0.350$; p=0.554
	Acute admissions reported	LRA t(1)=0.033; p=0.974
	Psych admissions reported	LRA t(1)=0.025; p=0.980
	Prison reported	LRA t(1)=0.168; p=0.866

Table A8. Impact of MAP psychological health score on process and 4 year outcomes

Independent (Predictor) Variable	Dependent (Process) variable	Statistics
Baseline MAP psychological health score **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention**	LDA $X^2(1)=0.302$; p=0.583
	Pos/neg discharge	LDA $X^2(1)=0.550$; p=0.458
	Drug screen done	LDA $X^2(1)=0.670$; p=0.413
	Methadone dose	QRA t(1)=1.271; p=0.204
	Diazepam dose	QRA t(1)=-1.295; p=0.196
	Dependent (outcome) variable	
	Employment status	LDA $X^2(1)=0.527$; p=0.468
	Family stability	LDA $X^2(1)=0.003$; p=0.956
	Any illicit drug use reported	LDA $X^2(1)=0.244$; p=0.621
	Heroin use reported	LDA $X^2(1)=1.205$; p=0.272
	Heroin days	QDA $X^2(5)=2.780$; p=0.734
	Heroin route	LDA $X^2(1)=0.662$; p=0.416
	Illicit Diazepam use	LDA **$X^2(1)=4.049$; p=0.044 >score predicts benzo use**
	Illicit diazepam days	QDA $X^2(5)=4.886$; p=0.430
	Ill meth use; days;	LDA $X^2(1)=0.690$; p=0.406
	Illicit methadone days	QDA $X^2(4)=6.511$; p=0.089
	Illicit painkillers	LDA $X^2(1)=1.840$; p=0.175
	+ve opiates	LDA $X^2(1)=0.045$; p=0.832
	+ve benzos	LDA $X^2(1)=1.474$; p=0.225
	Acute admissions reported	LRA t(1)=0.548; p=0.584
	Psych admissions reported	LRA t(1)=0.545; p=0.586
	Prison reported	LRA t(1)=0.645; p=0.519

Table A9. Impact of baseline heroin days used on process and 4 year outcomes

Independent (Predictor) Variable	Dependent (Process) variable	Statistics
Heroin use days **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention**	LDA $X^2(1)=0.072$; p=0.789
	Drug screen done	LDA $X^2(1)=0.124$; p=0.724
	Methadone dose	LRA t(1)=1.821; p=0.069
	Diazepam dose	LRA t(1)=-0.316; p=0.752
	Dependant (outcome) variable	
	Employment status	LDA $X^2(1)=1.482$; p=0.224
	Family stability	LDA $X^2(1)=0.303$; p=0.582
	Any illicit drug use reported	LDA $X^2(1)=2.991$; p=0.084
	Heroin use reported	**LDA $X^2(1)=5.231$; p=0.022 More days predicts no use**
	Heroin days	LDA $X^2(5)=4.931$; p=0.424
	Heroin route	LDA $X^2(1)=2.308$; p=0.129
	Ill Diazepam use	LDA $X^2(1)=2.263$; p=0.132
	Illicit diazepam days	LDA $X^2(5)=3.727$; p=0.589
	Illicit methadone use	LDA $X^2(1)=3.497$; p=0.061
	Illicit methadone days	LDA $X^2(3)=0.283$; p=0.963
	Illicit painkillers use	LDA $X^2(1)=0.100$; p=0.751
	Illicit painkillers days	LDA $X^2(1)=0.970$; p=0.325
	+ve opiates	LDA $X^2(1)=2.832$; p=0.092
	+ve benzos	LDA $X^2(1)=0.157$; p=0.692
	Acute admissions reported	LRA t(1)=-0.199; p=0.843
	Psych admissions reported	LRA t(1)=0.211; p=0.833
	Prison reported	LRA t(1)=0.272; p=0.786

Table A10. Impact of baseline diazepam illicit use on process and 4 year outcomes

Independent (Predictor) Variable	Dependent (Process) variable	Statistics
Benzodiazepine use - test **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention**	Chi square $X^2(2)=0.034$; p=0.983
	Drug screen done	Chi square $X^2(4)=0.856$; p=0.931
	Methadone dose	KWH $X^2(1)=2.163$; p=0.141
	Diazepam dose	KWH $X^2(1)=0.579$; p=0.447
	Dependent (outcome) variables	
	Employment status	Chi square $X^2(12)=5.629$; p=0.934
	Family stability Negative predicts stability	**Chi square $X^2(4)=10.699$;p=0.030**
	Any illicit drug use reported	Chi square **$X^2(6)=12.494$ p=0.052**
	Heroin use reported; days	Chi square $X^2(6)=6.266$; p=0.394
	Heroin days Negative predicts more heroin use	**Chi square $X^2(16)=28.293$p=0.029**
	Heroin route	Chi square $X^2(8)=3.647$; p=0.887
	Illicit Diazepam use	Chi square $X^2(6)=6.805$; p=0.339
	Illicit diazepam days	Chi square $X^2(16)=18.766$; p=0.281
	Illicit methadone use	Chi square $X^2(6)=5.010$; p=0.543
	Illicit methadone days	Chi square $X^2(12)=11.820$; p=0.460
	Illicit painkillers use	Chi square $X^2(6)=5.218$; p=0.516
	Illicit painkillers days	Chi square $X^2(18)=6.401$; p=0.602
	+ve opiates	Chi square $X^2(8)=8.656$; p=0.372
	+ve benzos	Chi square $X^2(6)=8.664$; p=0.193
	Acute admissions reported	KWH $X^2(1)=0.002$; p=0.968
	Psych admissions reported	KWH $X^2(1)=0.012$; p=0.912
	Prison reported	KWH $X^2(1)=0.037$; p=0.848

Table A11. Impact of injecting risk (baseline IRQ total score) on process and 4 year outcomes

Independent (Predictor) Variable	Dependent (Process) variable	Statistics
Risk taking – injecting total score 1-17 in IRQ (71 of 87 IV cases/537) **No significant impact identified**	**Retention**	LDA $X^2(1)=1.003$; p=0.317
	Drug screen done	Chi square $X^2(4)=6.389$; p=0.172
	Methadone dose	LRA t(1)=-1.125; p=0.267
	Diazepam dose	LRA t(1)=0.531; p=0.598
	Dependent (outcome) variable	
	Employment status	LDA $X^2(1)=0.047$; p=0.828
	Family stability	LDA $X^2(1)=0.136$; p=0.712
	Any illicit drug use reported	LDA $X^2(1)=0.134$; p=0.715
	Heroin use reported; days; route	LDA $X^2(1)=0.134$; p=0.715
	Heroin days	LDA $X^2(2)=1.324$; p=0.516
	Heroin route	LDA $X^2(1)=1.286$; p=0.257
	Illicit Diazepam use	LDA $X^2(1)=0.727$; p=0.394
	Illicit diazepam days	LDA $X^2(3)=3.431$; p=0.330
	Ill meth use; days;	Not tested
	Illicit painkillers use	Not tested
	Illicit painkiller days	Not tested
	+ve opiates	Chi square $X^2(8)=11.926$; p=0.155
	+ve benzos	Chi square $X^2(8)=11.043$; p=0.087
	Acute admissions reported	LRA t(1)=-1.015; p=0.316
	Psych admissions reported	LRA t(1)=-1.013; p=0.317
	Prison reported	LRA t(1)=-1.008; p=0.319

Table A12. Impact of Pain and its characteristics on process

Independent (Predictor) Variable	Dependent (Process) variable	Statistics
Pain **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied** 1. Present - No associations 2. Duration - No associations 3. Chronic (12/12) – 4. Intensity 5. Intensity quintiles	**Retention : High intensity (score)predicts poor retention**	1.Chi square $X^2(1)=0.033;p=0.856$ 2.LDA $X^2(1)=0.238$; p=0.626 3. Chi square $X^2(1)=0.055;p=0.815$ **4.LDA $X^2(1)=6.301$; p=0.012** 5. Chi square $X^2(4)=6.208;p=0.184$
	Pos/neg discharge : More severe (quintiles)predicts negative discharge	1.Chi square $X^2(1)=0.548;p=0.459$ 2.LDA $X^2(1)=0.003$; p=0.958 3. Chi square $X^2(1)=0.001;p=0.979$ 4.LDA $X^2(1)=0.748$; p=0.387 **5. Chi square $X^2(4)=13.151;p=0.011$**
	Drug screen done: Higher intensity (score) =less likely to be screened	1.Chi square $X^2(2)=0.869;p=0.647$ 2. LDA $X^2(1)=0.022$; p=0.883 3. Chi square $X^2(2)=0.254;p=0.881$ **4.LDA $X^2(1)=4.874$; p=0.027** 5. Chi square $X^2(8)=10.979;p=0.203$
	Methadone dose	1. KWH $X^2(1)=0.810$; p=0.368 2.LRA t(1)=0.284; p=0.777 3. KWH $X^2(1)=0.145$; p=0.704 4.LRA t(1)=1.598; p=0.111 5. KWH $X^2(4)=6.887$; p=0.142
	Diazepam dose	1. KWH $X^2(1)=0.010$; p=0.920 2.LRA t(1)= 1.189; p=0.236 3. KWH $X^2(1)=0.107$; p=0.744 4.LRA t(1)=1.503; p=0.134 5. KWH $X^2(4)=3.739$; p=0.442

Table A13. Impact of Pain and its characteristics on 4 year outcomes

Independent (Predictor) Variable	Dependent (Outcome) variable	Statistics
Pain **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied** 1. Present - No associations 2. Duration - No associations 3. Chronic (12/12) 4. Intensity 5. Intensity quintiles	**Employment status**	1.Chi square $X^2(6)=8.002$; p=0.238 2. LDA $X^2(1)=0.001$; p=0.972 3. Chi square $X^2(6)=7.645$; p=0.265 4.LDA $X^2(1)=0.370$; p=0.543 **5. Chi square $X^2(24)=36.718$; p=0.047**
	Family stability	1.Chi square $X^2(2)=0.634$; p=0.729 2. LDA $X^2(1)=0.914$; p=0.339 3. Chi square $X^2(2)=2.713$; p=0.258 4.LDA $X^2(1)=1.455$; p=0.228 5. Chi square $X^2(8)=9.062$; p=0.337
	Any illicit drug use reported	1.Chi square $X^2(2)=0.851$; p=0.654 2. LDA $X^2(1)=0.160$; p=0.689 3. Chi square $X^2(2)=0.063$ p=0.969 4.LDA $X^2(1)=3.206$; p=0.073 5. Chi square $X^2(8)=10.368$; p=0.240
	Heroin use reported; days; route	1.Chi square $X^2(3)=2.632$; p=0.452 2. LDA $X^2(1)=0.045$; p=0.831 3. Chi square $X^2(2)=0.843$; p=0.656 4.LDA $X^2(1)=0.295$; p=0.587 5. Chi square $X^2(8)=8.142$; p=0.420
	Heroin days: **Chronic pain predicts moredays**	1.Chi square $X^2(7)=11.644$; p=0.113 2. LDA $X^2(3)=4.308$; p=0.230 **3. Chi square $X^2(6)=12.942$; p=0.044** 4.LDA $X^2(5)=8.747$; p=0.120 5. Chi square $X^2(24)=35.542$; p=0.061
	Heroin route	1.Chi square $X^2(4)=1.573$; p=0.814 2. LDA $X^2(1)=0.508$; p=0.476 3. Chi square $X^2(4)=1.211$; p=0.876 4.LDA $X^2(1)=0.012$; p=0.913 5. Chi square $X^2(16)=16.987$; p=0.386
	Ill Diazepam use	1.Chi square $X^2(3)=1.594$; p=0.661 2. LDA $X^2(1)=0.389$; p=0.533 3. Chi square $X^2(2)=0.682$; p=0.711 4.LDA $X^2(1)=1.268$; p=0.260 5. Chi square $X^2(8)=6.744$; p=0.564
	Illicit diazepam days	1.Chi square $X^2(8)=3.880$; p=0.868 2. LDA $X^2(1)=1.756$; p=0.882 3. Chi square $X^2(8)=7.728$; p=0.460 4.LDA $X^2(5)=7.772$; p=0.169 5. Chi square $X^2(32)=27.901$; p=0.674
	Illicit methadone use;	1.Chi square $X^2(3)=3.952$; p=0.267 2. LDA $X^2(1)=0.334$; p=0.563 3. Chi square $X^2(2)=0.443$; p=0.802 4.LDA $X^2(1)=2.791$; p=0.095 5. Chi square $X^2(8)=6.274$; p=0.617
	Illicit methadone days	1.Chi square $X^2(6)=3.958$; p=0.682 2. LDA $X^2(3)=0.409$; p=0.938 3. Chi square $X^2(6)=1.293$; p=0.972 4.LDA $X^2(3)=2.047$; p=0.563 5. Chi square $X^2(24)=23.425$; p=0.495
	Illicit painkillers use	1.Chi square $X^2(3)2.188$; p=0.534 2. LDA $X^2(1)=1.387$; p=0.239 3. Chi square $X^2(2)=0.422$; p=0.810 4.LDA $X^2(1)=0.153$; p=0.696 5. Chi square $X^2(8)=11.023$; p=0.200
	+ve opiates	1.Chi square $X^2(4)=4.019$; p=0.403 2. LDA $X^2(1)=0.249$; p=0.618 3. Chi square $X^2(4)=0.703$; p=0.951 4.LDA $X^2(1)=2.164$; p=0.141 5. Chi square $X^2(16)=18.961$; p=0.271
	+ve benzos	1.Chi square $X^2(3)=0.245$; p=0.970 2. LDA $X^2(1)=0.546$; p=0.460 3. Chi square $X^2(3)=0.579$; p=0.901 4.LDA $X^2(1)=1.660$; p=0.198 5. Chi square $X^2(12)=16.202$; p=0.182

	Acute admissions reported (18)More intense=more admissions	1.ANOVA F(1,9)=-0.012; p=0.912 2. LRA t(1)=-0.339; p=0.735 3.KWH $X^2(1)=0.000$; p=0.993 4.**LRA t(1)=2.366; p=0.018** 5. KWH $X^2(4)=5.495$; p=0.240
	Psych admissions reported (14)More intense=more admissions	1.ANOVA F(1,9)=-0.014; p=0.905 2. LRA t(1)=-0.341; p=0.734 3. KWH $X^2(1)=0.044$; p=0.834 4. **LRA t(1)=2.391; p=0.017** 5. KWH $X^2(4)=5.961$; p=0.202
	Prison reported (48) More intense=more admissions	1.ANOVA F(1,9)=-0.054; p=0.816 2. LRA t(1)=-0.338; p=0.736 3KWH $X^2(1)=0.158$; p=0.691 **4LRA t(1)=2.367; p=0.018** 5.KWH $X^2(4)=6.690$; p=0.153

Table A14. Impact of Social Phobia (SPDQ) on process and 4 year outcomes

538 screened of whom 215 socially phobic, 323 not.

Independent (Predictor) Variable	Dependent (Process) variable	Statistics
Social phobia (SPDQ) 1. **Diagnosis y/n** 2. **Social phobia total score** **No significant impact identified**	**Retention**	1.Chi square $X^2(1)=2.293$; p=0.130 2.LDA $X^2(1)=2.219$; p=0.136
	Pos/neg discharge	1.Chi square $X^2(1)=0.140$; p=0.708 2.LDA $X^2(1)=0.117$; p=0.732
	Drug screen done	1.Chi square $X^2(2)=2.203$; p=0.332 2.LDA $X^2(1)=0.445$; p=0.505
	Methadone dose	1.KWH $X^2(1)=0.151$; p=0.697 2.LRA t(1)=0.-1.188; p=0.235
	Diazepam dose	1.KWH $X^2(1)=1.804$; p=0.179 2.LRA t(1)=-1.575; p=0.116
	Dependent (Outcome) variable	
	Employment status	1.Chi square $X^2(6)=12.212$; p=0.057 2.LDA $X^2(1)=2.623$; p=0.203
	Family stability	1.Chi square $X^2(2)=2.744$; p=0.254 2.LDA $X^2(1)=0.237$; p=0.626
	Any illicit drug use reported	1.Chi square $X^2(2)=2.954$; p=0.228 2.LDA $X^2(1)=1.056$; p=0.304
	Heroin use reported	1.Chi square $X^2(3)=3.672$; p=0.299 2.LDA $X^2(1)=0.403$; p=0.525
	Heroin days	1.Chi square $X^2(8)=7.784$; p=0.455 2.LDA $X^2(5)=8.082$; p=0.152
	Heroin route	1.Chi square $X^2(1)=4.627$; p=0.328 2.LDA $X^2(1)=3.744$; p=0.053
	Illicit Diazepam use	1.Chi square $X^2(3)=3.482$; p=0.323 2.LDA $X^2(1)=0.003$; p=0.955
	Illicit diazepam days	1.Chi square $X^2(8)=10.829$; p=0.212 2.LDA $X^2(5)=6.093$; p=0.297
	Illicit methadone use	1.Chi square $X^2(3)=5.177$; p=0.159 2.LDA $X^2(1)=1.557$; p=0.212
	Illicit methadone days	1.Chi square $X^2(6)=8.628$; p=0.196 2.QDA $X^2(3)=4.713$; p=0.194
	Illicit painkillers use	1.Chi square $X^2(3)=3.678$; p=0.298 2.LDA $X^2(1)=1.697$; p=0.193
	+ve opiates	1.Chi square $X^2(4)=2.658$; p=0.617 2.LDA $X^2(1)=0.002$; p=0.966
	+ve benzos	1.Chi square $X^2(3)=3.057$; p=0.383 2.LDA $X^2(1)=1.238$; p=0.266
	Acute admissions reported	1.KWH $X^2(1)=1.705$; p=0.192 2.LRA t(1)=-1.512; p=0.131
	Psych admissions reported	1.KWH $X^2(1)=2.104$; p=0.147 2.LRA t(1)=-1.520; p=0.129
	Prison reported	1.KWH $X^2(1)=3.205$; p=0.073 2.LRA t(1)=-1.446; p=0.149

Social phobia as measured by SPDQ at baseline has <u>no significant impact</u> on 2009 outcomes

Table A15. Impact of ADHD symptoms (CSS) on process and 4 year outcomes. 368 of original cohort screened. Of these: 51 had Inattentive symptoms; 28 had hyperactive/impulsive symptoms; 20 combined 59 had "any ADHD" symptoms – 31 inattentive; 8 hyperactive; 20 combined

Independent (Predictor) Variable	Dependent (Process) variable	Statistics
1. ADHD symptoms **2. ADHD types** **3. Impairment (19)** **Significant impact set at thep<0.05 level** **Significant impact at the appropriate level once Bonferroni Correction applied**	**Retention**	1. Chi square $X^2(1)=0.423$; p=0.515 2. Chi square $X^2(2)=4.248$; p=0.120 3. Chi square $X^2(1)=0.046$; p=0.529
	Pos/neg discharge	1. Chi square $X^2(1)=1.347$; p=0.246 2. Chi square $X^2(1)=0.022$; p=0.881 3. Chi square $X^2(1)=0.063$; p=0.802
	Drug screen done	1.Chi square $X^2(2)=0.304$; p=0.859 2.Chi square $X^2(2)=2.813$; p=0.245 3. Chi square $X^2(2)=0.081$; p=0.960
	Methadone dose	1.KWH $X^2(1)=3.369$; p=0.066 2.KWH $X^2(2)=0.291$; p=0.865 3. KWH $X^2(1)=2.022$; p=0.155
	Diazepam dose	1.KWH $X^2(1)=3.327$; p=0.068 2.KWH $X^2(2)=1.273$; p=0.529 3. KWH $X^2(1)=2.304$; p=0.129
	Dependent (outcome) variable	
	Employment status	1.Chi square $X^2(6)=3.980$; p=0.679 2.Chi square $X^2(6)=7.274$; p=0.296 3. Chi square $X^2(6)=9.714$; p=0.137
	Family stability	1.Chi square $X^2(2)=1.140$; p=0.566 2.Chi square $X^2(4)=5.282$; p=0.260 3. Chi square $X^2(2)=0.438$; p=0.803
	Any illicit drug use reported	1.Chi square $X^2(3)=0.732$; p=0.866 2.Chi square $X^2(4)=5.323$; p=0.256 3. Chi square $X^2(2)=1.968$; p=0.374
	Heroin use reported	1.Chi square $X^2(3)=2.478$; p=0.479 2.Chi square $X^2(4)=4.316$; p=0.365 3. Chi square $X^2(3)=0.142$; p=0.986
	Heroin days	1.Chi square $X^2(8)=11.767$; p=0.162 2.Chi square$X^2(14)=17.946$; p=0.209
	Heroin route	1.Chi square $X^2(4)=7.981$; p=0.092 2.Chi square $X^2(8)=9.334$; p=0.315
	Illicit Diazepam use	1.Chi square $X^2(3)=5.481$; p=0.140 2.Chi square $X^2(4)=5.310$; p=0.257 3. Chi square $X^2(3)=0.279$; p=0.964
	Illicit diazepam days	1.Chi square $X^2(8)=7.371$; p=0.497 2.Chi square $X^2(12)=14.980$; p=0.243
	Illicit methadone use	1.Chi square $X^2(3)=2.672$; p=0.445 2.Chi square $X^2(4)=7.488$; p=0.112 3. Chi square $X^2(3)=0.179$; p=0.981
	Illicit methadone days	1.Chi square $X^2(5)=6.091$; p=0.297 2.Chi square $X^2(8)=7.404$; p=0.494
	Illicit painkillers use: **ADHD predicts painkiller use**	**1.Chi square $X^2(3)=8.804$; p=0.032** 2.Chi square $X^2(4)=6.483$; p=0.166 3. Chi square $X^2(3)=0.244$; p=0.970
	+ve opiates	1.Chi square $X^2(3)=3.199$; p=0.362 2.Chi square $X^2(6)=7.108$; p=0.311 3. Chi square $X^2(4)=0.360$; p=0.986
	+ve benzos	1.Chi square $X^2(3)=1.388$; p=0.708 2. Chi square $X^2(6)=3.998$; p=0.677 3. Chi square $X^2(3)=0.693$; p=0.875
	Acute admissions reported (18)	1.KWH $X^2(1)=0.525$; p=0.469 2.KWH $X^2(2)=4.833$; p=0.089 3. KWH $X^2(1)=0.006$; p=0.940
	Psych admissions reported (14)	1.KWH $X^2(1)=0.236$; p=0.627 2.KWH $X^2(2)=3.248$; p=0.197 3. KWH $X^2(1)=0.014$; p=0.905
	Prison reported (48)	1.KWH $X^2(1)=0.088$; p=0.767 2.KWH $X^2(2)=3.273$; p=0.195 3. KWH $X^2(1)=0.012$; p=0.911

Appendix 5 – Additional tables of results – Chapter 7

This Appendix contains the additional results tables for which no significant associations were demonstrated - HIC data linkage univariate analyses

Table A16. Impact of Area lived in on outcomes

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
Area **No significant impacts identified**	***Out-patient appointments*** SMR00 sessions 2005/10	KWH $X^2(2)=4.800$; p=0.091
	Acute Services Contacts	
	Ambulance service call-outs SAS attendances 2008/11	KWH $X^2(2)=0.700$; p=0.705
	Naloxone administrations 2008/11	KWH $X^2(2)=2.506$; p=0.286
	A&E attendances <2008	KWH $X^2(2)=1.904$; p=0.386
	General Hospital Admissions	
	SMR01 admissions (acute) - ALL	KWH $X^2(2)=0.816$; p=0.665
	SMR01 duration(nights) - ALL	KWH $X^2(2)=1.374$; p=0.503
	Psychiatric Admissions	
	SMR04 admissions(psych) 2005/11	KWH $X^2(2)=0.611$; p=0.737
	SMR04 total days	KWH $X^2(2)=1.176$; p=0.556
	Registrar General Death Data GROS dead/alive	Chi square $X^2(2)=0.387$; p=0.824

Table A18. Impact of deprivation score on outcomes

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
SIMD quintile **No significant impacts identified**	***Out-patient appointments*** SMR00 sessions 2005/10	KWH $X^2(4)=7.343$; p=0.119
	Acute Services Contacts	
	Ambulance service call outs SAS attendances 2008/11	KWH $X^2(4)=5.036$; p=0.284
	Naloxone administrations 2008/11	KWH $X^2(4)=4.090$; p=0.394
	A&E attendances <2008	KWH $X^2(3)=5.289$; p=0.152
	General Hospital Admissions	
	SMR01 admissions (acute) - ALL	KWH $X^2(4)=5.346$; p=0.254
	SMR01 duration(nights) - ALL	KWH $X^2(4)=3.072$; p=0.546
	Psychiatric Admissions	
	SMR04 admissions(psych) 2005/11	KWH $X^2(4)=6.280$; p=0.179
	SMR04 total days	KWH $X^2(4)=3.881$; p=0.422
	Registrar General Death Data GROS dead/alive	Chi square $X^2(4)=2.188$; p=0.701

Table A17. Impact of time at current address on outcomes

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
Time at address **No significant impacts identified**	***Out-patient attendances*** SMR00 sessions 2005/10	KWH $X^2(5)=1.634$; p=0.897
	Acute services contacts	
	Ambulance Service Call-outs SAS attendances 2008/11	KWH $X^2(5)=2.342$; p=0.800
	Naloxone administrations 2008/11	KWH $X^2(5)=5.784$; p=0.328
	A&E attendances <2008	KWH $X^2(5)=7.540$; p=0.183
	Acute Hospital Admissions	
	SMR01 admissions (acute) - ALL	KWH $X^2(5)=7.732$; p=0.172
	SMR01 duration(nights) - ALL	KWH $X^2(5)=2.903$; p=0.715
	Psychiatric Admissions	
	SMR04 admissions(psych) 2005/11	KWH $X^2(5)=1.416$; p=0.923
	SMR04 total days	KWH $X^2(5)=2.360$; p=0.797
	Registrar General Death Data GROS deaths	Chi square $X^2(5)=8.238$; p=0.144

Table A19. Impact of Living arrangements on outcome

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
Lives alone or not **No significant impacts identified**	***Out-patient Attendances*** SMR00 sessions 2005/10	KWH $X^2(1)=0.017$; p=0.896
	Acute Services Contacts	
	Ambulance service Call-outs SAS attendances 2008/11	KWH $X^2(1)=0.211$; p=0.646
	Naloxone administrations 2008/11	KWH $X^2(1)=0.020$; p=0.886
	A&E attendances <2008	KWH $X^2(4)=0.011$; p=0.918
	Acute Hospital Admissions	
	SMR01 admissions (acute) - ALL	KWH $X^2(1)=0.093$; p=0.760
	SMR01 duration(nights) - ALL	KWH $X^2(1)=0.218$; p=0.641
	Psychiatric Admissions	
	SMR04 admissions(psych) 2005/11	KWH $X^2(1)=0.572$; p=0.449
	SMR04 total days	KWH $X^2(1)=1.211$; p=0.271
	Registrar general Death Data GROS deaths	Chi square $X^2(5)=1.416$; p=0.923

Table A20. Impact of having children at baseline on outcomes

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
Has children **No significant impacts identified**	***Out-patient attendances*** SMR00 sessions 2005/10	MWU=18524; p=0.699
	Acute services contacts	
	Ambulance service Call-outs SAS attendances 2008/11	MWU=236.0; p=0.850
	Naloxone administrations 2008-11	MWU=63.5; p=0.604
	A&E attendances <2008	MWU=72.0; p=0.796
	Acute Hospital Admissions	
	SMR01 admissions (acute) - ALL	MWU=19459; p=0.821
	SMR01 duration(nights) - ALL	MWU=4187; p=0.580
	Psychiatric Admissions	
	SMR04 admissions(psych) 2005/11	MWU=144.5; p=0.654
	SMR04 total days	MWU=204.5; p=0.530
	Registrar General Death Data GROS deaths	Chi square $X^2(1)=0.140$; p=0.709

Table A21. Impact of living with children at baseline on outcomes

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
Living with children **No significant impact identified**	***Out-patient attendances*** SMR00 sessions 2005/10	MWU=14542.0; p=0.323
	Acute services contacts	
	Ambulance service Call-outs SAS attendances 2008/11	MWU=255.0; p=0.917
	Naloxone administrations 2008-11	MWU=34.0; p=0.261
	A&E attendances <2008	MWU=86.5; p=0.867
	Acute Hospital admissions	
	SMR01 admissions (acute) - ALL	MWU=3719.5; p=0.860
	SMR01 duration(nights) - ALL	MWU=3511.5; p=0.497
	Psychiatric Admissions	
	SMR04 admissions(psych) 2005/11	MWU=92.0; p=0.746
	SMR04 total days	MWU=85.0; p=0.530
	GROS deaths	Chi square $X^2(1)=1.847$; p=0.174

Table A22. Impact of Educational level achieved on outcome

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
Educational level achieved **No significant impact identified**	***Out-patient attendances*** SMR00 sessions 2005/10	KWH $X^2(4)=7.491$; p=0.112
	Acute Services Contacts	
	Ambulance service call-outs SAS attendances 2008/11	KWH $X^2(4)=6.043$; p=0.196
	Naloxone administrations 2008-11	KWH $X^2(4)=0.768$; p=0.857
	A&E attendances <2008	KWH $X^2(4)=1.412$; p=0.494
	Acute Hospital Admissions	
	SMR01 admissions (acute) - ALL	KWH $X^2(4)=1.817$; p=0.769
	SMR01 duration(nights) - ALL	KWH $X^2(4)=3.297$; p=0.509
	Psychiatric Admissions	
	SMR04 admissions(psych) 2005/11	KWH $X^2(4)=5.036$; p=0.284
	SMR04 total days	KWH $X^2(4)=5.418$; p=0.247
	Registrar General Death DataGros death	Chi square $X^2(4)=2.380$; p=0.666

Table A23. Impact of baseline MAP Psychological Health Score on outcome

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
MAP Psychological Health Score **No significant impact identified**	SMR00 sessions 2005/10	LRA t(1)=1.895; p=0.059
	Emergency Service Contacts	
	Ambulance service Call-outs SAS attendances 2008/11	LRA t(1)=-0.427; p=0.671
	Naloxone administrations 2008-11	LRA t(1)=-0.026; p=0.979
	A&E attendances <2008	LRA t(1)=1.120; p=0.270
	Acute Hospital Admissions	
	SMR01 admissions (acute) - ALL	LRA t(1)=0.645; p=0.519
	SMR01 duration(nights) - ALL	LRA t(1)=-0.096; p=0.924
	Psychiatric Admissions	
	SMR04 admissions(psych) 2005/11	LRA t(1)=0.557; p=0.580
	SMR04 total days	LRA t(1)=0.634; p=0.529
	Registrar General Death Data GROS death	LDA $X^2(1)=0.041$; p=0.840

Table A24. Impact of baseline diazepam dosage on outcome

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
Diazepam dose **No significant impact identified**	***Out-patient attendances*** SMR00 sessions 2005/10	LRA t(1)=-1.803; p=0.072
	Emergency Service contacts	
	Ambulance service Call-outs SAS attendances 2008/11	LRA t(1)=-0.489; p=0.626
	Naloxone administrations 2008-11	LRA t(1)=-0.700; p=0.489
	A&E attendances <2008	LRA t(1)=0.596; p=0.555
	Acute Hospital Admissions	
	SMR01 admissions (acute)	LRA t(1)=-0.222; p=0.825
	SMR01 duration(nights)	LRA t(1)=-0.535; p=0.593
	Psychiatric Admissions	
	SMR04 admissions(psych) 2005/11	LRA t(1)=-0.460; p=0.647
	SMR04 total days	LRA t(1)=-0.613; p=0.541
	Registrar general Death Data GROS death	LDA $X^2(1)=2.570$; p=0.109

Table A25. Impact of route of baseline heroin use (injecter/non-injector) on outcome

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
Heroin route **No significant impact identified**	***Out-patient attendances*** SMR00 sessions 2005/10	MWU=7581.500; p=0.277
	Emergency Service Contacts	
	Ambulance service call-outs SAS attendances 2008/11	MWU=122.500; p=0.885
	Naloxone administrations 2008-11	MWU=17.000; p=0.571
	A&E attendances <2008	MWU=14.500; p=0.435
	Acute Hospital Admissions	
	SMR01 admissions (acute)	MWU=1798.000; p=0.712
	SMR01 duration(nights)	MWU=1677.500; p=0.392
	Psychiatric Admissions	
	SMR04 admissions(psych) 2005/11	MWU=25.500; p=0.053
	SMR04 total days	MWU=30.500; p=0.121
	Registrar general Death Data GROS death	Chi square $X^2(2)=0.468$; p=0.791

Table A26. Impact of baseline illicit diazepam use on outcome

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
IV	**DV**	**Stats**
Diazepam use at baseline **No significant impact identified**	***Out-patient attendances*** SMR00 sessions 2005/10	MWU=5959.000; p=0.259
	Emergency Service Contacts	
	Ambulance Service Call-outs SAS attendances 2008/11	MWU=74.000; p=0.888
	Naloxone administrations 2008-11	MWU=2.500; p=0.286
	A&E attendances <2008	MWU=26.500; p=0.763
	Acute Hospital Admissions	
	SMR01 admissions (acute) - ALL	MWU=1528.000; p=0.562
	SMR01 duration(nights) - ALL	MWU=1590.500; p=0.823
	Psychiatric Admissions	
	SMR04 admissions(psych) 2005/11	MWU=34.000; p=0.113
	SMR04 total days	MWU=27.500; p=0.052
	Registrar General Death Data GROS death	Chi square $X^2(2)=0.511$; p=0.774

Table A27. Impact of baseline risk taking (IRQ total score) on outcome

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
Risk taking – injecting total score 1-17 in IRQ (71 of 87 IV cases/537) **No significant impact identified**	***Out-patient attendances*** SMR00 sessions 2005/10	LRA t(1)=-0.322; p=0.748
	Emergency Services Contacts	
	Ambulance Service Call-outs SAS attendances 2008/11	LRA t(1)=-0.410; p=0.696
	Naloxone administrations 2008-11	Not tested (numbers)
	A&E attendances <2008	LRA t(1)=-0.447; p=0.685
	Acute Hospital admissions	
	SMR01 admissions (acute)	LRA t(1)=-0.336; p=0.739
	SMR01 duration(nights)	LRA t(1)=-0.221; p=0.827
	Psychiatric Hospital Admissions	
	SMR04 admissions(psych) 2005/11	Not tested (numbers)
	SMR04 total days	Not tested (numbers)
	Registrar General Death Data GROS death	LDA $X^2(1)=0.160$; p=0.689

Table A28. Impact of baseline social phobia (SPDQ) on outcome

Independent (Predictor) Variable	Dependent (Process or outcome) Variable	Statistics
SPDQ diagnosis and score **No significant impact identified**	***Out-patient attendances*** SMR00 sessions 2005/10	1.MWU=27971.000; p=0.298 2.LRA t(1)=1.384; p=0.167
	Ambulance Service Call-outs SAS attendances 2008/11	1.MWU=392.000; p=0.393 2.LRA t(1)=0.323; p=0.748
	Naloxone administrations 2008-11	1.MWU=122.500; p=0.631 2.LRA t(1)=0.089; p=0.930
	A&E attendances <2008	1.MWU=105.000; p=0.560 2.LRA t(1)=1.019; p=0.316
	Acute Hospital Admissions	
	SMR01 admissions (acute) - ALL	1.MWU=6686.000; p=0.539 2.LRA t(1)=-0.366; p=0.715
	SMR01 duration(nights) - ALL	1.MWU=6731.000; p=0.709 2.LRA t(1)=0.146; p=0.884
	Psychiatric Admissions	
	SMR04 admissions(psych) 2005/11	1.MWU=262.000; p=0.629 2.LRA t(1)=0.960; p=0.342
	SMR04 total days	1.MWU=264.000; p=0.684 2.LRA t(1)=1.784; p=0.081
	Registrar general death Data GROS death	1.Chi square $X^2(1)=1.261$; p=0.262 2 LDA $X^2(1)=1.807$; p=0.179

Appendix 6 – Cross Validation demonstration of method

This appendix contains a description of a "test" regression analysis and cross validation exercise, undertaken to confirm the effectiveness of the cross validation approach taken in Chapter 9.

Introduction

In order to demonstrate the validity of the cross validation method used, an exercise was undertaken using test data. The exercise aimed to demonstrate cross-validation of a predictive model derived from *Group a* data to *Group b*. A test dataset was generated using the MATLAB programme. Overall, the data fitted y=2.1x+3.5. The total dataset was split into two elements - Group a split fitted y=2.0x+3.5; Group b split fitted y=2.1x+3.4. [Complete data used are attached in Appendix 6. Figure 1.]

Method

A multiple linear regression was undertaken using *Group a* data. SPSS outputs are shown (Tables 1-3). The R square was 0.816 – i.e. the model predicted 81.6% of the variance (Table 1). F is very high (therefore very unlikely to occur by chance) Accordingly, the significance level for the ANOVA is less than 0.001 (Table 2).

The model generated coefficients (Table 3) - B1 (the gradient of the line) and B0 (the Y intercept of line). These coefficients were incorporated into the equation y= bo + bx + 3.5 to generate a new variable "ca" – the predicted outcome ("y") using the *Group a* model. This was then correlated with the *Group b* observed outcome ("y2b"). These were highly correlated (Table 4 and scatterplot 1) – demonstrating that the *predicted* outcome "ca" correlates closely with (predicts) the *observed* outcome in the novel dataset "y2b". The model is generalizable.

Table 1. SPSS output 1 - model summary – Group a data

Model	R	R square	Adjusted R Square	Standard error of estimate
	.903	.816	.814	.273

Table 2. SPSS output 2 - ANOVA

Model	Sum of Squares	df	Mean Square	F	Significance
Regression	32.309	1	32.309	434.185	.000
Residual	7.292	98	.074		
Total	39.601	99			

Table 3. SPSS output 3 - Coefficients

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	3.517	.058		60.406	.000
	group a x values	2.027	.097	.903	20.837	.000

Cross validation

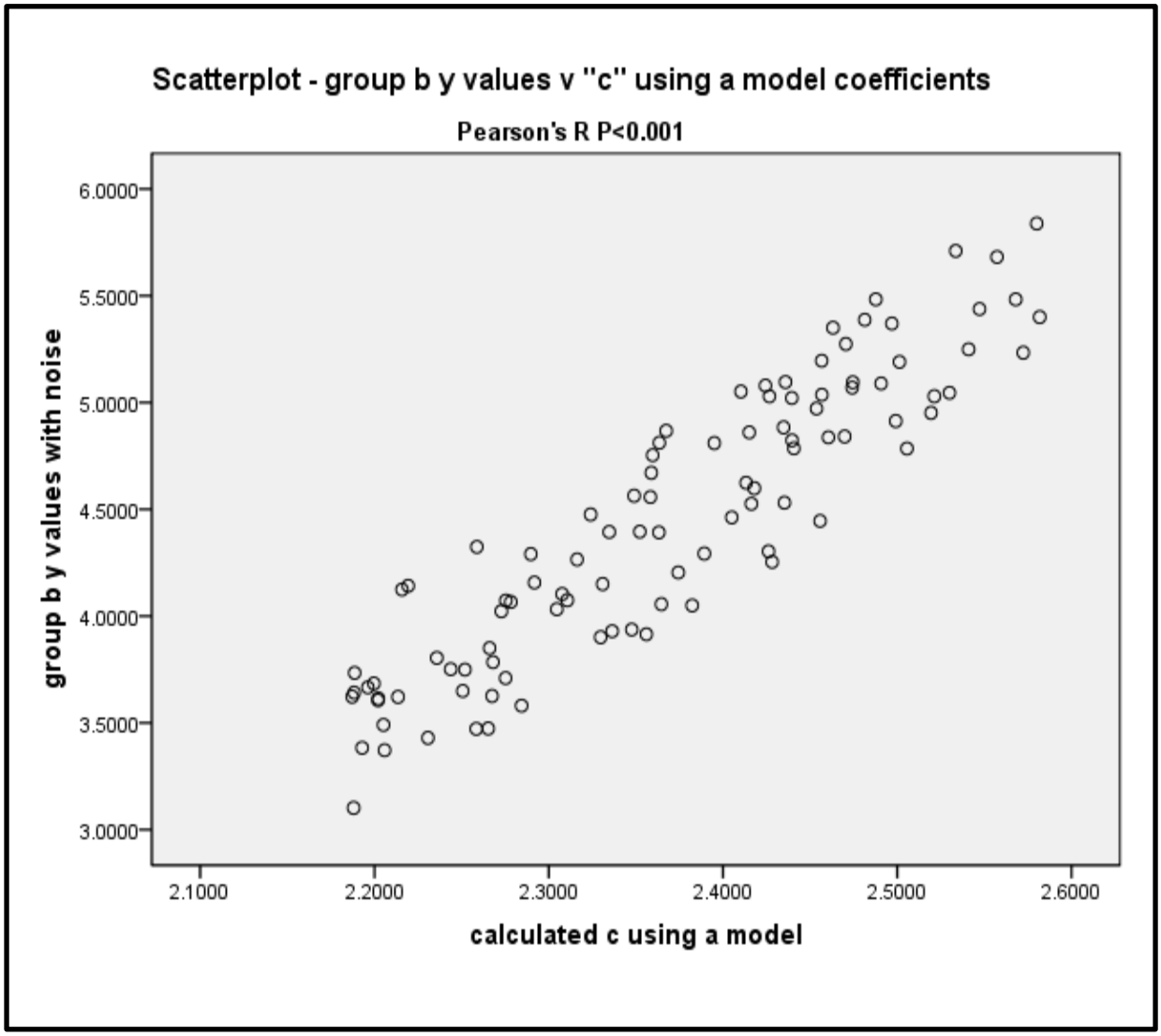
Coefficients from regression a, were used to compute variable “ca”. “ca” was then correlated with variable y2b (from dataset B).

Table 4. SPSS output 4 - Correlations

		Predicted outcome (calculated c using a model)	Observed outcome gp b - y values with noise
calculated c using a model	Pearson Correlation	1	.917**
	Sig. (2-tailed)		.000
	N	100	100
group b y values with noise	Pearson Correlation	.917**	1
	Sig. (2-tailed)	.000	
	N	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

SPSS Output 5. Scatterplot 1.



Repeat test

A further multiple linear regression was undertaken using *Group b* data. SPSS outputs are shown (Tables 5-7). The R square was 0.840 – i.e. the model predicted 84% of the variance (Table 5). F is very high (therefore very unlikely to occur by chance) Accordingly, the significance level for the ANOVA is less than 0.001 (Table 6). The model generated coefficients (Table 7) - B1 (the gradient of the line) and B0 (the Y intercept of line).

Table 5. SPSS output - model summary – Group b data

Model	R	R square	Adjusted R Square	Standard error of estimate
	.917	.840	.839	.262

Table 6. SPSS output - ANOVA

Model	Sum of Squares	df	Mean Square	F	Significance
Regression	35.320	1	35.320	515.898	.000
Residual	6.709	98	.068		
Total	42.029	99			

Table 7. SPSS output - Coefficients

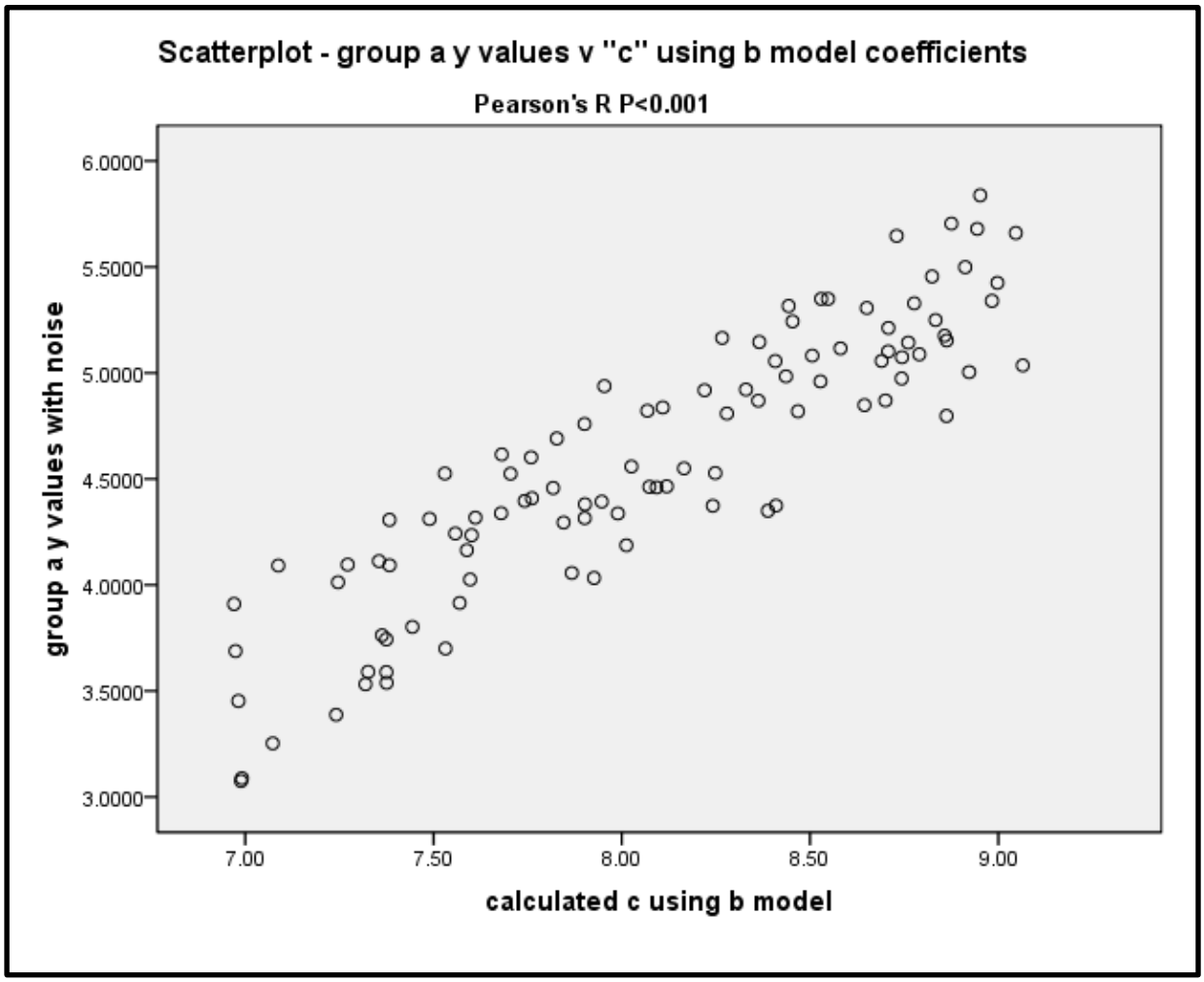
Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	3.449	.051		67.548	.000
	group b x values	2.141	.094	.917	22.713	.000

These coefficients were incorporated into y= bo + bx + 3.5 to generate a new variable "cb" – the predicted outcome ("y") using the *Group b* model. This was then correlated with the *Group a* observed outcome ("y2a"). These were highly correlated (Table 8 and scatterplot 2) – demonstrating that the *predicted* outcome "cb" correlates closely with (predicts) the *observed* outcome in the novel dataset "y2a". The model is generalizable.

Table 8. SPSS Output - Correlations

		Observed outcome group a y values with noise	Predicted outcome calculated c using b model
group a y values with noise	Pearson Correlation	1	.903**
	Sig. (2-tailed)		.000
	N	100	100
calculated c using b model	Pearson Correlation	.903**	1
	Sig. (2-tailed)	.000	
	N	100	100

SPSS Output. Scatterplot 2.



Conclusions

This exercise shows that the method of cross-validation undertaken is effective at demonstrating the predictive value of the model generated by regression analysis on novel datasets.

Figure 1. Data used in cross validation test exercise

	xa	xb	y2a	y2b	x	y	y2
1.	.9501	.5828	5.3400	4.5259	.9501	4.9003	5.3400
2.	.2311	.4235	3.8023	4.3955	.2311	3.4623	3.8023
3.	.6068	.5155	4.5279	4.2928	.6068	4.2137	4.5279
4.	.4860	.3340	4.3370	4.2652	.4860	3.9720	4.3370
5.	.8913	.4329	5.1758	3.9151	.8913	4.7826	5.1758
6.	.7621	.2259	5.1157	4.0230	.7621	4.5242	5.1157
7.	.4565	.5798	4.0327	4.8605	.4565	3.9129	4.0327
8.	.0185	.7604	3.0751	5.4830	.0185	3.0370	3.0751
9.	.8214	.5298	5.1014	4.8102	.8214	4.6428	5.1014
10.	.4447	.6405	4.7593	5.0210	.4447	3.8894	4.7593
11.	.6154	.2091	5.1651	3.8500	.6154	4.2309	5.1651
12.	.7919	.3798	4.8483	4.3939	.7919	4.5839	4.8483
13.	.9218	.7833	5.0039	5.3697	.9218	4.8436	5.0039
14.	.7382	.6808	5.3493	4.4456	.7382	4.4764	5.3493
15.	.1763	.4611	3.5904	4.8677	.1763	3.3525	3.5904
16.	.4057	.5678	4.4572	5.0516	.4057	3.8114	4.4572
17.	.9355	.7942	5.8378	5.1904	.9355	4.8709	5.8378
18.	.9169	.0592	5.4987	3.3719	.9169	4.8338	5.4987
19.	.4103	.6029	4.6909	5.0792	.4103	3.8205	4.6909
20.	.8936	.0503	4.7972	3.6139	.8936	4.7873	4.7972
21.	.0579	.4154	3.2528	4.5634	.0579	3.1158	3.2528
22.	.3529	.3050	4.5245	4.0322	.3529	3.7057	4.5245
23.	.8132	.8744	5.0565	5.7101	.8132	4.6263	5.0565
24.	.0099	.0150	3.9100	3.1021	.0099	3.0197	3.9100
25.	.1389	.7680	4.0127	5.0893	.1389	3.2778	4.0127
26.	.2028	.9708	4.0929	5.2337	.2028	3.4055	4.0929
27.	.1987	.9901	3.7436	5.8381	.1987	3.3974	3.7436
28.	.6038	.7889	4.3736	4.9135	.6038	4.2076	4.3736
29.	.2722	.4387	3.7000	4.5575	.2722	3.5444	3.7000
30.	.1988	.4983	3.5887	4.0501	.1988	3.3976	3.5887
31.	.0153	.2140	3.4530	3.7846	.0153	3.0305	3.4530
32.	.7468	.6435	5.3495	4.7853	.7468	4.4936	5.3495
33.	.4451	.3200	4.3804	4.0745	.4451	3.8902	4.3804
34.	.9318	.9601	5.6796	5.4827	.9318	4.8636	5.6796
35.	4660	.7266	4.3928	5.0699	.4660	3.9320	4.3928
36.	.4186	.4120	4.2947	3.9372	.4186	3.8373	4.2947
37.	.8462	.7446	5.1431	5.3874	.8462	4.6924	5.1431
38.	.5252	.2679	4.4625	4.2904	.5252	4.0503	4.4625
39.	.2026	.4399	4.3069	4.6710	.2026	3.4053	4.3069
40.	.6721	.9334	4.3499	5.6817	.6721	4.3443	4.3499
41.	.8381	.6833	4.9736	5.0367	.8381	4.6762	4.9736
42.	.0196	.2126	3.0884	3.6260	.0196	3.0393	3.0884
43.	.6813	.8392	5.0557	4.9516	.6813	4.3626	5.0557
44.	.3795	.6288	4.4091	4.8838	.3795	3.7590	4.4091
45.	.8318	.1338	5.6466	3.8044	.8318	4.6636	5.6466
46.	.5028	.2071	4.5583	3.4738	.5028	4.0056	4.5583

47.	.7095	.6072	4.8190	4.3034	.7095	4.4189	4.8190
48.	.4289	.6299	4.0566	4.5311	.4289	3.8578	4.0566
49.	.3046	.3705	4.2344	4.1500	.3046	3.6092	4.2344
50.	.1897	.5751	4.1127	4.6243	.1897	3.3793	4.1127
51.	.1934	.4514	3.7627	4.8118	.1934	3.3869	3.7627
52.	.6822	.0439	4.3743	3.6840	.6822	4.3644	4.3743
53.	.3028	.0272	4.0254	3.3833	.3028	3.6055	4.0254
54.	.5417	.3127	4.8370	4.1036	.5417	4.0833	4.8370
55.	.1509	.0129	4.0956	3.6229	.1509	3.3017	4.0956
56.	.6979	.3840	5.3158	3.9294	.6979	4.3958	5.3158
57.	.3784	.6831	4.6015	5.1957	.3784	3.7567	4.6015
58.	.8600	.0928	5.0878	4.1418	.8600	4.7200	5.0878
59.	.8537	.0353	5.3281	3.6662	.8537	4.7073	5.3281
60.	.5936	.6124	4.9184	4.2535	.5936	4.1871	4.9184
61.	.4966	.6085	4.1870	5.0292	.4966	3.9931	4.1870
62.	.8998	.0158	5.7044	3.6416	.8998	4.7995	5.7044
63.	.8216	.0164	5.2125	3.7342	.8216	4.6433	5.2125
64.	.6449	.1901	4.9216	3.4723	.6449	4.2898	4.9216
65.	.8180	.5869	4.8704	4.5987	.8180	4.6359	4.8704
66.	.6602	.0576	4.8692	3.4907	.6602	4.3205	4.8692
67.	.3420	.3676	4.6155	3.9013	.3420	3.6839	4.6155
68.	.2897	.6315	3.9146	5.0961	.2897	3.5795	3.9146
69.	.3412	.7176	4.3379	5.2739	.3412	3.6824	4.3379
70.	.5341	.6927	4.4601	4.8370	.5341	4.0682	4.4601
71.	.7271	.0841	5.0815	4.1248	.7271	4.4542	5.0815
72.	.3093	.4544	4.3177	4.0559	.3093	3.6186	4.3177
73.	.8385	.4418	5.0742	4.7536	.8385	4.6770	5.0742
74.	.5681	.3533	4.5498	4.4759	.5681	4.1361	4.5498
75.	.3704	.1536	4.3960	3.7514	.3704	3.7408	4.3960
76.	.7027	.6756	5.2431	4.9719	.7027	4.4055	5.2431
77.	.5466	.6992	4.4648	5.3501	.5466	4.0931	4.4648
78.	.4449	.7275	4.3150	5.0950	.4449	3.8898	4.3150
79.	.6946	.4784	4.9838	4.2041	.6946	4.3891	4.9838
80.	.6213	.5548	4.8084	4.4624	.6213	4.2426	4.8084
81.	.7948	.1210	5.3062	3.4300	.7948	4.5896	5.3062
82.	.9568	.4508	5.4250	4.3922	.9568	4.9137	5.4250
83.	.5226	.7159	4.8216	4.8410	.5226	4.0452	4.8216
84.	.8801	.8928	5.2496	5.2492	.8801	4.7603	5.2496
85.	.1730	.2731	3.5318	4.1571	.1730	3.3459	3.5318
86.	.9797	.2548	5.6601	3.5807	.9797	4.9595	5.6601
87.	.2714	.8656	4.5256	5.0455	.2714	3.5429	4.5256
88.	.2523	.2324	4.3113	4.0731	.2523	3.5047	4.3113
89.	.8757	.8049	5.4551	4.7848	.8757	4.7515	5.4551
90.	.7373	.9084	4.9596	5.4378	.7373	4.4746	4.9596
91.	.1365	.2319	3.3877	3.7097	.1365	3.2730	3.3877
92.	.0118	.2393	3.6884	4.0660	.0118	3.0235	3.6884
93.	.8939	.0498	5.1532	3.6056	.8939	4.7878	5.1532
94.	.1991	.0784	3.5383	3.6215	.1991	3.3983	3.5383
95.	.2987	.6408	4.1642	4.8230	.2987	3.5974	4.1642

96.	.6614	.1909	5.1459	4.3241	.6614	4.3229	5.1459
97.	.2844	.8439	4.2428	5.0295	.2844	3.5688	4.2428
98.	.4692	.1739	4.9379	3.7496	.4692	3.9384	4.9379
99.	.0648	.1708	4.0912	3.6493	.0648	3.1296	4.0912
100.	9883	.9943	5.0355	5.4002	.9883	4.9767	5.035
101.			.5828	4.1656	4.5259		
102				.4235	3.8470	4.3955	
103				.5155	4.0310	4.2928	
104				.3340	3.6679	4.2652	
105				.4329	3.8658	3.9151	
106				.2259	3.4519	4.0230	
107				.5798	4.1596	4.8605	
108				.7604	4.5207	5.4830	
109				.5298	4.0596	4.8102	
110				.6405	4.2811	5.0210	
111				.2091	3.4181	3.8500	
112				.3798	3.7596	4.3939	
113				.7833	4.5667	5.3697	
114				.6808	4.3617	4.4456	
115				.4611	3.9222	4.8677	
116				.5678	4.1357	5.0516	
117				.7942	4.5884	5.1904	
118				.0592	3.1184	3.3719	
119				.6029	4.2057	5.0792	
120				.0503	3.1005	3.6139	
121				.4154	3.8307	4.5634	
122				.3050	3.6100	4.0322	
123				.8744	4.7487	5.7101	
124				.0150	3.0300	3.1021	
125				.7680	4.5359	5.0893	

126	.9708	4.9417	5.2337
127	.9901	4.9802	5.8381
128	.7889	4.5777	4.9135
129	.4387	3.8773	4.5575
130	.4983	3.9966	4.0501
131	.2140	3.4279	3.7846
132	.6435	4.2870	4.7853
133	.3200	3.6401	4.0745
134	.9601	4.9202	5.4827
135	.7266	4.4533	5.0699
136	.4120	3.8239	3.9372
137	.7446	4.4891	5.3874
138	.2679	3.5359	4.2904
139	.4399	3.8798	4.6710
140	.9334	4.8668	5.6817
141	.6833	4.3667	5.0367
142	.2126	3.4251	3.6260
143	.8392	4.6785	4.9516
144	.6288	4.2576	4.8838
145	.1338	3.2675	3.8044
146	.2071	3.4143	3.4738
147	.6072	4.2144	4.3034
148	.6299	4.2598	4.5311
149	.3705	3.7410	4.1500
150	.5751	4.1503	4.6243
151	.4514	3.9028	4.8118
152	.0439	3.0878	3.6840
153	.0272	3.0544	3.3833
154	.3127	3.6254	4.1036

155	.0129	3.0257	3.6229
156	.3840	3.7679	3.9294
157	.6831	4.3662	5.1957
158	.0928	3.1857	4.1418
159	.0353	3.0707	3.6662
160	.6124	4.2248	4.2535
161	.6085	4.2171	5.0292
162	.0158	3.0315	3.6416
163	.0164	3.0327	3.7342
164	.1901	3.3801	3.4723
165	.5869	4.1738	4.5987
166	.0576	3.1152	3.4907
167	.3676	3.7351	3.9013
168	.6315	4.2629	5.0961
169	.7176	4.4353	5.2739
170	.6927	4.3853	4.8370
171	.0841	3.1682	4.1248
172	.4544	3.9087	4.0559
173	.4418	3.8837	4.7536
174	.3533	3.7065	4.4759
175	.1536	3.3072	3.7514
176	.6756	4.3513	4.9719
177	.6992	4.3984	5.3501
178	.7275	4.4550	5.0950
179	.4784	3.9568	4.2041
180	.5548	4.1097	4.4624
181	.1210	3.2421	3.4300
182	.4508	3.9015	4.3922
183	.7159	4.4318	4.8410

184	.8928	4.7857	5.2492
185	.2731	3.5462	4.1571
186	.2548	3.5095	3.5807
187	.8656	4.7312	5.0455
188	.2324	3.4647	4.0731
189	.8049	4.6097	4.7848
190	.9084	4.8168	5.4378
191	.2319	3.4638	3.7097
192	.2393	3.4786	4.0660
193	.0498	3.0995	3.6056
194	.0784	3.1568	3.6215
195	.6408	4.2816	4.8230
196	.1909	3.3818	4.3241
197	.8439	4.6877	5.0295
198	.1739	3.3478	3.7496
199	.1708	3.3416	3.6493
200	.9943	4.9886	5.4002

Appendix 7 – Multicollinearity diagnostic tests

This appendix contains the tables of outputs from the multicollinearity tests undertaken during the multiple regression analyses.

Introduction

In the case of the binary regression analyses undertaken to develop predictive models, all factors were inserted into a multiple regression as suggested by Field (2009). Outputs were recorded – the tolerance levels and Variance Inflation Factor (VIF). Menard (1995) proposes that a tolerance level of <0.1 implies there is a significant issue with collinearity of the independent variables. Myers (1990) suggests that a VIF of >10 implies significant collinearity.

The outputs below reflect the tests undertaken for the final proposed models.

Coefficients – Dependent variable = dead

Model	Collinearity statistics	
	Tolerance	**VIF**
Age	.973	1.028
Screen done	.999	1.001
Number of admissions	.974	1.027

Coefficients – Dependent variable = positive drug tests

Model	Collinearity statistics	
	Tolerance	**VIF**
Methadone dose	.990	1.010
Diazepam dose	.982	1.018
Where treated	.989	1.011

Coefficients – Dependent variable = self-report of drug use

Model	Collinearity statistics	
	Tolerance	**VIF**
Treatment setting	1.000	1.000
Route of heroin use	1.000	1.000

Coefficients – Dependent variable = Family stability

Model	Collinearity statistics	
	Tolerance	**VIF**
Age	.937	1.067
Area lived in	.697	1.435
Treatment setting	.907	1.102
Has children	.956	1.046
Has support from external agency	.893	1.120
Prescribed diazepam	.909	1.101
Illicit diazepam use	.772	1.295

Appendix 8 - Media coverage

This Appendix contains example screenshots of online headlines/articles covering the political debate around methadone prescribing in Scotland in 2012

Shocking picture shows woman licking methadone from pavement in front of child

31 Jan 2012 00:00

THIS shocking picture showing a woman licking methadone from a pavement as a child looks on has sparked fury.

THIS shocking picture showing a woman licking methadone from a pavement as a child looks on has sparked fury.

The photograph was taken by a stunned onlooker outside Edinburgh's Wester Hailes shopping centre after the woman dropped the heroin substitute.

The woman, in her 30s, had gone to a chemist for her weekly prescription for methadone. She was accompanied by her friend and a young girl. She was on her way home when she dropped the liquid. She then kneeled down and licked it from the dirty pavement.

The image has sparked outrage in the area, where the woman is a well-known addict.

Mum-of-four Debbie Notman, 28, said: "People are disgusted anyone would do this in front of a child. "My pal took the photo on Saturday. He couldn't believe what he was seeing. "She was so oblivious she didn't even notice the picture was being taken."

Campaigners say the woman needs help and should not be vilified. John Arthur, director of Edinburgh drugs group Crew 2000, said: "Addicts can go to extraordinary lengths to get their substances due to the cravings they can experience. "This is surely deserving of compassion rather than ridicule."

- By Dailyrecord.co.uk

Methadone is waste of money and failure as a treatment, says expert

20 Aug 2012 06:30

The destruction of Scotland's working base by Margaret Thatcher's Tories left a generation out of work and bereft of a future. The Heroin Age had begun.

IN the 1970s, I was on the drugs squad in Glasgow, dealing largely with LSD and cannabis users bringing drugs in from Amsterdam and North Africa, usually student types returning from holidays.

There were so few heroin users in Glasgow then that the head of the squad reckoned he knew every one personally.

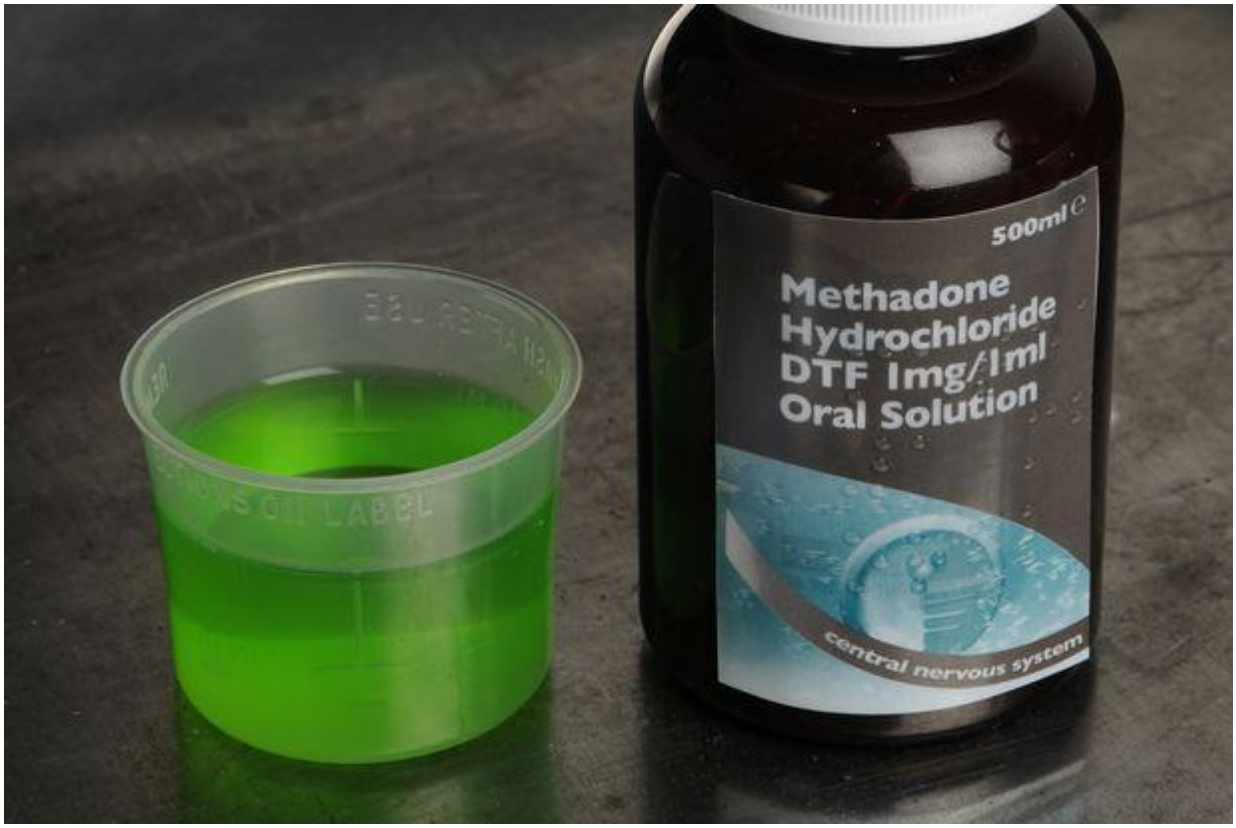
The subsequent destruction of Scotland's working base by Margaret Thatcher's Tories, however, left a generation out of work and bereft of a future. The Heroin Age had begun

- By John Ferguson

Methadone madness: Users slam claim that drug is being used to cure addiction

21 Aug 2012 06:30

MANY addicts we spoke to openly admitted to using methadone AND heroin – a combination that has resulted in hundreds of drug deaths.



Methadone

A CONSTANT stream of addicts file into Houlihan Pharmacy for their daily hit of methadone.

The shop sits in one of Glasgow's poorest areas and comprises a needle exchange on the left and a chemist shop, where the heroin substitute is handed out, on the right.

The chemist on Saracen Street, Possilpark, is Scotland's biggest single supplier of methadone, taking in £856,255 from 2006 to 2011.

Addicts we spoke to made a nonsense of the claim that the Class A drug is being used to cure their addiction

By John Ferguson, David Clegg

Methadone probe launched by Scottish Government after Daily Record reveals £36m-a-year heroin substitute scandal

5 Sep 2012 06:30

THE SNP's Community Safety Minister Roseanna Cunningham has initiated a probe into the controversial heroin substitute on the back of the Daily Record's campaign.

MSP Roseanna Cunningham speaks to the Daily Record's John Ferguson at the Scottish Parliament in Edinburgh

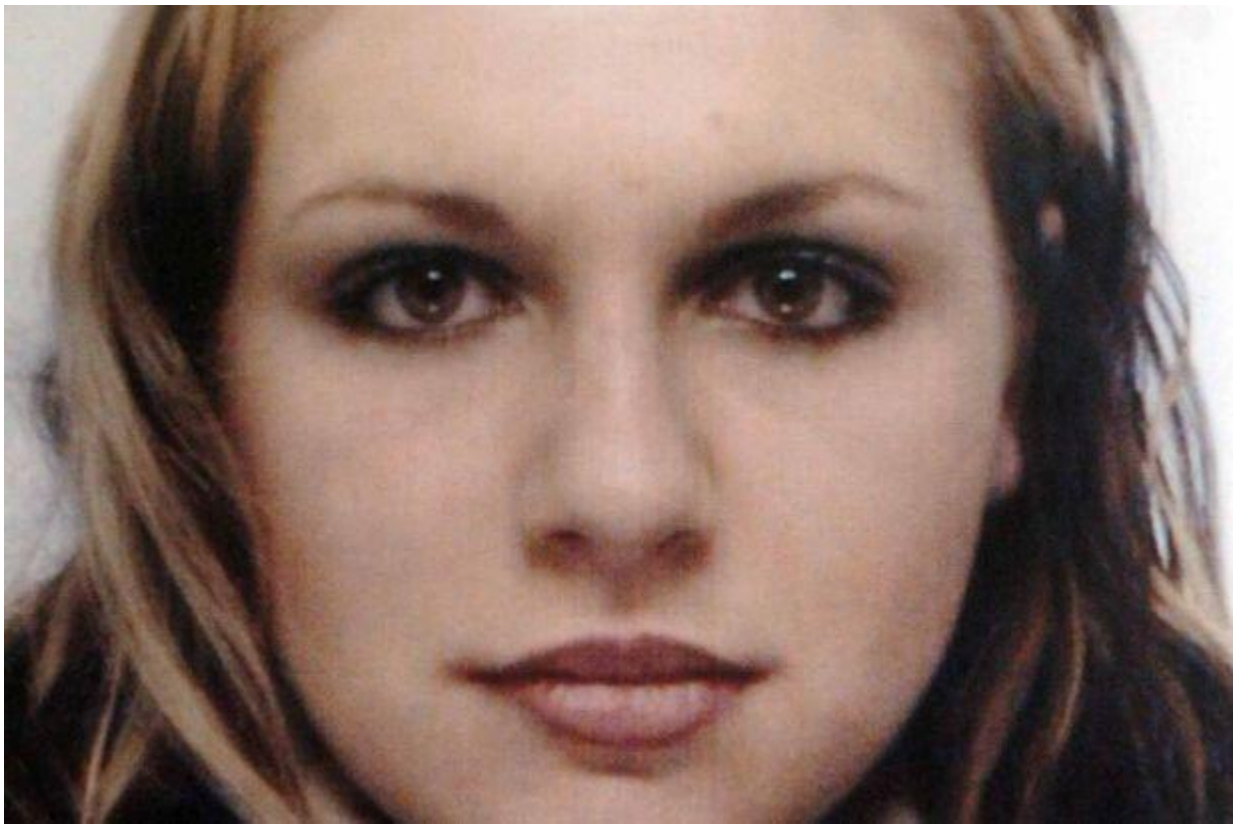
THE Scottish Government are carrying out an urgent inquiry into Scotland’s £36million methadone scandal demanded by the Daily Record.

By John Ferguson

Cycle of death and misery caused by black market methadone.. and it's all funded by the taxpayer

4 Sep 2012 06:30

PRESCRIPTION methadone is traded for street heroin leaving hundreds like teenager Danielle Scott dead.



Danielle Scott was one of many killed by methadone

DRUG addicts are selling NHS methadone to buy the heroin it’s meant to wean them off.

Hundreds have died taking methadone sold by addicts in a taxpayer-funded cycle of misery.

Victims include angel-faced Danielle Scott, 17, who was fed the heroin substitute by a dealer who got gallons of it on prescription.

Gallons of NHS-funded methadone are being sold in a deadly black market which costs hundreds of lives every year.

Almost half of all drug deaths in Scotland last year were linked to the heroin substitute – and most of the casualties had not been prescribed methadone