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EUROPE

Development of a framework to estimate the cost of opioid dependence

Emma Disley, Andrew Mulcahy, Mafalda Pardal, Jennifer Rubin, Kai Ruggeri

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Preface

RB Pharmaceuticals commissioned RAND Europe to identify and assess existing estimates of the costs of opioid dependence (on heroin or prescription opioid painkillers). Opioid dependence imposes a range of costs on individuals, families, communities and society, and understanding these costs is important to inform policy and decisionmaking in this area, especially when budgets for services to address challenges such as substance misuse are under pressure.

This report sets out the findings of a targeted review of the harms of opioid dependence, and an assessment of the existing estimates of the costs of opioid dependence. A proposed framework for developing new, more comprehensive estimates of the costs of opioid dependence is outlined.

This report will be of interest to those in national and local government charged with addressing challenges associated with opioid dependence, as well as academics and researchers working in the field.

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This report has been peer-reviewed in accordance with RAND's quality assurance standards.

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Summary

Dependence on heroin and on prescription and over-the-counter opioids can impose significant harms on the state, communities, families, patients and users.

Some of these possible harms are tangible – loss of life, poor health and the cost of healthcare and the criminal justice system. Others are less tangible, such as reduced quality of life and the psychological health of both users and their families.

Understanding the nature and size of these harms and where they fall is important for policymakers responding to opioid dependence. Assigning a monetary value to these harms, where possible, is one way in which they can be assigned a magnitude of importance, as well as help in assessing the relative effectiveness of programs aimed at assisting those affected by opioid dependence. This study identifies and assesses available estimates of the costs of opioid dependence.

RAND Europe was asked to independently assess available estimates (from the UK, other European countries and worldwide), identify possible gaps and develop a framework to generate more comprehensive and standardised cost estimates relevant for different dependence and treatment contexts taken from a truly societal perspective (which considers not just taxpayers or the government perspective, but also the lost quality of life of those suffering from dependence and their families/communities). The objectives were to:

- Better understand and map the various categories of costs of opioid dependence.
- Collect existing estimates (from the UK, other European countries and worldwide) of the magnitude of different costs.
- Identify those costs for which estimates are available, and those costs that have not been estimated.
- Review costing methodologies and data sources used in existing estimates.
- Identify upper and lower bounds to the range of existing estimates, and provide explanations for variations between estimates.

To identify and review existing estimates, a rapid evidence assessment (REA) was undertaken. To ensure the collation of estimates that were comparable, strict criteria were applied to select studies for inclusion. Studies must:

- Be published after 2000.
- Provide monetised estimates of the harms associated with dependence.

- Include at least some costs other than those of the cost of drug treatment.
- Isolate the costs of opioid dependence (from other drugs and substances).
- Contribute to an understanding of per-person, per-year costs of dependence for any given jurisdiction (we focus on the per-year costs associated with an individual opioid-dependent person, not an individual in the general population).

Included estimates were assessed and adjusted to facilitate standardisation and quality determination. This allowed us to map what was estimated and how, and convert estimates into a standards currency of 2012 euros.

Some nine studies providing 15 cost estimates met the inclusion criteria. Of these, seven were from the US, one was from Canada and one from Australia. Studies from the UK and Sweden were identified during the search but these did not meet the inclusion criteria.

Knowledge about the harms of opioid dependence is limited and patchy.

A targeted review of the literature highlighted the kinds of harms stemming from opioid dependence, but there is considerable scope to improve the knowledge base in this area. The available evidence tends to focus on dependence on heroin, whereas relatively little is known about the challenges faced by those who are dependent on prescription or over-the-counter medicines containing opioids. Some harms – for example the rates of drug-related deaths – are much better understood than others (such as the effects on families and communities of opioid dependence).

Existing estimates vary in geography, type of opioid use and definition of dependence.

The estimates included vary widely, in terms of their geographic spread, populations studied, methodological approach and the data on which they are based. The main similarity between the estimates is that they focus on estimating costs of healthcare, criminal justice and lost productivity costs.

Welfare and intangible costs are not well estimated but appear significant.

Only one included study estimated social welfare costs and none looked at intangible costs. Thus the included estimates omit several of the possible harms of opioid dependence. It is likely, therefore, that they are underestimates.

Costs to those who are dependent, their families and communities are not well estimated.

All the included estimates take a government or taxpayer perspective, thus not including costs borne by the dependent individual, his or her friends, family and community (such as quality of life or well-being). Total costs of opioid dependence were highly varied, ranging from €2,627 to €60,665 per person, per year.

It is not possible to select any one estimate as more accurate or useful. In addition, it was not the case that estimates that included more kinds of costs were higher in value. We suggest that the drivers of the size of these estimates lie in the methodological approach – including data sources and assumptions, etc. For studies to be truly comparable, they must share the same methods, which these do not.

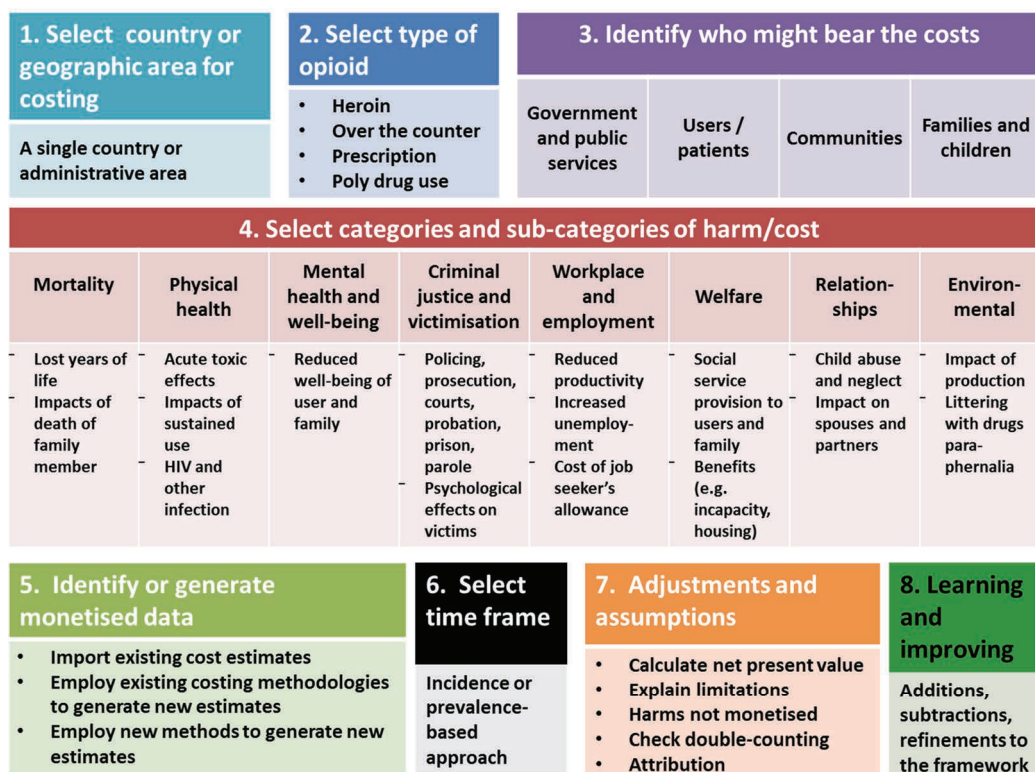
We propose a framework that can be used as a tool for calculating the costs of different types of opioid dependence in different contexts.

This framework sets out eight steps to guide decisions about cost estimation. The framework is intended to lead to estimates that:

- Are specific to a country or local administrative area.
- Separate (as far as possible) prescription opioid and heroin dependence.
- Cost harms to individuals, families and communities, as well as to the government.
- Are inclusive in the kinds of harms costed – including tangible and intangible costs that occur in the short, medium and long term.
- Are able to make the best use of available data to build a bottom-up estimate.
- Make appropriate adjustments for time period, attribution of costs to opioid dependence and avoid double counting.
- Facilitate continuous improvement to costing methodologies and the evidence base and are able to adapt to include new kinds of harms.

This framework draws on groupings and categorisations used to map drug-related harms (Advisory Council on the Misuse of Drugs, 2010; MacDonald et al., 2005) included in the wider health economics literature (National Institute for Health and Clinical Excellence, 2011; Sefton et al., 2002) and used in model approaches for costing substance abuse (Collins et al., 2006; Rehm et al., 2006; Single et al., 1996).

Figure S-1: Proposed framework to guide estimation of the costs of opioid dependence



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1.1 Why estimate the social and economic costs of opioid dependence?

The total costs to society of all Class A¹ drug use (including but not limited to opioids) in the UK in 2003/04 was estimated at around £15.4bn, or £44,231 per-year, per problematic drug user (Gordon et al., 2006, p.4). A lifetime ‘crime and health bill’ of £480,000 was estimated for each intravenous drug user in the UK (National Treatment Agency for Substance Misuse, 2012b, p.6).

Understanding the costs stemming from opioid dependence is important to policymakers and others considering how to improve outcomes for those affected. Decisions about what services and treatments to provide, how they should be designed and for whom they should be tailored are best taken with a good understanding of the range of challenges and costs that any treatment or service may be seeking to alleviate. When budgets are constrained it is important to know the opportunity cost associated with reducing or redirecting funds to alternative uses.

The usefulness of generating estimates of social and economic costs of certain behaviours can be illustrated by the use of estimates of the cost of crime in the UK (Brand & Price, 2000) and the US (Cohen, 2000). These provide a quantified measure of the relative costs of a range of types of crime and victimisation, and make more explicit the social, psychological and economic costs of crime to the individual, community and public sector. As such they are used to inform policy design and focus preventive measures, criminal justice resources and victim support. Cost estimates are vital inputs to cost-effectiveness and cost-benefit analysis to evaluate policy options or assess the impact of a chosen policy, programme or intervention.

1.2 Aims

In order to support the generation of cost estimates that could be drawn upon to inform policy and decisions in this area, it is important first to understand the existing evidence base regarding the costs of opioid dependence.

¹ In the UK the Misuse of Drugs Act 1971 divides all controlled drugs into three classes, A, B and C, according to their perceived harm. Class A drugs are considered the most dangerous substances and carry the heaviest criminal penalties. Class A includes crack cocaine, cocaine, ecstasy (MDMA), heroin, LSD, magic mushrooms, methadone, methamphetamine (crystal meth) (UK Drugs Policy Commission, 2008).

RAND Europe was asked to independently assess available estimates (from the UK, other European countries and worldwide), identify possible gaps and develop a framework to generate more comprehensive and standardised cost estimates. The objectives of the work were to:

- Better understand and map the various categories of costs of opioid dependence.
- Collect existing estimates (from the UK, other European countries and worldwide) of the magnitude of different costs.
- Identify those costs for which estimates are available, and those costs that have not been estimated.
- Review costing methodologies and data sources used in existing estimates.
- Identify upper and lower bounds on the range of existing estimates, and explanations for variation between estimates.

1.3 Scope

Types of opioid use included: prescription, over-the-counter and illicit opioids

‘Opioid’ is a generic term applied to alkaloids derived from the opium poppy (opiates), their synthetic analogues and compounds synthesised in the body.² This study looks at the costs associated with dependence on (illicit) heroin and on prescription and over-the-counter opioids, such as codeine, tramadol and fentanyl.³

The harms imposed and experienced by those using heroin are likely to be different from those associated with the use of prescription drugs, given evidence of differences in the personal, social and other characteristics of these two groups of users (Subramaniam & Stitzer, 2009). However, it is also noted that these populations frequently overlap, with users moving between illicit and prescription opioids or using both at the same time (Canfield et al., 2010).

Throughout this report, where possible, costs associated with dependence on prescription drugs are distinguished from those associated with illicit opioid use.

The terms used in this report: dependence, abuse, misuse and addiction

A variety of terms are used by those working in this field to indicate different levels and types of opioid use, including use, misuse, dependence and addiction (see Box 1). In line

² Opioids interact with specific receptors in the brain and reduce pain, induce sleep and may alter mood or behaviour. The main types of opioids are: *natural opiates*: alkaloids contained in the resin of the opium poppy, primarily morphine, codeine, and thebaine; *semi-synthetic opioids*: created from the natural opiates, such as hydromorphone, hydrocodone, oxycodone, oxymorphone, desomorphine, diacetylmorphine (heroin), nicomorphine, dipropanoylmorphine, benzylmorphine, ethylmorphine and buprenorphine; *fully synthetic opioids*: such as fentanyl, pethidine, methadone, tramadol and dextropropoxyphene.

³ There are two broad clinical uses of opioids: the management of acute or chronic pain and the management of opioid dependence through opioid substitution treatment (see Appendix B for a brief description of the treatment options for those dependent on heroin) (Larance et al., 2011). The focus of this report as regards prescription and over-the-counter opioids is on opioids prescribed for pain management, not on the use of opioids in substitution treatment.

with the aim of developing a comprehensive framework to estimate the broad range of costs associated with opioid dependence, this project included and considered costs associated with all of these types of use. In this report the term ‘dependence’ is used as an umbrella term.⁴

Box 1: Terminology to describe dependence

There are two main systems of classification for diagnosis of drug use disorders internationally: the International Classification of Diseases (ICD-10) produced by World Health Organization (WHO) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) provided by the American Psychiatric Association (APA).

The WHO definition in the ICD-10 (and in its earlier iterations) describes dependence as involving elements of tolerance, withdrawal, difficulty in controlling use, a focus on getting and using the substance to the detriment of other activities, and continued use despite harm (World Health Organization, 1990) (see Appendix C for a summary of the diagnosis criteria). The majority of studies included in the review reported using the ICD-9 definition.

This is similar to the criteria previously set by the APA in the DSM-IV (American Psychiatric Association, 1994). The DSM-IV has been recently updated and the DSM-V combines substance abuse and substance dependence into single substance use disorder, specific to each substance within a new ‘addictions and related disorders’ category (American Psychiatric Association, 2013).

The term ‘**physiological dependence**’ is generally used to describe the adaptation to the continuous presence of drugs in the body (Larance et al., 2011; Savage et al., 2003). Physical dependence may involve tolerance to the used dose or/and withdrawal symptoms. Proponents of the changed language of the DSM-V argue that employing the term ‘addiction’ helps distinguish physiological dependence from the psychological dependence manifested in drug abuse behaviour (Larance et al., 2011). As explained above, in this report we use the term ‘dependence’ as an umbrella term for physical and psychological aspects of opioid use.

‘**Non-medical use**’ is the term commonly used to describe taking prescription drugs to get high, using more than prescribed, or using prescription drugs in a manner other than that intended by the prescriber (Martins et al., 2007; UNODC, 2012, p.81). However, a number of different terms are used interchangeably in the literature including ‘abuse’, ‘illicit use’, ‘misuse’, ‘unsanctioned use’ or ‘extramedical use’ (Larance et al., 2011). There is little consensus around the terminology (Casati et al., 2012).

A distinction between untreated and undertreated dependence

This study was initially scoped to consider the costs of ‘untreated’ opioid dependence. In the course of the research we amended that term to ‘undertreated’ dependence. This is in recognition of the fact that while in treatment many users will continue to ‘top up’ or use additional opioids beyond their treatment regimes and will continue to suffer harm and impose costs.

This amendment was also in recognition of the chronic, relapsing character of opioid dependence (Aguilar de Arcos et al., 2008; Calabria et al., 2010; Dennis et al., 2005; Lobmaier et al., 2008; McLellan et al., 2000). Many people who seek treatment will have more than one treatment episode, engaging and exiting treatment several times (Best et al.,

⁴ Although it should be noted that not all opioid use or misuse entails dependence, we use this term as shorthand and are including all use that is associated with harm and costs, as opposed to controlled use that could be stopped at will and which is not associated with impacts on productivity, relationships, health, and so forth.

2006). For example, available data for England for the period 2005/06 to 2007/08 indicate that reappearances within the drug treatment system are common. Following treatment exit (i.e. having completed a treatment journey in remission from dependence, or having dropped out of treatment) more than one-third of all clients (including but not limited to opioid users) were readmitted to treatment within 12 months (Millar et al., 2012; National Treatment Agency for Substance Misuse, 2010b). Research in the US extrapolated a median time of nine years from first treatment episode to last use (based on users of a range of substances including but not limited to opioids).⁵ While this estimate is not specific to opioid use, it provides an indication of the long-term timeframe involved, and suggests that multiple episodes of treatment over several years are the norm (Dennis et al., 2005).

In relation to prescription opioids, national drug treatment data in the UK analysed by the National Treatment Agency for Substance Misuse (NTA) suggest that people who only report problems in relation to prescription or over-the-counter drugs, once in treatment engage well and achieve comparatively better outcomes than the illegal drug-using treatment population (National Treatment Agency for Substance Misuse, 2011).

Ideally, an estimate of the costs of opioid dependence should:

- Take into account costs associated with all opioid dependent people, whether or not in treatment.
- Distinguish between costs imposed by those in treatment and those not in treatment.

Box 2: Estimates of the proportion of opioid dependent individuals who are in treatment

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) provides estimates of the proportion of problem opioid users in treatment. These estimates relate primarily to those dependent on heroin rather than prescription or over-the-counter drugs. The most commonly reported type of treatment in Europe for dependence on heroin is opioid substitution treatment (EMCDDA, 2012) (see Appendix B for further information about treatment).

The number of individuals receiving opioid substitution treatment is estimated using a range of methods and is based on data collected at the national level. As such, caution must be exercised when comparing data from different countries.

The EMCDDA estimates that on average about 50 percent of all 'problem opioid users' in the EU and Norway are in substitution treatment (EMCDDA, 2012, p.75; Pirona, 2012). There are substantial differences between countries within the EU; much lower coverage levels are estimated for some countries, for example Latvia (2 percent) and Poland (8 percent) (EMCDDA, 2012, p.75; Solberg et al., 2002).

Considering harms associated with opioid dependence as a starting point

A distinction may be made between outcomes, harms and costs associated with opioid dependence:

- **Outcomes** are experiences, events and states associated with opioid use. Outcomes could be positive or negative: for example, a positive outcome could be relief from physical pain or psychological burden, while negative outcomes may include loss of productivity or loss of employment, criminality associated with the need to

⁵ In a sample of individuals in publicly funded treatment programmes in a metropolitan area.

fund addiction, etc. Positive and negative outcomes are experienced by individuals, families and society at large.

- **Harms** are the negative outcomes associated with opioid dependence.
- Harms can be quantified as monetised **costs**. Some harms are experienced directly as monetised costs, for example loss of income. Others have to be monetised using various methods, for example loss of a job not only entails lost income in the short to medium term, but also may have wider impacts on future employability, and these types of outcomes are not directly monetised.

The starting point for a comprehensive framework to estimate the costs of opioid dependence is empirical evidence of the harms associated with dependence. Once an inventory of these harms is undertaken, it is then possible to map which harms have already been monetised in existing estimates and which have not, thereby identifying the gaps to fill. Some potential harms of opioid dependence are less readily visible than others or may carry greater levels of uncertainty, and these can be challenging to measure and monetise.

Costs of drug treatment programmes are not included

In line with the original brief to consider untreated opioid dependence, the scope of this review was to examine costs other than those costs stemming from providing drug treatment (i.e. psychosocial interventions, substitution treatment and drug detoxification – see Appendix B). RB Pharmaceuticals has commissioned a separate study into the costs of providing drug treatment. Healthcare costs were included where they related to the treatment of health problems stemming from dependence rather than drug treatment per se.

Focus on per-person, per-year costs

The scope of the work was to identify existing estimates of opioid dependence and express these as per-person, per-year estimates. More specifically, we focus on the per-year costs associated with an individual opioid-dependent person, not an individual in the general population. Compared to aggregate, national-level cost estimates, per-person, per-year cost estimates may simplify comparisons across settings to the extent that they allow differences in population size to be controlled for (however, other challenges in making comparisons remain, such as differences in the cost of healthcare in different countries).

Geographic coverage

While this report aims to inform policy and decisionmaking in the UK and Europe, we sought to identify existing estimates from any country. However, we limited our search to studies published in English (see Appendix A).

Costs to individuals, families, communities, state and society

There are a range of costing perspectives that can and have been taken when seeking to inform decisions about whether or not, and how much, to invest in preventing or addressing harmful behaviours such as opioid dependence.

The most commonly taken approach is an accounting method, which seeks to add up the range of identifiable costs associated with the behaviour. Because the aim is to inform decisions about investment in treatment, prevention, etc., the costs that are most relevant and therefore included are those costs that are avoided when the behaviour is prevented

(Heaton, 2010). There is a range of possible levels at which costs can be counted. The individual may incur a range of costs themselves, as may their friends and family. Beyond that opioid dependence can have costly implications for communities, for example due to increased acquisitive crime committed to fund addiction or the presence of drug dealers who contribute to fear and insecurity.

Furthermore, public services and wider society incur costs in dealing with challenges associated with opioid dependence, such as problematic family environments, welfare or benefits payments, criminal justice system activity (both in seeking to prevent and deal with the aftermath of crime) and healthcare costs.

1.4 Approach

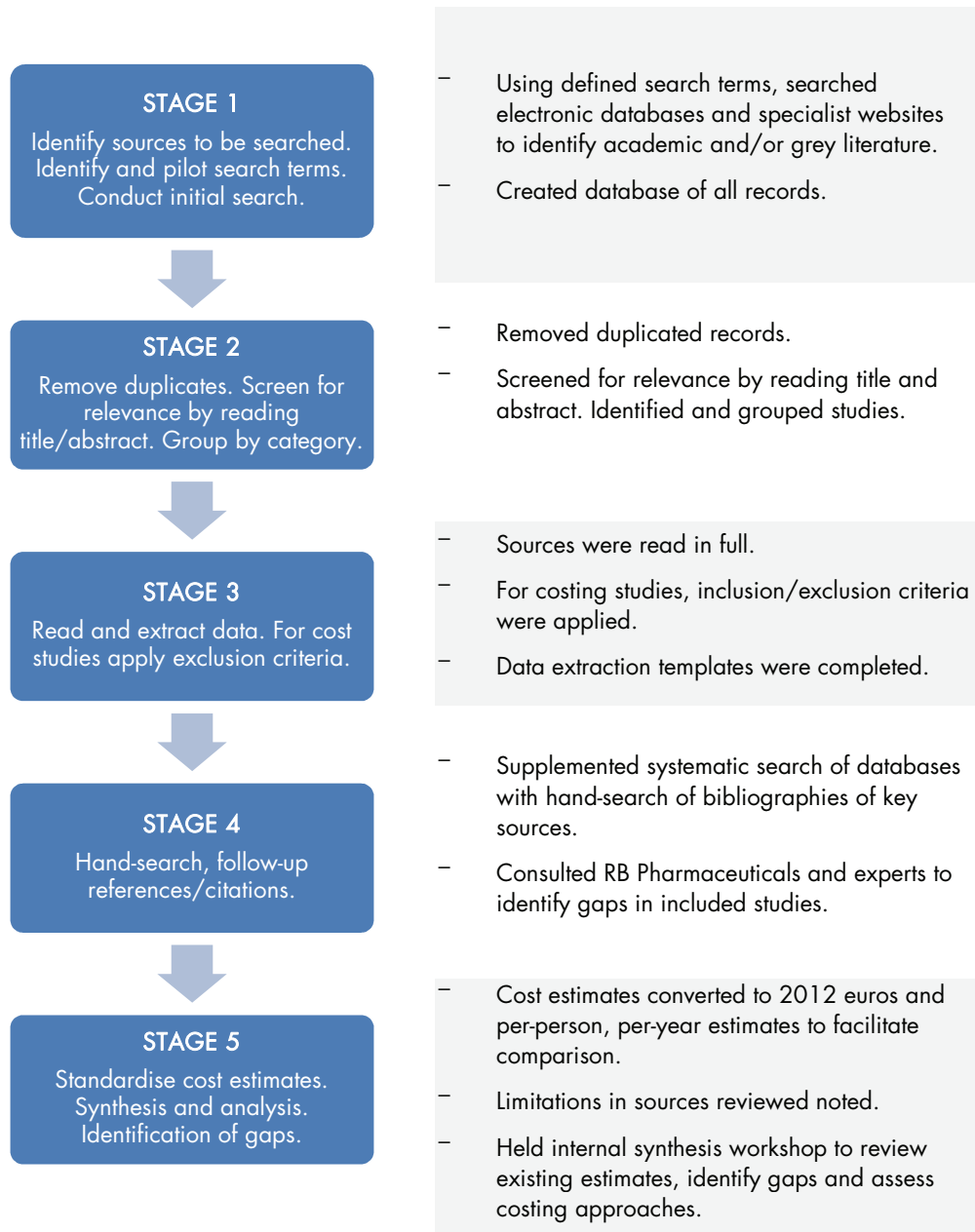
To address the questions set out in Section 1.2 the following reviews were undertaken:

- A rapid evidence assessment⁶ (REA) to identify and assess (i) existing estimates of the costs of untreated or undertreated opioid dependence and (ii) costing approaches used in those estimates.
- A targeted review of literature on the prevalence of and harms associated with opioid use and dependence. This provides context and background to the study and informs the appraisal of existing estimates.

Full details of how the REA was conducted are outlined in Appendix A. The approach is summarised in Figure 1.

⁶ Conducted within a limited timeframe and involving an overview of existing research on a carefully defined topic, rapid evidence assessments are rigorous and explicit in method but limit aspects of a full systematic review.

Figure 1: Overview of the REA approach



Criteria for including studies that provided cost estimates

Criteria were applied to ensure that only studies that were relevant to the research questions were included in the review of existing estimates. In order to be included, studies had to:

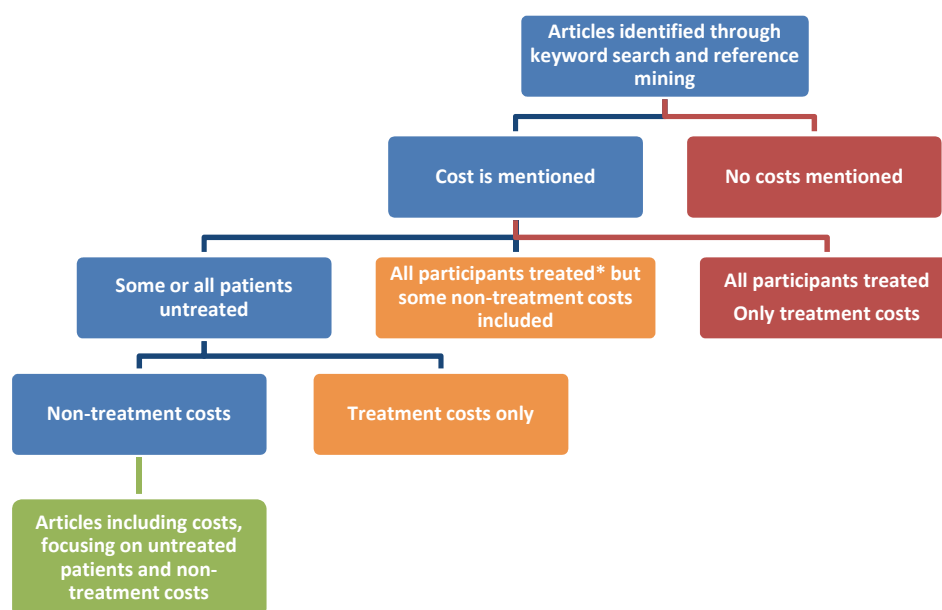
- Be published since 2000 – to ensure a manageable number of hits and that measured costs were relatively comparable to those borne in 2012.
- Provide monetised estimates of the harms associated with dependence – in line with the key research question to identify and compare existing cost estimates. Given limited project resources we excluded studies that report only, for example,

rates of crime attributed to opioid dependence, or lost days of work attributed to opioid dependence without reporting costs. While these studies provide useful information on the impacts of opioid dependence, the impacts must be combined with cost data to generate per-person, per-year cost estimates.⁷

- Include at least some costs other than those of the cost of drug treatment – as explained above, the scope of the review excluded drug treatment costs in line with the original aim to look at untreated (later amended to undertreated) dependence.
- Isolate the costs of opioid dependence from dependence on other drugs and substances – we aimed to identify only the harms and costs of opioid dependence, so excluded studies that estimated costs of, for example, all Class A drug use (although we drew on these studies for context – see Section 3.1).
- Contribute to an understanding of per-person, per-year costs of dependence (for reasons explained in Section 1.3, above).

The process of applying these criteria is illustrated in Figure 2.

Figure 2: Application of inclusion criteria for cost estimate studies



Green – included

Blue – decision point

Orange – case-by-case decision taken on inclusion

Red – excluded

* No assessment of the quality of treatment was undertaken

⁷ We recognise that a study with a broader scope could have included studies that did not provide monetised estimates and generated estimates of these costs independently.

Number of studies included

Some 470 sources were identified through the initial search for cost estimation studies (see Appendix A for search terms used). After excluding duplicates and applying the inclusion/exclusion criteria, 38 studies were identified for detailed review (this includes those identified through searching bibliographies). Having met all the criteria above, 15 cost estimates from 9 studies were finally included. These 15 estimates are described in detail in Chapter 13 and 4.

We recognise that this is a small number of studies, given that so much research has been conducted into the costs of drug use, but the exclusion criteria were applied strictly to ensure that included estimates were as comparable as possible. However, we draw upon some of the studies that did not meet the inclusion criteria to provide background to the study as well as information about the possible range of harms from opioid dependence. Some of the excluded studies also provided cost estimates, and these are reviewed in Section 3.1.

Data extraction

The research team recorded information about each cost study. A similar data extraction process was conducted for the background literature review. Questions asked of cost studies included:

- What costs are counted?
- For each cost, what data sources are used, and what estimation method is employed?
- How are costs attributed to opioid dependence rather than other factors?
- What time horizon is used?
- What population/sample are estimates based on – and related to this, how generalisable are the findings?

The full data extraction templates are provided in Appendix A.

Limitations of our approach

As a result of the application of strict inclusion criteria and search terms referring to ‘opioid’ and ‘cost’ (see Appendix A), some estimates that are well known to researchers and policymakers in this field were not included in the study. They were excluded not because they lack robustness but because, for example, they did not separate the costs of opioid dependence from dependence on other drugs. We have, however, drawn upon these estimates as vital context to the study (see Chapter 2 and Section 3.1).

1.5 Structure of this report

Chapter 2 examines harms from opioid dependence. Chapter 3 describes the studies included and Chapter 4 sets out the cost estimates. Chapter 5 sets out a framework to guide future estimation and a proposal to pilot the framework by developing cost estimates for opioid dependence in the UK.

CHAPTER 2 **Harms associated with opioid dependence**

Harms are the problematic outcomes associated with opioid dependence that are experienced by individuals, families and society. Harms associated with opioid dependence can be explored in part through analysis of large data sets and through qualitative studies that usefully explore patterns of drug dependence and harm (Back et al., 2011; French et al., 2004; McKeganey et al., 2002; Nilsson & Wadeskog, 2011). Once identified, these harms can be quantified as monetised costs.

This chapter is based upon a targeted review of the literature. The aim is to provide an overview of the kinds of harms associated with heroin and prescription drug dependence. Doing so puts us in a position to assess the comprehensiveness of existing estimates identified in the REA and informs the development of a framework to support more comprehensive estimates in the future.

As a starting point, two frameworks developed by researchers in the field of drug misuse are reviewed to illustrate how harms can be grouped and categorised. We recognise that there is a range of guidance and frameworks that could be drawn upon, including those used in international guidelines on estimating costs of substance abuse (Collins et al., 2006; Rehm et al., 2006; Single et al., 1996), and those used more broadly in health economics literature (National Institute for Health and Clinical Excellence, 2011; Sefton et al., 2002). The two frameworks reviewed below are intended to be illustrative. Other frameworks largely cover the same cost categories.

2.1 Two frameworks for categorising drug-related harms in the UK

The first framework consists of evaluation criteria of the harms caused by the misuse of drugs developed by the Advisory Council on the Misuse of Drugs (2010). As Figure 3 sets out, these criteria make a distinction between harms to the user and to others, and separate physical, psychological and social costs. Distinction is made between drug-specific harms resulting directly from use and secondary, knock-on effects that are drug-related.

This framework captures some intergenerational effects, since ‘future prospects of children’ are counted within the category of ‘family adversities’. It also captures community-level harms, with the category ‘harm to others’ including the immediate family and friends of drug users, their local community, and society more widely – through demands placed upon public services by drug use.

Figure 3: Evaluation criteria of the harms caused by the misuse of drugs developed by the ACMD

Harm to users
<ul style="list-style-type: none"> • <u>Physical</u> Drug-specific mortality – intrinsic lethality of the drug Drug-related mortality – extent to which life is shortened Drug-specific damage to physical health Drug-related damage to physical health, e.g. blood-borne viruses • <u>Social</u> Loss of tangibles – income, housing, education Loss of relationships with family and friends • <u>Psychological</u> Dependence – propensity or urge to use despite harm Drug-specific impairment of mental functioning Drug-related impairment of mental functioning – e.g. mood disorders
Harm to others
<ul style="list-style-type: none"> • <u>Social</u> Crime related to drug use Environmental damage – e.g. waste from production Family adversities – e.g. child neglect International damage – e.g. deforestation Economic cost – healthcare, prison, police, social services, lost productivity • <u>Community</u> Decline in social cohesion • <u>Physical and psychological</u> Direct and indirect (violence, road traffic accident)

Source: Advisory Council on the Misuse of Drugs (2010), Nutt et al. (2010)

A different framework is provided by the UK Drug Harm Index, which captures the harms generated by the ‘problematic use’ of any illegal drug. The Index focuses on health, criminal justice and community harms, as set out in Table 1.

The Drug Harm Index was developed to measure the impact of policies to tackle drug harms and is designed to weight some harms more heavily than others. It does not capture effects on relationships, friends and families and is primarily concerned with social costs borne by the public sector and society as a whole.

Comparing these frameworks, the Drug Harm Index is narrower in scope than that developed by the Advisory Council on the Misuse of Drugs, being limited to ‘a subset of harms for which robust data are available’ (MacDonald et al., 2005, p.v). The Advisory Council criteria include more intangible harms.

While useful to orient us to the range of possible harms, these frameworks have been developed with the use of illegal drugs such as heroin in mind. The implication for our review is that they may be less applicable to the misuse of prescription opioids, as they may not consider harms specific to this group of users and therefore may be less useful in

assessing the comprehensiveness of estimates of the costs of prescription opioid dependence.

Table 1: Harms of drug use included in Drug Harm Index

<p style="text-align: center;">Health impacts</p> <p>New HIV cases Hepatitis B and C cases due to intravenous drug use Drug-related deaths Drug-related mental health and behavioural problems Drug overdoses Drug-related neonatal problems</p>	<p style="text-align: center;">Community harms</p> <p>Community perceptions of drugs use/dealing Drug-dealing offences</p>
<p style="text-align: center;">Domestic drug-related crime</p> <p>Burglary Robbery Theft of and from vehicle, bike theft and other theft</p>	<p style="text-align: center;">Commercial drug-related crime</p> <p>Shoplifting Burglary Theft of and from vehicle</p>

Source: MacDonald et al. (2005)

2.2 Examples of harms associated with opioid dependence

Drawing on the framework proposed by the Advisory Council on the Misuse of Drugs and the Drugs Harm Index, this section provides an overview of some of the harms associated with opioid dependence: health impacts (mortality, morbidity), effects on employment, impacts on children and families, and crime and victimisation. For each type of harm we note whether available evidence distinguishes between harm associated with heroin use and that associated with prescription drug use, as well as who suffers the harm – individuals, families, communities and/or society. This section does not aim to describe all the possible kinds of harm associated with the use of opioids.

Health impacts

Mortality

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) reports that opioids (mainly heroin) are present in 80 to 90 percent of drug-induced deaths reported in Europe (EMCDDA, 2012).⁸ A systematic review of 58 studies from 20 countries found that the most common cause of mortality among opioid-dependent groups was overdose, followed by trauma, suicide and disease-specific mortality (for example, HIV/AIDS and liver disease). Mortality rates were 2.38 times higher for people out of treatment, compared to those in opioid substitution treatment (Degenhardt et al., 2011b).⁹ Studies included in this systematic review most commonly related to mortality in heroin users rather than those dependent on prescription drugs only.

The EMCDDA notes that evidence of deaths resulting from the use of prescribed opioid painkillers in Europe remains limited (EMCDDA, 2012, p.85). Data from the United Nations Office on Drugs and Crime (UNODC) relating to the US indicate that overdose deaths involving prescription opioids have quadrupled since 1999 (UNODC, 2012, p.5) and exceed those of heroin alone throughout the last decade (Paulozzi, 2012).

⁸ Although there is evidence that a substantial proportion of all drug-induced fatalities occur in the context of polydrug use.

⁹ See Appendix B for a description of available treatments.

Suicide-related risks tend to be higher for people dependent on opioids than for the general population (Kuramoto et al., 2012; Trémeau et al., 2008). Trémeau et al.'s study of 160 opioid dependent people enrolled in or starting maintenance treatment in France found that nearly half had attempted suicide.¹⁰ Those dependent on prescription opioids are also a high-risk group for suicide-related mortality (Kuramoto et al., 2012).

The harm of increased mortality not only falls on users themselves, but also on their families through grief and bereavement – which are more difficult to monetise and which may lead to reduced productivity and health problems (and thus further costs to society over the long term).

Physical and mental health impacts

Degenhardt & Hall (2012) distinguish four types of adverse health effects from illicit drug use:

- The acute toxic effects, including overdose
- The acute effects of intoxication, such as accidental injury and violence
- Development of dependence, as defined in ICD-10
- Adverse health effects of sustained use, such as chronic disease (e.g., cardiovascular disease and cirrhosis), blood-borne bacterial and viral infections (such as HIV), and mental disorders.

A systematic review found evidence of associations (not necessarily causal) between opioid use and an increase in fatal overdose, accidental injury, cardiovascular problems, pulmonary disease, liver disease and common mental disorders. Evidence regarding possible links with motor vehicle accidents and cancers is not conclusive (Degenhardt & Hall, 2012). The authors of the review note that they were unable to separately discuss the magnitude of adverse outcomes attributable to prescribed pharmaceutical opioids.

Another systematic review found that those who are dependent on opioids report lower health-related quality of life compared to the general population and to people with various medical illnesses (De Maeyer et al., 2010). Participation in substitution treatment had a positive effect on individuals' quality of life, but long-term effects remain unclear. The authors note that quality of life research related to dependence on opioids is 'still in its infancy', and where it is conducted it focuses on health-related quality of life rather than clients' subjective experiences about the 'goodness of life'.

The harms or costs discussed here fall directly on health and social care systems, through increased use of services by those who are opioid dependent. But there are also harms to users themselves and to their families and communities.

Identifying and separating out the health impacts of prescription opioid dependence is complicated by the fact that a substantial proportion of people using prescription opioids have pre-existing health conditions (Cicero et al., 2008).

¹⁰ The author noted that the incidence of suicidal behaviours varies between countries; this estimate is for France and might not be generalisable.

Effects on employment

Drawing on data from the 2007 US National Survey on Drug Use and Health,¹¹ Ruetsch concluded that patients who abuse opioids (both prescription and heroin) are more likely to be absent from work, missing around 2.2 days of work monthly, compared to 0.83 days per month missed by the average employee (Ruetsch, 2010). People who are dependent on opioids and are untreated also seem to register higher rates of underemployment and unemployment compared to the general population (Wall et al., 2000).

Reduced employment harms society at large through reduced productivity, as well as the individual and their family through reduced earnings and the psychological impacts of unemployment (Eardley, 2002).

Impacts on children and families

Data from the UK National Treatment Agency (NTA) indicate that just over half of all adults receiving drug treatment (not just in relation to opioid use) during 2011–12 were either parents or lived with children (National Treatment Agency for Substance Misuse, 2012a, p.3).

Evidence suggests that living with parents who have substance dependence compromises children's health and development (Advisory Council on the Misuse of Drugs, 2011). Children of drug users are at increased risk of negative outcomes in their emotional and cognitive development and are more likely to have behavioural problems (Peleg-Oren & Teichman, 2006). Drawing on interviews with 30 recovering heroin addicts, McKeganey et al. (2002) found that the children of addicts experienced material neglect associated with their parents' drug use, were exposed to drug use and drug dealing, and were at risk of violence and physical abuse, criminal behaviour and family break-up. Similarly, a US study that compared children of parents with opioid use disorders with those whose parents had no substance use disorders found that the children of opioid-dependent parents had significantly higher rates of psychopathology as well as more difficulties in academic, social, and family functioning (Wilens et al., 2002).

These effects are likely to be long term (Advisory Council on the Misuse of Drugs, 2011; Peleg-Oren & Teichman, 2006) and possibly intergenerational – with knock-on effects for future generations who are exposed to similar risks.

Impacts on the whole family, not just on children, are explored within the literature (for example, see Copello et al., 2009). A study in India illustrated the distress caused by those who are opioid dependent to their families and care providers (Shyangwa et al., 2008). While different cultural norms may impact on transferability of findings, many of the challenges identified in this study are likely to be experienced elsewhere, as families and carers in other countries also face the psychological implications of the dependence of someone close to them.

A survey of over 3,000 adults in Copenhagen, Helsinki, Oslo and Stockholm sought to determine the prevalence of specific types of harm among those who knew individuals who

¹¹ The National Survey on Drug Use and Health is conducted annually by the Substance Abuse and Mental Health Services Administration in the United States. It provides data on the use of a number of substances, both licit and illicit (such as tobacco, alcohol, illicit drugs, non-medical use of prescription drugs), as well as mental health data.

used illicit drugs (such as fear of violence, having to call the police and seeking professional help) and asked respondents to indicate how much they had been affected on a scale from 0 (no negative impact) to 10 (my life has been destroyed). The average reported harm was about 2, but a significant minority (10 percent) indicated that the harm was above 5 (Melberg et al., 2011).

The above noted harms fall directly on the children and family members of those who are dependent on opioids, as well as the communities in which those dependent on opioids live and on wider society – including through the demands placed on public services, such as child protection and health services.

The studies mentioned here relate primarily to the impacts of the use of heroin, but those dependent on prescription opioids are included in some studies as they are also likely to cause harm to those around them, especially if they are already dependent on family members and care-givers for underlying health conditions for which opioid-containing drugs have been prescribed. There is scope for further research into how impacts on families and care-givers differ for heroin and prescription drug dependence.

Crime and victimisation

Drug misusers (of all types, not just opioids) tend to have multiple contacts and experiences with drug treatment and criminal justice systems, although available evidence is limited as to the nature of the causal relationship between drugs and crime (French et al., 2004; Scott et al., 2003). A 2003–2006 survey of drugs and crime among individuals arrested in England and Wales found that regular users of heroin and crack cocaine were more likely (81 percent) to have engaged in acquisitive crime during the year before arrest (Boreham et al., 2007).

Some harms resulting from this association between drug use and crime fall on those who are dependent (through the negative impacts of imprisonment and having a criminal record, for example). Harms are also incurred directly by their families, victims of crime and society as a whole through the costs of policing, prosecution services, courts, prison and probation services.

Again, our targeted review identified fewer sources looking at the association between prescription dependence and crime. The higher frequency of property crime committed by those using heroin, crack and cocaine was not observed in the context of non-medical use of prescription opioids by individuals living in Canadian cities (Manzoni, 2006).

2.3 Prevalence of opioid use in Europe

Understanding the prevalence of opioid use is important for mapping both harms and costs. As indicated, we are primarily interested in per-person (per addicted/ dependent person), per-year cost estimates, and prevalence rates are important inputs to estimating these costs.

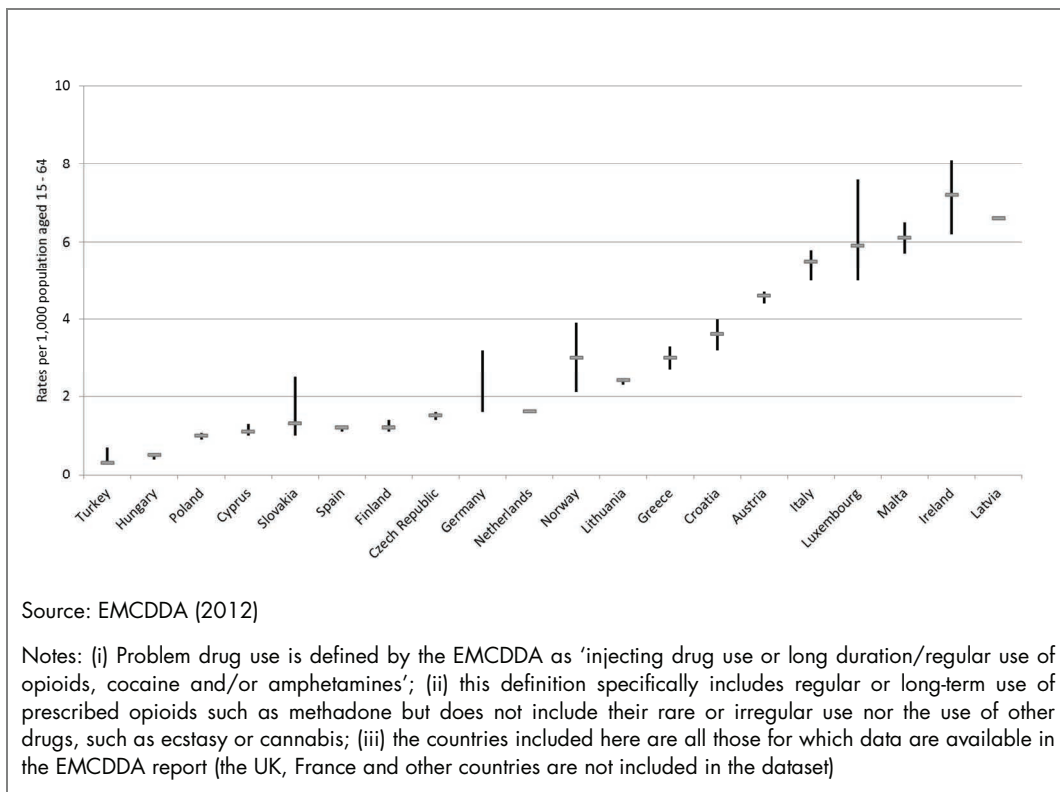
This discussion of prevalence is conducted with the recognition that there is no ‘objective’ measure of dependence to either heroin or prescription drugs (Lintzeris, 2013). Guided by the DSM and ICD criteria, diagnosis is a matter of both clinical interpretation and patient self-report, which are inevitably subjective.

EMCDDA – prevalence of heroin use

The EMCDDA provides estimates of the rates of problem opioid use in selected EU countries per 1,000 population aged between 15 and 64 years (EMCDDA, 2012). EMCDDA estimates include ‘use of prescribed opioids such as methadone’, and vary from less than one case per 1,000 population and seven cases per 1,000 population, with the average prevalence of problem opioid users in the EU and Norway estimated at 4.2 per 1,000 population, corresponding to approximately 1.4 million problem opioid users (EMCDDA, 2012, p.72). Figure 4 shows data from the 2012 EMCDDA report.

Although evidence of heroin opioid use or dependence is available for a large number of countries, any cross-national comparison is limited by a number of factors, such as the different definitions and data collection procedures employed at the national level and the differing methods used to generate the estimates (Degenhardt et al., 2011a; Degenhardt et al., 2011b).¹²

Figure 4: Estimates of the prevalence of 'problem opioid use'



¹² Data sets often vary by target groups (the EMCDDA estimates refer to ‘problem opioid users’; UNODC estimates just refer to ‘opioid’ use). Date of data collection also varies between sources. The most recent national study available has been cited by the EMCDDA, but there are discrepancies across countries. Estimation method might also have an impact – there is a mix of different direct (household surveys or school surveys, for instance) and indirect estimate techniques (such as capture-recapture, treatment multiplier, truncated poisson, among others).

Prevalence of prescription opioid dependence in Europe

A recent review aimed to estimate the prevalence of dependence following opioid treatment for pain management (Minozzi et al., 2013).¹³ The authors found that:

- Few studies report the onset of dependence
- The few studies which are available are of poor methodological quality
- There is heterogeneity across studies as to estimated rates of dependence (ranging from 0 to more than 50 percent).

Similar conclusions – that available data on prevalence of prescription opioid dependence are limited, particularly in European countries – were drawn by the UNODC (2012, p.3).

In 2011 the UK NTA analysed treatment and prescription data but was not able to establish a definite prevalence of addiction to prescription or over-the-counter medicines.¹⁴ They did find evidence that the majority of those currently in treatment for problems relating to prescription medicines have concurrent problems with illegal drugs (National Treatment Agency for Substance Misuse, 2011).

There is evidence that the problem of prescription opioid dependence is extensive in North America, where it has been estimated that prescription opioids are used more than heroin. In Eastern and Southeastern Europe heroin appears to be more prevalent (UNODC, 2012, p.9), although dependence on prescription opioids appears to be growing (Casati et al., 2012; UNODC, 2012).¹⁵

Investigating the possible drivers of dependence is beyond the scope of this report, but it is noted that the drivers of heroin dependence may differ from the factors driving prescription opioid dependence. Rates of dependence to prescription medicines may vary according to the type of pain disorder, setting (primary healthcare, chronic pain, psychiatric or addiction services) and how treatment is provided (for example, variation in the types, doses, duration and controls of opioid medications) (Lintzeris, 2013, p.699). Differences in marketing of prescription opioids, differences in cost of and access to these opioids through the medical system, and general differences in preferences are all additional explanations for rates of dependence. NTA analysis in the UK has indicated large geographical differences in the amounts of opioid-containing drugs prescribed and a correlation between areas of high prescribing and the numbers accessing treatment in relation to dependence on prescribed medicines (National Treatment Agency for Substance Misuse, 2011).

¹³ Patients receiving any of the following strong opioid analgesics (by any route of administration): morphine, methadone, buprenorphine, oxycodone, fentanyl, hydromorphone, levorphanol or pethidine.

¹⁴ Medicines included within the prescription category are: analgesics including opioids (excluding opioids prescribed for the treatment of addiction), benzodiazepines, z-drugs and barbiturates. Medicines included within the over-the-counter category are: over-the-counter opioids (mainly codeine containing compounds) and antihistamines (data suggests that these are less of an issue).

¹⁵ Global licit production of opioids (such as morphine, codeine, thebaine, hydrocodone, oxycodone and methadone) was reported by the UNODC to have increased between 2010 and 2012, which increases the risk that they are over prescribed or diverted (UNODC, 2012, p.82).

2.4 Summarising harms

Table 2 (at the end of this chapter) draws on the two existing frameworks reviewed above and the targeted review of literature to map the harms from opioid dependence. This mapping provides an initial structure for the assessment of existing estimates in the next chapter.

It is possible that the framework should be populated differently for prescription opioid dependence and for dependence on heroin, but for now we present a single framework.

2.5 Conclusion

In order to map the kinds of harms associated with dependence on heroin and prescription opioids this chapter has (i) reviewed two frameworks used by researchers in the field of drug misuse for categorising the harms of drug dependence, and (ii) reviewed existing studies on the correlates and problems associated with dependence.

Available evidence indicates some of the problems and challenges associated with opioid use. However, there is little evidence about how harms differ by type of use or among those dependent on prescription versus illicit opioids.

An understanding of the characteristics, correlates and harms of prescription opioid and illicit drug use is needed in order to enhance the design of interventions and provision of care (Back et al., 2011) and is an important preparatory step in developing a framework to provide monetised cost estimates of opioid dependence.

Table 2: Indicative framework to capture the harms of opioid dependence

Cost categories		Individual	Family	Community/society
Health impacts	Mortality	<ul style="list-style-type: none"> – Lost years of life 	<ul style="list-style-type: none"> – Psychological impacts of losing family member 	<ul style="list-style-type: none"> – Lost productivity – Healthcare costs
	Physical health impacts	<ul style="list-style-type: none"> – Acute toxic effects – Acute effects of intoxication – Adverse health effects of sustained, chronic, regular use 	<ul style="list-style-type: none"> – Increased risk of infection, such as HIV – Impact on care-givers – Impacts of child neglect, inadequate supervision, and domestic violence – Impacts on foetal and neonatal development 	<ul style="list-style-type: none"> – Healthcare cost (including additional GP visits) – Injuries from workplace accidents – Child protection and social care
	Psychological impacts and well-being	<ul style="list-style-type: none"> – Reduced well-being – Psychological conditions as a result of opioid dependence 	<ul style="list-style-type: none"> – Psychological impacts/distress from having a dependent person in the family – Family break-up and social isolation 	<ul style="list-style-type: none"> – Reduced social cohesion from family breakup – Healthcare costs
Employment and workplace		<ul style="list-style-type: none"> – Increased risk of unemployment and under-employment – Loss of income 	<ul style="list-style-type: none"> – Reduced household income – Intergenerational effects of having unemployed parent – Lost carer employment opportunities 	<ul style="list-style-type: none"> – Lost productivity – Cost of jobseeker's allowance and other similar benefits
Education		<ul style="list-style-type: none"> – Poorer educational outcomes 	<ul style="list-style-type: none"> – Reduced educational achievement of children – Intergenerational effects 	<ul style="list-style-type: none"> – Less skills available in workforce
Welfare (including housing)		<ul style="list-style-type: none"> – Impacts of problems securing housing 	<ul style="list-style-type: none"> – Impacts of inappropriate accommodation 	<ul style="list-style-type: none"> – Housing benefit – Social services
Crime		<ul style="list-style-type: none"> – Impacts of imprisonment – Impacts of having a criminal record – Opportunity cost of engaging in an unlawful (rather than lawful) career 	<ul style="list-style-type: none"> – Effects of imprisonment of family member – Family members victimisation – Intergenerational impacts 	<ul style="list-style-type: none"> – Fear of crime – Policing, prosecution, courts, probation, prison, parole – Psychological effects on victims – Lost earnings of victims (Brand & Price, 2000)
Environment				<ul style="list-style-type: none"> – Impacts of production – Litter of drug paraphernalia

CHAPTER 3 **Description of included estimates of the cost of opioid dependence**

This chapter describes the 15 cost estimates (from 9 studies) that were included in the review, as well as the corresponding issues for generalisation of and comparison between estimates. Estimates differed in terms of:

- Populations covered by the estimate – geography and type of opioid used
- Definitions of dependence
- Methodological approaches and data sources
- Categories of cost included.

These factors are discussed further in Section 3.1. The studies are described in detail in Appendix D, and the key features are set out in Table 4, later in this chapter. Chapter 4 presents and discusses the actual cost estimates.

Several studies presented more than one cost estimate that was consistent with our inclusion criteria. In these cases the multiple estimates sometimes reflected different methodological approaches or measurement techniques (such as estimates with and without controlling for observable covariates in Leider et al., 2011), different populations (such as clinical and non-clinical abusers in White et al., 2009), or different data sources (such as US SAMHSA or ONDCP data as a population denominator in Mark et al., 2001).

When studies presented more than one estimate we included each estimate that was (a) consistent with our study inclusion criteria, and (b) compatible with a ‘per-person, per-year’ presentation. Table 3 lists included studies with more than one cost estimate.

Table 3: Included studies with multiple cost estimates

Study	No. of Estimates	Description
White et al. (2009)	3	Clinical/non-clinical/aggregate populations
McAdam-Marx et al. (2010)	2	With and without controls
Mark et al. (2001)	2	Different prevalence estimates
White et al. (2005)	2	Study population and projected population
Leider et al. (2011)	2	With and without controls

3.1 Estimates not included

Our strict inclusion criteria, necessary to ensure that estimates could be (broadly) compared, as well as to ensure a manageable number of estimates, meant that some estimates that are well known to researchers and policymakers in this field were not included. These are briefly reviewed here.

Public costs of individuals with a history of crime and drug addiction in Sweden

A Swedish study (Nilsson & Wadeskog, 2011) calculated the public costs of six particular individuals with a history of crime and drug addiction who were employed by two social enterprises. The report – of which only the summary was available in English – looked at about 130 cost parameters for heroin, amphetamines and alcohol addiction. The parameters included healthcare and treatment, crime, housing and costs relating to the addicts' children. Welfare services used by addicts were described by addicts themselves.

Using an expert panel consisting of recovering addicts and practitioners the study mapped the addiction careers of the six individuals in question. The results show that the public costs per amphetamine or heroin addict per year range from 1.4 million to 2 million SEK (around £140,000 to £200,000). The limitation of this study is that it does not reflect the general public costs of drug abuse; it examined the possible public costs that specific six individuals of these two enterprises generated in their addictive careers in the three years before joining the enterprises.

Lifetime costs of problem drug users in the UK

PricewaterhouseCoopers (PwC) undertook work for the UK Ministry of Justice on prison-based drug testing, part of which involved the development of an economic framework to model the lifetime economic output, health, crime and social impacts of a 'problem drug user' compared to an 'average' person. The model estimates the lifetime costs for a male and a female in each group (PwC, 2008).

This study estimated excess mortality costs, excess morbidity, direct health costs, lost earnings, lost productivity, criminal justice system costs, costs to children of problem drug users in care and the intergenerational costs (children of problem drug users are more likely themselves to be problem drug users and incarcerated).

Based on assumptions about each of these costs, it was estimated that the costs of a male lifetime problem drug user are around £827,000, and £859,000 for a female. The authors stress that this estimate is an indicative guide to the magnitude of additional costs incurred by a lifetime of problem drug use. The study did not isolate the costs of opioid dependence from dependence on other substances and thus was not included.

The economic and social costs of Class A drug use in England and Wales

In work for the UK Home Office in 2006, Gordon et al. (2006) update previous estimates of the costs of Class A drug use (Godfrey et al., 2002). Their methodology classifies Class A drug users by type – young recreational, older regular and problematic.

The cost domains included are drug-related crime, health service use, drug-related deaths and social care. The cost of all Class A drug use (including but not limited to opioids and therefore not included in our analysis) in the UK in 2003/04 was estimated at £44,231 per year per problematic drug user. Based on these estimates, the NTA has estimated a lifetime 'crime and health bill' of £480,000 for each intravenous drug user (again, not limited to opioids) in the UK (National Treatment Agency for Substance Misuse, 2012b, p.6).

Crime costs of chronic drug users

French et al. (2004) estimated the incremental cost of crime associated with ‘chronic drug use’. This estimate was based on empirical information collected through a detailed survey¹⁶ that was administered to both chronic drug and non-drug users in the community. To be included in the sample individuals had to have consumed an illicit drug at least once a week during the previous 12 months and tested positive for cocaine and/or opiates. The study was not included as it is not limited to opioids and did not include prescription opioid use.

The survey data were combined with existing estimates of the costs of specific crimes to estimate the cost of crime for the average chronic drug user as a victim of criminal activity, a perpetrator of criminal activity, and overall. The findings were as follows:

- Chronic drug users were significantly more likely to be involved in all types of crime (around 73 percent more likely) than non-drug users.
- The average annual victim cost of crime was \$25,897¹⁷ for chronic drug users and \$13,718 for non-drug users.
- The average annual perpetrator cost of crime was \$29,205 for chronic drug users and \$3,697 for non-drug users.
- Combined (victim plus perpetrator) annual cost of crime was \$77,168 for chronic drug users and \$21,130 for non-drug users.

3.2 Included estimates

3.2.1 Variation in geography

Included studies estimate the cost of opioid dependence in American, Australian and Canadian populations.

National regulation, law enforcement, healthcare and social policies have profound effects on opioid supply, patterns of addiction and costs associated with opioid dependence. It is therefore important to identify the geography of study populations and to recognise differences when comparing estimates from different countries. For example, comparisons of the healthcare costs associated with opioid dependence should recognise that healthcare costs in the United States are, on average, considerably higher than costs in European countries, Canada and Australia (Organisation for Economic Co-operation and Development, 2010). Similarly, differences in the administration of criminal justice and welfare systems between countries mean that estimates should not be generalised.

Some reviewed studies estimate costs associated with opioid dependence in populations within specific regional or local areas. For example, Wall et al. (2000) calculate costs using a survey of individuals in Toronto. Differences in the nature of opioid dependence and the availability and cost of healthcare and social services across urban and rural settings should be considered before results from this or other studies are generalised to wider populations.

¹⁶ The questionnaire contained over 300 questions and was divided into seven sections: screening, general, medical, satisfaction, alcohol and drug use, demographics, and safety. The survey asked questions about both criminal acts that respondents had committed, and crimes of which they had been victims.

¹⁷ All averages are for data values constrained to the range defined by the 5th and 95th percentiles.

More broadly, each reviewed study raised concerns that hinder comparisons across studies. For example, several US-based studies were limited to individuals with employer-sponsored health insurance, or to low-income individuals insured by a state Medicaid programme. Wall et al. (2000) surveyed individuals at needle exchange programs and social service agencies in Toronto, most of whom were heroin users. Other studies focused on prescription opioid abuse. A minority of reviewed studies (including Wall et al., 2000) discussed threats to generalisability and, where possible, adjusted data inputs and results to mitigate these concerns.¹⁸

Our abstraction template (see Appendix A) collected extensive information on setting and context to facilitate comparisons across studies, and to accurately describe the caveats that must accompany any comparison.

3.2.2 Variation in type of opioid use

Two included studies looked only at heroin users (Mark et al., 2001; Wall et al., 2000), two looked only at prescription drug use (Birnbaum et al., 2011; White et al., 2009) and five did not specify (Heffernan et al., 2003; Leider et al., 2011; McAdam-Marx et al., 2010; McCarty et al., 2010; Riddell et al., 2008; White et al., 2005). This reinforces the impression from the targeted literature review, set out in Chapter 2, that available evidence does not allow the harms from and costs of heroin dependence to be distinguished from the harms from dependent use of prescription opioids.

3.2.3 Variation in definitions of dependence

Six studies used the ICD-9 definition of dependence (Birnbaum et al., 2011; Leider et al., 2011; Mark et al., 2001; McAdam-Marx et al., 2010; White et al., 2005; White et al., 2009), and one used the Australian version of ICD-10 (Riddell et al., 2008). Two used a definition created by the study authors (McCarty et al., 2010; Wall et al., 2000).

3.2.4 Variation in approaches

The studies that met our inclusion criteria fall into two main categories in terms of approach and methodology:

- Studies implementing the ‘cost-of-illness’ methodology.¹⁹ These estimate the burden of a condition from a governmental or public sector perspective. Cost-of-illness studies tended to combine readily available prevalence, event and unit cost data into aggregate cost estimates.
- Descriptive analyses of healthcare administrative data. These estimate costs from the health services perspective. Studies analysing routinely collected data used a combination of actual and projected healthcare utilisation and spending data to arrive at cost estimates.

3.2.5 Categories of cost

We identified three commonly estimated categories of costs in our review:

- Healthcare costs
- Criminal justice and victimisation costs
- Lost productivity.

¹⁸ In the case of Wall et al. (2000), the authors adjust their survey data to approximate the entire Toronto population of illicit opioid users, reporting the survey sample and adjusted results separately.

¹⁹ ‘Cost of illness’ is a widely used term in the health economics field (see Hodgson & Meiners, 1982; World Health Organization, 2009a).

Only one reviewed study estimated costs in another category: Mark et al. (2001) considered costs from welfare programmes that provide services to individuals dependent on opioids. These categories and other relevant information are presented in Table 4. Below we explain what kinds of costs were estimated within each of these categories, before mapping harms that have not been costed.

Table 4: Description of included cost estimates

Study	Estimate	Country	Type of costs estimated				Type of opioids included			Definition of dependence	Methodology
			Health	Crime and Justice	Productivity	Welfare	All/ not specified	Heroin	Prescription		
Wall et al. (2000)	[1]: Study sample [2]: Projected population, Toronto	Canada	X	X	X			X		Daily opiate users currently not in or seeking treatment	Cost of illness
White et al. (2005)	[1]: Base	USA	X				X			ICD-9	Analysis of administrative data (claims data)
White et al. (2009)	[1]: Projected population, clinical abusers [2]: Projected population, non-clinical abusers [3]: Projected population, all abusers	USA	X						X	ICD-9	Analysis of administrative data (claims data)
McAdam-Marx et al. (2010)	[1]: Univariate [2]: Controlling for covariates	USA	X				X			ICD-9	Analysis of administrative data (claims data)
Leider et al. (2011)	[1]: Controlling for covariates [2]: Univariate	USA	X				X			ICD-9	Analysis of administrative data (claims data)
Birnbaum et al. (2011)	[1]: Base	USA	X	X	X				X	ICD-9	Cost-of-illness based on augmented administrative data
Mark et al. (2001)	[1]: SAMSHA prevalence [2]: ONDCP prevalence	USA	X	X	X	X		X		ICD-9	Analysis of health service and survey data
Riddell et al. (2008)	[1]: Base	Australia	X				X			ICD-10 (Australian Modification)	Analysis of administrative data (claims data)
McCarty et al. (2011)	[1]: Base	USA	X				X			Individuals with diagnoses of opioid dependence (two or more diagnoses per year)	Analysis of claims data across five calendar years

Healthcare costs

Costs in this category include costs of providing healthcare services to individuals dependent on opioids. These costs reflect dispensed pharmaceuticals, emergency treatment, hospital visits to treat symptoms of opioid abuse, and other healthcare services resulting from opioid dependence. In accordance with the inclusion criteria the costs of treatment specifically for opioid dependence were excluded from this category.

Healthcare costs may be borne by health insurers who make payments to providers in exchange for delivering services, out-of-pocket payments by patients, or combinations of the above.

Most reviewed studies apply standard tariffs from fee schedules or provider cost estimates reported to national health systems, combined with data on utilisation to arrive at total per-person, per-year costs. Studies using insurance claims data (primarily from the US) are an exception: they report actual (not estimated or average) paid amounts to providers.

Criminal justice and victimisation costs

This cost category includes three main components, each of which capture a dimension of the social costs of crimes committed by individuals who are dependent on opioids:

- Policing costs
- Court and corrections costs (including prosecution, incarceration and community supervision costs)²⁰
- Victimisation costs (including damages to individuals as a result of crime).

In most reviewed studies, costs in this category are estimated by multiplying crime event data by per-crime cost estimates provided by governments.

Lost productivity

This cost category reflects lost economic productivity due to opioid dependence, where the lost productivity is due to presenteeism, absenteeism, disability or death. Costs in this category are often estimated by multiplying a measured or imputed duration of lost work by a given wage (minimum, average or median).

Social programme costs

This cost category considers resources used to provide non-healthcare services for individuals dependent on opioids, including job placements, nutrition, housing and welfare payments. As with criminal justice and victimisation costs, costs in this category can be calculated by multiplying estimates of social programme utilisation by a per-use or per-person, per-year cost estimate provided by governments or social programmes. Only one reviewed study, Mark et al. (2001), estimated social programme costs.

3.2.6 Harms that have not been costed

The included estimates did not consider several of the harms identified in Chapter 3. All the estimates take a healthcare or a taxpayer perspective, thus not including costs to the dependent individual, his or her friends and family (such as reduced quality of life and well-being).

²⁰ None of the studies distinguishes between crimes related to selling/supplying drugs versus crimes attributed to abuse.

Such costs are more difficult to quantify in monetary terms (McCollister & French, 2003). For example, psychological status is typically assessed using clinical instruments and numerical scales to indicate the degree of mental illness or distress. These scales do not translate easily into meaningful economic terms (McCollister & French, 2003). However, economic studies have devised approaches to quantifying these costs, and there have been attempts to generate monetised estimates (Copello et al., 2009).

From a theoretical perspective, these costs should be salient for policymakers deciding how to allocate scarce public resources. While costs in this category were not estimated by any reviewed study, they have the potential to be large in magnitude – for example, around 50 percent of the estimated cost of crime in England and Wales is due to the physical and emotional impact of crime on victims (Dubourg et al., 2005, p.12).

3.2.7 Attribution challenges

A shared challenge across all three of the costing methodologies described above is the need to attribute costs in the data to opioid dependence as opposed to any other aspect of a person's lifestyle or health. The aim is to isolate costs that would not be incurred if the individual dependent on opioids were not dependent.

To do so studies must estimate the incremental costs, on top of 'baseline' costs, that are directly attributable to opioid dependence. All individuals, including those who are and those who are not dependent on opioids, can incur healthcare costs, commit or be victims of crime, miss work, use social services, and so on. Researchers would overestimate costs if they attributed all costs in these categories to opioid dependence in a population dependent on opioids.

Reviewed studies used a variety of approaches to attribution:

- Five studies used non-dependent individuals as matched controls (Birnbaum et al., 2011; Leider et al., 2011; McAdam-Marx et al., 2010; White et al., 2005; White et al., 2009). The usefulness of this approach hinges on how well the observable characteristics used to match individuals predict those outcomes that are of interest, which in this case are those costs associated with opioid dependence.
- One reviewed study, however, made no attempt to attribute costs to opioid dependence (Riddell et al., 2008). This study simply reports cost levels or trends without claiming the costs are necessarily due to opioid dependence.

3.3 Conclusion

This chapter has provided an overview of the 15 estimates of costs of opioid dependence included in this review. The following chapter sets out the actual values arrived at in these estimates.

CHAPTER 4 **Existing estimates of the costs of opioid dependence**

This chapter explains the method used to standardise estimates to arrive at comparable per-person, per-year costs.

4.1 Adjusting for changes in prices and different currencies

Each of the reviewed studies indicated the calendar year used as a baseline for cost estimates. We inflated monetary values from the reported baseline year to 2012 using local inflation rates reported by the Royal Bank of Canada, the Reserve Bank of Australia and the US Department of Labor's Bureau of Labor Statistics. We then used 2012 exchange rates²¹ to convert inflated 2012 US dollars, Canadian dollars and Australian dollars to 2012 euros. The exchange and inflation rates and calculations for each estimate are set out in Appendix E.

4.2 Estimating per-person, per-year costs

Some studies reported per-person, per-year costs, or in other words the costs of opioid dependence accrued by a single person over a calendar year. Other studies, however, did not. We adjusted results to conform to the per-person, per-year cost format using methods summarised in Table 5. Table 5 also lists adjustments to apportion costs into the categories described in Chapter 3. All adjustments rely on data and results reported in the specific study: no data external to the study in question were used to calculate per-person, per-year estimates.

²¹ www.oanda.com

Table 5: Adjustments to study results to calculate per-person, per-year costs

Study	Adjustment
Wall et al. (2000)	(1) Divide reported aggregate costs by the study sample size [for study sample estimate]; (2) apportion reported total per capita costs to cost categories using reported percentages [for projected estimate]
Birnbaum et al. (2011)	Apportion reported total per capita costs to cost categories using reported percentages
Mark et al. (2001)	Apportion reported total per capita costs to cost categories using reported percentages
White et al. (2005)	Calculate average difference between costs in subjects with an opioid abuse-related diagnosis code and in matched controls
White et al. (2009)	No adjustments necessary
McAdam-Marx et al. (2010)	Calculate average difference between costs in subjects with an opioid abuse-related diagnosis code and in matched controls
Leider et al. (2011)	No adjustments necessary. Report results only for the non-adherent population
Riddell et al. (2008)	No adjustments necessary. Report results only for opioids
McCarty et al. (2011)	No adjustments necessary

4.3 Assessing scope and generalisability

In order to describe the variation in cost estimate magnitudes, we scored reviewed studies in terms of the scope of costs considered and the generalisability of results across geography and populations. Reviewers ranked each study from 1 to 5 on both dimensions.

Scope of costs

For scope of costs, lower scores connote fewer estimated cost components and fewer or narrower costs measured within each component. Studies with higher scores estimated multiple cost components in a more comprehensive fashion.

Scope of costs scores align with the following rubric:

1. Cost narrowly estimated within one cost category (e.g. costs for a single type of healthcare service; no study received this score).
2. Costs partially estimated for only one cost category (e.g. costs for all healthcare provided in one clinical setting).
3. Costs comprehensively estimated for one cost category.
4. Costs comprehensively estimated for at least two categories.
5. Costs estimated for healthcare, criminal justice and productivity.

Generalisability

For generalisability, lower scores indicate estimates that were calculated based upon more narrowly defined populations while higher scores indicate larger, more diverse study samples. Generalisability scores align with the following rubric:

1. Small convenience samples (e.g. surveys) with no mention of differences between the sample and the entire population of individuals dependent on opioids.
2. Small convenience samples (e.g. surveys) where the authors identify but do not address differences between their sample and all individuals dependent on opioids.

3. Large convenience sample (e.g. from administrative data) with selection concerns, for example due to medical care seeking, or a small convenience sample where the authors control for observable drivers of differences in costs.
4. Large, nationally representative sample of individuals dependent on some opioid categories but not others.
5. Large, nationally representative sample of all individuals dependent on illicit and prescription opioids (no study received this score).

4.4 Adjusted cost estimates

Table 6 reports adjusted (for inflation, exchange rate and to arrive at per-person, per-year cost) cost estimates in aggregate and by cost component. Full details regarding adjusted cost estimates are provided in Appendix E.

Total costs range from €2,627 to €60,665 per-person, per-year. Estimates of the health component alone range from €890 to €15,078 per-person, per-year. The estimates reported in Table 6 suggest two main observations:

- Estimates of the costs associated with opioid dependence are highly variable.
- In the handful of studies considering non-healthcare costs, these account for a significant portion of total costs.

Table 6: Adjusted per-person, per-year cost estimates in included studies (2012 euros)

Study	Estimate	Total costs (€)	Cost components (€)		
			Health	Criminal justice	Productivity
Wall et al. (2000)	[1]: Study sample	45,915	2,806	39,915	3,194
Wall et al. (2000)	[2]: Projected population, Toronto	13,495	890	8,129	4,476
White et al. (2005)	[1]: Base	13,668	13,668	-	-
White et al. (2009)	[1]: Projected population, clinical abusers	15,078	15,078	-	-
White et al. (2009)	[2]: Projected population, non-clinical abusers	5,322	5,322	-	-
White et al. (2009)	[3]: Projected population, all abusers	7,273	7,273	-	-
McAdam-Marx et al. (2010)	[1]: Univariate	5,712	5,712	-	-
McAdam-Marx et al. (2010)	[2]: Controlling for covariates	14,704	14,704	-	-
Leider et al. (2011)	[1]: Controlling for covariates	2,627	2,627	-	-
Leider et al. (2011)	[2]: Univariate	2,725	2,725	-	-
Birnbaum et al. (2011)	[1]: Base	27,003	12,001	2,455	12,547
Mark et al. (2001)	[1]: SAMSHA prevalence	60,665	14,023	14,572	32,070
Mark et al. (2001)	[2]: ONDCP prevalence	21,904	5,063	5,261	11,579
Riddell et al. (2008)	[1]: Base	2,933	2,933	-	-
McCarty et al. (2011)	[1]: Base	10,631	10,631	-	-

Figure 5 and Figure 6 illustrate the magnitude of cost estimates relative to the scope and generalisability scores. Figure 5 includes total costs while Figure 6 includes only the health

cost component (health costs were separated in order to illustrate the extreme variability in the quantum of the estimates, even within one cost category). The size of the circles in the figures represents the cost estimate magnitudes reported in Table 6. Three additional observations follow from Figure 5 and Figure 6:

- First, **estimates that scored highly on scope (ranked 4 or 5) have small healthcare costs relative to total costs, and large total cost estimates overall.** These estimates were generated using variations on the cost-of-illness methodology, were US- and Canada-based, and examined a range of populations including a sample of heroin users in Toronto and individuals represented in US-wide administrative data.
- Secondly, **the most generalisable estimates (ranked 4) are highly variable in magnitude.** The two largest estimates are from a study that applied an adaptation of the cost-of-illness methodology to a US-wide population. The considerable difference in estimates from this study is due to assumptions about the prevalence of opioid dependence in the US.
- Thirdly, **no study received the maximum score in both scope and generalisability.** This gap in current research reflects the complexity and difficulty of conducting a study that considers all relevant cost components in detail, assembles data on each cost component, and is based on study samples that allow results to be generalised.

Figure 5: Total cost estimates relative to study scope and generalisability

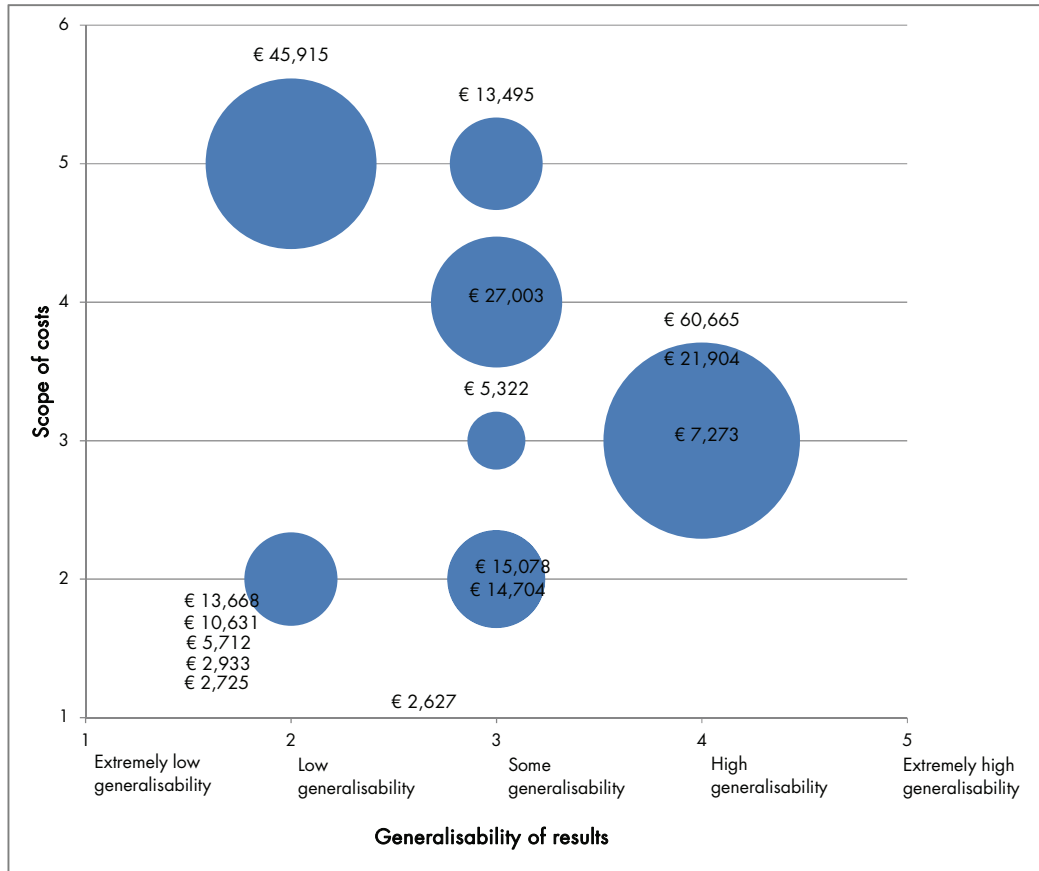
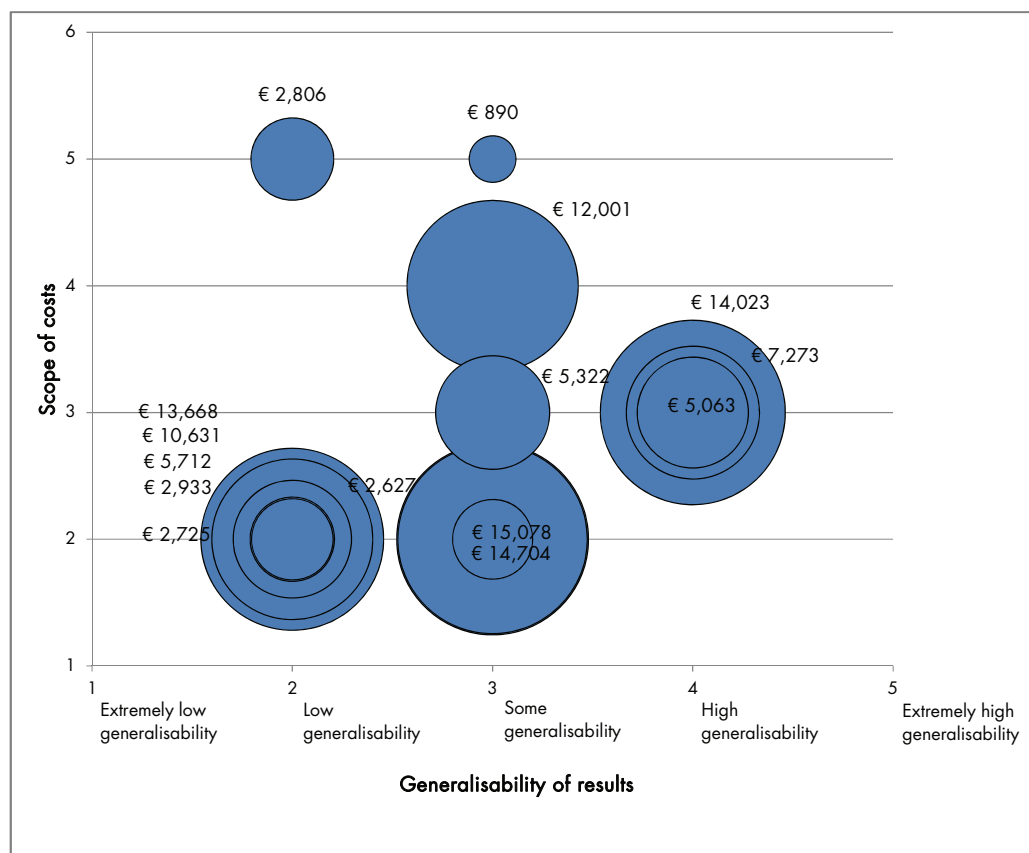


Figure 6: Healthcare cost estimates relative to study scope and generalisability

4.5 Conclusion

This chapter has set out the estimates of the cost of opioid dependence calculated in studies included in our review. Total costs of opioid dependence were highly varied, ranging from €2,627 to €60,665 per person, per year. Given the differences in geography, approach and populations, as described in Chapter 3, it is not possible to select one as a more accurate or useful estimate.

It is not the case that estimates that included more kinds of costs were always higher in value. We suggest that the drivers of the size of these estimates lie in the methodological approach – including data sources, assumptions, etc.

The next and final chapter sets out a framework that could be used to generate more comparable and comprehensive estimates in the future.

CHAPTER 5 **A framework to estimate the costs of opioid dependence**

5.1 Developing a framework for cost estimation

In this section we propose a framework that can be used as a tool for calculating the costs of different types of opioid dependence in different contexts. An overview of the framework is set out in Figure 7. Below we explain what each step of the framework includes, in terms of the estimation of costs. This framework has similarities to those presented in Section 2.1 and to systems for categorising harms and costs included in both the broader health economics literature (National Institute for Health and Clinical Excellence, 2011; Sefton et al., 2002) and guidance for costing substance abuse (Collins et al., 2006; Rehm et al., 2006; Single et al., 1996).

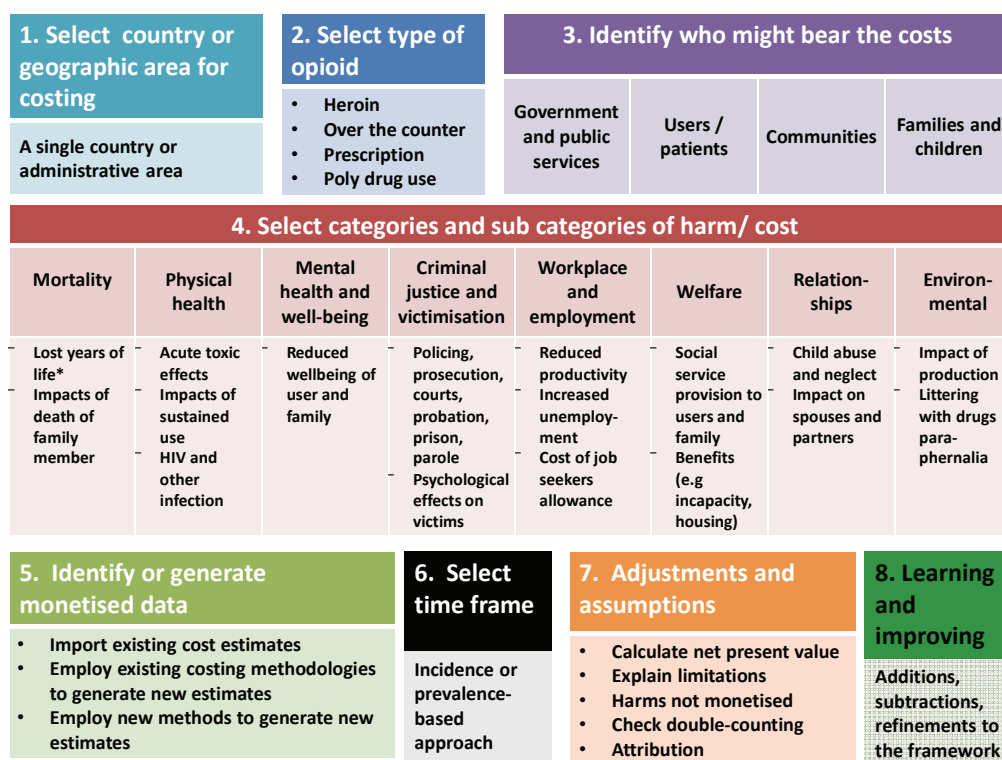
5.1.1 Step 1: Select a country or geographic area in which the costs should be estimated

Given the variability in healthcare, criminal justice and welfare systems (such as state benefits for unemployment, housing and long-term sickness), an estimate of the cost of opioid dependence must be specified for a particular country, or even a particular geographic or administrative area within a country, if this is likely to have implications for costs. For example, in some countries, such as the UK, drug treatment services are increasingly commissioned locally, so information about the harms and costs of opioid dependence locally could inform commissioning choices. Average wages may vary greatly between different parts of a country, entailing separate calculations for lost productivity in different regions.

5.1.2 Step 2: Select the type of opioids for which an estimate will be generated

A framework should break down costs for dependence on different opioids. Those dependent on heroin are likely to incur different costs than those dependent on prescription drugs, and harms and costs incurred by those groups might be different from populations who are dependent on both illicit and medical opioids.

The quality of information on these various forms of opioid dependence is varied – estimates of the prevalence of prescription opioid dependence is relatively lacking in the UK, as it is elsewhere in Europe – which has implications for the confidence with which it is possible to produce estimates for different kinds of users.

Figure 7: Proposed framework to guide estimation of the costs of opioid dependence

5.1.3 Step 3: Select the costing perspective

The framework distinguishes between government and public services, users/patients, communities and families and children. Choices about whose costs to count will be driven by the purpose for which an estimate is being calculated. In an economic analysis, for example, the groups for which costs are estimated must be the same as the groups for which benefits are being quantified. In seeking an overall estimate of the costs of opioid dependence, the costs incurred by all groups would be counted, with care taken to avoid double counting where the same or similar costs are incurred in different groups or at different levels.

5.1.4 Step 4: Select the categories and sub-categories of harm to cost

The framework sets out headings and sub-headings of different kinds of harm associated with opioid dependence. Those developing cost estimates should select those harms for which they would like to develop cost estimates. As above, in seeking an overall estimate of the costs of opioid dependence, all of these would be selected to obtain as comprehensive a costing as possible with available data.

It might not be possible to calculate estimates for each kind of harm in every country or geographic area, depending on available data and research. Such limitations would be made explicit in the estimates generated so that it is always clear what is and is not included in a given estimate.

5.1.5 Step 5: Identify or generate monetised data

There is a range of ways in which this step may be undertaken:

- There may be an existing estimate for a particular harm that can be used directly, or which can be used with little additional calculation (for example, an existing estimate can be adjusted to present-day prices).
- There may be an existing estimate for a particular harm that can be used with modification or additional calculation (for example, an existing estimate of harm stemming from all drug use from which the opioid-specific cost might be disaggregated if relevant information such as prevalence rates are known).
- A cost estimate might be calculated by combining existing data about (i) the prevalence of the harm within the group of interest and (ii) existing cost data monetising that harm (for example, if the average number of work days lost because of opioid dependence is known, this can be combined with appropriate estimates of the cost of lost work days used by government economists).
- There may be a data gap relating to either (i) prevalence of a harm within the group of interest and/or (ii) monetised estimates of that harm. Here new data must be generated or extrapolated from other sources, or sufficiently useful proxies must be identified.

Overall, it is preferable to base estimates on empirical data about the costs actually imposed by different forms of opioid dependence. Research estimating the costs of crime is a helpful example here. Costs of crime estimates are based upon empirical information about the (large) number of crimes of different types. Similar data sources about those who are dependent on opioids do not currently exist at a similar scale. This means we have limited information from which to estimate average costs of different types of dependence (this has been possible in relation to the cost of crime, where, for example, the cost of an average burglary compared to average theft has been estimated).

Some existing studies have employed qualitative methodologies to shed light on the experiences of opioid dependence. Examples include work by Wall et al. (2000), who surveyed individuals using a needle exchange programme, and research in Sweden by Nilsson & Wadeskog (2011) that developed a description of the costs of drug use by consulting expert panels consisting of recovering addicts and agency officials (see Back et al., 2011; McKeganey et al., 2002; Nilsson & Wadeskog, 2011).

This kind of qualitative information is important for supporting a ‘bottom-up’ approach to costing, which attempts to piece together the experiences, behaviours and outcomes that together generate the total cost of opioid dependence. Each ‘category’ generating a cost is identified and then all costs are aggregated to arrive at a total cost for a particular dependent population.

5.1.6 Step 6: Select the costing timeframe

In this review, estimates of per-person, per-year costs have been generated. This is useful for estimating cost savings from intervention programmes. An incidence-based approach might be useful in some contexts, measuring the lifetime costs of opioid dependence.

Either costing timeframe can take into account the longer-term and intergenerational impacts of dependence, including those that persist once a person is no longer dependent.

5.1.7 Step 7: Establish adjustments and assumptions

Costs that appear in the future (i.e. more than one year ahead) need to be discounted in order to account for their present value. For example, costs of crime estimates have used a rate of between 2 and 3.5 percent per year (Brand & Price, 2000; Cohen, 1988; Dubourg et al., 2005).²²

Double counting is a risk in any bottom-up cost estimate, and occurs when the same cost has been included more than once. For example, an existing estimate of the cost of drug-induced mortality might include both individual losses and losses to the economy from reduced productivity. If an existing estimate of the workplace costs of dependence is also relied upon, there is a risk that this also includes productivity losses from increased mortality.

It is also important that any estimate is accompanied with information about harms that have not been costed. Given the challenges in assigning a monetary value to intangible costs, it is likely that some important harms cannot be adequately captured.

Researchers and policymakers should be clear about what is taken into account in a costing framework, and what is not. There is likely to be a tension between being comprehensive but with potentially significant inaccuracy, and being more limited in coverage but only including those harms for which reliable cost estimates are available. One suggested way of mediating this tension is to provide a comprehensive framework, to populate this with costs that have been estimated with relative certainty (with ranges where appropriate), and to make clear what is missing and the likely significance of that gap for the overall estimate.

5.1.8 Step 8: Learning and refinements to the framework

A policy-relevant framework could help surface relatively unexamined costs within existing categories and should be reviewed and be able to adapt to accommodate new kinds of harm. These might stem from improvements in the evidence base on the nature of harms, improvements in costing methodologies or changes in prescribing practices, quality and purity of heroin, the demographics of the dependent population, and so on.

5.2 Piloting the framework to generate a new estimate for the UK

A study could be conducted that builds and pilots the framework in the UK and then tests and validates it in additional countries

The biggest challenge in conducting such a study is identifying data that allow cost estimation other than criminal justice and healthcare costs. Table 7 sets out a preliminary scoping of possible data sources. We separate two different kinds of information: (i) information about the prevalence or nature of a particular harm (for example 1 in 10 children of heroin users miss 1 day of school per week), and (ii) information about the monetized cost of that harm (the average cost of one lost school day is £x to the school, £y to the economy in terms of long-term lost productivity and £x to the child in terms of lost quality of life).

²² This is consistent with the inflation-adjusted discount rate.

Table 7: Possible data sources to explore in piloting the framework in the England

Type of harm	Possible data sources to understand prevalence and nature	Approach to monetising
Physical health impacts and mortality – individual	Office for National Statistics – drug-related deaths Build on existing work identifying the effects of illicit drug use (Degenhardt & Hall, 2012)	Update existing cost estimates in Drug Harm Index (MacDonald et al., 2005) Review estimates for all Class A and extrapolate for opioids (based on prevalence data)
Physical health impacts and mortality – healthcare costs	Data on the type and frequency of medical and psychiatric services consumed from hospital episode statistics	Service-specific cost estimates to determine the reduction in (or avoided) client healthcare costs
Perceptions of drug-dealing	British Crime Survey asks ‘how much of a problem are people using or dealing drugs?’	Draw on work that monetises the fear of crime (Dolan et al., 2005) Explore stated or revealed preference methods
Drug-related crime	Data from the Arrestee Survey (Boreham et al., 2007), the National Treatment Outcome Research Study (Stewart et al., 2000), the Drug Outcome Research in Scotland (DORIS) Study (McKeganey et al., 2008), the Drug Treatment Outcomes Research Study (DTORS) (Donmall et al., 2009), the Treatment Outcomes Profile (Donmall et al., 2009)	Draw on/update cost of crime estimates (Brand & Price, 2000; Dubourg et al., 2005)
Employment	Estimates of days’ work	Data on average earnings for different kinds of employment
Impacts on children and families	Build on existing work to estimate prevalence	Draw on monetising methods (for example, Copello et al., 2009)

REFERENCES

Reference List

- Advisory Council on the Misuse of Drugs (2010) *Consideration of the Use of Multi-Criteria Decision Analysis in Drug Harm Decision Making*. As of 8 October 2013:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/119154/ACMD-multi-criteria-report.pdf
- Advisory Council on the Misuse of Drugs (2011) *Hidden Harm – Responding to the Needs of Children of Problem Drug Users*. As of 8 October 2013:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/120620/hidden-harm-full.pdf
- Aguilar de Arcos, F., Verdejo-García, A., Ceverino, A., Montañez-Pareja, M., López-Juárez, E., Sánchez-Barrera, M., López-Jiménez, A., & Pérez-García, M. (2008) 'Dysregulation of emotional response in current and abstinent heroin users: negative heightening and positive blunting', *Psychopharmacology*, 198(2), 159–66.
- Amato, L., Minozzi, S., Davoli, M., & Vecchi, S. (2011a) 'Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification', *Cochrane Database Of Systematic Reviews*, 9.
- Amato, L., Minozzi, S., Davoli, M. and Vecchi, S. (2011b) 'Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence', *Cochrane Database Of Systematic Reviews*, 10.
- American Psychiatric Association (1994) *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, American Psychiatric Association.
- American Psychiatric Association (2013) *Substance-Related and Addictive Disorders Fact Sheet*. As of 8 October 2013:
<http://www.dsm5.org/Documents/Substance%20Use%20Disorder%20Fact%20Sheet.pdf>
- Back, S., Lawson, K., Singleton, L., & Brady, K. (2011) 'Characteristics and correlates of men and women with prescription opioid dependence', *Addictive Behaviors*, 36(8), 829–34.
- Best, D., Day, E., & Morgan, B. (2006) *Addiction Careers and the Natural History of Change*. NTA research briefing 20. As of 8 October 2013:
http://www.misbrugsnet.dk/fagligt/self_change/nta_addiction_careers_2006.pdf
- Birnbaum, H., White, A., Schiller, M., Waldman, T., Cleveland, J., & Roland, C. (2011) 'Societal costs of prescription opioid abuse, dependence, and misuse in the United States', *Pain Medicine*, 12(4), 657–67.

- Boreham, R., Cronberg, A., Dollin, L., & Pudney, S. (2007) *The Arrestee Survey 2003–2006*, Home Office Statistical Bulletin, London: Home Office.
- Brand, S., & Price, R. (2000) *The economic and social costs of crime*, Home Office Research Study 217. London: Home Office.
- Calabria, B., Degenhardt, L., Briegleb, C., Vos, T., Hall, W., Lynskey, M., Callaghan, B., Rana, U., & McLaren, J. (2010) 'Systematic review of prospective studies investigating "remission" from amphetamine, cannabis, cocaine or opioid dependence', *Addictive Behaviors*, 35(8), 741–49.
- Canfield, M., Keller, C., Frydrych, L., Ashrafioun, L., Purdy, C., & Blondell, R. (2010) 'Prescription opioid use among patients seeking treatment for opioid dependence', *Journal Of Addiction Medicine*, 4(2), 108–13.
- Casati, A., Sedefov, R., & Pfeiffer-Gerschel, T. (2012) 'Misuse of medicines in the European Union: a systematic review of the literature', *European Addiction Research*, 18, 228–45.
- CIAR (2008) *Quality of Treatment Services in Europe: Drug Treatment Situation and Exchange of Good Practice*, Health and Consumer Protection Directorate General.
- Cicero, T., Lynskey, M., Todorov, A., Inciardi, J., & Surratt, H. (2008) 'Co-morbid pain and psychopathology in males and females admitted to treatment for opioid analgesic abuse' *Pain*, 139, 127–35.
- Cohen, M. (1988) 'Pain, suffering and jury awards: a study of the cost of crime to victims' *Law and Society Review*, 22(3), 537–55.
- Cohen, M. (2000) 'Measuring the costs and benefits of crime and justice', in *Measuring and Analysis of Crime and Justice*, Washington DC: National Institute of Justice, 263–315. As of 8 October 2013: http://www.ncjrs.org/criminal_justice2000/vol_4/04f.pdf
- Collins, D., Lapsley, H., Brochu, S., Easton, B., Pérez-Gómez, A., Rehm, J., & Single, E. (2006) *International Guidelines for the Estimation of the Avoidable Costs of Substance Abuse*. Ottawa: Health Canada.
- Copello, A., Templeton, L., & Powell, J. (2009) *Adult Family Members and Carers of Dependent Drug Users: Prevalence, Social Cost, Resource Savings and Treatment Responses (Report for the UKDPC)*. London: UK DPC.
- Day, E., Ison, J., & Strang, J. (2008) 'Inpatient versus other settings for detoxification for opioid dependence', *Cochrane Database Of Systematic Reviews*, 2.
- Degenhardt, L., Bucello, C., Calabria, B., Nelson, P., Roberts, A., Hall, W., Lynskey, M., Wiessing, L., Mora, M., Clark, N., Thomas, J., Briegleb, C., & McLaren, J. (2011a) 'What data are available on the extent of illicit drug use and dependence globally? Results of four systematic reviews', *Drug And Alcohol Dependence*, 117(2–3), 85–101.
- Degenhardt, L., Bucello, C., Mathers, B., Briegleb, C., Ali, H., Hickman, M., & McLaren, J. (2011b) 'Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies', *Addiction*, 106(1), 32–51.
- Degenhardt, L., & Hall, W. (2012) 'Extent of illicit drug use and dependence, and their contribution to the global burden of disease', *The Lancet*, 379(9810), 55–70.

- De Maeyer, J., Vanderplasschen, W., & Broekaert, E. (2010) 'Quality of life among opiate-dependent individuals: a review of the literature', *International Journal of Drug Policy*, 21(5), 364–80.
- Dennis, M., Scott, C., Funk, R., & Foss, M. (2005) 'The duration and correlates of addiction and treatment careers', *Journal Of Substance Abuse Treatment*, 28(Suppl 1), S51–S62.
- Dolan, P., Loomes, G., Peasgood, T., & Tsuchiya, A. (2005) 'Estimating the intangible victim costs of violent crime' *British Journal of Criminology*, 45(6), 958–76.
- Donmall, M., Jones, A., Davies, L., & Barnard, M. (2009) *Summary of Key Findings from the Drug Treatment Outcomes Research Study (DTORS)*, Home Office Research Report 23. London: Home Office. As of 8 October 2013:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/116599/horr23.pdf
- Dubourg, R., Hamed, J., & Thorns, J. (2005) *The Economic and Social Costs of Crime Against Individuals and Households 2003/04*, Home Office Online Report 30/05. London: Home Office.
- Eardley, T. (2002) 'Identifying and quantifying the costs of unemployment', in Saunders, P., & Taylor, R. (eds), *The Price of Prosperity: The Economic and Social Costs of Unemployment*, Sydney: University of New South Wales Press, 44–65.
- EMCDDA (2002) *Key Role of Substitution in Drug Treatment*, Drugs in focus, EMCDDA.
- EMCDDA (2012) *The State of the Drugs Problem in Europe. Annual Report 2012*, EMCDDA.
- Ferri, M., Davoli, M., & Perucci, C. (2011) 'Heroin maintenance for chronic heroin-dependent individuals', *Cochrane Database Of Systematic Reviews*, 12.
- French, M., McCollister, K., Alexandre, P., Chitwood, D., & McCoy, C. (2004) 'Revolving roles in drug-related crime: the cost of chronic drug users as victims and perpetrators', *Journal of Quantitative Criminology*, 20(3), 217–41.
- Godfrey, C., Eaton, G., McDougall, C., & Culyer, A. (2002) *Economic and Social Costs of Class A Drug Use in England and Wales, 2000*. Home Office Research Study 249, London: Home Office. As of 8 October 2013:
<http://webarchive.nationalarchives.gov.uk/20110218135832/http://rds.homeoffice.gov.uk/rds/pdfs2/hors249.pdf>
- Gordon, L., Tinsley, L., Godfrey, C., & Parrott, S. (2006) 'The economic and social costs of Class A drug use in England and Wales, 2003/04', in Singleton, N., Murray, R., & Tinsley, L. (eds), *Measuring Different Aspects of Problem Drug Use: Methodological Developments* (2nd edition), Home Office Online Report 16/06, London: Home Office, 41–45. As of 8 October 2013:
<http://webarchive.nationalarchives.gov.uk/20110218135832/http://rds.homeoffice.gov.uk/rds/pdfs06/rdsolr1606.pdf>
- Heaton, P. (2010) *Hidden in Plain Sight: What Cost-of-Crime Research Can Tell Us About Investing in Police*. RAND Center on Quality Policing Occasional Paper. As of 8 October 2013:

- http://www.rand.org/pubs/occasional_papers/OP27.html
- Heffernan, E., Finn, J., Saunders, J., & Byrne, G. (2003) 'Substance-use disorders and psychological distress among police arrestees', *Medical Journal Of Australia*, 179(8), 408–11.
- Hodgson, T. & Meiners, M. (1982) 'Cost-of-illness methodology: a guide to current practices and procedures', *The Milbank Memorial Fund Quarterly. Health and Society*, 429–62.
- Kuramoto, S., Chilcoat, H., Ko, J., & Martins, S. (2012) 'Suicidal ideation and suicide attempt across stages of nonmedical prescription opioid use and presence of prescription opioid disorders among U.S. adults', *Journal Of Studies On Alcohol And Drugs*, 73(2), 178–84.
- Larance, B., Degenhardt, L., Lintzeris, N., Winstock, A., & Mattick, R. (2011) 'Definitions related to the use of pharmaceutical opioids: extramedical use, diversion, non-adherence and aberrant medication-related behaviours', *Drug And Alcohol Review*, 30(3), 236–45.
- Leider, H., Jatinder Dhaliwal, M., Davis, E., Kulakodlu, M., & Buikema, A. (2011) 'Healthcare costs and nonadherence among chronic opioid users', *American Journal of Managed Care*, 17(1), 32–40.
- Lintzeris, N. (2013) 'Commentary on Minozzi et al. (2013): Diagnosing opioid dependence in the context of long-term opioid use for chronic pain – counting shades of grey in a black and white world', *Addiction*, 108(4), 699–700.
- Lobmaier, P., Kornor, H., Kunoe, N., & Bjørndal, A. (2008) 'Sustained-release naltrexone for opioid dependence', *Cochrane Database Of Systematic Reviews*, 2.
- MacDonald, Z., Tinsley, L., Collingwood, J., Jamieson, P., & Pudney, S. (2005) *Measuring the Harm from Illegal Drugs Using the Drug Harm Index*, Home Office Online Report 24/05, London: Home Office. As of 8 October 2013: <http://library.npia.police.uk/docs/hordsolr/rdsolr2405.pdf>
- Manzoni, P., Brochu, S., Fischer, B., & Rehm, J. (2006) 'Determinants of property crime among illicit opiate users outside of treatment across Canada' *Deviant Behavior*, 27(3), 351–76.
- Mark, T., Woody, G., Juday, T., & Kleber, H. (2001) 'The economic costs of heroin addiction in the United States', *Drug And Alcohol Dependence*, 61(2), 195–206.
- Martins, S., Ghandour, L., & Chilcoat, H. (2007) 'Profile of dependence symptoms among extramedical opioid analgesic users', *Addictive Behaviors*, 32(10), 2003–19.
- Mattick, R., Breen, C., Kimber, J., & Davoli, M. (2009) 'Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence', *Cochrane Database Of Systematic Reviews*, 3.
- Mattick, R., Kimber, J., Breen, C., & Davoli, M. (2008) 'Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence', *Cochrane Database Of Systematic Reviews*, 2.
- Mayet, S., Farrell, M., Ferri, M., Amato, L., & Divoli, M. (2010) 'Psychosocial treatment for opiate abuse and dependence', *Cochrane Database Of Systematic Reviews*, 4.

- McAdam-Marx, C., Roland, C., Cleveland, J., & Oderda, G. (2010) 'Costs of opioid abuse and misuse determined from a Medicaid database', *Journal Of Pain & Palliative Care Pharmacotherapy*, 24(1), 5–18.
- McCarty, D., Perrin, N., Green, C., Polen, M., Leo, M., & Lynch, F. (2010) 'Methadone maintenance and the cost and utilization of health care among individuals dependent on opioids in a commercial health plan', *Drug And Alcohol Dependence*, 111(3), 235–40.
- McCollister, K., & French, M. (2003) 'The relative contribution of outcome domains in the total economic benefit of addiction interventions: a review of first findings', *Addiction*, 98(3), 1647–59.
- McKeganey, N., Barnard, M., & McIntosh, J. (2002). 'Paying the price for their parents' addiction: meeting the needs of the children of drug-using parents', *Drugs: Education, Prevention, and Policy*, 9(3), 233–46.
- McKeganey, N., Bloor, M., McIntosh, J., & Neale, J. (2008) *Key Findings from the Drug Outcome Research in Scotland (DORIS) Study*, University of Glasgow Centre for Drug Misuse Research Occasional Paper.
- McLellan, A., Lewis, D., O'Brien, C., & Kleber, H. (2000) 'Drug dependence, a chronic medical illness', *Journal Of The American Medical Association*, 284(13), 1689–95.
- Melberg, H., Hakkarainen, P., Houborg, E., Jääskeläinen, M., Skretting, A., Ramstedt, M., & Rosenqvist, P. (2011) 'Measuring the harm of illicit drug use on friends and family', *Nordic Studies On Alcohol And Drugs*, 28(2), 105–21.
- Millar, T., Ahmad, M., Richardson, A., Skodbo, S., Donmall, M., & Jones, A. (2012) *The Drug Data Warehouse: Linking Data on Drug Misusers and Drug-Misusing Offenders*, Home Office Research Report 63, London: Home Office.
- Minozzi, S., Amato, L., & Davoli, M. (2013) 'Development of dependence following treatment with opioid analgesics for pain relief: a systematic review', *Addiction*, 108(4), 688–98.
- National Institute for Health and Clinical Excellence (2011) *Assessing Cost Impact Methods Guide*, London: National Institute for Health and Clinical Excellence.
- National Treatment Agency for Substance Misuse (2010a). *Drug Treatment in 2009–10*, London: NTA. As of 8 October 2013:
http://www.nta.nhs.uk/uploads/nta_annualreport_0910.pdf
- National Treatment Agency for Substance Misuse (2010b) *A Long-Term Study of the Outcomes of Drug Users Leaving Treatment*, London: NTA. As of 8 October 2013:
http://www.nta.nhs.uk/uploads/outcomes_of_drug_users_leaving_treatment2010.pdf
- National Treatment Agency for Substance Misuse (2011) *Addiction to Medicine*, London: NTA. As of 8 October 2013:
<http://www.nta.nhs.uk/uploads/addictiontomedicinesmay2011a.pdf>
- National Treatment Agency for Substance Misuse (2012a) *Parents With Drug Problems: How Treatment Helps Families*, London: NTA. As of 8 October 2013:
<http://www.nta.nhs.uk/uploads/families2012vfinali.pdf>
- National Treatment Agency for Substance Misuse (2012b) *Why Invest? How Drug Treatment and Recovery Services Work for Individuals, Communities and Society*,

- London: NTA. As of 8 October 2013:
<http://www.nta.nhs.uk/uploads/whyinvest2final.pdf>
- Nilsson, I., & Wadeskog, A. (2011) *From the Public Perspective: A Summary of Reports on Socioeconomic Reports for Vägen ut! kooperativen and Basta Arbetskooperativ*, Stockholm: Swedish Agency for Economic and Regional Growth.
- Nutt, D., King, L., & Phillips, L. (2010) 'Drug harms in the UK: a multicriteria decision analysis', *The Lancet*, 376(9752), 1558–65.
- Organisation for Economic Co-operation and Development (2010) *OECD Health Data 2012*. As of 8 October 2013:
<http://www.oecd.org/health/health-systems/oecdhealthdata.htm>
- Paulozzi, L. (2012) 'Prescription drug overdoses: a review', *Journal of Safety Research*, 43, 283–89.
- Peleg-Oren, N., & Teichman, M. (2006) 'Young children of parents with substance use disorders (SUD): a review of the literature and implications for social work practice', *Journal of Social Work Practice in the Addictions*, 6(1–2), 49–61.
- Pirona, A. (2012) 'Trends, availability and access to opioid substitution treatment in the European Union, Norway, Croatia and Turkey', EMCDDA.
- PwC (2008) *Report to the Department of Health and Ministry of Justice: Review of Prison-Based Drug Treatment Funding – Final Report*.
- Rehm, J., Baliunas, D., Brochu, S., Fischer, B., Gnam, W., Patra, J., Popova, S., Sarnocinska-Hart, A., & Taylor, B. (2006) *The Costs of Substance Abuse in Canada 2002*. Ottawa: Canadian Centre on Substance Abuse.
- Riddell, S., Shanahan, M., Degenhardt, L., & Roxburgh, A. (2008) 'Estimating the costs of drug-related hospital separations in Australia', *Australian And New Zealand Journal Of Public Health*, 32(2), 156–61.
- Ruetsch, C. (2010) 'Empirical view of opioid dependence', *Journal of Managed Care Pharmacy*, 16(1–b), S9–S13.
- Savage, S., Joranson, D., Covington, E., Schnoll, S., Heit, H., & Gilson, A. (2003) 'Definitions related to the medical use of opioids: evolution towards universal agreement', *Journal Of Pain And Symptom Management*, 26(1), 655–67.
- Scott, C., Foss, M., Lurigio, A., & Dennis, M. (2003) 'Pathways to recovery after substance abuse treatment: leaving a life of crime behind', *Evaluation and Program Planning*, 26(4), 403–12.
- Sefton, T., Byford, S., McDaid, D., Hills, J., & Knapp, M. (2002) *Making the Most of It: Economic Evaluation in the Social Welfare Field*. Joseph Rowntree Foundation. As of 8 October 2013: <http://www.jrf.org.uk/sites/files/jrf/1842631322.pdf>
- Shyangwa, P., Tripathi, B., & Lal, R. (2008) 'Family burden in opioid dependence syndrome in tertiary care centre' *Journal Of The Nepal Medical Association*, 47(171), 113–19.
- Single, E., Collins, D., Easton, B., Harwood, H., Lapsley, H., & Maynard, A. (1996) *International Guidelines on Estimating the Costs of Substance Abuse* (1st edition), Ottawa: Canadian Centre on Substance Abuse.

- Solberg, U., Burkhart, G., & Nilson, M. (2002) 'An overview of opiate substitution treatment in the European Union and Norway', *International Journal of Drug Policy*, 13, 477–84.
- Stewart, D., Gossop, M., Marsden, J., & Rolfe, A. (2000) 'Drug misuse and acquisitive crime among clients recruited to the National Treatment Outcome Research Study (NTORS)', *Criminal Behaviour & Mental Health*, 10(1), 10–20.
- Subramaniam, G., & Stitzer, M. (2009) 'Clinical characteristics of treatment-seeking prescription opioid vs. heroin-using adolescents with opioid use disorder', *Drug And Alcohol Dependence*, 101(1–2), 13–19.
- Trémeau, F., Darreye, A., Staner, L., Corrêa, H., Weibel, H., Khidichian, F., & Macher, J. (2008) 'Suicidality in opioid-dependent subjects', *American Journal On Addictions / American Academy Of Psychiatrists In Alcoholism And Addictions*, 17(3), 187–94.
- UK Drugs Policy Commission (2008) *The UK Drug Classification System: issues and challenges*. London: UKDPC.
- UNODC (2012) *World Drug Report 2012*, Vienna: UNODC.
- Wall, R., Rehm, J., Fischer, B., Brands, B., Gliksman, L., Stewart, J., Medved, W., & Blake, J. (2000) 'Social costs of untreated opioid dependence' *Journal Of Urban Health: Bulletin Of The New York Academy Of Medicine*, 77(4), 688–722.
- White, A., Birnbaum, H., Mareva, M., Daher, M., Vallow, S., Schein, J., & Katz, N. (2005) 'Direct costs of opioid abuse in an insured population in the United States', *Journal of Managed Care Pharmacy*, 11(6), 469–79.
- White, A., Birnbaum, H., Rothman, D., & Katz, N. (2009) 'Development of a budget-impact model to quantify potential cost savings from prescription opioids designed to deter abuse or ease of extraction', *Applied Health Economics and Health Policy*, 7(1), 61–70.
- Wilens, T., Biederman, J., Bredin, E., Haesy, A., Abrantes, A., Neft, D., Millstein, R., & Spencer, T. (2002) 'A family study of the high-risk children of opioid- and alcohol-dependent parents', *American Journal On Addictions / American Academy Of Psychiatrists In Alcoholism And Addictions*, 11(1), 41–51.
- World Health Organization (1990) *The ICD-10 Classification of Mental and Behavioural Disorders*, Geneva: WHO.
- World Health Organization (2009a) *WHO Guide to Identifying the Economic Consequences of Disease and Injury*. Geneva: WHO.
- World Health Organization (2009b) *Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence*, Geneva: WHO.

APPENDICES

Appendix A: Methodology for the REA and review of background literature

Stage 1: Identify sources to be searched, identify and pilot search terms, conduct initial search and create initial database of references

The first step was used for both the REA of existing cost estimates as well as the background literature review. Two databases were searched:

1. EBSCOhost

We used this database to search the following:

EconLit, the American Economic Association's electronic database – covers virtually every area related to economics.

Medline – contains journal citations and abstracts for biomedical literature.

Social Sciences Abstracts – contains indexing for 620 publications on a wide range of interdisciplinary fields such as addiction studies, anthropology, corrections, economics, gender studies, gerontology, minority studies, political sciences, psychology, sociology, and more.

Criminal Justice Abstracts – contains more than 300,000 records from the most important sources in the field.

National Criminal Justice Reference Service Abstracts – provides information covering the fields of law enforcement and criminal justice.

2. Cochrane Library

The Cochrane Library is a collection of six databases that contain different types of high-quality, independent evidence to inform healthcare decisionmaking, and a seventh database that provides information about groups in the Cochrane Collaboration. We used this database to search the Cochrane Database of Systematic Reviews.

In addition, a number of specialist websites were searched by hand to identify relevant studies and information. These are outlined in Table A-1.

Table A-1: Specialist websites searched by hand

	Name	URL
1.	European Monitoring Centre for Drugs and Drug Addiction	http://www.emcdda.europa.eu/
2.	United Nations Office on Drugs and Crime	http://www.unodc.org/
3.	Home Office National Statistics	https://www.gov.uk/government/publications/drug-misuse-declared-findings-from-the-2011-to-2012-crime-survey-for-england-and-wales-csew-second-edition
4.	World Health Organization	http://www.who.int/en/
5.	BMA Board of Science	http://bma.org.uk/about-the-bma/how-we-work/professional-activities-and-special-interest/board-of-science
6.	National Treatment Agency for Substance Misuse	http://www.nta.nhs.uk/
7.	American Psychiatric Association	http://www.psych.org/practice/dsm
8.	National Institute on Drug Abuse	http://www.drugabuse.gov/

Search terms were developed and piloted. The search terms used are outlined in Table A-2 and A-3.

Table A-2: Search terms used in EBSCOhost

Questions posed	Search terms
What is opioid dependence? <ul style="list-style-type: none"> Do definitions vary between licit and illicit? 	Opioi* AND depend* AND defin* (Prescrip* AND opioi*) AND depend* (Prescrip* AND opioi*) AND defin*
What does it mean to be treated or untreated? <ul style="list-style-type: none"> What definitions of 'in treatment' are used in the literature? Any evidence about treatment journeys? 	Heroin AND depend* AND recovery Defin* AND opioi* AND drug treatment Opioi* AND depend* AND relapse
What estimates are there of percentages of people who are opioid dependent who are in treatment? <ul style="list-style-type: none"> What methods/data are used to estimate rates in treatment? What are the likely limitations of these estimates? 	Opioi* AND depend* AND treatment rate (Opioi* AND depend*) AND estimate* AND 'not in treatment' (Opioi* AND depend*) AND population AND treatment (Opioi* AND depend*) AND population AND character*
What are the characteristics of the in-treatment population? <ul style="list-style-type: none"> How does this differ from opioid dependent population at large? 	
What are the life experiences/problems of those who are dependent on opioids? Any benefits of opioid use?	Opioi* AND depend* AND ethnogra* Opioi* AND depend* AND quality of life (Opioi* AND depend*) AND family
What estimates have been made of the social and economic costs of opioid dependence? <ul style="list-style-type: none"> How are the costs categorised? 	Opioi* AND depend* AND cost* Heroin AND depend* AND cost* Opioi* AND depend* AND social

Table A-3: Search terms used in Cochrane Library

Questions posed	Search terms
What are the available treatments for opioid dependence? <ul style="list-style-type: none"> What are the expected effects of different kinds of treatment? 	Opioid dependence treatment

Search terms were entered into each of the identified databases. The research team kept detailed notes of how the search terms were entered to ensure transparency, and to ensure that the approach could be replicated. The approach taken to searching is set out in Table A-4.

Table A-4: Methods of searching databases

Database	Details of search
EBSCOhost	Advanced search Selected to search in 'abstract or author-supplied abstract' Selected 'find all search terms' Limited publication date between 2000 and 2012 Selected 'exact duplicates removed from the results'
Cochrane Library	Advanced search Searched in 'title, abstract or keywords' Selected 'reviews only' Word variations have been searched Limited publication date between 2000 and 2012

The research team used the reference management software Endnote to keep a record of the references identified. Each relevant 'hit' was downloaded or entered manually into Endnote.

Stage 2: Remove duplicates, screen for relevance by reading title/abstract, group into (1) cost studies (2) background review

Duplicates were removed by employing the 'remove duplicates' function within Endnote. Further duplicated references were then removed by hand when encountered.

A member of the research team then screened all references by title and abstract, initially excluding references that were not of relevance.

Box A-1: Examples of topics considered irrelevant

Studies including on the following topics were excluded for lack of relevance to research questions:

- Chemistry of opioids
- Testing substitutes in a laboratory setting
- Substance abuse amongst physicians
- Satisfaction with treatment
- Development of scales to measure dependence
- Complications arising from treatment
- Treatment of alcohol dependency
- Opioids and Parkinson's disease

Following initial screening each source was categorised into one or more of the following categories:

1. Cost studies
2. Background and context
 - a. Cochrane reviews
 - b. Cost studies
 - c. Life experiences of being opioid dependent
 - d. Prescription opioids
 - e. Prevalence studies
 - f. Treatment rates
 - g. Treatment journeys
 - h. General background and context

Stage 3: Read and extract data, apply exclusion criteria for cost studies

Research team members read each of the sources. For costing studies the exclusion criteria were applied. Information was extracted from each source using a data extraction template. This template allowed researchers to both describe studies and extract the information needed to make a quality assessment. Table A-5 shows the template used to extract data used for studies including cost estimates. Table A-6 shows the template used to extract data used for studies relevant to background and context.

Table A-5: Data extraction template for cost studies

Study background
Aim/purpose of the study and research questions/hypothesis <i>Write in authors' description if there is one</i> <i>Elaborate if necessary, but indicate which aspects are reviewers' interpretations</i>
Broad type of study <i>(1) Randomised experiment; (2) non-randomised experiment [control and experimental group, tested before and after intervention]; (3) one group pre-post-test [no control group, measured before and after intervention]; (4) one group post-test only [no control group, measured only after not before intervention – e.g. just ask study participants about perceived effects]; (5) case study; (6) secondary data analysis; (7) systematic review; (8) non-systematic (narrative) review; (9) other</i>
Are some or all subjects untreated? (y/n)
Are some or all costs unrelated to treatment? (y/n)
Summary rationale for inclusion if either of the above are 'n'
Population (brief summary)
Perspective
Country in which the study is conducted
Study years
Currency units
Currency year
Inflation factor (local currency -> 2012)
Conversion rate (local -> USD, 2012)
Per capita denominator
Rand adjustments to estimates reported in study
Total estimates
Dependence
Is dependence defined (y/n)
If so, how is dependence defined?
Any discussion of meaning of dependence?
Risks that lead to dependence
Methods
Methods – general
Overall approach (choose from cost-of-illness, analysis of claims/health system data, trial, or other)
Notes/concerns regarding overall cost approach
Sample – strategy
Is this study exclusively a secondary analysis of healthcare or other administrative data? (y/n) if yes, skip '*'
*recruitment method (e.g. consecutive admissions, public campaign, university hand-outs)
Eligibility criteria
Did the study focus on heroin, other non-RX opioids, or RX opioids? (identify as many as needed or mark 'no focus')
Did any of the sample drop-out over time, and if so, were the members of the sample who dropped out different?
Were subjects recruited or measured at a particular stage in the treatment journey?
Did the study follow the prevalence or incidence-based approach?
Do the authors produce findings that are representative of a given population? If so how 'representative' was their sample?
Notes/concerns on selection and potential bias
Overall generalizability rating: 1 (results not generalisable out of study) to 5 (results generalisable to all opioid dependent individuals in country), for cost components measured.

Methods – data collection
Methods used to collect data: <i>(1) interviews; (2) observations; (3) self-complete questionnaire; (4) focus groups; (5) administration of psychological or other tests; (6) secondary data</i>
Type of data collected
Timeline of testing/collection
Is data separated between positive/negative outcomes, treated/non-treated?
Were new measures validated in some way?
Notes/concerns on validity of tools, problems with data collection methods?
Methods – data analysis
Which methods were used to analyse qualitative data: for example, thematic analysis using n-vivo or other software – do the authors say how they got from their data to their results? Is there any discussion of contradictory data?
Which methods were used to analyse quantitative data: for example, type of regression or other statistical analysis technique
Do the authors describe strategies used in analysis to control for bias from confounding variables: any attempt to isolate effects of intervention from other factors – such as growing out of crime, changes in life circumstances of programme participants, etc.
Notes/concerns regarding overall cost approach
Methodological strength (1 – simple descriptive, likely biased, stats; 5 – cleanly identified cost impact of opioid dependence)
Demographics
N
Ages
Sex
Ethnicity
Any other useful information about study participants
Notes/concerns on demographics abstracted
Treatments
Treatments
Is there a specific treatment definition?
If yes, what are the key steps of the treatment?
Is it a trial therapy or widely used?
Is there a control? (y/n)
If there is a control, describe
Is there a clear indicator for effectiveness/outcomes? If yes, describe
Are failed cases reported? (e.g. relapses, non-adherence, dropouts)
List any ambiguities related to treatment and costs
Costs
Health costs of opioid dependence
What is counted?
Data sources?
Time horizon
Estimation methods used
Approach to attribute costs to opioid dependency
Limitations of methods/estimates
Estimate
Notes/concerns on costs abstracted
Criminal justice
What is counted?
Data sources?
Time horizon
Estimation methods used
Approach to attribute costs to opioid dependency
Limitations of methods/estimates
Estimate
Notes/concerns on costs abstracted
Workplace costs
What is counted?
Data sources?

Time horizon
Estimation methods used
Approach to attribute costs to opioid dependency
Limitations of methods/estimates
Estimate
Notes/concerns on costs abstracted
Welfare costs
What is counted?
Data sources?
Time horizon
Estimation methods used
Approach to attribute costs to opioid dependency
Limitations of methods/estimates
Estimate
Notes/concerns on costs abstracted
Other costs
What is counted?
Data sources?
Estimation methods used
Approach to attribute costs to opioid dependency
Limitations of methods/estimates
Estimate
Notes/concerns on costs abstracted
General notes

Table A-6: Data extraction template for background studies

Last author name and endnote reference
Study background
Aim/purpose of the study and research questions/hypothesis <i>Write in authors' description if there is one</i> <i>Elaborate if necessary, but indicate which aspects are reviewers' interpretations. Other, more specific questions about the research questions and hypotheses are asked later</i>
Broad type of study <i>Quantitative or qualitative</i> <i>(1) Randomised experiment; (2) non-randomised experiment [control and experimental group, tested before and after intervention]; (3) one group pre-post test [no control group, measured before and after intervention]; (4) one group post-test only [no control group, measured only after NOT before intervention – e.g. just ask study participants about perceived effects]; (5) case study; (6) secondary data analysis; (7) systematic review; (8) non-systematic (narrative) review; (9) other</i>
Country in which the study is conducted
Dependence
Is dependence defined (y/n)
If so, how is dependence defined?
Any discussion of meaning of dependence?
Rates of dependence estimated?
If so, describe estimation method
Limitations of methods
Other definitions
Treatments
How is treatment defined (in general)?
What kind of treatment is referred to?
Availability/coverage of treatment
Effectiveness/outcomes (evidence that opioid dependent in treatment are different from opioid dependent not in treatment)
Advantages
Disadvantages
Definition of in treatment? Any discussion of treatment journeys?
Estimate of the population of drug users undergoing drug treatment?
If so, describe estimation method

Limitations of methods
Substances used
Reasons for not receiving treatment
Reviewer concerns regarding overall cost analytics
Excludes? Concerns
Includes? Concerns
Health costs of opioid dependence
Data sources?
Estimation methods used
Timeframe
Limitations of methods/estimates
\$/£ estimate
Criminal justice
What is counted?
Data sources?
Estimation methods used
Timeframe
Limitations of methods/estimates
Estimate
Workplace costs
What is counted?
Data sources?
Estimation methods used
Timeframe
Limitations of methods/estimates
Estimate
Welfare costs
What is counted?
Data sources?
Estimation methods used
Timeframe
Limitations of methods/estimates
Estimate (include whether individual or aggregate)
Other costs
What is counted?
Data sources?
Estimation methods used
Timeframe
Limitations of methods/estimates
Estimate
Sample – strategy
Countries of the participants
Ages
Sex
Ethnicity
Any other useful information about study participants
Sampling frame and method used to select study participants <i>Of all participants in a given intervention, how many took part in the study? How were study participants selected? Any issues around voluntary participation in the study? Were incentives given to recruit people into the study?</i>
Did any of the sample drop out over time, and if so, were the members of the sample who dropped out different?
Are the authors trying to produce findings that are representative of a given population? If so how 'representative' was their sample?
Methods used to collect data <i>(1) Interviews; (2) observations; (3) self-complete questionnaire; (4) focus groups; (5) administration of psychological or other tests; (6) secondary data</i>
Any issues about validity of tools, problems with data collection methods?
Methods – data analysis

Which methods were used to analyse qualitative data? <i>For example, thematic analysis using n-vivo or other software – do the authors say how they got from their data to their results? Is there any discussion of contradictory data?</i>
Which methods were used to analyse quantitative data? <i>For example, type of regression or other statistical analysis technique</i>
Do the authors describe strategies used in analysis to control for bias from confounding variables? <i>Any attempt to isolate effects of intervention from other factors – such as growing out of crime, changes in life circumstances of programme participants, etc.?</i>

Stage 4: Hand-search and follow-up references and citations

The systematic search of databases and specialist websites was supplemented by hand-searching the contents and bibliographies of relevant texts and articles. Doing this provided the research team with confidence that the key texts and studies in a particular field had been included (or at least considered and excluded if they did not meet the inclusion criteria).

Experts in the field as well as from RB were asked to suggest sources that had not been identified in the search. In particular, we reviewed previous work commissioned by RB to estimate the global costs of opioid dependence.

Stage 5: Standardise cost estimates, synthesis and analysis, identification of gaps

Cost estimates were converted to 2012 euros and per-person, per-year estimates to facilitate comparison.

The data extracted from the studies were used to write the report. In the write-up researchers describe in detail the strengths and limitations of the studies.

Rather than assigning a grade or score to each study, as is often done in a rapid evidence assessment, the research team considered that it was more helpful to describe the different strengths and weaknesses of each study, since this provides a more comprehensive and nuanced way of communicating the quality of the evidence.

Appendix B: Treatments available for opioid dependence

The focus of this study is on the non-treatment costs of opioid dependence. To guide the exclusion of non-relevant studies, here we provide an overview of treatments for opioid dependence.²³ These can be used to treat dependence on legal and illegal opioids.

Table B-1: Treatments for opioid dependence

Psychosocial interventions	Description Aims to offer support to opioid users in the process of managing or overcoming their drug addiction, improving well-being and quality of life and stimulating behavioural change (EMCDDA, 2012; Mayet et al., 2010; World Health Organization, 2009b).
	Setting and complementary interventions Can be used in combination with pharmacotherapy treatments or as a separate and independent intervention (Amato et al., 2011a, 2011b; Mayet et al., 2010).
	Examples of interventions Includes counselling, motivational interviewing, cognitive behavioural therapy, case management, group and family therapy, and relapse prevention (EMCDDA, 2012).
Substitution treatment (or maintenance treatment)	Description The most common treatment option for opioid users in Europe (EMCDDA, 2012). Involves the administration of a similar substance to the drug normally used by the opioid user, in order to reduce risky behaviour. The stable level of the dosage administered does not allow for an experience of intoxication or withdrawal (EMCDDA, 2012; World Health Organization, 2009b).
	Setting and complementary interventions Typically provided in an outpatient setting, but available in inpatient settings in some countries (for instance, in prisons). Substitution treatment is usually complemented with psychosocial interventions (CIAR, 2008; EMCDDA, 2012; World Health Organization, 2009b).
	Examples of substances Some of the main substances normally included in substitution treatment are methadone, buprenorphine, naltrexone or pharmaceutical diamorphine (heroin) (Ferri et al., 2011; Mattick et al., 2009; Mattick et al., 2008; Solberg et al., 2002).
Drug detoxification (or managed withdrawal)	Description A medically supervised intervention aimed at managing withdrawal symptoms associated with the cessation of opioid use. May be a requirement for admission into long-term, abstinence-based inpatient treatment (Day et al., 2008; EMCDDA, 2012; World Health Organization, 2009b).
	Setting and complementary interventions Typically provided in an inpatient setting,

²³ We are aware that some methods of treatment may be specific to the population dependent on prescription opioids (for example, allowing someone to take an alternative pain medication that is less addictive or providing other behavioural counselling therapies).

	normally within specialised medical centres. May be complemented with psychosocial interventions (CIAR, 2008; EMCDDA, 2002).
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Drug treatment data from the UK's National Treatment Agency for Substance Misuse indicated that in 2009–2010 approximately half of those in treatment received prescription-based substitution treatment. One third of these clients have further received complementary treatment, including psychosocial interventions or inpatient detoxification (National Treatment Agency for Substance Misuse, 2010a).

Some of the key substances usually included in substitution treatment are methadone, buprenorphine or naltrexone. An overview of their main characteristics is presented in Table B-2.

Table B-2: Characteristics of the main substances used in opioid substitution treatment

Methodone	Buprenorphine	Naltrexone
<ul style="list-style-type: none"> • Oral administration • Slow onset of action • Long half-life 	<ul style="list-style-type: none"> • Administered sublingually • Active for approximately 24 to 36 hours 	<ul style="list-style-type: none"> • Oral administration • Blocks the actions of heroin for 48 to 72 hours
<i>Agonist</i> : reinforcing or pleasurable	<i>Partial Agonist</i> : reinforcing or pleasurable, but patients feel more alert (when compared with the use of agonists)	<i>Antagonist</i> : does not produce euphoria nor dysphoria in abstinent patients, free of addictive risk

Source: McLellan et al. (2009); Nutt et al. (2010)

Table B-3: Estimates of problem opioid users and numbers of clients in opioid substitution treatment

	Problem Opioid Users	Clients in Opioid Substitution Treatment
European Union and Norway	1,400,000	710,000
USA	1,200,000	660,000
Australia	90,000	43,000

Source: Adapted from EMCDDA (2012)

Notes: The estimates refer to opioid substitution treatment only.

Appendix C: Definitions of dependence

Table C-1: DSM-IV and ICD-10 definitions of substance dependence

DSM-IV: substance dependence	ICD-10: dependence syndrome
<p>'When an individual persists in use of alcohol or other drugs despite problems related to use of the substance, substance dependence may be diagnosed. Compulsive and repetitive use may result in tolerance to the effect of the drug and withdrawal symptoms when use is reduced or stopped.'</p>	<p>'Cluster of physiological, behavioural, and cognitive phenomena in which the use of a substance or a class of substances takes on a much higher priority for a given individual than other behaviours that once had greater value.</p> <p>A central descriptive characteristic of the dependence syndrome is the desire (often strong, sometimes overpowering) to take the psychoactive drugs (which may or not have been medically prescribed), alcohol, or tobacco.'</p>

Source: American Psychiatric Association (1994); World Health Organization (1990)

Box C-1: DSM-IV and ICD-10 criteria of substance dependence**DSM-IV Substance Dependence Criteria**

Substance dependence is defined as a maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by three (or more) of the following, occurring any time in the same 12-month period:

1. Tolerance, as defined by either of the following: (a) a need for markedly increased amounts of the substance to achieve intoxication or the desired effect or (b) markedly diminished effect with continued use of the same amount of the substance.
2. Withdrawal, as manifested by either of the following: (a) the characteristic withdrawal syndrome for the substance or (b) the same (or closely related) substance is taken to relieve or avoid withdrawal symptoms.
3. The substance is often taken in larger amounts or over a longer period than intended.
4. There is a persistent desire or unsuccessful efforts to cut down or control substance use.
5. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.
6. Important social, occupational, or recreational activities are given up or reduced because of substance use.
7. The substance use is continued despite knowledge of having a persistent physical or psychological problem that is likely to have been caused or exacerbated by the substance (for example, current cocaine use despite recognition of cocaine-induced depression or continued drinking despite recognition that an ulcer was made worse by alcohol consumption).

ICD-10 Diagnostic Guidelines

A definite diagnosis of dependence should usually be made only if three or more of the following have been present together at some time during the previous year:

1. A strong desire or sense of compulsion to take the substance.
2. Difficulties in controlling substance-taking behaviour in terms of its onset, termination, or levels of use.
3. A physiological withdrawal state when substance use has ceased or have been reduced, as evidenced by: the characteristic withdrawal syndrome for the substance; or use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms.
4. Evidence of tolerance, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses (clear examples of this are found in alcohol- and opiate-dependent individuals who may take daily doses sufficient to incapacitate or kill non-tolerant users).
5. Progressive neglect of alternative pleasures or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects.
6. Persisting with substance use despite clear evidence of overtly harmful consequences, such as harm to the liver through excessive drinking, depressive mood states consequent to periods of heavy substance use, or drug-related impairment of cognitive functioning; efforts should be made to determine that the user was actually, or could be expected to be, aware of the nature and extent of the harm.

Source: American Psychiatric Association (1994); World Health Organization (1990)

Appendix D: Description of included studies

Box D-1: included studies

1. Birnbaum, H., White, A., Schiller, M., Waldman, T., Cleveland, J., & Roland, C. (2011) 'Societal costs of prescription opioid abuse, dependence, and misuse in the United States', *Pain Medicine*, 12(4), 657–67.
2. Leider, H., Jatinder Dhaliwal, M., Davis, E., Kulakodlu, M., & Buikema, A. (2011) 'Healthcare costs and nonadherence among chronic opioid users', *American Journal of Managed Care*, 17(1), 32–40.
3. Mark, T., Woody, G., Juday, T., & Kleber, H. (2001) 'The economic costs of heroin addiction in the United States', *Drug And Alcohol Dependence*, 61(2), 195–206.
4. McAdam-Marx, C., Roland, C., Cleveland, J., & Oderda, G. (2010) 'Costs of opioid abuse and misuse determined from a Medicaid database', *Journal Of Pain & Palliative Care Pharmacotherapy*, 24(1), 5–18.
5. McCarty, D., Perrin, N., Green, C., Polen, M., Leo, M., & Lynch, F. (2010) 'Methadone maintenance and the cost and utilization of healthcare among individuals dependent on opioids in a commercial health plan', *Drug And Alcohol Dependence*, 111(3), 235–40.
6. Riddell, S., Shanahan, M., Degenhardt, L., & Roxburgh, A. (2008) 'Estimating the costs of drug-related hospital separations in Australia', *Australian And New Zealand Journal Of Public Health*, 32(2), 156–61.
7. Wall, R., Rehm, J., Fischer, B., Brands, B., Gliksman, L., Stewart, J., Medved, W., & Blake, J. (2000) 'Social costs of untreated opioid dependence', *Journal Of Urban Health: Bulletin Of The New York Academy Of Medicine*, 77(4), 688–722.
8. White, A., Birnbaum, H., Mareva, M., Daher, M., Vallow, S., Schein, J., & Katz, N. (2005) 'Direct costs of opioid abuse in an insured population in the United States' *Journal of Managed Care Pharmacy*, 11(6), 469–79.
9. White, A., Birnbaum, H., Rothman, D., & Katz, N. (2009) 'Development of a budget-impact model to quantify potential cost savings from prescription opioids designed to deter abuse or ease of extraction', *Applied Health Economics and Health Policy*, 7(1), 61–70.

Table D-1: Detailed description of included studies

Study	Summary
Wall et al. (2000)	Wall et al. used a cost-of-illness methodology to estimate the social costs associated with untreated opioid dependence in four cost domains: (1) healthcare; (2) law enforcement; (3) victimization; and (4) lost productivity. This study did not separate services that were related to treatment of opioid dependence from other services (e.g. emergency department visits, hospital stays, etc.). As a result we assume that some or all costs were unrelated to treatment. The authors relied heavily on inputs from the literature and the administrative datasets, having also undertaken a primary survey. The primary data collection (survey) mainly involved heroin users recruited at needle exchange and social service sites. It remains unclear whether non-heroin subjects were included. Data were collected in a 10-month period, one collection per participant. The study followed a prevalence-based approach. The survey population was composed of 114 individuals, 82 percent of which were male. In terms of age distribution, 55 percent of the population was 31–40 years old. A cost-of-illness methodology was used to analyse the quantitative data, with some imputation (mix of direct elicitation and imputation on frequency and list costs). The authors described strategies used in the analysis to improve generalisability. For instance, they reweighted their survey results to better approximate the general Toronto population. Wall et al. collected information on how often people committed crimes, saw doctors or missed work, amongst others. They then multiplied these 'frequencies' by estimates of the average

	<p>cost per event (i.e. unit costs) to arrive at estimates of the total costs of crime, healthcare services and workplace in their study population. The authors estimated a \$13,100 ('96 CAN\$) cost per user, roughly CAN\$50 per capita over entire population – all estimates were annualised. Comprehensive healthcare costs were counted (i.e., inpatient, ER, outpatient, pharma, ambulance). Healthcare costs represent 6.6 percent of the total figure (\$865). In the domain of law enforcement, the authors included police, court and corrections costs. The authors employed a direct elicitation on frequency, costs provided by government and opioid 'fraction' of responsibility from literature. Criminal justice costs represent 39.1 percent of the total costs (\$5,122.1). In terms of workplace costs, the authors considered morbidity and mortality (projected over lifetime). While all other estimates were annualised, workplace costs estimates considered a time horizon ranging up to retirement (65 years old). The authors applied a direct elicitation of hours worked and estimates from the literature. Productivity loss costs represent 33.2 percent of the total costs (\$4349.2). Victimization costs were counted separately from criminal justice, through direct elicitation, costs reported by government, and opioid 'fraction'. Victimization costs represent 21.2 percent of the total figure (\$2,777.2).</p>
White et al. (2005)	<p>This study compared healthcare costs associated with opioid abusers (i.e. those with a diagnosis) to similar non-abusers. The authors analysed administrative data (claims data), which might have resulted in potential selection and accounting issues. All individuals in the study interacted with the healthcare system either due to (1) acute care related to opioid abuse; or (2) seeking treatment related to dependence. This study did not separate services that were related to treatment of opioid dependence from other services (e.g. emergency department visits, hospital stays, etc.). As a result we assume that some or all costs were unrelated to treatment. The study followed a prevalence-based approach. Data collected included healthcare utilisation and cost. The main method employed was a cost comparison in a propensity score-matched sample of patients with and without opioid dependence diagnosis. The sample comprised 740 patients with diagnosis and 2220 without. About 83 percent of the individuals were aged 18–54; the majority of the sample population was male. The sample was matched on age, gender and region. Regarding healthcare costs of opioid dependence, data were retrieved from commercial claims databases, over a time horizon of one year per subject. The authors estimated an eight times higher spending (\$15,884 vs \$1,830) for opioid abusers than for non-abusers. One possible explanation for this is that cost outcomes likely included treatment costs and reflect significant differences in patient population in terms, for instance, of comorbidities.</p>
White et al. (2009)	<p>This study estimated the potential cost savings from a hypothetical abuse-deterrent/resistant prescription opioid (after estimating costs). The authors undertook a claims-based analysis comparing a cross section of abusers to a matched set of non-abusers, with assumptions on clinical versus non-clinical abusers based on self-reported prevalence data. Data was collected from Ingenix, ASI-MV Connect drug surveillance data, 2005 NSDUH survey, DAWN/TEDS to validate, covering one year of records. This study did not separate services that were related to treatment of opioid dependence from other services (e.g. emergency department visits, hospital stays, etc.). As a result we assume that some or all costs were unrelated to treatment. Potential selection and accounting issues may be present in this analysis of administrative data given that all individuals in the study interacted with the healthcare system either due to (1) acute care related to opioid abuse; or (2) seeking treatment related to dependence. The study followed a prevalence-based approach. Estimates are meant to be representative of the US. We note that although all individuals had a medical claim with abuse diagnosis or self-reported abuse it is unclear how much of this was due to opioids only. The study employed cost comparison in a propensity score-matched sample of patients with and without opioid dependence diagnosis, plus extrapolation of costs for non-clinical abusers using factors derived from expert opinion. Samples were matched on age, gender, region and employment status. The sample population comprised 300,000 clinical abusers and 1.2 million non-clinical abusers. In terms of healthcare costs, the study considered medical and drug costs, relying on Ingenix claims data and self-reported abuse prevalence (used to estimate non-clinical abuser costs) over a period of one year per subject. The authors estimated costs of \$17,000 per 'clinical abuser' and \$6,000 per 'non-clinical abuser'.</p>
McAdam-Marx et al. (2010)	<p>This study described healthcare costs associated with opioid abusers (with a diagnosis for abuse, dependence, or poisoning) compared to matched controls. The authors developed a claims-based analysis comparing a cross section of abusers to a matched set of non-abusers.</p>

	<p>This study did not separate services that were related to treatment of opioid dependence from other services (e.g. emergency department visits, hospital stays, etc.). As a result we assume that some or all costs were unrelated to treatment. Potential selection and accounting issues are associated with the analysis of administrative claims only as all individuals in the study interacted with the healthcare system either due to (1) acute care related to opioid abuse; or (2) seeking treatment related to dependence. Eligibility criteria were based on Medicaid diagnosis for opioid abuse, dependence, or poisoning in the Medicaid inpatient, outpatient, or long-term care files. Attrition is likely to have occurred in the Medicaid sample due to changes in eligibility and access. The sample was built using 12-month continuous enrolment criteria, which resulted in the exclusion of 50 percent of the patients (as these did not remain enrolled for 12 months). A prevalence-based approach was adopted in the study. Data collected covered all healthcare utilisation and costs, over one year of records. The authors undertook a cost comparison in a propensity scored-matched sample of patients with and without opioid dependence diagnosis. The sample population included 50,162 patients with opioid abuse-related diagnosis and 3:1 matched controls (150,486). The mean age was about 42 years old in both groups, and the majority of the patients were female. We acknowledge that the US Eastern region accounted for 60 percent of the study participants. Samples were matched on age, gender and region. All healthcare claims in Medicaid MAX file (national sample) were considered on a time horizon of one year per subject. As with other claims analysis the diagnosis typically shows up only for expensive inpatient care. The costs considered likely included treatment costs. Opioid users had significantly higher health spending (\$14,537 vs. \$8,663 baseline, \$23,556 vs. \$8,436 after controlling for observable baseline characteristics) than non-users. Costs were higher for the abuse population except for long-term care claims LTC (which is expected if there is a residual selection concern).</p>
<p>Leider et al. (2011)</p>	<p>This study described healthcare costs associated with chronic opioid use (rather than abuse) and estimated whether adherence affected costs. The authors conducted a claims-based analysis comparing a cross section of chronic users to a matched set of non-abusers. This study did not separate services that were related to treatment of opioid dependence from other services (e.g. emergency department visits, hospital stays, etc.). As a result we assume that some or all costs were unrelated to treatment. Given that this analysis relied exclusively on administrative data (claims data) there might have been significant selection and accounting issues. The key eligibility criteria consisted of a diagnosis for opioid abuse, dependence, or poisoning in the Medicaid inpatient, outpatient, or long-term care files. The study focused on prescription opioids for the sample selection but did not exclude heroin users. As this study focused on chronic users (and not abusers), users who may not have been dependent might have been included. A prevalence-based approach was followed. The administrative claims data (US commercial, Medicaid, and Medicare managed care patients) covered all medication costs as well as other healthcare costs for the period of one year. The authors applied a cost comparison in a propensity score-matched sample of patients with and without long-term opioid use. The samples were matched on age, gender, region, insurance type, mental health benefit, and Charlson comorbidity score. A total of 49,425 users and non-users were included, from which 1659 were chronic, non-adherent users. About half of the sample population was aged 45–64; the majority was female. All healthcare claims in data were counted, including ambulatory, emergency, inpatient, other medical, total medical and pharmacy, in a period of one year per subject. According to this study estimate, opioid users had significantly higher health spending (\$23,049 vs. \$4,975) than non-users.</p>
<p>Birnbaum et al. (2011)</p>	<p>This descriptive study estimated the social costs associated with untreated opioid dependence in three cost domains: (1) healthcare; (2) criminal justice; and (3) workplace. The authors undertook a claims-based analysis relying heavily on cost estimates from elsewhere. This study did not separate services that were related to treatment of opioid dependence from other services (e.g. emergency department visits, hospital stays, etc.). As a result we assume that some or all costs were unrelated to treatment. The study population comprised three samples: (1) privately insured prescription opioid abuse patients (n=4474); (2) caregivers of privately insured prescription opioid abuse patients (n=5987); and (3) Florida Medicaid opioid abuse patients (n=4667). A prevalence-based approach was followed. The authors employed costing with some imputation, attempting to control for bias from confounding variables by matching opioid users to non-users. We note that all individuals in the study interacted with the healthcare system either due to (1) acute care related to opioid abuse; or (2) seeking treatment related to dependence. The total US</p>

	<p>estimated costs are of \$55.7 billion. Regarding healthcare costs, the authors considered healthcare claims from FL Medicaid (1997 Q3 to 2006 Q2) plus ESI database (1999–2007). Samples matched 1:1 on age, gender, geographic location, employment status for privately insured, and race for FL Medicaid. Healthcare costs accounted for 44 percent of total costs. In the domain of criminal justice, the authors considered apportioned costs from aggregates, including property lost to crime, correctional facilities, and legal and police protection, relying on various aggregate cost estimates and opioid utilisation estimates. This study assumed that aggregate costs can be apportioned uniformly. About 9 percent of total costs were associated with criminal justice costs. Workplace costs were estimated on the basis of several costs estimates and opioid utilisation estimates, and included apportioned costs from aggregates, including presenteeism, disability and medically related absenteeism, incarceration, unemployment and premature death. As with the criminal justice estimates, the study assumed that aggregate costs can be apportioned uniformly. The authors estimated that 46 percent of total costs result from lost productivity (mostly due to premature death).</p>
<p>Mark et al. (2001)</p>	<p>This study documented the costs of heroin addiction in the US to individuals and society, relying on several different sources such as household surveys and expert panel reports (from 1996 to 1998). The authors adopted a prevalence-based approach. This study did not separate services that were related to treatment of opioid dependence from other services (e.g. emergency department visits, hospital stays, etc.). As a result we assume that some or all costs were unrelated to treatment. While the study provided detail and specificity regarding its findings, the methodological approach was not outlined in a clear manner (e.g., no descriptive information about study samples was provided). We further note the risks associated with relying on and combining different datasets. In terms of healthcare costs of opioid dependence, the study considered medical care costs/treatment and medical complication costs from heroin addiction. Data was extracted from the following datasets (from 1996 to 1997): Uniform Facility Data Set, Treatment Episode Data Set, National Association of State Alcohol and Drug Abuse Directors, National Treatment Improvement Evaluation Study, Drug Abuse Warning Network, National Ambulatory Medical Care Survey. An estimate of \$6281bn was presented – this is the presumed national, annual cost for all heroin use and not cost-per-patient/treatment. We note that nearly 50 percent of costs were attributed to AIDS. This secondary analysis has large potential for confounds or errors, with little description on each use. Criminal justice cost estimates included incarceration, crime, policing and costs to crime victims. A mixture of data sources was consulted, including: NHSDA, Justice Expend. And Empl. Extracts 1992, Uniform Crime Reports 1997, Drug Use Forecasting 1996, NCVS, Profile of Jail Inmates, Survey of Inmates in the State Correctional Facilities – between 1992 and 1997. Average costs were applied to activity estimates, resulting in an estimate of US\$1816bn costs on incarceration; US\$1,751bn costs on policing and US\$796m costs to victims. The information and assumptions based on which these estimates were produced were to some extent unclear and ambiguous. In the domain of workplace costs, the authors counted mortality (i.e., the removal of productive citizens), applying average costs to activity estimates based on the following data sources: US DoL, US DoComm, CPS, NHSDA, TEDS, NLAES – between 1996 and 1999. The mortality ‘best guess’ was of US\$5,027bn; unemployment costs estimates accounted for US\$4,557bn and lower earnings represented US\$113m. Welfare costs estimates covered social insurance, public aid and direct human services. The authors relied on prior studies from 1994 to 1998, applying average costs to activity estimates arriving at an estimated cost of US\$99m. We acknowledge the discrepancy between welfare cost estimates and cost estimates for other domains.</p>
<p>Riddell et al. (2008)</p>	<p>This study estimated total hospital costs related to illicit drug classes (one of which is opioids). The authors carried a secondary data analysis of discharge-based data. This study did not separate services that were related to treatment of opioid dependence from other services (e.g. emergency department visits, hospital stays, etc.). As a result we assume that some or all costs were unrelated to treatment. The study covers opiates in general, with the sample population being recruited or measured while in hospitalisation. Hospital diagnosis data was collected, in particular discharge data and reimbursement prices, at one single point in time (single discharge). On this costing exercise, diagnosis rates were separated by drug category using aetiological fraction reported in the literature. Healthcare costs considered hospital costs only, with no matched control group. Opioid-related inpatient costs amounted to \$11.4m between 1999/2000 and 2001/2002, with a modest increase</p>

	<p>from 2002 to 2005.</p>
<p>McCarty et al. (2011)</p>	<p>This study assessed the costs of treating opioid dependence in a commercial health plan and the implications of methadone maintenance on cost of care. The overall approach consisted of an analysis of claims data across five calendar years. This study did not separate services that were related to treatment of opioid dependence from other services (e.g. emergency department visits, hospital stays, etc.). As a result we assume that some or all costs were unrelated to treatment. We note that the region considered is limited and with relatively strong social programmes available. Individuals with a diagnosis of opioid dependence (i.e. with two or more diagnosis per year) and at least nine months of health plan eligibility were included in the sample. The focus of the study is not entirely specific, mentioning heroin and prescription opioids. A prevalence-based approach was followed. Although the timeline of testing covered five years, not all patients were included for all five years (only those with two or more diagnosis per year). The authors carried out a simple multiplication of visits by care received and costs recorded in claims, averaged across observations. Parameter estimates were used for multivariate analysis of some factors. A total of 2523 'observations' were registered. Emergency visits, primary care visits, non-addiction medical visits, inpatient stays were included, relying on claims data from 2000 to 2004. No external costs were considered and no legitimate control was used thus possibly generating confounds given the large use of emergency care. The study estimated (per year) a total cost of US\$7,163.08 regarding any methadone use; \$18,694.82 for no methadone use and one/no addiction care; \$14,694.82 for no methadone use and two or more addiction care visits.</p>

Appendix E: Adjusted cost estimates

Table E-1: Calculations for adjusted cost estimates

Study	Description of estimate	Costs reported in the study					Description of the cost					Inflation rates to 2012		Exchange rates to EUR			Estimate in 2012 EUR						
		Health care	Criminal justice	Productivity	Total	Non-health	Unit of the cost	Population denominator	Additional calculations (as described in table 4)	Original year and currency	USD*	CAN** or AUD***	USD to EUR (2012)	CAN to EUR (2012)	AUD to EUR (2012)	Health	Criminal justice	Productivity	Total	Non-Health	Generalisability	Scope (costs)	
Wall et al. (2000)	[1] Study sample	\$2,727	\$38,785	\$3,104	\$44,615	\$41,888	Per Addict	Survey respondents, small n	Yes	1999CAN	1.38	1.32	0.78	0.78	0.81	2,806	39,915	3,194	45,915	43,109	2	5	
	[2] Projected population, Toronto	\$865	\$7,899	\$4,349	\$13,113	\$12,248	Per Addict (Enrolled)	Toronto users	Yes	1999CAN	1.38	1.32	0.78	0.78	0.81	890	8,129	4,476	13,495	12,605	3	5	
White et al. (2005)	[1] Base	\$14,054			\$14,054		Per diagnosed abuser	Diagnosed patients, in administrative health datasets	Yes	2003USD	1.25		0.78	0.78	0.81	13,668			13,668		2	2	
White et al. (2009)	[1] Projected population, clinical abusers	\$17,000			\$17,000		Per abuser	Diagnosed patients, US	No	2006USD	1.14		0.78	0.78	0.81	15,078			15,078		3	2	
	[2] Projected population, non-clinical abusers	\$6,000			\$6,000		Per abuser	Survey respondents, US	No	2006USD	1.14		0.78	0.78	0.81	5,322			5,322		3	3	
	[3] Projected population, all abusers	\$8,200			\$8,200		Per abuser	Mixed, US	Yes	2006USD	1.14		0.78	0.78	0.81	7,273			7,273		4	3	
McAdam-Marx et al. (2010)	[1] Univariate	\$5,874			\$5,874		Per diagnosed abuser	Diagnosed patients, in administrative health datasets	Yes	2003USD	1.25		0.78	0.78	0.81	5,712			5,712		2	2	
	[2] Controlling for covariates	\$15,120			\$15,120		Per diagnosed abuser	Diagnosed patients, in administrative health datasets	Yes	2003USD	1.25		0.78	0.78	0.81	14,704			14,704		3	2	
Leider et al. (2011)	[1] Controlling for covariates	\$3,156			\$3,156		Per non-adherent user, average difference	Prescription opioid, adherent and non-adherent users	No	2008USD	1.07		0.78	0.78	0.81	2,627			2,627		3	2	
	[2] Univariate	\$3,273			\$3,273		Per non-adherent user, average difference	Prescription opioid, adherent and non-adherent users	No	2008USD	1.07		0.78	0.78	0.81	2,725			2,725		2	2	
Birnbaum et al. (2011)	[1] Base	\$14,416	\$2,949	\$15,072	\$32,437	\$18,021	Per DSM-IV criteria diagnosed abuser, study reported prevalence	US prescription opioid abusers	Yes	2009USD	1.07		0.78	0.78	0.81	12,001	2,455	12,547	27,003	15,001	3	4	
Mark et al. (2001)	[1] SAMSHA prevalence	\$12,346	\$12,829	\$28,234	\$53,408	\$41,063	Per self-reported US heroin user	All US self-reported heroin users	Yes	1996USD	1.46		0.78	0.78	0.81	14,023	14,572	32,070	60,665	46,642	4	3	
	[2] ONDCP prevalence	\$4,458	\$4,632	\$10,194	\$19,284	\$14,826	Per self-reported US heroin user	All US self-reported heroin users	Yes	1996USD	1.46		0.78	0.78	0.81	5,063	5,261	11,579	21,904	16,841	4	3	
Riddell et al. (2008)	[1] Base	\$2,985			\$2,985		Per separation	All Australian separations with diagnosis	Yes	2005AUD	1.22	1.22	0.78	0.78	0.81	2,933			2,933		2	2	
McCarty et al. (2011)	[1] Base	\$11,200			\$11,200		Per diagnosed abuser	Diagnosed patients, study population	No	2004USD	1.22		0.78	0.78	0.81	10,631			10,631		2	2	

* Bureau of Labour Statistics ** Royal Bank of Canada (year of study) *** AUD: Reserve Bank of Australia