# Deliverable 8.1:

# Determinants of harmful substance use and harmful gambling: an interdisciplinary review

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## Abstract

This report focuses on the determinants of engagement in harmful behaviour in relation to substance use and gambling, where harms may be a direct result of a given behaviour or may be a consequence of societal reactions to the behaviour. The determinants of harmful substance use and harmful gambling are presented within four themed areas of research including socio-economic, cultural and environmental conditions, living and working conditions, cellular and molecular factors, and multidisciplinary models of harmful substance use. Determinants identified from across the natural and social sciences include marketing, marginalisation, previous substance use, intra-individual vulnerabilities, biological vulnerabilities and compulsion. These determinants operate across three different levels, the innate, our environment and the societies in which we live, however there is also considerable overlap between determinants at different levels. For example, drinking culture develops in the context of drug control policies, the history of alcohol consumption in a given culture and the availability of alcohol products, whilst previous abuse of an illicit substance use may be influenced by the availability of illicit drugs, personality characteristics, drug control policies and cultural norms or attitudes towards drug use. Thus all three levels of influence are important for understanding the range of determinants of harmful substance use and gambling in European populations. A key challenge related to this specific interdisciplinary work was the scarcity of research in many disciplines relating to our focus on the transition from risky to harmful substance use and gambling. Across most of the disciplines included here, research has traditionally focused on the determinants of harmful use versus no use or any use, rather than the determinants of the transition from risky use of harmful use. Thus, future research could examine this key stage on the continuum of addictive behaviour.

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# 1. INTRODUCTION

The science of addiction emerges from diverse fields of study, such as genetics, sociology, neurobiology, psychology and economics. This research has resulted in significant advances in our understanding of addictive substance use and addictive behaviours, what predicts them and the outcomes they may lead to. However, our understanding is fractured and knowledge from across the scientific disciplines is too rarely brought together. As a result, addiction science as a whole is rather like the tale of "The elephant and the blind men"; each man touches and describes one part of the animal, but none can describe the whole beast.

Even when analysing the same underlying questions, scientific disciplines often vary in their research foci, methods, data and outcomes. These differences are not trivial and can act as hindrances to the integration of scientific knowledge as well as prompting much debate and disagreement. Overcoming these obstacles would permit more interdisciplinary approaches to science, in which data from a range of disciplines could be more effectively synthesised. By allowing us to see the 'whole beast', such approaches can enhance our understanding of current evidence, highlight new solutions to problems and signpost productive avenues for future, possibly cross-disciplinary, research.

A prime target for interdisciplinary study in addiction science is the identification and analysis of factors associated with the process of engaging in addictive substance use and gambling. In different ways and to different degrees, scientific disciplines have sought to understand the characteristics of individuals and the contexts of engagement which are associated with particular behaviours or outcomes. Identifying these behavioural determinants or risk factors can lead to better targeting and design of preventative and clinical interventions and public policy at all societal levels. It can also provide a more comprehensive understanding of how and why individuals and societies engage with and respond to addictive substance use and gambling in particular ways.

However, when identifying the determinants of engagement in addictive substance use and gambling, it is important to remember that all forms of engagement cannot be seen as equal and that determinants may vary for different forms of engagement. For example, regular heroin use is different to regular alcohol use, a small weekly bet on a football match is different to compulsively playing internet poker and drinking two alcoholic drinks a day is different to drinking fourteen alcoholic drinks once a week. Therefore, addictive substance use and gambling need to be broken down into more narrowly defined behavioural concepts, such as initial use, risky use, harmful use,

addiction, cessation or chronic relapsing. Understanding the determinants of these specific forms of behaviour allows a more focused understanding of where interventions are required and how addictive substance use and gambling behaviours may emerge, extinguish, escalate, diminish or fluctuate over time. Further, it allows addiction science to move away from a narrow focus on addiction per se and onto other important concepts such as risky behaviour, harmful behaviour in general and 'recovery' and their associated developmental processes.

## 1.1 Scope and Purpose

This is the second of a series of three reports describing the findings of an interdisciplinary study on identifying the determinants of different stages of addictive substance use and gambling behaviour using evidence from a range of scientific disciplines. This report focuses on identifying determinants of harmful substance use or harmful gambling. The preceding report focused on the determinants of risky substance use and risky gambling, whilst the following report will focus on the determinants of chronic relapse and cessation of problematic substance use or gambling respectively.

This report focuses on the determinants of individuals engaging in harmful behaviour in relation to substance use and gambling. Harms may be a direct result of a given behaviour or may be a consequence of societal reactions to the behaviour. The definition of harmful behaviour used in this report is:

*"Substance use or gambling which has caused material harms of social, mental or physical nature which are experienced by the user, other individuals or society at large, where cause means outcomes which would not have occurred without the substance use or gambling".*

This report includes dependence within the definition of harmful use but it is important to note that there are distinct clinical definitions for harmful use and for dependence. The World Health Organisation ICD-10 diagnostic criteria describes these as:

Harmful use: A pattern of psychoactive substance use that is causing damage to health. The damage may be physical (as in cases of hepatitis from the self-administration of injected drugs) or mental (e.g. episodes of depressive disorder secondary to heavy consumption of alcohol).

Dependence: Applied to alcohol and other drugs, dependence refers to the need for repeated doses of the drug to feel good or avoid feeling bad. Clinically, ICD-10 criteria can be used to assess dependence with fulfilment of three or more criteria resulting in a diagnosis of dependence. The term addiction is often used interchangeably with dependence.

Therefore, 'dependence' is viewed in this report as a harmful outcome of addictive substance use or behaviours where the harm in question is the need to continue to engage in the substance use or behaviour in order to regulate one's emotional state.

The aim of this report is to compile and integrate the existing evidence of determinants of harmful substance use or harmful gambling from seven disciplines: anthropology, economics, genetics, neurobiology, psychology, public policy and sociology. The substances covered by the report are predominantly alcohol, tobacco and illicit drugs but our findings can be viewed as valid for the developmental processes of all psychotropic substances. Further additional information on gambling is covered to illustrate specific aspects of the processes involved in developing 'behavioural addictions' like pathological gambling. A set of determinants will be drawn from each discipline and these will be single factors, either individual-specific or environmental, which may influence whether an individual engages in harmful substance use or harmful gambling. Models or theories describing the interactions of multiple determinants and how these interactions lead to harmful behaviour will also be identified. These will contribute to our efforts to synthesise evidence from across scientific discipline as such models and theories often draw on evidence from multiple disciplines.

This research report will outline the principal current evidence from each discipline, highlight complimentary and contrasting data and discuss the implications of this body of evidence for both policy makers and researchers. A companion report will seek to present an interdisciplinary logic model mapping the determinants of harmful substance use and harmful gambling, the evidence for these determinants and, where evidence permits, how these determinants interact to influence harmful behaviour. The companion report will also, where data and evidence permit, provide estimates of transition probabilities describing the likelihood of an individual, under a specific set of both innate and environmental conditions, progressing from one behavioural stage to the next (e.g. from binge drinking to chronic harmful drinking).

In conjunction with the other two reports in this series, it is hoped that the synthesis of current scientific knowledge on different forms of engagement with addictive substances and gambling will

afford policy makers a comprehensive understanding of this topic and assist them in the planning of strategies to tackle problematic engagement with addictive substances and behaviours across Europe. Further, by taking an interdisciplinary approach, substantial gaps in current evidence or missing links between disciplines may be more easily identified, thereby providing a focus for future research and funding. Finally, it is hoped that this report begins to better integrate the different disciplines dealing with addiction studies and provides a model of how these diverse sciences can come together to foster interdisciplinary research that translates into policy responses which improve societal well-being.

The remainder of this introductory chapter provides an overview of two areas which frame this research: firstly, a description of different scientific methods is provided with a view to identifying how these impact on interdisciplinary studies such as this one, and secondly, an overview of the harms of substance use and gambling and how harmful substance use or gambling is differentiated from the concept of risky substance use or gambling described in the previous report.

## 1.2 The challenge of integrating evidence from different scientific methods

Scientific disciplines take a number of different approaches towards understanding the world. These include positivism, realism, interpretivism, objectivism and constructivism. Each has a different perspective on what can be considered valid sources of evidence and a set of principles about the way in which the object of study (e.g. society) functions to which new evidence can be applied. The most common approach to understanding the different underlying approaches of scientific disciplines is to make the somewhat crude distinction between the positivist natural sciences and the constructivist social sciences.

The natural sciences, including physics, biology, chemistry and parts of psychology, fit more comfortably within this distinction as their approaches are overwhelmingly positivist. The key feature of positivism is an emphasis on the use of repeated observation and measurement as a means to explain the underlying reasons for certain behaviours. This approach, which essentially proposes that the world can be understood through objective and rational quantification and categorisation, lies at the core of what became known as 'the scientific method'. To identify determinants of a particular outcome, statistical tests are typically used to measure how closely associated the determinants and the outcome are, how accounting for additional factors may alter this relationship and whether other potential explanations for this association can be ruled out. To

enable this, both the determinant and the outcome must be amenable to objective measurement or categorisation and considerable effort is often invested in constructing suitable tools which can reliably measure complex concepts such as personality, well-being and addiction. The positivist approach has been criticised for, amongst other things, reducing a hugely complex social world to numbers and categories and for adopting an approach which prioritises reductive measurement and analysis by distant scientists over the detailed observations of individuals with close personal experience of the phenomena in question.

In contrast, social science has tended towards a more constructivist approach whereby objective measurement is not ignored but is de-prioritised, partly due to the perceived difficulty of objectively measuring or classifying important concepts for understanding society such as power relations, political philosophy or youth culture. Instead, concepts are often subjectively defined through detailed description. Particular attention is paid to how different constructions of the meaning and purpose of a concept may emerge when viewed in the context of interrelations between individuals and different levels of society, such as families, subcultures, institutions and nation states, and the practices, values and beliefs which are embedded within each of these social units. Constructivist approaches have been particularly criticised for treating subjective opinion or anecdote as robust evidence and for providing deep understanding that lacks validity beyond the case in point.

A comparison of the criticisms of positivism and constructivism highlights that, at the heart of the distinction between these two approaches is a debate as to whether there is an objective reality which can be understood with sufficient scientific effort or whether, to some extent, the world should be understood subjectively as humans and societies act on the basis of viewing the world through their own lens rather than through a universal set of well-defined truths.

The crudity of the positivist vs. constructivist distinction is worth noting, as although it highlights important differences between scientific disciplines, it is particularly caricatured for social science. Some social sciences, such as psychology and economics, have strong positivist slants and many of those working in other disciplines, such as sociology and anthropology, do not reject objective measurement per se, but simply try to provide further evidence to interact with it. Nor are positivism and constructivism the only approaches used across the scientific disciplines; however, they provide a useful dichotomy for demonstrating key divergences in scientific methods.

The underlying approaches which inform scientific disciplines are not solely philosophical points. As described above, they contribute to decisions about the kind of data that is regarded as acceptable evidence and where scientific effort is focused. As such, different disciplines have developed starkly different methods of conducting research. For example, the repeated experimentation and sophisticated well-defined measurement tools of natural science contrast sharply with the text-based description and recorded speech reflections collected in many sociological and anthropological studies. Similarly, the carefully quantified statistical relationships between determinant and outcome identified by positivist science sit uncomfortably with the richly contextualised processes of cause and effect which are theorised using constructivist data.

These divergences present important challenges for this project. Although, determinants of harmful behaviour drawn from positivist research are often straightforward to list and statistical analyses allow them to be arranged into evidence-based models, the broad concepts discussed in constructivist research and their varying meanings and complex interconnections make them less easy to succinctly summarise or to arrange into easily accessible models in informative ways. Part of our work represents an attempt to develop working practices and research methods which can address these challenges.

## 1.3 Harmful substance use and gambling

The harms identified with harmful substance use and gambling are diverse, including negative consequences for physical and mental health as well as financial, legal and social costs for the individual and those around them. An understanding of why humans engage in harmful activities and how societies make decisions in response to behaviour perceived to be harmful is required to frame our understanding of the determinants of harmful substance use and gambling. First, we elucidate the distinction between risky substance use and gambling that were the focus of the previous report, and harmful substance use and gambling that are the focus of this report.

### 1.3.1 How does harmful substance use differ from risky substance use?

Harmful substance use and gambling should be situated in relation to risky behaviour which was the focus of the first report in this series. The first report for Work Package 7 of ALICE RAP described the determinants of risky substance use and gambling, where risk was defined as:

"*All expressions of substance use and gambling, in terms of quantity, frequency, pattern and situational circumstances (e.g. location, time) which are material predictive factors for short- or long-term individual harm, or harm to others including society at large*"

This synthesis report for WP8 of ALICE RAP is focused on the determinants of harmful substance use and harmful gambling defined as:

*"Substance use or gambling which has caused material harms of social, mental or physical nature which are experienced by the user, other individuals or society at large, where cause means outcomes which would not have occurred without the substance use or gambling".*

The distinction between risky and harmful use can be conceptualised as the difference between behaviour that has the potential to cause harm and behaviour that is actually causing social, mental or physical harm. For example, an example of *risky* use in relation to alcohol consumption might be drinking to the point of intoxication, which can place you and those around you at risk of harms such as accidents and violence. *Harmful* use would be drinking to the point of intoxication and as a result actually experiencing harms such as being involved in a traffic accident or a violent fight. Thus harmful substance use or harmful gambling presupposes the experience of a negative consequence of behaviour in which the behaviour is a necessary cause of the outcome.

### 1.3.2 Overview of harmful substance use and harmful gambling

Our understanding of the nature of harmful substance use and harmful gambling is informed by our position as European societies which place a high value on economic productivity and on perpetuating individual physical health. Framed within this context, harmful substance use and gambling can be identified as problematic because they result in negative physical or mental health outcomes and economic, legal, financial or social costs for the individual, family and friends or for wider society. In this section both the harms common to addictive substances and gambling and the harms specific to different substances are identified. Although epidemiological research on harm from licit substances is relatively well-developed, research on illicit substances is often less developed and so data on the harms of illegal drugs is drawn from a comparatively narrow evidence base. In addition to exploring direct harms of addictive behaviours, the idea that society's response to a particular behaviour may modify the harm experienced as a result of that behaviour is explored.

Before engaging in a description of harmful substance use and harmful gambling, it is important to acknowledge that there are benefits associated with substance use and gambling. For example, moderate alcohol consumption is associated with health benefits including reduced risk of coronary heart disease (Corrao et al. 1999) and psychosocial benefits including sociability, mood enhancement and stress reduction (Peele and Brodsky 2000). Substance use and gambling behaviour may be considered harmful where the total costs to the individual or society outweigh such benefits.

#### 1.3.2.1 Harms to the individual common to addictive substances and gambling

As a result of consuming licit or illicit substances, or gambling, individuals may experience a range of negative health or non-health consequences. Potential non-health consequences of substance use and gambling include financial problems (such as debt or bankruptcy), domestic problems or the disruption of personal relationships (such as family disintegration and relationship breakdown), difficulties in obtaining and maintaining employment, and engagement in violent or drug-related crime (Advisory Council on the Misuse of Drugs 2006;Shaw et al. 2007) (Reith 2006).

Whilst many health consequences of substance use are specific to the drug of choice, there are a number of health problems that are common to different types of substance use and gambling. Substance use and problem gambling may impair psychological functioning and reduce quality of life (Costenbader et al. 2007;Grant and Kim 2005). Among individuals who use substances and gamble problematically, the prevalence of depression and rates of suicide are high compared with the general population (Reith 2006;Stenbacka et al. 2010). Injecting drug use, for example including heroin and crack cocaine, is associated with secondary harms resulting from the mode of drug administration (Nutt et al. 2007). Secondary harms include the transmission of blood-borne viruses (such as HIV and Hepatitis B and C), septicaemia, abscesses, vein collapse and thrombosis.

#### 1.3.2.2 Harms to the individual from different addictive substances and gambling

Harms to the individual specific to different addictive substance and gambling are predominantly health related harms: non-health consequences are often common to multiple licit or illicit substances and gambling. An exception is heroin use, which is associated with social exclusion and prostitution, where the use of many other drugs such as nicotine, alcohol and cannabis is not (Advisory Council on the Misuse of Drugs 2006).

Many illicit substances encourage repeated use, driven by various factors including the nature of the drug experience, their power to induce dependence and withdrawal reactions (Nutt et al. 2007).

Some drugs, for example cannabis, result in a psychological dependence where habitual use is based on cravings rather than the drug withdrawal that is associated with physical dependence (such as a habitual user of heroin might experience on quitting attempts). The half-life of a drug (the speed at which it is cleared from the body), the pharmacodynamic efficiency of the drug, and the degree of tolerance that develops from repeated use, are all factors in the development of dependence and withdrawal. Evidence on the tendency of different substances to induce dependency is varied as we have more population-based estimates of addictiveness for the more commonly used drugs: evidence suggests that smoked tobacco is the most addictive commonly used drug, with heroin and alcohol somewhat less so; psychedelics have a low addictive propensity (Nutt et al. 2007).

Evidence for harmful health consequences of substance use in relation to licit substances is well documented within epidemiological studies. Harmful alcohol users may experience a range of negative health outcomes including maternal and perinatal disorders, cancer, neuropsychiatric disorders, cardiovascular diseases, cirrhosis of the liver, and unintentional or intentional injuries (Rehm et al. 2010). In 2004, 94,452 men and 25,284 women aged 15-64 years died of alcohol attributable causes in the EU, corresponding to 11.9% of all deaths (Rehm et al. 2012). Alcohol dependence makes up 71% of the net burden of alcohol-attributable mortality. The negative health consequences of tobacco use are wide ranging and include cancers (such as oropharyngeal and laryngeal cancer), cardiovascular diseases (such as ischemic heart disease and heart failure) and respiratory diseases (such as pneumonia, influenza and chronic obstructive pulmonary disease)(Rehm et al. 2006b). In 2000, 18.0% of deaths (13,491,000 people) in developed regions of the world and 12.2% of the global burden of disease among men and women combined was attributable to smoking and oral tobacco (Rehm, Taylor, & Room 2006b). Tobacco use contributes to the deaths of some 650,000 European Union (EU) citizens a year (World Health Organisation 2012).

Harms from illicit substance use are inextricably linked to the type of drug, the way it is used (e.g. intravenous versus smoked), the social context of use and how it is combined with other substances (Centre for Public Health 2011). Illicit substances including cannabis, cocaine, opioids, nitrites and dissociative anaesthetics are associated with a range of acute and chronic physical and psychiatric harms, as described below.

Cannabis is a psychoactive preparation of the marijuana plant. Harmful cannabis use is that which results in physical morbidity such as irritant effects on the respiratory system, difficulty in motor-coordination and inhibition of reproductive functions, and psychiatric consequences such as

impairment of higher cognitive functions and personality changes (Ashton 2001). No cases of fatal overdose from acute cannabis use have been reported but cannabis use has been implicated in driving fatalities and fatal cardiac accidents in young users. Cannabis use may be an important risk factor for chronic respiratory diseases such as chronic bronchitis and there are a number of reports in the literature of an association between cannabis use and rare forms of oropharyngeal cancer in relatively young users (Ashton 2001).

Opioids are psychoactive chemicals that have analgesic effects but can also create strong sense of euphoria. Harmful opioid use is associated with health problems that include urinary retention, depressed nervous system activity, sedation, mental confusion and hallucinations (Centre for Public Health 2011). Intravenous opioid use carries the greatest risk of addiction and health complications. Intravenous use is associated with additional risks such as the transmission of infectious diseases including HIV, hepatitis B and hepatitis C, as described above (Rehm, Taylor, & Room 2006b). Mortality from opioid use may be a result of overdose or be linked to a range of complications including respiratory depression and profound decreases in blood pressure leading to respiratory arrest (Centre for Public Health 2011). Opioids, mainly heroin or its metabolites, are present in the majority of drug-induced deaths reported in Europe, even if a substantial proportion of all drug-induced fatalities occur in a context of polydrug use (EMCDDA 2012). In 23 European countries providing data in 2009/10, opioids accounted for the overwhelming majority of cases, with 15 countries reporting proportions of 80% or more. Drawing on an analysis of data from over 30 cohort studies following patients up to 2010, it was estimated that 10,000–20,000 opioid users die each year in Europe, with most deaths occur among males in their mid-thirties (EMCDDA 2012).

Stimulants are psychoactive substances such as ecstasy, amphetamines and cocaine that induce temporary enhancements in either mental or physical function. Some of the risks of stimulant abuse are illustrated here by focusing on the harms of cocaine. Both acute and chronic cocaine use are associated with a number of negative physical and psychological outcomes. Potential physical health harms of acute use include cardiovascular, respiratory, neurological and genitourinary complications and adverse psychological effects include personality or mood changes such as anxiety, sleep disturbance and paranoia (Kaye and Darke 2004). Acute complications may lead to death, for example as a result of toxic reactions which may lead to cardiac or respiratory arrest (Kaye & Darke 2004). Mortality from chronic cocaine use is most often linked to cardiovascular complications such as inflammation and injury of the heart muscle. Morbidity related to chronic cocaine use may affect

a range of body systems including the vascular, renal, neurological and reproductive systems (Centre for Public Health 2011).

Hallucinogens are a class of psychoactive drugs that can cause changes in perception, emotion and consciousness, inducing experiences that are completely different to familiar states of mind. There are three broad categories of hallucinogen: psychedelics (such as LSD), dissociatives (such as Ketamine), and deliriants (such as diphenhydramine). There is little evidence for deaths resulting from acute or chronic consumption of hallucinogens, with the exception being risk of injury and accidental death due to perceptual distortions and impaired decision making (Centre for Public Health 2011). Acute harms are associated with self-harm, accidents or violence whilst intoxicated and a range of personality and mood changes such as dysphoria, impaired concentration and derealisation. Long-term hallucinogen use is not associated with physical morbidity and few users show signs or symptoms of dependence. After chronic exposure some users experience persistence of low level hallucinations, brief flashbacks, delirium and depression (Centre for Public Health 2011).

In addition to the harms of illicit substance use evidence supports an associated between problem gambling and a number of chronic health problems. Although a direct causal relationship is not always evident, problem gambling is also associated with chronic medical conditions, obesity, and the use of expensive forms of medical care (such as psychiatric hospitalization)(Black et al. 2013).

#### 1.3.2.3 Harms to others from addictive substances and gambling

The use of addictive substance and gambling may bring about harm or costs to those not engaged in the behaviour, such as the users' family or friends, as well as wider society.

The friends and family of harmful substance users or gamblers may experience a range of health and non-health consequences of the addictive behaviour. During pregnancy and early childhood there is a risk of harms to the foetus and the breastfeeding baby as a result of substance use, as well as risk of childhood neglect and abuse (Nutt et al. 2007). Intravenous drug use is associated with the transmission of blood-borne viruses and may harm others through the transmission of infection to sexual partners and needle-sharers (Nutt et al. 2007). Smoking, including nicotine and cannabis, is associated with harms of passive or second-hand smoke (such as cancer and cardiovascular disease) (Advisory Council on the Misuse of Drugs 2006). Substance users may inflict verbal and or physical abuse on family and friends (Laslett et al. 2011). Research exploring the impact of drug use on family

found that many reported declining in physical and psychological health due to stress (Velleman et al. 1993) and had sought professional help for themselves to cope with stress (Melberg et al. 2011).

Aside from harm to family and friends, other individuals in society might experience harm from others' substance use or gambling, through being a victim of crime. Alcohol intoxication is a common cause of car and other accidents (Nutt et al. 2007) and violent crimes including homicide, sexual assault, robbery and assault.

Non-health consequences of association with a harmful substance user or gambler include having to live with and suffer exposure to an intoxicated person (Nutt et al. 2007), fear of violence (Melberg et al. 2011) and being threatened or verbally abused (Laslett et al. 2011). Families of drug users have also described negative consequences such as the introduction of the family to crime and criminal activity (Nutt et al. 2007), exposure to drugs, altered family functioning e.g. loss of close relationship and theft of goods and money from the home (Barnard 2005). Outside of the user's immediate family and friends, negative consequences of alcohol use that have been reported include being kept awake at night, being annoyed by people vomiting or urinating and feeling unsafe waiting for public transport (Laslett et al. 2011).

The harms to others resulting from substance use and gambling vary by gender with females reporting more negative harm as a result of knowing drug users than males (Melberg et al. 2011).

The implications for wider society of harmful substance use and gambling include health care costs, economic costs, law enforcement costs and social care costs. Smoking, alcohol consumption and illicit drug use all burden the health care system to different degrees through wholly and partially attributable acute and chronic health problems (Easton 1997;Rehm et al. 2009). The healthcare costs of the use of addictive substance are immense, with tobacco estimated to cause up to 40% of all hospital illness and alcohol involved in over half of visits to accident and emergency departments in the UK (Nutt et al. 2007). Healthcare costs include hospitalisations, inpatient and outpatient specialist treatment, general practitioner costs and prescription drug costs (Rehm et al. 2006a). Economic costs refer to lost productivity related to harmful substance use and gambling, for example absenteeism and reduced performance at work (Easton 1997). Law enforcement costs of harmful substance use and gambling are also high, including the cost to society of crimes (such as property loss or damage), policing, criminal charges and incarcerations as well as costs for licensing premises and costs for specialised drug enforcement (Rehm et al. 2006a). Finally, substance use and

gambling may result in social care costs, including for substance misuse services and children and families services (Centre for Public Health 2011; Rehm et al. 2009).

#### 1.3.2.4 Influence of societal perceptions of substance use and gambling on harm

Whilst it is evident that use of illicit substances might directly threaten health, societal perceptions of the harm associated with the use of different drugs is mediated by factors including culture, the media and political views. For example, public perception of the dangers of ecstasy have been influenced by the media's excitement about the drug since its rise to popularity in the late 1980s (Independent Scientific Committee on Drugs 2013). Most people who take the drug have no serious side effects and there is limited evidence for a dependence syndrome related to taking MDMA or related substances (Centre for Public Health 2011). The harms of ecstasy are linked to how people take the drug and poly drug consumption rather than ecstasy itself. As such, the harms associated with ecstasy use are much less than other Class A drugs such as Heroin, Cocaine and Crystal Meth. Thus societal restrictions on addictive substance use do not always appear to logically reflect the epidemiological evidence of harm from use of that substance and, in some cases, prohibitions, restrictions and policy responses may contribute to the harm through the imposition of punitive sanctions, the creation of problematic illicit markets and the withholding of protective measures. As such, harms to health from a behaviour may be outweighed by harms which are wholly the produce of how society has developed its response to that behaviour. Evidence on the determinants of a particular harmful behaviour therefore, should be seen as socially produced, rather than purely a reflection of inherent harmfulness. Evidence for the influence of society as a determinant of harmful substance use and gambling is presented in Section 3.1.1 (p.25).

### 1.3.2 Prevalence of harmful and dependent substance use and gambling in Europe

The prevalence of harmful and dependent substance use and gambling varies across the countries of Europe. Harmful alcohol use is defined in this report as that which has caused material harms of social, mental or physical nature which are experienced by the user, other individuals or society at large, that would not have occurred without the alcohol use. A threshold for harmful alcohol consumption or a level above which we can identify drinking as being harmful is not evident: there is a dose response relationship between many negative outcomes and alcohol but the experience of harm is dependent upon a range of contextual factors so that individuals consuming the same level of alcohol in two different situations may experience different outcomes. The prevalence of alcohol abuse, a maladaptive pattern in which alcohol intake is sufficient to adversely affect health or social functioning, and alcohol dependence have been measured across Europe. The point prevalence of

alcohol use disorders among men ranges from 15.29% aged 15 years and older in Hungary and 13.39% in Lithuania, to 1.07% in Spain and 0.50% in Italy. Among women the point prevalence of alcohol use disorders ranges from 2.55% in Norway and 2.27% in Hungary and Sweden to 0% in Cyprus and 0.17% in Spain (World Health Organisation 2013). Alcohol dependence among the adult population of the EU was 5.4% of men and 1.5% of women in 2005 (Rehm et al. 2012). The Mediterranean wine drinking countries had lower rates of alcohol dependence than the EU average, perhaps as a result of the pattern of drinking in these countries, whilst the countries of Eastern Europe had a higher than average rate of both alcohol dependence and drinking to intoxication. The Nordic countries sit in between these two parts of Europe, having relatively high rates of alcohol dependence compared to overall consumption levels (Rehm et al. 2012).

Smoking prevalence is measured more frequently in research than nicotine dependence; however, a few studies have examined nicotine dependence measured using tools such as the Fagerström Test for Nicotine Dependence (FTND) which is a standard test for assessing the intensity of nicotine addiction. Examining tobacco use across 13 countries (of which 12 were European), Fagerström and Furberg (2008) found that smoking prevalence ranged from 16% in Sweden to 39% in Denmark and nicotine dependence measured using the FTND score from 2.8 in Germany to 4.6 in Sweden, with higher scores reflecting greater dependence among a general population sample of smokers. Countries with lower smoking prevalence appear to have smokers with higher depence scores than those where smoking is more prevalent (Fagerstrom et al. 1996). Andlin-Sobocki et al. (2005) estimated the prevalence of smoking dependence across Europe based on the prevalence of smoking using a German national study that measured smoking prevalence and dependence. They estimated that nicotine dependence in Europe ranges from 5.5% in Portugal and 5.9% in Sweden and the Czech-Republic to 11.1% in Greece and 12.7% in Slovakia.

The overall prevalence of problem drug use among adults aged 15-64 years in Europe ranges from a high of 12.3/1000 population in Latvia to a low of 1.5/1000 population in Cyprus (EMCDDA 2012). Injecting drug use is most prevalent in the Czech Republic at 5.0/1000 and Slovakia at 4.9/1000 population and is least prevalent in the Netherlands at 0.22/1000 population. The available country level data on problem opioid use shows that Ireland has the highest prevalence at 7.2/1000 population and Turkey the lowest at 0.3/1000 population (EMCDDA 2012). Data is missing for a number of countries in the three categories of overall, injecting and opioid use, but only Romania, Slovenia and Estonia are missing data across all three categories of problematic illicit drug use. Data on injecting drug use in these three countries was reported by Aceijas et al. (2004) based on a review

of published and unpublished documents from 1998-2003, with IDU prevalence reported at 6.6/1000 in Romania, 3.7/1000 in Slovenia and 20.6/1000 in Estonia. Prevalence of IDU is particularly high in Estonia compared with the rest of Europe.

Problem and pathological gambling, measured using the South Oaks Gambling Screen (Lesieur et al. 1986) or the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV), varies widely between European countries. Data from 11 countries in Europe shows that lifetime prevalence of problem and pathological gambling (scoring 5 or more on DSM-IV) combined ranges from 1.1% in Italy and Spain to 6.5% in Estonia. Past year prevalence ranges from 1.3% in Germany to 3.1% in Finland (Kun et al. 2012). Such high rates of problem gambling as can be found in Estonia (and Finland and Switzerland) are much higher that the typical rates of 0.5-2% found across most of Europe and indeed around the world.

### 1.3.3 Population groups with higher rates of harmful substance use and gambling

Harmful alcohol use is more common among men than women, for example the prevalence of alcohol dependence in the European Union is 1.5% among women and 5.4% among men, and approximately three-quarters of deaths due to alcohol consumption occur in men (Rehm, Shield, Rehm, Gmel, & Frick 2012). Across Europe a mixed picture emerges relating to age differences in the prevalence of alcohol use disorders, with higher rates found among young, middle and older age groups depending upon the country and diagnosis (Rehm et al. 2005). Alcohol abuse is often more prevalent in younger age groups, however it is suggested that this may represent a transitory life phase rather than psychopathology (Caetano 1999). Co-morbidity of mental health and alcohol abuse or alcohol dependence in Europe has been measured using data from the European Study of the Epidemiology of Mental Disorders. Among individuals with a 12-month mood or anxiety disorder, prevalence of alcohol abuse was 20.8% and alcohol dependence was 27.7% (Alonso et al. 2004). Among people with Schizophrenia across five European countries, an average of 35% were identified as abusing alcohol. This average masks large between country variations, with 11.5% of participants from Verona and 75% of participants in London alcohol abusers (Gaite et al. 2002).

Data on sex and age differences in nicotine dependence is scant, so we rely on smoking prevalence data to examine demographic variations in smoking. Smoking prevalence in the European Union is higher among men than women, at 37.0% and 26.9% respectively (Zatonski et al. 2012). Prevalence of current smoking declines with age; for example 39.5% of men aged 20-44 years in the EU are current smokers compared with 32.7% of men aged 45-64 years (Zatonski, Przewozniak, Sulkowska,

West, & Wojtyla 2012). Nicotine dependence is more prevalent in people with mental disorders, and in particular mood disorders and schizophrenia, with smoking rates among those with a mental disorder estimated to be between 55-90% compared with general population smoking rates of 22% in the USA (de Leon et al. 2002). Among nicotine dependent adults, the prevalence of at least one additional mental disorder has been reported at 52.4% (Schmitz et al. 2003).

Across Europe more men use illicit drugs and attend drug treatment services than women (EMCDDA 2005). The ratio of men to women in opioid outpatient treatment is on average 3.5:1 in Europe, although this does vary by country with a higher proportion of female outpatients in northern Europe than southern Europe (EMCDDA 2001). Data on the gender composition of injecting drug users is scant, however a few studies have reported the proportion of the IDU population that are men and women. For example, in England 24% of IDU and in Russia 25% of IDU are women (Hickman et al. 2004;Platt et al. 2004). Co-morbidity between drug use disorders and mental health disorders is generally higher than for alcohol use disorders, with 30-45% of women and 15-25% of men with a drug use disorder meeting criteria for one or more mental disorders (Jane-Llopis and Matytsina 2006). Co-morbidity increases with severity of drug use, with drug dependent subjects displaying the highest prevalence of mental health problems.

Problem gambling is more common among men and younger adults (Johansson 2006); for example, in a Swedish population study men had a 271% high risk of lifetime problem gambling compared with women and those aged 15-24 years had a 151% higher risk of exhibiting lifetime problem gambling than those aged over 25 years (Volberg et al. 2001), whilst in Great Britain the prevalence of problem gambling among adolescents is reported to be 2-4 times greater than among adults (Forrest and McHale 2012). High rates of mental health problems including mood, psychotic, personality and attention-deficit disorder are also reported among problem gamblers; for example, compared with non-gamblers those with problem gambling were 3.3 times more likely to report ever having had major depression and 3.5 times more likely to have a history of schizophrenia (Potenza et al. 2001).

# 2. METHODS

## 2.1 Research method and process

This report is based on a synthesis of evidence from seven disciplines on the determinants of harmful substance use and harmful gambling. The disciplines involved are anthropology, economics, genetics, neurobiology, psychology, public policy and sociology. Further evidence was provided by experts on gambling, comparative European studies and marketing. The research team is made up of leading addiction scientists from each discipline in addition to the project management team and a science writer responsible for evidence synthesis.

The report was completed through three overlapping processes. First, each expert produced a review of the relevant evidence from their discipline; second, these reviews were integrated into a synthesis report by the science writer and, third, consensus meetings were held to discuss evidence from each discipline and drafting of the synthesis report. The descriptions of the research process below outline how and when this process took place.

### 2.1.1 Timings of process

An initial meeting of the project's partners in May 2011 defined the work schedule for this research project; including a preliminary timeline for meetings, the outcomes for dissemination and the proposed format and content of the discipline reviews.

At a consensus meeting in May 2012, discipline experts presented early drafts of their expert reviews and the partners agreed the definition of harmful behaviour. Experts then worked independently or in collaboration with epistemologically-similar disciplines to review relevant literature and draft expert papers by October 2012. Using each of these reviews, a draft of this synthesis report was produced by a science writer outlining key concepts, theories and determinants identified by the different disciplines. This draft report was circulated to the research team in April 2013 prior to a second consensus meeting in the same month. Following this consensus meeting the science writer responded to the comments and discussion of the discipline experts to produce this final version of the report in May 2013.

### 2.1.2 Structure of reviews

Each disciplinary review was a comprehensive and objective review of the state of the art within that discipline. Addictive substances or behaviours covered by the reviews include alcohol,

amphetamines, cannabis, cocaine, ecstasy, gambling, hallucinogenic substances, opioids, synthetic drugs, and tobacco. Reviews were narrative and between 7000 and 10,000 words. Each review contained a statement of methods including any inclusion and exclusion criteria used to select studies as well as evidence on both theory and determinants of potentially harmful substance use or gambling. To aid and foster interdisciplinary working, single disciplines were separated into four clusters representing their typical level and methods of analysis:

***Social and environmental focus***

Cluster 1: Public policy and economics

Cluster 2: Sociology and anthropology

***Individual focus***

Cluster 3: Economics and psychology

***Cellular and molecular focus***

Cluster 4: Genetics and neurobiology

The social and environmental level includes anthropology, sociology, public policy and economics, and analyses the interactions between and within large groups or societies, their perspectives and motivations and the characteristics of those groups or societies which influence harmful substance use or gambling. The individual group contains psychology and economics which examine the thoughts, emotions, behaviours and decision-making processes of individuals engaging in harmful behaviours and how these vary from those who abstain from doing so. The cellular and molecular level examines how harmful behaviour may stem from inherent or environmentally-induced biological changes. Economics operates at both the individual- and the social environmental-level depending upon whether one is considering micro- or macro-economics. To a lesser extent, this is true for other disciplines, although, for convenience, they have been included within a group which contains the majority of their focus.

### 2.1.3 Literature search and study selection

Experts in each discipline considered literature using the agreed definition (p.6). Consultation with other discipline experts as well as between disciplines aided identification of relevant literature. No limits were put on the design or methodologies of studies included in reviews and, consequently, the studies are as diverse as the sciences represented and span historical analyses, qualitative research

and micro- or macro-level quantitative methods to laboratory-based, clinical and epidemiological approaches. This inclusive approach is beneficial as each discipline has different approaches to reporting and analysing evidence. Rigid systematic review methods were not used since the aim of this analysis was to summarise rather than catalogue the scope of available evidence. Appropriate research databases were used for each discipline. Only English language articles were reviewed.

### 2.1.4 Evidence synthesis

Each discipline review was examined to identify the key determinants and models of interactions between disciplines that contribute to harmful substance use and harmful gambling. Determinants that were mentioned in multiple disciplines were examined further to understand whether combining information between the two or more reports may provide further insight into the role of this determinant of harm. As this process developed, disciplinary boundaries were blurred and, consequently, results are not presented by discipline but are instead structured around four areas of research; socio-economic, cultural and environmental conditions, living and working conditions, cellular and molecular factors, and multidisciplinary models of harmful substance use.

## 2.2 Comparison with previous multi-disciplinary models of addiction

Previous attempts to develop multi-disciplinary models of addiction have been conducted by groups including the Missouri Alcoholism Research Centre (Jacob et al. 2001) and individual authors such as West (n.d.). West has produced the most comprehensive review of models of addiction to date, including a systematic literature search that was conducted and experts were consulted to identify the main theoretical approaches for understanding addiction from across scientific disciplines. The result of this systematic literature search was a detailed reported outlining 10 different groups of models of addiction, including those modelling the individual (such as automatic processing theories, reflective choice theories and goal-focused theories) and population level theories (such as social network theories and economic models). Work by West (n.d.) and Jacob et al. (2001) has drawn together evidence from across disciplines such as genetics and psychology to improve understanding of the determinants of addiction in relation to alcohol, nicotine and illicit drugs.

The current project differs from such previous work as that by West in that it focuses more broadly on harmful substance use and gambling rather than addiction or dependence. In contrast to West, we also explore, alongside broader constructs, specific mechanisms relating to individual addictive

behaviours. We are a team of experts working across Europe and our international expertise has facilitated the inclusion of a broader range of evidence within our multi-disciplinary approach. We include evidence from disciplines that are more frequently drawn together in multi-disciplinary research (such as genetics and psychology) alongside disciplines that are less often examined within such endeavours (such as sociological and anthropological work). Our multi-disciplinary research team meets twice a year, so over the duration of the project we have had multiple opportunities for experts from different fields to engage in challenging but fruitful discussion around our work.

# 3. RESULTS

This section presents a synthesis of the discipline reviews. The determinants of harmful substance use and harmful gambling are presented within four themed areas of research:

1. Socio-economic, cultural and environmental conditions
2. Living and working conditions
3. Cellular and molecular factors
4. Multidisciplinary models of harmful substance use

These four sections are developed from evidence across the disciplines, with no section the domain of a single scientific discipline. The first three sections focus on individual concepts that are determinants of harmful substance use and gambling and this evidence is drawn together in the fourth section on 'multidisciplinary models of harmful substance use and gambling'. At the end of the chapter individual determinants of risky behaviour are presented in Table 1.

## 3.1 Socio-economic, cultural and environmental conditions

The determinants described here are drawn from economics, sociology and anthropology and describe the influence on harmful substance use and gambling of broader social, economic and political environmental conditions.

### 3.1.1 Societal framings of harmful substance use and harmful gambling

The social and cultural context within which substance use and gambling take place is important for framing our understandings of what is considered harmful behaviour. A behaviour may be considered harmful due to:

1. Inherent negative consequences of use, for example alterations in brain chemistry that result in down regulation of the dopamine system (a reduction in the number of dopamine receptors) from persistent drug use.
2. Harms to the individual caused by how society handle's substance use, for example the criminalisation of illicit drugs resulting in the production of unregulated substances that may contain harmful cutting agents.
3. Harms to society that result from the individual's substance use, for example lost economic productivity resulting from alcohol-related morbidity and mortality.

This section is focused on the latter two types of harm, particularly focusing on how social and cultural contexts form perceptions of harms and how these are managed on a societal or local level, rather than physical harms at the individual level.

Within Europe there is evidence that the harm experienced from a given level of alcohol consumption varies between different drinking cultures and within cultures over time. For example epidemiological analyses show a much stronger relationship between changes in per-capita consumption of alcohol and changes in homicide and suicide rates in northern than in southern countries in western Europe (Norstrom 2002). The mechanisms underlying such differences in the experience of harm might include engagement with drinking and seriousness of drinking (Partanen 1991). In this context engagement with drinking is the extent to which drinking is ritualised and integrated within, as opposed to separate from, daily life and seriousness of drinking reflects the prevalence and degree of intoxication from drinking.

As described in Section 1.3, the harms experienced as a result of addictive behaviours may be influenced by societal perceptions of substance use and gambling. As such, within a given culture or society the harm related to the use of a substance may change over time as a result of moral panic. A moral panic occurs when a condition, episode, person or group is suddenly regarded as a threat to societal values and interests (Cohen 1972). This can causes harm in a number of different ways, for example, public hostility towards deviants, the strengthening of laws around a particular behaviour and the awarding of unusually harsh punishments for deviant behaviour (Critcher 2008). Under these circumstances behaviour that might previously have been considered risky becomes harmful

because of society's changed reaction to the behaviour. Drug use has been repeatedly an object of moral panic (Cheung 2000) with harms of different substances appearing in the limelight suddenly and often in stereotyped form when reported by mass media. The determinants of such moral panics can be explored in reference to public concern around crack cocaine use in the mid-1980s in the USA. The determinants of this moral panic included a general decline in the public's acceptance of illegal drug use, growing interest of media and action groups in the phenomenon of drug use, over dramatization of the actual prevalence of drug use and growing concern among politicians and lawmakers about the issue. The situation was exacerbated by the increase in measurable harm from illicit substance use, but the societal reaction may have been disproportionate to the harm and appeared to be fuelled by factors such as the novelty of crack cocaine and the overdoses of some prominent athletes. The harms of this moral panic included a law enforcement crackdown and a crisis mentality among the population, both of which may have contributed to the seriousness of the crack cocaine problem (Goode and Ben-Yehuda 1994).

In addition to the acute or transient threats posed by moral panics, local or regional cultural norms and religious beliefs may influence societal response to and the harm experienced from an addictive behaviour. Addictive substances and behaviours may be heavily moralised and are often subject to either prohibitory or regulatory frameworks which vary from place to place and change over time. Engagement with addictive substances often conveys strong social meaning and may lead to stigma, which can be particularly focused on the marginalised 'misusers' as opposed to a supposedly more responsible mainstream (Peele 1987;Room 2011). This can lead to punitive societal responses which are potentially harmful in themselves and, conversely, a lack of intervention into mainstream behaviour which allows harms to occur unchecked. Where evidence of harms associated with use of illicit substances is available, it does not always translate logically into policy responses as policy decisions are shaped by moral judgements, narratives of social order and cultural histories as well as empirical judgements around objectively measurable harms. Restrictions that develop from such policy responses and decisions may vary between societies presenting sharp disconnects in what the harms of engagement in a particular behaviour are in different contexts. For example, many Western cultures embrace drinking but risks of censure are high in Islamic states, and provision of needle exchanges for intravenous drug users may greatly reduce risk of blood-born infection but are nonetheless only sporadically available in certain contexts.

Public, policy and media reactions to substance use and gambling influence how society handles substance use through drug control, harm minimisation and treatment systems. Drug control policy

may affect drug users experience of harm through drug laws and law enforcement. For example, if caught using drugs in a country with a zero tolerance approach to illicit substance use, individuals may be subject to criminal sanctions with potential negative implications for health, social and financial circumstances. Countries may also change drug laws or law enforcements' response to substance use over time, perhaps resulting in the reclassification of a drug or a law enforcement crackdown, with implications for the experience of harm for those individuals continuing to use particular substances.

Drug control policy also frames and influences drug users' health, for example through laws around the provision or lack of access to clean needles and syringes (Campbell and Shaw 2008). Lack of access to clean needles is one example of how it may not be drug use in itself that causes health problems, but a lack of services that societies offer to drug users than would enable people to take drugs in less harmful ways (Bourgois et al. 1997). Since the mid-1980s, the concept of harm reduction has challenged the traditional basis of drug policy which focused on ideas of supply reduction and use reduction. Arising from the HIV/AIDS epidemic among injecting drug users, ideas around harm reduction as a concept and harm reducing initiatives have developed over time from discussions among researchers and policy makers (Inciardi and Harrison 1999;Stimson 2007). The underlying principle of harm reduction is that drug policy should direct efforts towards mitigating the health problems caused to drug users rather than on moral and political decisions about whether drug use per se is good or bad and tolerable to society or not (Marlatt 1998). Within a harm reduction culture, abstinence is considered a valuable goal, but so are alternative goals such as reductions in pain, illness and other harms related to drug use. Harm minimisation strategies might include a range of services for drug users including needle exchanges, street level nursing, easy access to substitution prescription medication and hostels for the homeless among whom rates of alcoholic and illicit drug dependence are high (Fazel et al. 2008;Marlatt 1998). The extent to which harm reduction is pursued as a policy objective in a given society influences the experience of negative consequences resulting from the use of an addictive substance.

In addition to the harms experienced as a result of the use of illicit drugs, harms may be experienced from the use of prescription or over the counter (OTC) medications, for example Benzodiazepines and codeine. In the context of OTC medications, misuse is the use of a drug for its intended purpose but at a higher than recommended dose or for a longer period of time, whilst abuse is non-medical use, e.g. to experience a high or to lose weight (Wazaify et al. 2005). Literature on societal framing by legal status of a drug is scarce, with research on this subject focused on awareness of misuse and

abuse of OTC medicines and potential solutions to the problem, rather than exploring perceptions of OTC medicine misuse and abuse. As such it is difficult to comment on the potential harms to those using OTC medicine inappropriately resulting from how society perceives their behaviour.

Substance use may result in a number of harms to society such as the harms associated with drug users consuming and dealing drugs in a neighbourhood, including the risk of children being in contact with illegal drugs and psychical or verbal harms. In order to protect those affected by others' substance use, society may engage in processes that can result in the experience of harm by substance users: for example, the strategy of "pushing around" drug users from open drug scenes in populated areas of a city to less visible spots that are more remote from the city centre. Dahl (2008) illustrates this idea using the Danish open drug scene where nuisance related to such drug scenes has increasingly become a matter of public concern and law enforcement is often regarded as a matter of public protection. Requests by shopkeepers and residents to disperse such scenes have resulted in strategies that move drug users to less visible areas that are often remote from the city centre and increase the risk of being robbed or visited by the police. Given the isolation and insecurity of these places they never became attractive to drug users (Dahl 2008). This scenario illustrates the conflict between minimising harm to others and causing harm to the individual.

### 3.1.2 Marginalisation

Marginalisation is the relative exclusion of individuals or groups from goods or services as a result of their circumstances. Deprivation, poverty and social exclusion are all forms of social and economic marginalisation. Individuals and groups may be marginalised along such divisions as economic status, ethnicity and education, with engagement in harmful substance use and harmful gambling often, although not always, seen to occur along similar societal divisions. Marginalisation is proposed to be a determinant of the transition to harmful substance use and harmful gambling, as evidenced below.

Indicators of social marginalisation such as not being in the workforce and not being stably housed are strong predictors for harmful substance use (Storbjörk and Room 2008). Death is one possible harmful outcome from substance use and has been associated with indicators of marginalisation; lower education, lower income and lower housing stability all contribute significantly to predicting death from an alcohol-specific condition (Makela 1999). Lower education and lower income have also been significantly associated with higher rates of nicotine dependence (Siahpush et al. 2006). The socio-economic gradient of alcohol-related mortality that is observed across nations is intriguing given that socio-economic class has been inversely associated within harmful alcohol consumption

(e.g. Siegler et al. 2011) and suggests that there is a disconnect between the gradient of consumption and gradient of harm in some contexts.

Exploring reasons for the social class gradient in mortality and other alcohol-related negative consequences, Room et al. (2006) suggest that higher socioeconomic status groups might have more resources to protect themselves from the hazards of drinking, for example taking a taxi home instead of driving or walking. Additionally, they suggest that men in higher SES groups are usually advantaged in terms of having a family, which may be a motivating factor in the decision to do something about an alcohol problem before severe consequences occur. Elsewhere, it has been suggested that different drinking patterns (e.g. binge drinking versus regular drinking) (Makela 1999) and the clustering of risk factors (such as malnutrition, poor access to health services and low income) in some populations (Schmidt et al. 2010) may also explain why some groups suffer harm from addictive substances whilst others do not.

Treatment and control systems may influence the marginalisation experienced by substance users. Individuals in substance misuse treatment are often excluded from or on the periphery of society for the duration of their treatment. Following treatment recovering addicts may not adequately reintegrate into society, having undergone treatment in an environment in which their everyday lives may have been constrained (Jöhncke 2009). Drug policy can also keep users in a marginalised position, for example by criminalising the distribution and use of many addictive substances, thus criminalising and facilitating punishment of the behaviour of those with drug dependencies (Campbell & Shaw 2008). Thus, substance abusing individuals may experience a cycle of marginalisation that is difficult to break.

Societal responses to problematised addictive behaviours may result in the formation of subcultures or countercultures of individuals who group together in response to social ostracism. Such societal exclusion might results when agencies that deal with drug related problems impose a label on particular forms of deviance or social problems. Individuals exposed to labelling may take on the associated identity and develop groupings (Goode 2004), perhaps as a form of defence, attack or adjustment. The actions that result from the formation of countercultures have been identified as “secondary deviance”, particularly used in relation to illicit drug use because of the illegality of the behaviour. “Primary deviance” is the behaviour that was socially disproved in the first place and “secondary deviance” is the deviant identity and behaviour of the counterculture that develops from punishment or ostracism related to the “primary deviance” (Lemert 1967). The subcultures that

develop are often marginalised from wider society. For example, following a criminal conviction an individual may find it impossible to secure work and may therefore be forced into a life of crime to survive. Thus marginalisation is a determinant of harmful substance use and harmful substance use may result in further marginalisation.

### 3.1.3 Marketing

Addictive behaviours have been associated with various elements of the marketing mix: price, place, product and promotion (the 4 P's). Evidence for marketing as a determinant of harmful substance use is focused on alcohol and tobacco use because evidence for marketing as a determinant of harmful illicit substance use is limited.

There is strong evidence for place and price as determinants of harmful alcohol use. Place has a strong influence on harmful alcohol use, particularly dependency or addiction, through the channels of alcohol distribution and availability of alcohol selling outlets (Bryden et al. 2012;Foster and Ferguson 2012;Lachenmeier et al. 2011). For example, the likelihood of heavy drinking has been linked to a higher density of off-sale shops and on-sales premises such as bars and restaurants (Bryden, Roberts, McKee, & Petticrew 2012). Extending the definition of harmful use beyond dependency to include harms to the user or others, Hughes et al. (2011) reported that "*a permissive environment, discounted drinks promotions, poor cleanliness, crowding, loud music and poor staff practice*" (p.42) contributed to alcohol-related problems including aggression, crime, injury and drink driving. Outlet opening hours and controls on the availability of alcohol have also been found to impact on drink driving and related fatalities (Grube and Stewart 2004). Price is a determinant of harmful alcohol use, with drinkers who have access to cheap alcohol more likely to drink more regularly and consume more alcohol per drinking occasion (Chaloupka et al. 2002). Evidence suggests that the affordability of alcohol is likely to affect high, but not the highest, levels of alcohol use, with price influencing whether people have any dependence symptoms at all but not the number of dependence symptoms (Farrell et al. 2003).

Harmful tobacco use evidenced to be associated with all four Ps. Tobacco promotion may perpetuate or increase harmful smoking by acting as an external cue to smoke (Capella et al. 2011) and smoking in movies is associated with positive attitudes towards smoking (National Cancer Institute 2008). Point of sale advertising stimulates opportunistic purchases with 25% of adult smokers reporting impulse cigarette purchases after seeing a tobacco display (Paynter and Edwards 2009). Point of sale advertising may also influence perceived social norms around smoking and can

undermine efforts to quit (Hastings et al. 2008). Alternative tobacco products such as menthol cigarettes may inhibit cessation and promote smoking relapse (Gardiner and Clark 2010) whist brand descriptors such as 'light' and 'mild' can undermine perceptions of risk with many health concerned smokers switching to regular use of such brands as an alternative to quitting (Hammond 2010). Tobacco pricing may also influence harmful use, with low income and less educated populations most sensitive to price increases (National Cancer Institute 2008). Harmful tobacco use, for example smoking during pregnancy, has been shown to be responsive to price with a 10% increased in price resulting in a 10% decrease in smoking among pregnancy women (Cawley and Ruhm 2011).

A small number of studies have examined the link between illicit drug prices and harms. There is reasonable evidence that affordability influences harmful use of drugs, with increased prices leading to reduced harmful use of drug such as heroin (Dave 2008) and cocaine (Markowitz 2005). Overall, the strength of the relationship between price and drug use is difficult to evaluate because of the challenges of conducting research in this area.

Harmful gambling is most strongly associated with product and place, although the importance of promotion should not be overlooked as 46% of problem gamblers in America reported that TV, radio and billboard adverts were triggers for them to gamble (Grant and Kim 2001). A range of product characteristics including a high gambling event frequency, probability of winning, cash or credit basis, stake size and skill needed to participate all influence the onset of problem gambling (Abbott et al. 2003). A large win early in a gambling career can also negatively influence long-term gambling behaviour, with new media technologies such as online casinos able to exploit novice gamblers by artificially creating a situation in which they experience an early big win (King et al. 2010). Countries with a high availability of gambling opportunities have among the highest prevalence rates of problem gambling (Sharpe 2002). The accessibility and ubiquity of opportunities to gamble may make it difficult for vulnerable individuals and problem gamblers to self-exclude from gambling and may lead to increased gambling problems (Griffiths 2004;King, Delfabbro, & Griffiths 2010).

## 3.2 Living and working conditions

The macro- and micro-economic environment, as well as individual level determinants including previous substance use and behavioural conditions, all have the potential to influence the transition to harmful substance use and gambling. Captured by the term living and working conditions here, these determinants are largely drawn from the disciplines of economics and psychology.

### 3.2.1 Economic cycles and unemployment

The macro economy has a direct effect on the consumption of intoxicating substances through causal pathways that include income, time, stress, opportunities for socialising and prices (Cawley & Ruhm 2011;Deb et al. 2011;Pacula 2010). Through these causal pathways the economic cycle may have a varying impact on harmful substance use, for example economic downturns may reduce income which constrains people's ability to purchase substances, but downturns may also reduce hours of work which increases the amount of time people have in which to use substances. Research on the impact of the economic cycle on harmful substance use and gambling looks at changes in harm from different behaviours during economic peaks and troughs. Pro-cyclical behaviour is positively correlated with the overall state of the economy, so when the economy is growing the behaviour becomes more common. Counter-cyclical behaviour is negatively correlated with the economic cycle, so when the economy is growing the behaviour becomes less common.

Consistent evidence is reported for the impact of the economic cycle on heavy drinking and traffic accidents, which are both pro-cyclical: in the peak of the economic cycle heavy drinking and traffic accidents increase. Inconsistent evidence has been found for the pro-cyclicity of liver disease, cardiovascular disease and homicide, although no significant evidence has been reported demonstrating counter-cyclical patterns related to the economic cycle (Pacula 2011). Tobacco use also appears to be pro-cyclical: economic downturns reduce the risks of smoking with declines concentrated in heavier smokers (Xu and Kaestner 2010). Illicit substance use is reported to be counter-cyclical amongst teenagers and young adults, with use increasing during downturns, but may be pro-cyclical among older adults (Arkes 2007;Chalmers and Ritter 2011). Drug users faced with income constraints may search for more 'efficient' ways to take drugs, for example injecting, which may further increase levels of harmful use during economic downturns.

The aggregate level data used to examine macro economic relationships can only be used to explore change in levels of harm and not the transition from risky to harmful use. Additionally, evidence for the impact of economic cycles on harmful substance use is based on ecological studies and is therefore at risk of the ecological fallacy, drawing conclusions on the behaviour of individuals based up analyses of group level, macro-economic data. The process of aggregating data may conceal considerable heterogeneity in response among individuals in the population under study. Therefore, researchers must be careful to not overstate population level relationships and should examine individual level relationships in addition to ecological analyses where possible in order to support

conclusions drawn at the aggregate level. For example, in considering the impact of economic cycles on alcohol consumption at the population level we cannot measure the switch between on and off-trade alcohol consumption that may affect harm patterns.

Moving from the broader macro-economic level to that of individual unemployment, there is evidence for a negative impact of unemployment on harmful substance use. Significant and often sizable relationships have been found for unemployment as a cause of alcohol abuse/ dependence, with odd ratios for alcohol abuse/dependence among the unemployed compared to the employed ranging from 1.7 to 3.7 in studies from the USA, Australia, the UK and Finland (Henkel 2011). Long-term unemployment has also been reported to predict alcohol-related deaths for both men and women (Garcy and Vagero 2012), whilst plant closures raise risk of hospitalisation due to alcohol-related disorders and alcohol-related mortality (Eliason and Storrie 2009). There is little research examining the relationship between unemployment and nicotine dependence, however one study among 16-18 year olds found that unemployment raised the risk of nicotine dependence (Fergusson et al. 1997). Illicit substance use and abuse/dependence, including cannabis, cocaine and heroin use, is also more common among unemployed people (Henkel 2011). The evidence in this field is focused on harmful use per se rather than the transition from risky to harmful substance use.

### 3.2.2 Previous substance use

Previous substance use may lead to further substance use or abuse of harder illicit drugs. Evidence for this gateway theory (Kandel 1975) has been found for a range of addictive substances, with cannabis and alcohol as particularly common 'gateway' drugs. For example, Swendsen et al. (2010) reported an association between prior illicit drug use and subsequent alcohol dependence.

Gateway theory has been criticised for overstating the importance of previous alcohol, tobacco and cannabis use for the subsequent development of problematic substance use. Criticisms include that studies exploring gateway theory are often derived from population based samples which have a low prevalence of hard drug use, are often limited to adolescents despite little evidence that adolescents who try hard drugs become regular users, and that similar findings have lead to divergent conclusions as a result of ambiguity around the interpretation of research findings (Reid et al. 2007). Additionally, evidence from the Arrestee Drug Abuse monitoring programme found that an increasing proportion of problematic illicit substance users do not follow the gateway sequence of substance use progression (Golub and Johnson 2002). Finally, where evidence has found an

association between cannabis use and subsequent use, abuse or dependence on other illicit drugs, the causal mechanisms underlying the relationship remain unclear (Fergusson et al. 2006).

### 3.2.3 Intra-individual factors

A range of behavioural determinants of harmful substance use and harmful gambling have been proposed from the scientific discipline of psychology. Determinants of harmful substance use and gambling include personality traits, cognitions, executive functions and mental health. The range of single determinants included within these four broad categorisations can be combined within integrative theoretical models that are described later in the report (see Section 3.4, p.39). Similar to the economic determinants described above, this evidence relates to the determinants of harmful use rather than the transition from risky to harmful use, around which evidence is scarce.

Personality traits are individual aspects of character that contribute to determining personality and behaviour. Substance use disorders involving alcohol, nicotine and illicit drugs have been strongly associated with high negative emotionality as well as low level constraint at age 17 (Elkins et al. 2006). Psychoticism and low openness to experience are correlated with alcohol dependence, high openness to experience and low consciousness are correlated with tobacco dependence, and novelty seeking is associated with higher risk of illicit drug and tobacco dependence (Grekin et al. 2006;Sher et al. 2000). Extraversion may be associated with alcohol dependence but evidence for this relationship is mixed with some authors reported a relationship (Grekin et al. 2006) and others finding no associated between substance use disorders and extraversion (Kotov et al. 2010). Elevated impulsivity is associated with dependence on cocaine, amphetamine, alcohol and opiates (Verdejo-Garcia et al. 2008). Higher impulsivity in substance users is not solely a result of drug use but has been found to be a stable personality trait after a prolonged phase of abstinence. Meta-analyses from cross-sectional studies found high disinhibition, low consciousness and low agreeableness to have the strongest association with substance use disorders (Kotov et al. 2008).

Cognitions are the higher-level functions of the brain that encompass mental processes involved in acquiring knowledge and understanding, including processes such as thinking, knowing, remembering, judging, and problem-solving. Cognitions play an important role in the transition to harmful substance use. Social images and descriptive norms at ages 12-13 were predictive for heavy drinking aged 14 to 18 years in the US (Andrews et al. 2011). Among adults, social and escape reasons for drinking and positive expectations towards drinking influenced heavy drinking (Greenfield et al. 2009), and drinking to cope was associated with more drinking problems over 10

years (Holahan et al. 2001). The research around cognitions as a determinant of harmful substance use are limited as most of the research is on alcohol rather than the wider range of addictive substances, most studies use correlation analysis and within the evidence base there is a lack of criteria for defining harmful substance use.

Executive functions describe the ability to control cognitions or behaviour in relation to future goals rather than immediate stimuli (Nigg et al. 2004). Executive control functions include set shifting (the ability to move back and forth between tasks), interference control (protecting the contents of working memory from interference), response inhibition (keeping goals in mind and prioritising actions), working memory (the system that actively holds multiple pieces of transitory information in the mind) and verbal fluency (listing related words in a given time period). Longitudinal research exclusively examining the relationship between executive control functions and substance misuse is weak and findings are inconsistent. Among children, poor response inhibition has been reported to predict alcohol-related problems at seven years independent of familial risk of alcoholism or anti-personality disorder (Nigg et al. 2006). Conversely, executive function deficits were not found to be predictive of stable cigarette smoking or substance use disorders in adolescents with attention deficit hyperactivity disorder (ADHD) over five years (Wilens et al. 2011).

Mental disorders and substance use disorders are often highly co-morbid (Kendler et al. 2003). Major depression is associated with alcohol, nicotine and illicit drug misuse (Swendsen et al. 2010). Dysthymia, hypomania and mania have all been associated with subsequent cannabis use disorders (Buckner et al. 2012). Bipolar disorders, non-alcohol substance use disorders and social phobia were predictive of alcohol dependence (Behrendt et al. 2011), as were disruptive behaviour disorders, post-traumatic stress disorders and panic disorders (Swendsen et al. 2010). In adolescents, ADHD and conduct disorder were strong predictors for later alcohol dependence at age 40 years (Knop et al. 2009). Major predictors for nicotine dependence include bipolar disorders, agoraphobia (Swendsen et al. 2010) and ADHD (Lee et al. 2011). Finally, problematic illicit drug use has been associated with most of the disruptive disorders and separation anxiety (Swendsen et al. 2010) as well as bipolar disorder and ADHD (Lee et al. 2011).

## 3.3 Cellular and molecular factors

The factors described here are drawn from genetics and neurobiology and describe the influence on harmful substance use and gambling of single determinants at the cellular and molecular level.

### 3.3.1 Biological vulnerabilities

Family, twin and adoption studies have been used to examine the heritability of addiction, with twin and adoption studies used to distinguish whether familial similarity is a result of environment or genetics. Heritability estimates describe, at a population level, the proportion of variability in a trait that can be attributed to genetic factors. Results from twin studies suggest that 50-70% of the variation in liability to alcohol dependence can be attributed to heritable factors, 34-78% of the variation in problematic cannabis use and 42-79% of the variation in problematic cocaine use (Agrawal and Lynskey 2008). Such wide ranging heritability statistics might illustrate uncertainty around the extent to which harmful substance use and gambling is heritable. The most recent adoption studies to date suggest environmental and genetic risk factors might interact, with environmental effects on drug abuse stronger in those with high genetic risk (Kendler et al. 2012).

Molecular genetic studies using modified animals have been used to examine and confirm partial genetic contributions to alcohol and drug abuse and, since the advent of human genome mapping, to test the role of different polymorphisms in addictive behaviours using genetically modified animals. Studies using genetically modified mice have found that mice lacking the dopamine and/or serotonin transporters show no preference for cocaine (Hall et al. 2004) and that under-expressed monoamine transporters, opioid receptors and monoamine receptors affect addiction to psychostimulant drugs (Sora et al. 2010). Transgenic mice that have had foreign genes introduced to their genetic material can be used to examine the impact on addictive behaviours of the over-expression of different single-nucleotide polymorphisms that encode neurotransmitter receptors or the influence of new genes on addictive behaviours (Koob 2006). For example, over-expression has been identified in the role of the dopamine transporter for the rewarding effects of cocaine (Donovan et al. 1999), in the serotoninergic receptor for the rewarding effects of alcohol (Bowers 2000) and in the nicotinic receptor for the effects of nicotine (Wilking et al. 2010).

Molecular genetic studies using human subjects have searched for DNA sequences that might contribute to individual variation in liability to develop an addiction. The principle genetic approaches used to identify variation in genetic markers are linkage and association. Linkage mapping searches for genetic markers that run the same way in affected families whilst association is a technique that aims to identify whether single-locus alleles or genotype frequencies differ between two groups of individuals (Ball 2008). Association techniques using candidate genes often have more power than linkage studies for identifying genes associated with addictive disorders as

such disorders are influenced by genes that influence multiple phenotypic traits and are usually of limited phenotypic effect. The two approaches are not mutually exclusive: genetic regions for exploration may be identified by linkage mapping and follow-up using association (Ball 2008). For example, the role of alcohol dehydrogenase was discovered using a linkage design and subsequently the aldehyde dehydrogenase alleles were identified using association techniques (Reich et al. 1998).

Epigenetic research studies changes in gene transcription without modifying underlying DNA sequences and has been used to explore drug-induced alterations and changes in gene expression (Maze and Nestler 2011;Renthal and Nestler 2008). Levels of histone acetylation are increased in mice exposed to acute or chronic cocaine consumption as well as other stimulant drugs (Kumar et al. 2005) suggesting that different levels of drug use can result in neural adaptations. Ribonucleic acids (RNAs) that are not translated into proteins may also play an important role in transcriptional regulation, epigenetic signalling, stress response and neural plasticity (Sartor et al. 2012). For example, micro-RNAs play a role in synaptic neuroplasticity in genetically modified mice (Edbauer et al. 2010) and evidence has been found for micro-RNA up- and down-regulation following cocaine, nicotine, alcohol and opioid use (Sartor, St Laurent, & Wahlestedt 2012).

Relatively few research studies have been conducted using human subjects because of the difficulties of epigenetic measurement in living individuals. The strongest evidence available finds a relationship between genetics and alcohol, nicotine and opiate dependence. Altered GABRA2 genes, which are a subunit of the chief inhibitory neurotransmitter in the central nervous system, have been linked to alcohol dependence (Ariza et al. 2012). The DRD2 gene that encodes the D2 dopamine receptor, which is a neurotransmitter expressed mainly in the striatum involved in the reward pathways of the brain, has also been linked to alcohol addiction (Ariza et al. 2012) and addiction vulnerability in general (Verdejo-Garcia et al. 2008). The role of the MOP-r gene which encodes μ-opioid receptor 1 in opiate and alcohol addiction has been reviewed by Kreek et al. (2012). When the MOP-r genes are bound biologically to active metabolites (e.g. morphine) the result is the release of dopamine leading to rewarding effects. Two single-nucleotide polymorphisms of the MOP-r gene have been associated with alcoholism and opiate dependence (Bart et al. 2004;Glatt et al. 2007). Smoking initiation, quantity and cessation may be influenced by a cluster of genes encoding subunits of the neuronal acetylcholine receptor that mediates fast signal transmission at synapses (Liu et al. 2010). Additionally, the CYP2A6 gene encodes a cytocrome that is involved in the oxidation of nicotine and cotinine, and alterations in this gene have been found to affect smoking quantity (Thorgeirsson et al. 2010). The genes identified are mainly related to either

the expression of proteins related to alcohol and nicotine metabolism or neurotransmitter reception.

Problem gambling shares genetic vulnerability factors with alcohol dependence, major depressive disorders and antisocial behaviours. The heritability of problem gambling is estimated at 50-60%, with genetic factors underlying the association between exposure to traumatic events and problem gambling (Lobo and Kennedy 2009). Reduced sensitivity of the reward system of the brain and other neurotransmitter dysfunctions may account for vulnerability to gambling problems. Genes for dopamine, serotonin and norepinephrine metabolism may influence problem gambling with individuals who inherit a number of these genes at increased risk of developing a one of number of impulsive, compulsive and addictive behaviours (Comings et al. 2001). Gender differences in the clinical manifestations of problem gambling may also have genetic influences given differences in the genetic contributions to problem gambling for men and women (Ibanez et al. 2003).

### 3.3.2 Compulsion

Neuroadaptations resulting from regular substance use might lead to a physical dependence on addictive substances that manifests as compulsion.

At a neurobiological and psychological level, individuals may engage in psychoactive substances to increase sensations including pleasure, sedation, pain relief, and to alter mood or thinking processes (World Health Organisation 2004). Humans have evolved natural mechanisms that reward behaviours useful for ensuring the continuation of the species, such as eating and drinking. Critical neuroadaptations may render the brain reward system hypersensitive to drugs and drug-associated stimuli (Robinson and Berridge 1993). Repeated drug use may result in neuroadaptations such as initiating a stress response via the hypothalamic pituitary axis system. The hypothalamic pituitary axis system is a feedback system that coordinates the activity of major peptide and catecholamine hormones, including dopamine. The hypothalamus synthesizes releasing hormones, which act on the pituitary, which evokes end-organ responses. This forms part of the brain's reward system for useful behaviours. Drugs such as cocaine and nicotine can result in an increase in hormones such as dopamine in the mesolimbic reward pathway of the brain, triggering the brain's reward system and reinforcing positive effects of drug use, potentially motivating further experimentation (Nestler 2005). As a result of regular drug use baseline dopamine (and other hormone) transmission may drop below normal levels resulting in dysphoric withdrawal symptoms when not taking the drug. In order to maintain homeostasis within the reward system of the brain and avoid the adverse state

that is a result of the down-regulation of hormone systems, individuals may feel compelled to continue their harmful drug use (Koob and Moal 1997). Prolonged heavy alcohol consumption may also induce changes in the neural circuits controlling motivational processes such as arousal and reward. Such changes affect systems including, among others, the dopamine, glutamate and serotonin, producing changes in sensitivity to alcohol's effects, for example tolerance. Following the discontinuation of use of alcohol a withdrawal state may follow and the individual remains susceptible to relapse evening after long periods of abstinence (Gilpin and Koob 2008).

Chronic drug use may interfere with several brain circuits leading to dysregulation through a cascade affect whereby one adaptation leads to another and so forth (Volkow et al. 2001;Volkow et al. 1993;Volkow et al. 2007). This can result in both impairment of the frontal cortex system, which plays a key role in executive functions such as decision making and delayed gratification, and in reductions in metabolism. These adaptations then drive harmful substance use as users seek to maintain homeostasis or avoid negative moods and withdrawal symptoms.

## 3.4 Multidisciplinary models of harmful substance use and gambling

The previous sections have introduced the range of individual determinants from across the scientific disciplines. Section 3.4 outlines multidisciplinary models of harmful substance use that draw together determinants from the range of disciplines to develop an understanding of how the factors affecting the transition to harmful substance use or gambling may interact. The four multidisciplinary models described here are the vulnerability-stress model, the complex vulnerability model, the behavioural learning model and dislocation theory.

### 3.4.1 Vulnerability-stress model and the complex vulnerability model

The vulnerability-stress model and complex vulnerability models emphasise the importance of the relationship between social and environmental factors on one hand, and psychological impairments and neurobiological differences on the other, for the development of problematic substance use.

The vulnerability-stress model is a general model for understanding the development and cessation of a broad range of mental disorders (Buhringer et al. 2008). Within the model, it is proposed that proximal and distal vulnerability factors could cumulatively lead to substance use, abuse or dependence. Distal vulnerabilities are innate or acquired dispositions such as gender, perinatal factors, adverse social events/conditions, and personality or neurobiological factors. Proximal

factors represent later event or characteristics such as life events and adverse social conditions, social support, stress coping and resilience, and internalising and externalising psychopathologies. Proximal and distal factors are so called because of their proximity to harmful drug use, with distal factors as early risk factors for initiation of substance use and proximal factors as later risk factors that influence the transition from intermittent or regular use to harmful substance use. Distal factors are assumed to be of greater importance for the first contact with psychotropic substances, making it hard to say no to experimentation with addictive behaviour, whilst progression into problematic use is influenced by proximal factors such as psychological impairments and individual neurobiological differences, such as mental disorders and personality traits (Le Moal and Koob 2003). This model draws together individual level characteristics and circumstances with sub-individual genetic and neurobiological vulnerabilities.

The complex vulnerability model (Iacono et al. 2008) emphasises the association between behavioural disinhibition, resulting from innate factors, environmental risks and possible childhood disruptive disorders and the development of early-onset substance use disorders. The early appearance of problem behaviours such as academic difficulties, substance use and antisocial behaviour may be influenced by the liability to behavioural disinhibition, childhood disruptive disorders and environmental risks, with problem behaviour potentially leading to an externalising psychopathology. The liability to behavioural disinhibition can originate from innate factors such as the personality traits of aggressiveness of impulsivity. Childhood disruptive disorders might include ADHD or conduct disorders and can be influenced by the liability to behavioural disinhibition and environmental risks such as the parent-child relationship, stressful and traumatic events and peer affiliations (Iacono et al. 2008). Harmful substance use or gambling might emerge as a consequence of an externalising psychopathology, in which problem behaviours are directed outwards towards other people, for example through disobedience, aggression and delinquency. Parts of the model have been confirmed for personality (Kotov, Gamez, Schmidt, & Watson 2010), childhood disruptive disorders (Lee et al. 2011) and early appearance of problem behaviours (Behrendt et al. 2011).

### 3.4.2 Behavioural learning model

The behaviour learning model (Buhringer 1998) identifies many risk factors for the development of problematic substance use and proposes a specific temporal ordering among the determinants, thus is differentiated from other models such as the vulnerability-stress model which only distinguish between proximal and distal risk factors. For example, there are several factors that might influence first substance use including the availability of a substance within a peer group, peer pressure and

expectation of positive advantages of use (Buhringer 1998). Behaviour may be driven by negative social or emotional situations, for example children might learn to escape from unpleasant situations by engaging in a particular behaviour. This first stage of initial consumption may lead on to regular or irregular usage, which may in turn result in positive or negative consequences at a pharmacological or emotional level that result from, for example, neuroadaptations. Frequent reinforcement may result in operant conditioning, a type of learning whereby behaviour is modified by its consequences, and/or substance related cue conditioning, where people who are addicted to drugs react to drug-related stimuli (Buhringer 1998).

Continued use may result in physical dependence as the body metabolism adapts to the substance and develops a biological necessity for it. If substance consumption is stopped at this point the user may experience unpleasant withdrawal symptoms, which can be prevented by consuming the substance again, resulting in maintenance of addictive behaviour. An important factor in continued substance use at this stage is the balance between positive consequences of substance use and failures in everyday life. Ordinary everyday life may become less and less important for problematic substance users, particularly if they already display behavioural deficits in different life domains, such as academic failure or relationship breakdown. Eventually the individual may be motivated solely by substance consumption to relieve withdrawal symptoms (Buhringer 1998).

### 3.4.3 Dislocation theory

Dislocation theory combines sociological and cultural explanations of addiction and is centred around the concept of psychosocial integration. Psychosocial integration in this context is conceptualised as interdependence, belonging, wholeness and social cohesion (Polyani 1944). The causes of dislocation may be diverse, including a natural disaster, debilitating accident, conflict or violence and economic change (Alexander 2008). For example, in relation to economic change, psychosocial integration may be undermined as societies alter over time as a result of the expansion of globalised free-market societies that seek to de-symbolise society to make people responsive to a continually changing economy. Through this loss of psychosocial integration individuals and groups in society become dislocated or alienated to a greater or lesser extent, as free markets require participants take the role of individual economic actors, unencumbered by family and friendship obligations, charitable feelings or clan loyalties (Alexander 2008). The lack of cultural and religious restraint in post-modern society generates an egocentric human species that is preoccupied with merchandise, difficulties of socialisation, hyperactivity and drug addiction (Dufour 2003).

Severely dislocated individuals may struggle to find psychosocial integration and therefore construct a lifestyle that substitutes it, for example by developing weak or unstable social relationships. Substitute lifestyles might be creative, for example a high-tech wizard or eccentric artist, but are often dangerous and clichéd, for example a youth gang member (Alexander 2008). Substitute lifestyles are often constructed on the margins or periphery or society and may centre on the use of drugs. The more barriers an individual experiences to psychosocial integration, the more likely they will be to lapse or relapse into harmful patterns of substance use.

Evidence in support of dislocation theory can be found across the world. Examples of first nation or aboriginal people who were dislocated and among whom alcoholism subsequently became endemic are widespread. Among people who have been allowed to resume their original cultural connections alcoholism problems have since decreased or disappeared. For example, Canadian Indians in the Vancouver area were disrupted and developed rampant alcohol problems following the introduction of, amongst others, the assimilation laws that forced them to learn only English at school. The reestablishment of previous traditions and ties at the community level has greatly decreased problems with addiction in this population (Alexander 2008). Another example of the impact of dislocation can be found in the history of the Hudson's Bay Company, Chartered by Charles II of England in 1670, that maintained forts and trading outposts throughout the Canadian north. The company included volunteers from London and the Orkney Island in the northern extreme of Scotland where the ships stopped on route from London. Men from Orkney were preferred as employees for reasons including that they were accustomed to life at sea and their characteristics of sobriety and obedience. In joining the Hudson's Bay Company these men severed their ties to traditional Orkney society, with contact from home once a year from a single ship that brought mail and supplies. After joining the Company, most of the men were never part of any society outside of the fur trade, gradually forgetting their ancestral roots. Alcoholism appears to have been rampant, with many accounts of smuggling brandy cases on ships, alcohol-related work accidents and alcohol-fuelled suicide. Among the Londoners it is plausible that the men could already have been alcoholic before joining the Company, but the men from Orkney were preferred employees because of their natural sobriety, suggesting that dislocation may have transformed them (Alexander 2008).

## 3.5 Determinants identified

From the disciplinary reviews, and the above synthesis of their findings, a list of determinants of harmful substance use and harmful gambling was extracted (see Table 1).

Table 1: Key determinants for harmful use categorised by discipline.

| Determinant | Anthropology & Sociology | Economics | Psychology | Genetics | Neurobiology |
|---|---|---|---|---|---|
| **Gender** | E.g. being male and increased risk of public disorder | E.g. alcohol price elasticities larger for women | E.g. male gender as risk factor, but depending on substance | E.g. different rates of alcohol and aldehyde dehydrogenases | |
| **Age** | E.g. age or life stage, youth | E.g. youth unemployment | E.g. early age of onset | | |
| **Ethnicity** | E.g. some groups at greater risk of arrest for cannabis use | | E.g. being Islamic is protective factor for SU in pregnancy | | |
| **Adaptation** | | | Impaired learning, e.g. reward learning, impaired cognitive control, e.g. response inhibition | Epigenetic adaptations (changes in gene transcription): histone acetylation & methylation, DNA methylation & non coding RNAs. Influence on neurobiological processes & structural changes in reward system | Change from homeostatic to allostatic states: down-regulation of dopamine system, alleviation of withdrawal system, initiation of stress response system, adaptations in metabolism |
| **Cognitions** | | | E.g. social image, social and escape reasons for drinking, descriptive norms & positive expectations | | |
| **Governance/ policy** | Availability, affordability, time, power & social relations | Availability, affordability, time | | | |
| **Macro-economic conditions** | Economic downturns, market promotion, industrialisation/ commodification/ commercialisation, income | Economic downturns, marketing (place, price, product, promotion), income, stress | | | |
| **Mental disorders** | | | E.g. major depression, social anxiety disorders, dysthymia, ADHD, phobias, & PTSD | | |

| Determinant | Anthropology & Sociology | Economics | Psychology | Genetics | Neurobiology |
|---|---|---|---|---|---|
| **Metabolism** | | | Tolerance and positive expectancies towards alcohol consumption | Variations in drug metabolism: e.g. availability of aldehyde dehydrogenases for alcohol and cytocrome P450 oxidase system for nicotine and opiates. | Adaptations in metabolism |
| **Neurocircuitry** | | | Psychopathology linked to specific brain alterations; specific neurocircuits to mediate the transition between occasional use to loss of behavioural control which defines harmful use/ addiction | Effects on neuroreceptor and transporter expression. | Impairment in pre-frontal cortex, decreased function of serotonin & opioid systems, cascade of neuroadaptations from ventral striatum to orbitofrontal cortex |
| **Personality traits** | | | E.g. impulsivity, psychoticism, novelty seeking, high negative emotionality & behavioural disinhibition | Sensation seeking, novelty seeking and impulsivity affected mainly by the expression of dopamine receptors: DRD2-4. | |
| **Socio-cultural norms** | Societal acceptance and public concern, lifestyle, historical and social transitions, religiosity | | Lack of willingness to oppose consumption (in self-regulation view of addiction), positive expectations, availability (in individual's environment) | | |
| **Socio-economic status** | Low socio-economic status, marginalisation | Unemployment, opportunity to socialise | Unemployment | | |
| **Substance use norms** | Heavy drinking as normative, user definitions of use, changes in use & social reactions to use | | Prior drug abuse (including heavy alcohol use and illicit drug abuse) | | |

# 4. DISCUSSION

In reframing addiction, ALICE-RAP aims to expand policy debates beyond a reductionist approach of focusing solely on addiction itself and, instead, facilitate discussion of broader aspects of addictive substance use and addictive behaviours. Addiction as a clinically defined disorder does not develop "overnight", but can be characterized as a developmental process with critical thresholds from low risk to risky and harmful use (including, but not limited to addiction as a mental disease). These processes are highly individual concerning duration, pattern and problem severity. A better understanding of individual and social risk and protective factors that modulate these developments is needed to improve public policy, prevention and early intervention. The primary aim of this report was to examine current evidence on the determinants of the transition to harmful substance use and harmful gambling, collating evidence from across several disciplines.

The commentary in this report goes beyond the rigid structure of a meta-analysis to interpret a disparate and diverse range of evidence that has rarely been brought together. Despite the variation between disciplines in the volume and quality of evidence on harmful outcomes of the use of different substances, for example, there is very little evidence around the impact of marketing strategies on harmful illicit drug use, it has been possible to identify a range of determinants of harmful addictive behaviour. The determinants drawn out from the different disciplines included within the synthesis are diverse, but there are also areas of overlap suggesting a scientific convergence on some of the key determinants of harmful substance use and gambling. Such areas of overlap are summarised in the following section.

## 4.1 Key findings on the determinants of harmful substance use and gambling

The harm experienced as a result of engagement in addictive behaviours varies between individuals and from one society to the next. Whilst some individuals can experiment with illicit drugs and then stop using without having experienced negative consequences or can drink in moderation, others develop harmful patterns of behaviour that are detrimental to their health, social or financial circumstances as well as wider society. In drawing together evidence from across scientific disciplines on the determinants of harmful substance use and gambling, this report has identified determinants that are associated with the experience of harm from addictive behaviours. These determinants fall in to three broad categories of influence on the transition to harmful behaviour: innate factors, our experiences, and the societies in which we live.

### 4.1.1 Innate factors

Individuals who experience harm from addictive substances may have innate vulnerabilities that promote continued use of a substance to and beyond the point at which harm is experienced. Gender is one such vulnerability, for example, men and women exhibit different responses to naltrexone treatment and different rates of alcohol and aldehyde dehydrogenases (Kim 2009). Additionally, inherited 'faulty' genes may affect brain systems. Genetic variations mainly affect the expression of proteins related to metabolism or neurotransmitter reception, including the reward system (affecting alcohol and illicit drug abuse) and the oxidation of cotinine and nicotine (affecting nicotine dependence). Finally, innate vulnerabilities might influence harmful substance use and gambling through mental disorders, such as ADHD and bi-polar disorder, which have genetic links and have been associated with the development of substance use disorders. Not all individuals who experience innate factors such as these develop problems with addictive behaviours and not all people who do engage in problematic substance use or gambling have these innate vulnerabilities, suggesting there are other determinants of harmful behaviour, which have been identified within this review as relating to our life experiences and the societies in which we live.

### 4.1.2 Our experiences

Our experiences throughout life can act as individual level determinants for harmful substance use and gambling. Unemployment is associated with alcohol and nicotine abuse and dependence, alcohol-related hospitalisations and mortality, and illicit drug use. Unemployment, low income and a low level of education are all risk factors for marginalisation and the experience of marginalisation can influence addictive behaviours through loss of psychosocial integration, which has been linked to substance abuse in dislocation theory. Similarly, early problem behaviour such as academic difficulties and antisocial behaviour is a determinant of harmful substance use and gambling that may indicate a risk of future marginalisation, e.g. from the workforce.

Harmful behaviour is associated with cognitions, for example social images, descriptive norms and positive expectations of behaviour. We may be better able to understand why some individuals participate in harmful substance use or gambling through exploring their cognitions: for example, a member of a social group that participates in illicit drug use will have different descriptive norms around drug taking behaviour and may have different expectations of that behaviour that someone who has no friends who use illicit drugs. Such cognitions are relevant for understanding why some individuals transition from risky to harmful behaviour. Mental disorders that are associated with harmful substance use may also be influenced by our experiences, for example, post-traumatic

stress disorder is a severe anxiety disorder that can develop after exposure to any event that results in psychological trauma, and has been linked to alcohol dependence (Swendsen et al. 2010). Additionally, mental disorders that have been identified as resulting from innate vulnerabilities, such as ADHD, may be triggered by environmental factors such as relationships with family or friends.

Previous substance abuse is a risk factor for future substance use and abuse, so individuals who have experienced problems with addictive behaviours in the past are more likely to experience behavioural problems again. Substance use can also result in drug induced alterations or neuroadaptations, for example histone acetylation increases after cocaine exposure and drug use may decrease baseline dopamine transmission leading to withdrawal symptoms in the absence of drugs. Thus, through drug use harmful substance users may induce alterations in brain chemistry that lead to physical dependency where the body then requires drugs to maintain homeostasis.

### 4.1.3 The societies in which we live

The society that provides the context in which individuals engage in addictive behaviours plays an important role in both harm minimisation and the generation of additional harms from substance use and gambling. Thus, in addition to inherent negative consequences of use, individuals may experience harm as a result of how society deals with substance misuse. Through this interdisciplinary review a number ways in which the society in which we live can impact on harm from substance use and gambling have been identified including: drinking cultures, harm minimisation policies, drug control policy and treatment systems, marginalisation and inequality, marketing, economic cycles and moral panics. These determinants can be categorised as political, economic or socio-cultural environmental influences on harmful behaviour.

The political environment includes the state, government and its institutions and legislations as well as stakeholders who influence the political system. Within the political environment determinants of harmful substance use and gambling include drug control policies (such as the criminalisation of substances), harm minimisation policies (such as the availability or absence of needle exchange programmes) and treatment systems (such as the availability of treatment for addictive behaviour). A range of political stakeholders including politicians, the media and healthcare professionals influence these broader determinants of harm from addictive behaviours. Policies around drug control, harm minimisation and drug treatment can all contribute to the marginalisation of problem substance users and gamblers, with political, economic and social marginalisation a strong determinant of engaging in harmful behaviours.

The economic environment includes a broad range of economic factors such as employment, income, productivity, and wealth, which shape our lives and provide opportunities for engaging in work and leisure activities. Determinants of harm within the economic environment include the economic system (such as free market societies which may result in dislocation), the stage of the economic cycle (such as an economic recession) and marketing (including price, place, product, promotion). The influence of these determinants varies by addictive behaviour, for example product and promotion are not associated with harmful alcohol use but both have been associated with harmful tobacco use and product with problem gambling.

Finally, the socio-cultural environment is the immediate physical and social setting in which people live as well as the culture in which they were educated and the people and institutions with whom they interact. Socio-cultural environmental determinants of harmful substance use and gambling include culture and moral panics. Evidence suggests that components of drinking culture such as the degree of ritualisation and integration of drinking within daily life and the extent to which individuals in a population drink to intoxication are determinants of harm from alcohol consumption. Epidemiological evidence supports that countries in which drinking to intoxication is more prevalent and drinking is separated from daily life have higher rates of harm from alcohol consumption. The cultural acceptability of behaving in a certain way influences both the prevalence of that behaviour and the associated harms. Individuals may also experience harm as a result of moral panics surrounding particular addictive behaviours, such as the moral panic surrounding crack cocaine use in the USA in the 1980s that resulted in a law enforcement crack down on users and a crisis mentality among the population. Moral panics can contribute to the marginalisation of problem substance users and gamblers, for example labelling certain behaviours as deviant can result in the development of subcultures, further exacerbating marginalisation and its associated harms.

### 4.1.4 Summary of the key determinants

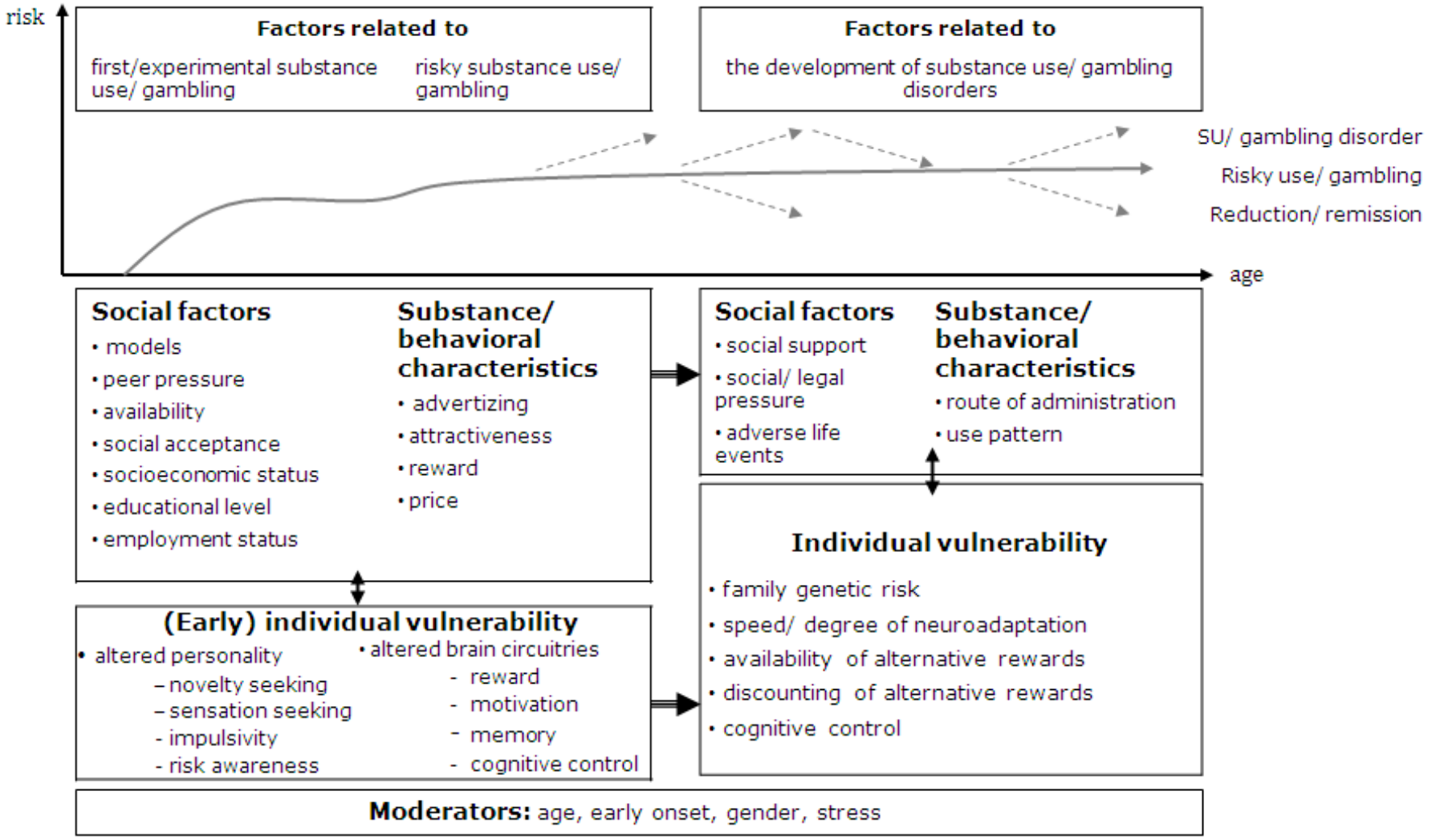
Section 4.1 has summarised the factors which were identified as important determinants of harm across multiple disciplines at three different level of influence: the innate, our environment and the societies in which we live. Whilst these categories are useful for outlining the different levels at which determinants of harmful substance use and gambling operate, they do not necessarily best illustrate the extent of overlap between determinants that are innate, experiential and environmental. Indeed, there is a substantial amount of interaction between some of these determinants: for example, drinking culture develops in the context of drug control policies, the

history of alcohol consumption in a given culture and the availability of alcohol products, whilst previous abuse of an illicit substance use may be influenced by the availability of illicit drugs, personality characteristics, drug control policies and cultural norms or attitudes towards drug use. Thus all three levels of influence are important for understanding the range of determinants of harmful substance use and gambling in European populations.

Multidisciplinary models of harmful substance use and gambling suggest that these individual determinants of harmful substance use and gambling may also interact in a cumulative way. For example, innate vulnerabilities may only lead to addictive behaviours in the context of environmental risks such as family conflict and academic failure. Given that the transition to harmful addictive behaviours is part of a progression of behaviour that begins with first experimentation, such multidisciplinary models have also sought to separate factors that influence any use from those that may determine progression to harmful use. For example LeMoal & Koob (2007) posit that distal factors may be of greater importance for the first contact with psychotropic substances whilst progression into problematic use is influenced by proximal factors such as psychological impairments and individual neurobiological differences. It is therefore important to move beyond knowledge of the determinants of harmful substance use and gambling to understand interactions between the various determinants.

As such, we suggest that certain social factors and characteristics of the substance, such as social acceptance, availability and price, are important in the transition to risky substance use and gambling, whilst others, such as adverse life events and route of administration are more important in the transition from risky to harmful substance use and harmful gambling (see Figure 1). Additionally, harmful substance use and gambling is influenced by individual vulnerabilities such as family genetic risk, speed and degree of neuroadaptations, and cognitive control to a greater extent than is the transition to risky substance use or gambling.

Figure 1: determinants of risky and harmful substance use and gambling



## 4.2 Limitations

Expert researchers from several disciplines appraised the most relevant literature and models available from their own discipline's perspective. Whilst this should ensure a representative view of each discipline and coverage of major works, it is possible that certain models or studies have been excluded and the expert consensus in choosing models for incorporation into the report has overlooked specific concepts. Resources also meant that relevant disciplines such as history, evolutionary biology and politics were not included in the interdisciplinary work. Were other experts from each discipline or from different disciplines recruited to the project it is likely that the nature of the evidence and the models and determinants selected would change. However, this limitation is inherent in the nature of any project of this kind, and only by means of increasing the number of transdisciplinary projects within this field to allow comparative studies will a full reflection of the field be allowed.

A key challenge related to this specific interdisciplinary work was the scarcity of research in many disciplines relating to our focus on the transition from risky to harmful substance use and gambling. Across most of the disciplines included here, research has traditionally focused on the determinants of harmful use versus no use or any use, rather than the determinants of the transition from risky use of harmful use. Given this limitation of the current evidence base, this report has focused on evidence for the transition from risky to harmful substance use and gambling where possible, highlighting areas in which the evidence focuses on the transition from any use to harm rather than risky use to harmful use.

## 4.3 Implications for research

A number of implications for research have been identified based upon this interdisciplinary review. Firstly, given the scarcity of previous research that has focused on the transition from risky to harmful substance use and gambling, future research could examine on this key stage on the continuum of drinking behaviour. For certain disciplines, for example genetics and neurobiology, it is not possible or extremely challenging to develop the evidence in this way; however, there may be scope within other disciplines, such as psychology, to further examine what determines whether or not risky behaviour transitions to harmful behaviour. Additionally, so much of the literature is about addiction or dependence, only one piece of the harmful substance use and gambling picture that we have considered here, making our definition of harm challenging to map on to the literature. Future research might consider exploring this broader concept of harmful substance use and gambling.

The volume and quality of evidence on the determinants of transition to harmful substance use varies by substance, with illicit drugs having far received far less attention in previous research than alcohol or nicotine. Whilst research on illicit drug use may be more challenging that research on licit substances, this gap in the evidence base could be addressed to improve our understanding of the determinants of the transition to harmful use of illegal substances. Similarly, evidence around harm to others is scarce in the literature; certain harms, such as second-hand smoke from cigarettes, have been well researched, whilst evidence around harm to others from illicit substance use is far less developed.

Another area we consider interesting for future research is cultural definitions of harmful use, addiction and dependence. For example, cultural definitions of addiction vary, so people drinking at different levels in different cultures might think differently about whether or not they're addicted. Our perspectives are an important element of our understanding of behaviour, for example a youth worker may see a situation differently to a policy maker. Acknowledging and embracing these different perspectives of harmful substance use and behaviour across research may improve our understanding of the determinants of different harmful behaviours.

Finally, further work could be developed to explore the ways in which diverse disciplines such as those involved in this project can better work together to enhance the evidence base around substance use and gambling. We continue to explore alternative approaches to blending research across our disciplines, in particular working with our anthropology and sociology partners to continuously improve the way that we engage with evidence from diverse fields within an overall project framework that is largely positivist in nature.

## 4.4 Implications for practice

Three key implications for practice have been identified based upon this multidisciplinary review. Firstly, the determinants of harmful substance use and gambling are often a combination of proximal and distal factors interacting to influence harmful behaviour. Individual vulnerability, such as family genetic risk and speed of neuroadaptations, has a larger role in the transition from risky to harmful substance use and gambling than the transition from use to risky use, but not the only role.

Secondly, the definition of harm has a social element so for some harms the harm depends on, for example, societal conditions, the legal status of a substance, or societal norms. Thus, drinking a given level of alcohol consumption may be relatively safe in certain contexts but harmful in another context. Some societies moderate the risk from substance use by developing harm minimisation policies, for example, providing clean needles to intravenous drug users to reduce the risk of transmitting blood borne viruses. We need recognition that harm reduction around drugs has been important in Europe; a number of European countries have made harm reduction choice, for example introducing methadone therapy to help prevent the spread of HIV/AIDS.

Finally, harms change over time in response to changes in patterns of use, public perceptions of use and policy. As an indicator of how the harm related to a given behaviour may change over time, in Denmark the laws around drink and drug driving have recently changed; there is now a zero tolerance policy for alcohol and people will lose their licence for 3 years if found with cannabis in their system. Prior to the zero tolerance policy for alcohol being introduced, individuals with a low level of alcohol consumption would not have been penalised but under the new law the same behaviour is illegal, thus illustrating how changes in policy can result in changes in harm from a given behaviour. The result of such a change in policy might be to reduce harm to others from substance use whilst increasing harm to the substance user. Thus, we should acknowledge that harmful substance use and gambling are not static concepts and that changes in policy have the potential to both increase and reduce harmful substance use and gambling.

## 4.5 Conclusions

This report has presented an integrated review of the determinants of harmful substance use and gambling. Such multidisciplinary syntheses as these are rare, but, valuable for understanding what drives harmful addictive behaviour. The findings of this research can be used to aid decision making for future funding and research to develop the multidisciplinary evidence base on the determinants of harmful substance use and gambling. It is hoped this knowledge can also be used to inform future policy making decisions across Europe and provide a basis for progress in treating outcomes related to harmful substance use and gambling.

Producing a coherent multidisciplinary synthesis on a topic such as harmful substance use and gambling is challenging given the diversity of scientific approaches to research across different disciplines. Some social sciences have strong positivist slants (e.g. economics) and others (e.g.

anthropology), whilst not rejecting objective measurement per se, focus on trying to provide further evidence to interact with such objective measurement. The underlying approaches which inform scientific disciplines contribute to decisions about the kind of data that is regarded as acceptable evidence and where scientific effort is focused; for example, the repeated experimentation and sophisticated well-defined measurement tools of natural science contrast sharply with the text-based description and recorded speech reflections collected in many sociological and anthropological studies. Whilst the determinants of harmful behaviour drawn from positivist research are often straightforward to list and statistical analyses allow them to be arranged into evidence-based models, the broad concepts discussed in constructivist research and their varying meanings and complex interconnections make them less easy to succinctly summarise or to arrange into easily accessible models in informative ways. This work has attempted to develop working practices and research methods which can address these challenges.

It is evident from the discussion around the key determinants of harmful substance use and gambling that only by examining the determinants of harm across the range of disciplines can we understand the diverse factors that influence the transition to harmful use. Individual determinants of harm have been identified at the cellular, individual and societal levels. Despite the variety of approaches to the subject in terms of different scientific perspectives and methodological techniques, there is a convergence of individual determinants across several subject areas (e.g. adaptations in body chemistry, marginalisation and availability). Multidisciplinary models of harmful substance use and gambling have also been identified that suggest individual determinants of harm interact in a cumulative way, with a range of innate and acquired risk factors influencing first contact which may ultimately, through a number of other determinants such as environmental, experiential and neurobiological factors, lead to the development of harmful behaviour. It is therefore important to move beyond knowledge of the determinants of harmful substance use and gambling to develop an understanding of interactions between the various determinants that operate at different levels. The greater understanding of harmful behaviours developed through interdisciplinary reviews such as this may help us to intervene earlier in behavioural trajectories to prevent individuals from progressing into harmful substance use or gambling.

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