



ALICE RAP WA3: WP7

Deliverable 7.2: Determinants of risky substance use and risky gambling: model and transition probabilities

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1. INTRODUCTION

This is the first of three reports outlining the development of a series of models that map the determinants of different stages of addictive behaviour. These reports run in parallel to the synthesis reports of the multidisciplinary group of Work Area 3 of ALICE-RAP. Work Area 3 (WA3) examines evidence surrounding the determinants of different stages of addiction, derived from expert reviews of the prevailing literature within a range of scientific disciplines. The disciplines that have contributed to this project are; anthropology, economics, genetics, neurobiology, public policy, psychology and sociology, with further input from experts on marketing, history, youth studies, cross-European perspectives and, finally, gambling as a behavioural addiction.

The project examines three stages of the addiction process; 1) the transition from use or no use to risky substance use and gambling, 2) the transition from risky use to harmful substance use and gambling, and 3) reductions in harmful substance use and gambling. This report focuses on the development of models concerned with the first stage: transition from none use or use to risky use of substances and gambling. The aim of the model presented here is to demonstrate topologically, the available evidence concerning the determinants of risky substance use and gambling. Use of alcohol, tobacco and illicit drugs are included, along with gambling as a representation of behavioural addictions. The models are intended for use by policy makers and researchers within the addiction field, both to guide policy decisions and highlight areas for future research. By bringing together research in a visual format from the wide range of disciplines that inform addiction studies, we have been able to identify knowledge gaps where research is needed to improve our current understanding and allow for the development of new multidisciplinary theories on substance use and gambling.

1.1 Model and Transition Probabilities - Aims and Approach

1.1.1 Model

The companion synthesis report integrated current expert opinion from a range of disciplines that inform addiction studies (Lees et al. 2012). Discrete determinants which influence an individual's progression from use to risky use of substances or gambling were identified across the breadth of disciplines which input into ALICE RAP and these are discussed further within the synthesis report. The aim of the work reported here was to provide a visual representation of the factors that influence complex behaviours such as substance use and gambling. Furthermore, we wished to explore how evidence from multiple disciplines, which differ



in their scientific approach, may be brought together into an accessible visual format. The initial inspiration for our work was that of the Foresight Obesity Systems Map (Foresight, 2007), and it was our intention to construct a map of addiction in a similar manner. We endeavoured to include key criteria within our logic model, in order to produce a model of use for both policy makers and addiction researchers. The criteria we aimed to include were:

- clear display of the different determinants identified across all disciplines
- demonstration of the relationships and dynamics between the different determinants
- inclusion of determinants with very different levels of abstraction
- clear display of previous multidisciplinary research
- highlighting determinants researched by multiple disciplines for possible future multidisciplinary collaborations.

Through mapping our work we are able to highlight knowledge gaps and potentially important interactions where multidisciplinary research may further our understanding. Thus, through the use of these models new interactions, relationships and theories may be postulated and researched. These models are intended for use by addiction researchers to aid in the process of hypothesis and theory development around risky use of addictive products. We also envisage policy makers engaging with these models to facilitate better design and targeting of future policy responses.

Following a brief conceptualisation of our understanding of risk, this report describes the process of development of the model including challenges in the presentation of data, the level of abstraction of certain determinants and the availability of evidence. Subsequently, we present the model and describe key findings such as determinants that vary by substance and those found in multiple disciplines. Finally, we discuss the limitations of our approach and implications for research and policy.

1.1.2 Transition probabilities for alcohol

As a companion to this report the probabilities of transitioning from one of the stages above to another have been calculated and are presented by Rehm and Probst (2013).

The literature-based approach taken within the synthesis reports permits the investigation of as many factors as desired. However, a problem with the listing of influential factors within reports is that the interaction of such factors is not clear, with different factors listed in different papers, and thus the relative importance of the different factors is open to subjective judgment. Moreover, even if systematic reviews are carried out and data quantitatively summarized in meta-analyses (e.g. Stroup et al. 2000), the numerical values given for different epidemiologic indicators are often inconsistent; incidence derived from one meta-



analysis may be inconsistent with prevalence estimates derived from another meta-analysis, or with the known case fatality or duration rates. The only remedy against this is joint analyses, and thus all these epidemiological indicators have to be analysed by substance to examine if they are consistently or inconsistently estimated. Various efforts to model epidemiological parameters have been undertaken, with most resulting in the development of software to consistently estimate key parameters of incidence, prevalence, duration, remission, and case-fatality in light of general population developments (<http://winthrop.ihme.washington.edu/>; see also Mathers et al. 2002; Barendregt et al. 2003). Such modern modelling approaches are not possible for many of the factors considered herein, as all the interactions between factors have to be integrated. Consistency requires that the number of included factors be limited, with concentration upon those factors considered most important.

The structure of our work schedules a successive analysis of each transition across all substances as well as gambling. Nevertheless, working with one dataset it is more beneficial to calculate and model transitions substance by substance. It might make sense theoretically to model the development of substance use disorders as a linear process that starts with use, progresses to risky use and ends with the substance use disorder, followed by cessation or the development of chronic problematic behaviour. However, empirically this linear process is not the only progression we observe, for example some people progress quickly from use to substance use disorders whilst others may skip risky use and move straight from use to harmful use. To statistically map reality requires the integration of those people that do not conform 100% to our theoretical model. Therefore we calculate not only the probability for one transition (use to risky use) but for all possible transitions (use to abstinence/use/risky use/harmful use). Modelling in this manner means that it is both more useful and more practical to work substance by substance instead of transition by transition.

This report presents a first attempt to model transition probabilities for the transition between different stages of alcohol use. As described above the use of the modelling approach requires the analysis of a discrete set of factors. Across multiple studies there are a few basic characteristics that have been shown to influence alcohol use in different stages of use. Age and gender have consistently been shown to be related to almost all stages of alcohol consumption. First of all, there still is a gender gap in alcohol consumption with men consuming more alcohol than women (World Health Organization, 2011). This gender gap is to a large extent influenced by social factors and life events. Risky patterns of alcohol use, such as binge drinking, have been shown to be related to gender as well as age (Wiltsack et al. 2000; Kuntsche et al. 2004). Furthermore, age and gender differences in the prevalence of alcohol use disorders have been shown (Rehm et al. 2009; Whiteford et al. 2013). Other studies show gender and age differences in the course of alcohol use disorders (Keyes et al. 2010) as well as in remission/cessation (Dawson et al. 2005; Bravo et al. 2013).



However, concerning age there has been a debate if it is the actual age that influences substance use behaviour or if it is rather the years since first use. These two aspects are hard to separate, as the long history of discussion in the different fields of age-period-cohort studies shows.

Another factor known to influence substance use behaviour is comorbidity, in particular psychological disorders. Comorbidity has been shown to impact alcohol use behaviour in a negative way (Regier et al. 1990). Compared to age and gender, comorbidity shows much more complex relations to substance use and substance use disorders: the effects differ by mental disease categories (e.g. internalizing vs. externalizing; distress vs. fear), substance of interest (alcohol, nicotine, illicit drugs etc.), and stage of substance use (use, risky use, harmful use) (Regier et al. 1990; Swendsen et al. 2010). Instead of looking at comorbidity as a risk factor preceding substance use behaviour, we could also look at lifetime comorbidity as a gross marker for vulnerability, which could be genetic or based on a certain environment or from an interaction of both.

Within this report on the determinants of risky use we aim to describe the course of alcohol consumption over time and to estimate the probabilities of transition from one stage of alcohol use to another. We will initially establish a simple model of use and test the feasibility of modelling, using only four factors: 1) stage of use (four categories: abstinence, use, risky use, harmful use) as an outcome variable, which of course in a final general population model would have to be supplemented by death, especially given the high relative risk of harmful use compared with the general population (Roerecke and Rehm, 2013), and three influencing factors: 2) age, 3) sex and 4) co-morbidity. Even though conceptually simple, this model will be more complicated than that which is currently used most often in epidemiological modelling, where only sex and age are controlled, and only two categories of outcome considered (abstinence, use disorders; Whiteford et al. 2013). Given this framework, we will attempt to estimate the transition probabilities between the different categories of outcome, which will allow us to track the course of a population over time.

1.3 Definition of risky substance use and risky gambling

Risk is not a straightforward concept. It can be inherent to a particular behaviour or may be attributable to social reactions to the behaviour. It is a relative concept with no fixed, quantitative threshold that experts agree can be used to distinguish risky from risk-free behaviour. Risky behaviour can be categorised into short term and long term risk. Short term risk, such as drink-driving or the use of unsterilized needles for injecting practice, is limited in duration with risk levels returning to baseline following the event. However, long-term risks, such as persistent cannabis use or drinking whilst pregnant, extend beyond the initial use of the drug with risk of harm typically accumulating over the duration of drug use. For an individual, short-term risks may be observed during a particular act, whereas long-term risks often rely on individual and societal



knowledge around risk. Both short and long term risks can pose harm to the individual, society, or both. Harms to society may be to individuals (e.g. through theft to fund drug purchases) or to society at large (e.g. through costs to public services such as the criminal justice or healthcare systems). For the purposes of this report the research team agreed the following definition of risky behaviour:

“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”

Within the above definition, the term ‘material predictive factors’ refers to the standards by which risk is judged to be of sufficient magnitude to be considered relevant by the research team and it should be noted that this may vary across disciplines.

1.3.1 Why do we engage in risky behaviours?

An understanding of why humans engage with risky activities and how societies make decisions in response to this is required to frame our descriptions of determinants of risky substance use and risky gambling.

Although addictive substances and behaviours are typically discussed, particularly in policy debates, in terms relating to their harmful aspects, clearly human engagement with them is not simply motivated by a desire to harm ourselves. Instead, these substances and behaviours serve several purposes for individuals that should not be overlooked in the development of policy and practice to reduce risky use. For example, psychoactive substances typically increase sensations of pleasure, sedation, pain relief or alertness, through altering the delicate balance of chemical messengers in the brain’s neuronal circuits (Di Chiara and Imperato, 1988). Additionally, the social values attached to engaging in such behaviours often encourage use; for example, alcoholic drinks are assigned strong cultural meanings and values including signifying fellowship and other ritual meanings when toasting, taking Holy Communion or celebrating sporting victory (Room, 1974; Room, 1976; Room, 2001; Skog, 1985). Equally sharing a cannabis joint is both an intoxicating experience and a social ritual. How, when, where, how much and how often engagement with addictive substances and behaviours occurs is likely to be determined by the complex interplay between both individual and the societal factors. To focus exclusively on any one aspect of these domains underplays the inextricably intertwined nature of individuals and societies.

1.3.2 Types of risk

Substance use and gambling have been documented extensively by epidemiologists as posing risks to the health of the individual (NIDA, 2013). The adverse effects of smoking and drinking alcohol have been



publicised widely through public health campaigns, with legislation and low risk guidelines implemented to inform the public and influence behaviour (e.g. drink-driving limits, minimum purchase ages) (NHMRC, 2009; Room, 2004a; Room, 2004b). Whilst there is less evidence describing the health impacts of consumption of most illicit substances, the overall health implications involved in taking such substances are largely believed to be negative and, despite some exceptions, are generally regarded as such by wider society. However, the concept of risk surrounding the engagement in such behaviours is a result of more than the inherent properties of the substances themselves. Legislation, historical precedent and popular culture surrounding the use of illicit substances adds a further layer of associated risk. Use of addictive substances can be heavily moralised, resulting in stigmatisation and marginalisation of users from society. Further, legislating against such activities can create extra risk through the imposition of punitive sanctions, the creation of problematic illicit markets and the withholding of protective measures (Rolles, 2010). These restrictions may vary between societies presenting sharp disconnects in what the risks 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. Similarly, high provision of needle exchanges may greatly reduce risk of blood-borne infection in some contexts but be only sporadically available in others. Consequently, any risk to health from a particular behaviour may be outweighed by societal-induced risks emerging from cultural or policy responses to the behaviour in question.

Identification of risky behaviour is further complicated where consumption may have potential beneficial effects at lower-levels but potential harmful effects at higher levels; for example, the apparent J-shaped relationship between level of alcohol consumption and risk of Ischaemic heart disease (Roerecke and Rehm, 2012). For other outcomes there may be threshold effects where risks only increase above certain levels and, in other cases, risks may increase sharply beginning with minimal levels of use.

These multiple understandings of risk in terms of substance use and gambling present challenges in identifying, categorising and understanding interactions between determinants, which often operate at numerous levels and describe different types of risk. Consequently, structuring a model around the determinants of the transition to risky substance use and gambling, given the complexity of interactions and level of operation, was challenging. However, in tackling this complexity we may further our understanding and highlight future effective strategies for both addiction research and policy interventions.



2. METHODS

2.1 Definition of a determinant

The term determinant may be perceived as inferring that a factor is predictive of behaviour, yet many of the disciplines involved in ALICE RAP conduct research that does not offer such direct extrapolative causal factors. Thus, it has been important for the progress of our multidisciplinary work, to define what we, as the ALICE RAP WA3, mean by the term determinant. During a WA3 meeting the expert panel agreed upon the following definition:

“A factor which alone or in combination acts to increase or decrease the likelihood of whether something happens or not. That influence can operate directly or through other factors. For this work package, determinants are used to describe the range of factors at the molecular and cellular, individual, and social environmental levels which, alone or together, increase the likelihood of risky use. To use the word determinant does not mean that we believe that any of these factors or combination of factors are deterministic in a causal manner.”

2.2 Methods for extracting determinants from the discipline reviews

The model includes each of the determinants identified from analysis of the individual discipline reports on the transition from no use or use to risky use of substances and gambling. These determinants were classified according to the substance to which they related, the age group to which they were applicable and the level of analysis at which they operated (cellular and molecular, individual or social and environmental). Following extraction of the determinants from the discipline reviews, an early version of the model was circulated to the research team to ensure that no determinants had been omitted from the model.

2.3 Process for the development of the model

The inspiration for the generation of a model for the determinants of different transition stages in the use of addictive substances was derived from the Foresight model of obesity (Foresight, 2007). The Foresight map outlines the interaction of all of the different factors at play in the development of obesity, with contributions from social and individual psychology, physiology and topics including food production and the environment in which food is marketed, purchased and consumed. The obesity system map is broken down into a series of derivative maps, each with a different focus such as the strength of evidence, and pathways that are relevant to policy approaches e.g. tax on food, improving food literacy and penalising parents



(Foresight, 2007). We set out to map the determinants of addiction, in a similar manner; however, early in the development of our model it became apparent that two key limitations would restrict our ability to replicate the obesity approach. Firstly, there is limited overlap between the different addiction disciplinary research fields which has resulted in a lack of available evidence to suggest relationships and interactions between determinants. Secondly, given this general lack of multidisciplinary, making judgements about the relative influence of the determinants from different disciplines was not possible. Given these challenges we examined alternative approach to the development of the model informed by two questions: 1) what could we say with the evidence available to use? 2) what techniques were available for visually displaying this information we had collated?

We developed and discussed four alternative conceptualisations of the model, each of which facilitated the process of model refinement, before settling on a final approach. The challenges we encountered during our development of different visual approaches is outlined in Table 1 and Figure 1 below. Subsequently, we present the key learning that informed the final model. The model that we present in Section 3 (p.20) illustrates our consensus on the optimal way of displaying current multidisciplinary evidence on the determinants of risky substance use and gambling.

2.4 Barriers to the development of testable models

Our ambition was to use the evidence generated to develop interdisciplinary testable models of addiction. These testable models would illustrate evidenced and hypothesised relationships between different determinants of addiction, providing a road-map for future addiction researchers. However, during the collation of evidence from the disciplines around the determinants of the transition to risky substance use and gambling, it became evident that developing such testable models would not be possible for two key reasons.

Firstly, there was an absence of evidence. After consideration of the available research pertaining to harmful substance use or gambling we concluded that there is a lack of evidence to support a comprehensive mapping of hypothesised relationships between determinants. Given that lack of supporting evidence, we felt that illustrating these relationships in the model may mislead researchers and policymakers regarding the importance of different determinants and the relationships between them.

Secondly, the diversity of disciplinary approaches to generating evidence around the factors influencing the transition to harmful substance use and gambling has hampered the process of drawing together evidence from across the disciplines. The determinants displayed in Figures 2-9 span a wide range of levels of



abstraction, from broad constructs such as institutions of social control to narrowly defined concepts such as features of neurocircuitry. To develop coherent testable models that incorporate such fundamentally different constructs requires the development and nurturing of multidisciplinary relationships that will enable scientific debate around the intricacies of such relationships. Whilst we have initiated such connections over the duration of this project, to produce models with greater interactions between determinants and which consider the range of research methods and types of data the disciplines use would require substantially more interaction between researchers.

Given these challenges, we have prioritised utility of the models and have focused on clarity and accessibility for policy makers. At the same time, we have sought to capture and display the full complexity of determinants contributed from all the research disciplines involved. The models that we present below do illustrate some of the relationships between determinants by the level of analysis at which they have been included in the model (e.g. molecular and cellular, individual or social environmental) and through the themes under which they have been grouped. Such broad research themes can be used as a guide for further research, highlighting areas for potential multidisciplinary collaboration which would enable to develop more detailed testable models in the future.

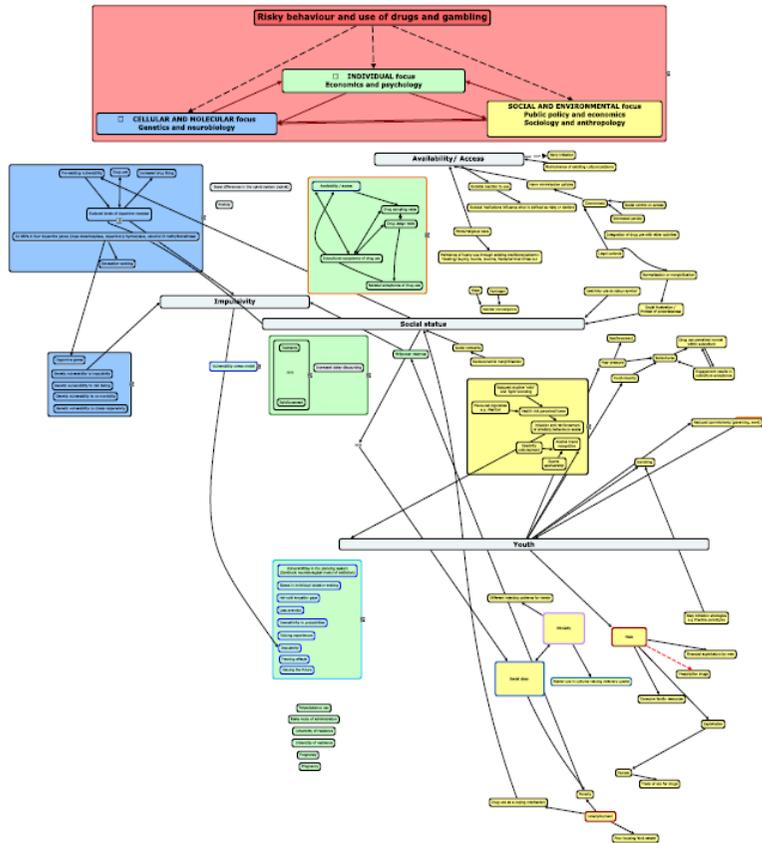


Model Variation	Description	Strengths	Limitations
1	A network-like model created using CMAP software that mapped the determinants from different disciplines and showed the relationships between determinants where evidence permitted.	<ul style="list-style-type: none"> • Illustrate different levels of abstraction of determinants. . • Easy to display links between determinants. • Contains search function and cross-referenced data. • Link determinants to evidence source through embedded HTML links. 	<ul style="list-style-type: none"> • Complexity hindered reading and created practical challenges for printing. • Lack of evidence for the relationships between many determinants and feedback loops.
2	A model that illustrates the different determinants that influence the transition to risky substance use and gambling at different stages of the life course (e.g. in utero, childhood, adolescence, and adulthood).	<ul style="list-style-type: none"> • An alternative approach that could be useful for policy makers targeting specific age groups. • Further understanding of the determinants that are most important at each age. 	<ul style="list-style-type: none"> • Not well-integrated with expert reviews informing model development. • Evidence is lacking around certain stages of the lifecourse. • Unclear whether to display data at life stage where a determinant was causal or where it took effect.
3	A model that illustrates through the use of concentric circles and vertical/ horizontal axes, the determinants, the number of disciplines in which they appear, whether an individual can effect the determinant, and if the determinant is substance specific.	<ul style="list-style-type: none"> • Concentric circles illustrate different levels of research focus. • Vertical /horizontal axes add. • Size of the determinant in the model used to illustrate the number of disciplines within which each determinant arose. 	<ul style="list-style-type: none"> • The size of the determinants could be confused with representing importance. • Begins to illustrate which determinants influence which substance, but doesn't make explicit to which addictions each determinant refers.
4	An earlier version of the final model that displayed the determinants in a hierarchy of concentric circles, illustrating multidisciplinary through colour.	<ul style="list-style-type: none"> • Clear illustration of multi versus single disciplinary through use of colour. • Concentric circles illustrate different levels of research focus. • Could cluster determinants based on theme. 	<ul style="list-style-type: none"> • Multidisciplinary determinants represented using multiple colours become difficult to read. • Clustering based on theme cluttered due to a lack of space within the concentric circles.

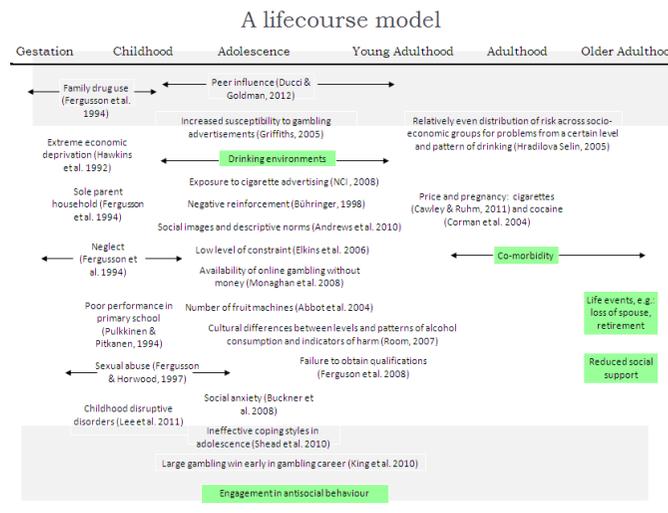


Figure 1: illustration of some of the previous models

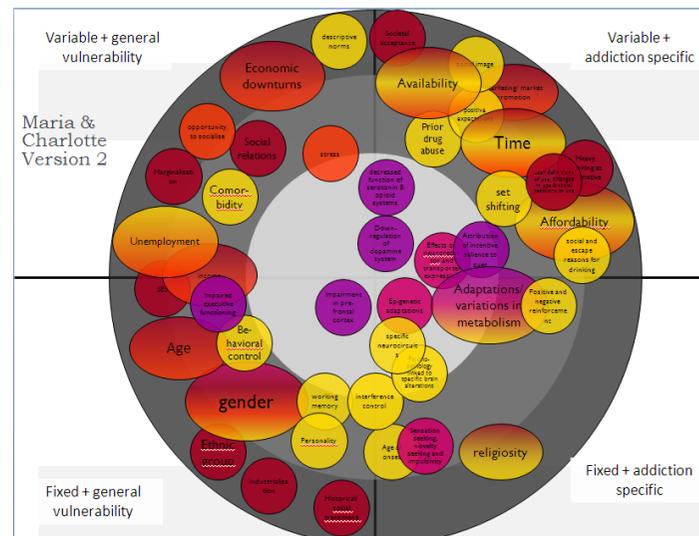
Model Variation 1: the CMAP model



Model Variation 2: the life course model



Model Variation 3: a concentric circle model





These themes were determined by the group to be the key themes, which are important for the transition to risky substance use and gambling. Individual determinants are listed within each theme, with determinants that were reported by two or more discipline represented in two or more themes, as relevant.

- 2) The second version of the model presents each determinant within an individual circle (Section 3.3, p.43). Determinants are coloured either light blue or dark red. The light blue colour indicates that just one discipline presented evidence on this determinant within their expert review, whilst the dark red colour represents that two or more disciplines presented research on this determinant. This model therefore serves to highlight those determinants where there is the potential for multidisciplinary research in the future.

In both versions of the model, we represent the three broad levels of analysis at which the different disciplines operate, as presented in the accompanying synthesis report on determinants of risky substance use and gambling (Lees et al. 2012). This serves both to direct the reader and allow easy groupings of determinants containing similar theories.

2.5.2 Determinants that vary by substance/gambling

Early versions of the model sought to display all the determinants relating to every substance from each discipline in one model. This approach resulted in a model that was very complex and difficult to understand. Given that the experts had collated substance specific information in the discipline reviews, we wanted to reflect this learning within the model. Additionally, it was apparent that some determinants only influenced the transition to risky use for some behaviours and so it was reductionist to remove the evidence around specific behaviours. The models that we present below thus comprise a set of maps, with each map representing one of the following substances or behaviours: alcohol, tobacco, cannabis, stimulants, opioids, club drugs and gambling. For the purposes of this report and the model presented herein our use of the term club drugs refers to ecstasy, alkyl nitrates, GHB, ketamine and also includes studies which in themselves use the category of club drugs. The final map identifies determinants that are influential across multiple substances and gambling, to illustrate determinants that are not behaviour specific (Section 3.2, p.40).

2.5.3 Level of abstraction

The different disciplines represented within this project conduct research at different levels of focus and analysis ranging from the societal to the molecular. Inevitably therefore, the determinants of risky substance use and gambling that we have identified vary in the level of abstraction to which



they refer, from the very specific (e.g. ALDH2) to greater theories and constructs (e.g. life course normative behaviours and institutions of social control). Further, different disciplines working at the same level of analysis may also identify determinants that differ in the level of their abstraction as a result of variations in their approach to research.

The WA3 team discussed this issue of the level of abstraction and decided to theme determinants (see Section 2.3.4 below) to facilitate the reader in understanding the model, given the varying levels of abstraction of the determinants. Thus, within a broad theme such an environment of use, the determinants include plastic glasses and sink estates, which vary greatly in their level of abstraction. However, this was the best available solution without losing much of the complexity of the evidence.

2.5.4 Clustering of determinants

To allow readers to interact with the models and quickly interpret results, key themes which were representative of the identified determinants were selected by the expert panel. Having identified key themes, experts allocated all of the determinants across each of the different substance models to the relevant theme domain, with determinants appearing in multiple domains where applicable. During this process there was much discussion around the suitability of certain themes and flexibility to modify themes where they did not accurately reflect individual determinants.

We clustered the identified determinants of risky substance use and gambling according to key themes rather than according to discipline as it was perceived by the panel that this would encourage engagement from non-specialist audiences and policy makers. Using themes facilitates the quick identification of key messages from our work and may help to target policy responses for different substances. Separating the determinants according to the different theme also aids understanding of the different levels of abstraction included within the models and simplifies and clarifies the model layout enabling readers to engage more easily with our work.

2.5.5 Multidisciplinary evidence

Identification of the determinants of risky substance use and gambling from each of the different disciplines contributing to this work resulted in a number of determinants being cited by multiple disciplines. These meeting points of the disciplines within the addiction field do not indicate that multidisciplinary research is already being carried out, rather that a number of disciplines have carried out research upon this topic within their separate disciplinary silos. We have developed a separate more to highlight these determinants (Section 3.3, p.43).



2.5.6 Evidencing the model

All determinants within the model are derived from discipline specific reports contributed by the discipline experts. These represent the evidence-based literature resulting from the different disciplines within the field of addiction studies, and are outlined within the companion synthesis report (Lees et al. 2012). We have not included the citation for each determinant within the model because it was perceived that this would make the model too cluttered and difficult to read. However, the evidence is presented within the D7.1 synthesis report and the references for the evidence are included at the end of this report.

2.6 Model validation

The scientific disciplines that contribute to ALICE-RAP arise from different epistemological traditions, which prioritise different forms of evidence. This evidence is challenging to combine in work such as this, and so opportunities to bring together discipline experts through teleconferences and face-to-face meetings have been important. Such sessions enable us to identify issues and work together to find solutions to emerging problems.

During the development of the final model, we engaged frequently with discipline experts. Experts were consulted regarding which determinants were included and excluded from the model at an early stage. Early versions of the model were circulated to all discipline experts for comment. The science writer subsequently held a teleconference with each of the disciplines to discuss the models and gather feedback. This round of feedback was highly informative, stimulating discussion around the advantages and limitations of different aspects of the models presented. In November 2013 the Steering Group (Gerhard Bühringer, Anne Lingford-Hughes, Petra Meir, John Holmes, Lucy Gell, Jane McLeod and Maria Neumann) met in the UK to discuss this feedback and share ideas on how to further develop the model.

In addition to consultation with the research group members during the development stages of the model, we presented a later version of the model to team members for validation at a meeting in Manchester in December 2013. This meeting involved experts from the following disciplines: sociology, anthropology, public policy, cross-European studies, psychology, neurobiology, genetics and gambling. At the meeting the panel of disciplinary experts developed key themes for each of the levels of analysis, and assigned each of the determinants to these themed domains within the



models. Decisions, based upon expert consensus opinion, were made as to whether determinants should be included, excluded (as they were represented more clearly by an alternative determinant within the models), renamed for clarification, and to which themed domain they should be assigned.

Throughout the process of model development therefore, there have been many discussions between members of the ALCIE RAP WA3 team. This process of progressing our work by circulating ideas for discussion and then meeting to provide feedback has been very informative and has greatly shaped the output of our work. In particular, where individuals felt strongly about how we should present data in a different way or target our model differently for the audience, this triggered challenging discussions between team members around how best to present the wealth of data we have collated over the past two years. These discussions have substantially influenced the final models we present in this report.

2.7 Calculation of transition probabilities

We initially identified a large dataset from one European member country, where transition probabilities as described above could be modelled (criteria for selection: large sample size, representativeness for general population, young age of participants, as many of the transitions to first use in Europe happen early in life (Kuntsche et al. 2004; Pitkänen et al. 2005), cohort design with as many follow-up points as possible). We have additionally attempted to cross-validate these results with similar analyses in the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; Chen et al. 2004).

2.7.1 EDSP: Dataset description

We used a German sample from a prospective-longitudinal study called the 'Early Developmental Stages of Psychopathology Study' (EDSP) as a database. The study aimed to investigate and describe the course of substance use and related disorders in youth and early adulthood. The design is described in detail elsewhere (Wittchen et al. 1998; Lieb et al. 2000). The study consists of one baseline assessment in 1995 (T0) and three follow-ups. Since the first follow-up comprised only a subsample, we used the second and third follow-up that took place in 1998/1999 (T2) and 2003 to 2005 (T3), respectively.

In 1994 the randomized sample was drawn from the population register of Munich and surrounding areas. Age groups 14-15, 16-21, and 22-24 were sampled in a ratio 4:2:1. 71% of the 4,263 persons



initially drawn completed the assessment. The resulting sample consists of 3,021 persons (49.3% women and 50.7% men) with German citizenship that were 14 to 24 years of age at baseline. Of this baseline sample 36.2% went to school and 26.4% went to university. Another 19.7% had a job at that point of time and 1.1% were unemployed (Lieb et al. 2000). The majority of the sample were still living with their parents (62.4%) and only a few were married (3.4%). The large majority of participants were part of the middle or upper socioeconomic strata (87.4%). This conforms with socio-demographic features of the region (Lieb et al. 2000). Response rates of T2 and T3 are 84% and 73% of baseline participants, respectively (Behrendt et al. 2008). At T2 only 12.8% were still attending school and 36.2% were employed. The proportion of persons living with their parents decreased to 40.2%, whilst 7.8% were married (Lieb et al. 2000).

Data were assessed using different questionnaires as well as the Computer-Assisted Personal Interview version of the Munich-Composite International Diagnostic Interview (M-CIDI; Wittchen and Pfister, 1997). Validity and reliability of the M-CIDI have been investigated and shown to be satisfactory (Lachner et al. 1998; Reed et al. 1998). The M-CIDI assesses information about symptoms, syndromes and diagnosis of 48 different mental disorders, as well as information on their onset, duration, and severity in a fully standardized manner. Both, lifetime and 12-month related questions were asked. The interview section assessing information on alcohol use and alcohol use disorders was only accomplished when the participant reported at least 13 drinking occasions in the past year. Information on quantity and frequency of present alcohol consumption, age of onset and offset were assessed, followed by questions concerning abuse and dependence.

In most cases the interview was carried out by psychologists during their psychotherapy training following the completion of two weeks interview training and several exercise interviews. The participants or their parents gave consent. Most interviews were accomplished at the participant's home.

2.7.2 Operationalisation: Use, risky use, harmful use, and cessation

In order to calculate transition probabilities we had to work with precise operationalisations instead of broad theoretical concepts. For that purpose we had to modify and in some way reduce the working definitions of WA3. Just like the consequences of alcohol use vary from a headache to death from alcoholic liver cirrhosis, definitions of risky or harmful consumption vary considerably. When one considers riskiness of drinking there are generally three dimensions of use: quality, quantity and pattern of use (Rehm et al. 2010). Since quality of alcohol is less important in the European context



due to strict control of alcoholic beverage by state controls and a relatively low proportion of unrecorded consumption (Rehm et al. 2010), we decided to use mean daily consumption as well as frequency of binge drinking for our operationalisations.

The operationalisations we applied for calculating transition probabilities differ from the working definitions used in WA3 in the following respects:

First of all, we focused on concrete features of drinking behaviour: average daily consumption, binge drinking occasions and alcohol use disorders. Of course one time use in a certain setting can be associated with (an elevated risky for) mortality (e.g. drunk driving), but we do not see how this behaviour would conceptually fit into a model aimed at the representation of systematic changes over time in the drinking behaviour of certain subgroups. Therefore, the drinking situation was not part of our concept. Second, we did not look at harm to others but at harm and risk to the drinking person itself. Harm and risk were mainly defined with respect to health consequences and mortality. Research has shown that mean daily consumption is clearly linked to increased mortality and morbidity of the drinking person (Di Castelnuovo et al. 2006; Rehm et al. 2010), and reduction in heavy use is related to a reduced mortality risk (Rehm and Roerecke, 2013). Last, we did not include any kind of social or financial harm. However, these kinds of consequences are known to be related to the level of use (Rehm et al. 2013).

Since the calculated transition probabilities depend upon the operationalisations we include, we decided to construct two sets of operationalisations that would enable us to compare the resulting transition probabilities. Referring to the on-going debate about our concepts of substance use disorders (Rehm et al. 2013) we decided to implement two versions of operationalization for harmful use: one that included alcohol use disorders only and one that included harmful patterns of use as shown in Table 2. Abstinence was in all cases defined as 12 or less drinking occasions in the past year and use was defined as at least 13 drinking occasions in the past year.

The main differences between the two versions are that version A uses lower limits for risky use and defines harmful use by alcohol use disorders, only. Version B is more strictly oriented to the definitions of the WHO by applying the commonly known thresholds for harmful use of 40 and 60g of pure alcohol per day for women and men, respectively (World Health Organization, 2001). All calculations were performed for both versions in order to compare results.



Table 2: Operationalisations for risky use and harmful use, Versions A and B.

Risky use	Women	<u>Mean daily consumption:</u> At least 15 g per day <u>Binge drinking:</u> At least 40 g per occasion 1-3 times per week	<u>Mean daily consumption:</u> 20 to 39 g per day <u>Binge drinking:</u> At least 40 g per occasion 1-3 times per week
	Men	<u>Mean daily consumption:</u> At least 25 g per day <u>Binge drinking:</u> At least 50 g per occasion 1-3 times per week	<u>Mean daily consumption:</u> 30 to 59 g per day <u>Binge drinking:</u> At least 50 g per occasion 1-3 times per week
Harmful use	Women	<u>Substance use disorder:</u> any alcohol use disorder	<u>Mean daily consumption:</u> At least 40 g per day <u>Binge drinking:</u> At least 40 g per occasion at least 4-5 times <u>Substance use disorder:</u> any alcohol use disorder
	Men	<u>Substance use disorder:</u> any alcohol use disorder	<u>Mean daily consumption:</u> At least 60 g per day <u>Binge drinking:</u> At least 50 g per occasion at least 4-5 times <u>Substance use disorder:</u> any alcohol use disorder

2.7.3 Operationalisation of age, gender, and comorbidity

In order to have sufficient data for all calculations, we had to focus on major risk factors to include in the model. For reasons described above we decided on gender, age, and comorbidity. Age was split into three groups: 14-17, 18-22, and 23-28. This grouping was done according to practical considerations on the one hand. On the other hand in Germany and most European countries the minimum legal drinking age is 18 years, which is relevant not least for the legal aspects of alcohol consumption. In order to calculate transition probabilities for all these age groups we had to work with the baseline as well as the two follow-ups mentioned above. The first two age groups refer to ages at baseline followed up to T2. The last group refers to ages at T2 followed up to T3. This means that the transitions for ages 23-28 go back to the same individuals as the transitions for the first two age groups. Comorbidity was defined as lifetime comorbidity of any other mental disorder (another substance dependence, an affective disorder, an anxiety disorder, an eating disorder, or a psychotic disorder (assessed only at T2 and T3)), diagnosed in the M-CIDI.

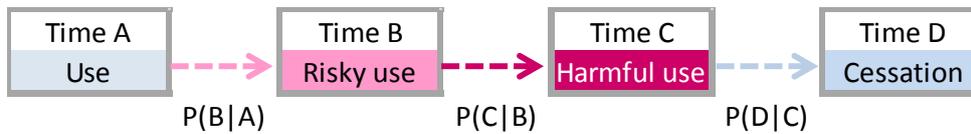


2.7.4 Statistical analysis

2.7.4.1 Calculation of transition probabilities

In the first instance, conditional probabilities to shift from one status at time A to another status at time B were calculated. For example, the probability of fulfilling the criteria for harmful use at time C when one was classified as a risky user at time B (see **¡Error! No se encuentra el origen de la referencia.**).

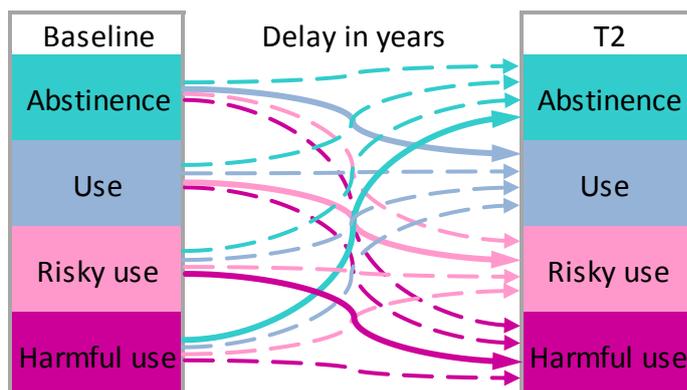
Figure 2: Basic model applied in first calculations



This model does not reflect the transitions of major interest in WA3, but it does not reflect reality to a satisfactory degree. The model in Figure 2 does not take into account that only a fraction of people do conform to the theoretical model of progression from use to risky use to harmful use and so on. Also, the delay of three to four years between follow-up makes it impossible to follow each person as closely as is desirable. Even if a person passed through a phase of risky use between use and harmful use, it is possible to miss that phase somewhere in the delay of several years.

Two things changed in the second step in order to depict the on-going processes entirely and more precisely: abstinence was included in the model and each possible transition was calculated separately as shown in the model in Figure 3. Transition probabilities were calculated for each subgroup (2 genders x 2 values of comorbidity x 3 age groups). The twelve resulting groups each contained the four patterns of use, leading to twelve transitions to another category of use to be

Figure 1: Transition model applied in final calculations.



calculated in each group. Of course in each subgroup a fraction of individuals stayed within one category of use from baseline to T2 (or T2 to T3, respectively). The transition probability is the probability of a person being in use category B at time 2 given he/she



was in use category A at time 1. In other words it is the number of individuals that switched from category A at time 1 to category B at time 2, divided by the total number of individuals that were in category A at time 1. Considering the multitude of transitions combined with partially small N in each group, we decided to refrain from calculating logistic regressions. All transition probabilities were weighted in order to account for age-stratification in sampling as well as age, gender, and regional differences in response rates at baseline. No measurement errors were taken into account and no confidence intervals were calculated. This work is essential in future analyses. All calculations were performed using STATA 12.

2.7.4.2 From transition probability to annual rate

The calculated transition probabilities depend on the delay between the two times of assessment. Logically the number of individuals (and thereby the transition probability) switching from one consumption category to another is larger when we observe individuals for several years instead of just a few months. We consequently broke down the calculated transition probabilities to annual rates with respect to the group-specific delay between the assessments. We calculated rates per year in Excel based on this formula:

$$\text{Rate per year} = \left(\sqrt[n]{\frac{P(B|A)}{100} + 1} \right) * 100$$

n= Group specific delay in years

P(B|A) = Calculated transition probability in %

2.7.4.3 Simulation

Based on those annual rates we started simulating the course of prevalence over youth and young adulthood (age 14 to 30) for 100,000 fictitious individuals in each of the four groups: females with no comorbidity, females with comorbidity, males with no comorbidity, and males with comorbidity. We took prevalence for use and abstinence from the German subsample in the ESPAP report (Hibell et al. 2012) as starting values at age 13 within our model. We applied the calculated annual rates in the following manner: for each consumption-pattern it was calculated how many individuals within one consumption group changed to another consumption group and how many joined the respective consumption group different consumption groups within one year. For example in order to calculate the number of risky drinkers in year X, we took the number of risky drinkers in the preceding year X-



1 and subtracted the number of people switching to abstinence (annual transition probability from risky use to abstinence multiplied by the number risky drinkers in year X-1), the people switching to use, and those switching to harmful use. Then we added the people that switched into risky patterns of use from other patterns of use in the preceding year (annual transition probability from abstinence to risky use multiplied with the number of abstinent people in year X-1 and so on). The results were then used to calculate the simulated N in the next year and so forth. For each age group the respective annual transition rates were used, leading to four gender- and comorbidity-specific models, each containing transition probabilities for three different age groups. These simulations were calculated using Excel.

2.7.4.4 Smoothing

To come up with smoothing, we tried to discover patterns in transition probabilities in two ways:

- Differences between transition probabilities between sex and age groups were tested for significance.
- A minimal effect size was used for determining whether transition probabilities were meaningfully different. This was done by expert interviews, and the limit was determined as +/- 30%.

Based on these criteria, several clusters of transition probabilities were estimated to be the same, with the transition probabilities of the two older age groups largely being able to be combined into one probability (for results see below).

3. RESULTS

3.1 The model

A series of models displaying the determinants identified from each of the different disciplines were constructed for the addictive behaviours addressed by our working group; alcohol, tobacco, cannabis, stimulants, opioids, club drugs and gambling. The substance to which each map refers appears in the top left hand corner of the map (see Figure 4, p. Figure 4: the alcohol model

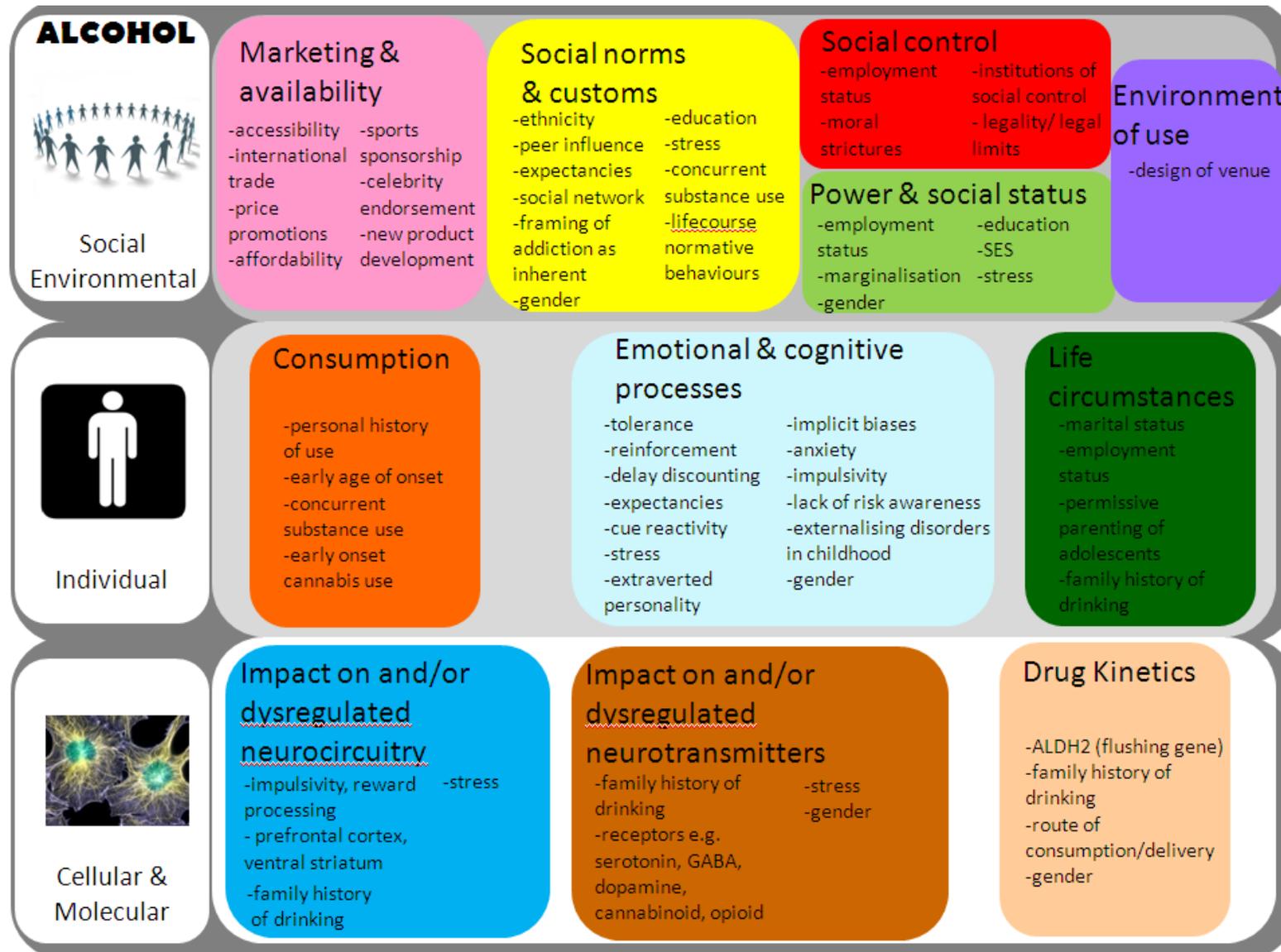
27). Within these substance-specific models the determinants are grouped by level of analysis (molecular and cellular, individual, and social environmental), with each of the three levels of focus



distinguished by three layers that darken in colour from the bottom to the top. The base of this model represents the molecular and



Figure 4: the alcohol model





cellular focus, the middle layer represents the individual focus, and the top, darkest layer represents the influence of social and environmental factors (see Figure 4).

Within the model, determinants are grouped according to different expert-agreed themes within each level of analysis. At the molecular and cellular level the themes identified are 'Impact on and/or Dysregulated Neurocircuitry', 'Impact on and/or Dysregulated Neurotransmitters' and 'Drug Kinetics'. At the individual level the themes identified are 'Consumption', 'Emotional and Cognitive Processes' and 'Life Circumstances'. At the social environmental level of analysis the themes identified are 'Marketing and Availability', 'Social Norms and Customs', 'Social Control', 'Power and Social Status' and 'Environment of Use'. Those determinants which influence multiple themes appear once in each of the themes where they exert effect e.g. stress is present within the themes of 'Social norms and customs', 'Power and social status', 'Emotional and cognitive processes', 'Impact on and/or dysregulated neurotransmitters' and 'Drug kinetics'.

We now present each of the substance specific models followed by a brief description of the meaning and content of each expert-agreed theme.



Figure 5: the tobacco model

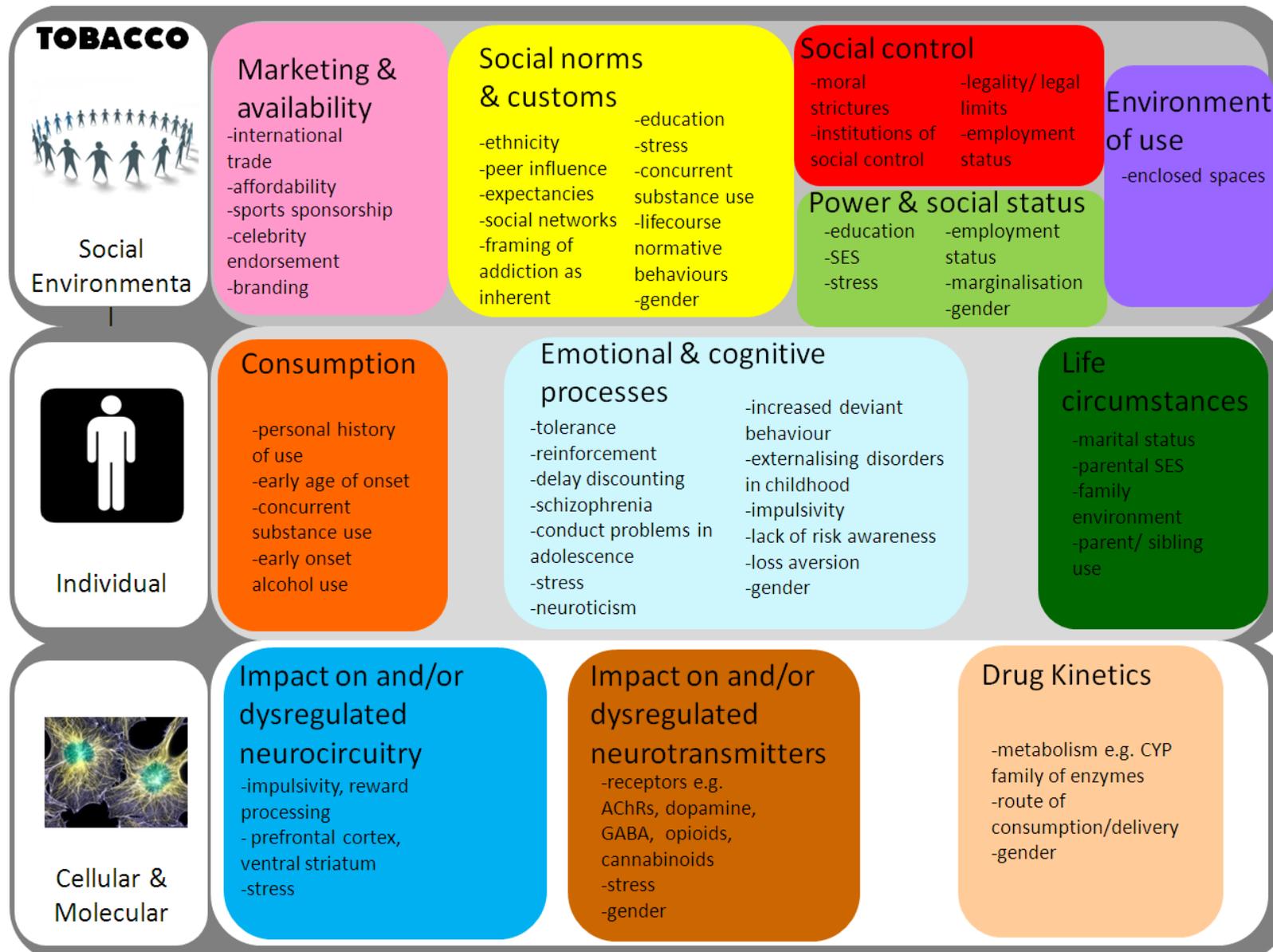




Figure 6: the cannabis model

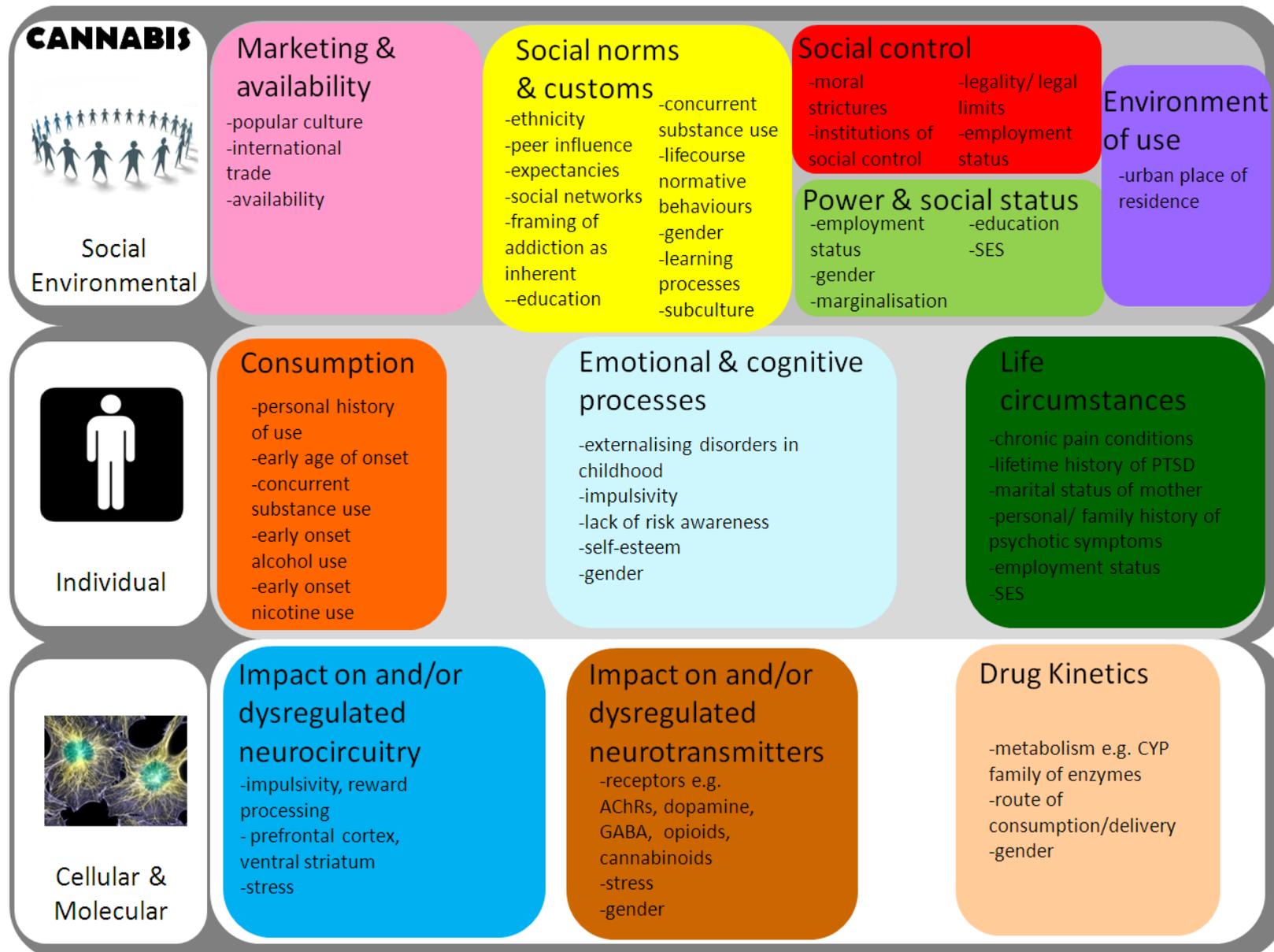




Figure 7: the stimulants model

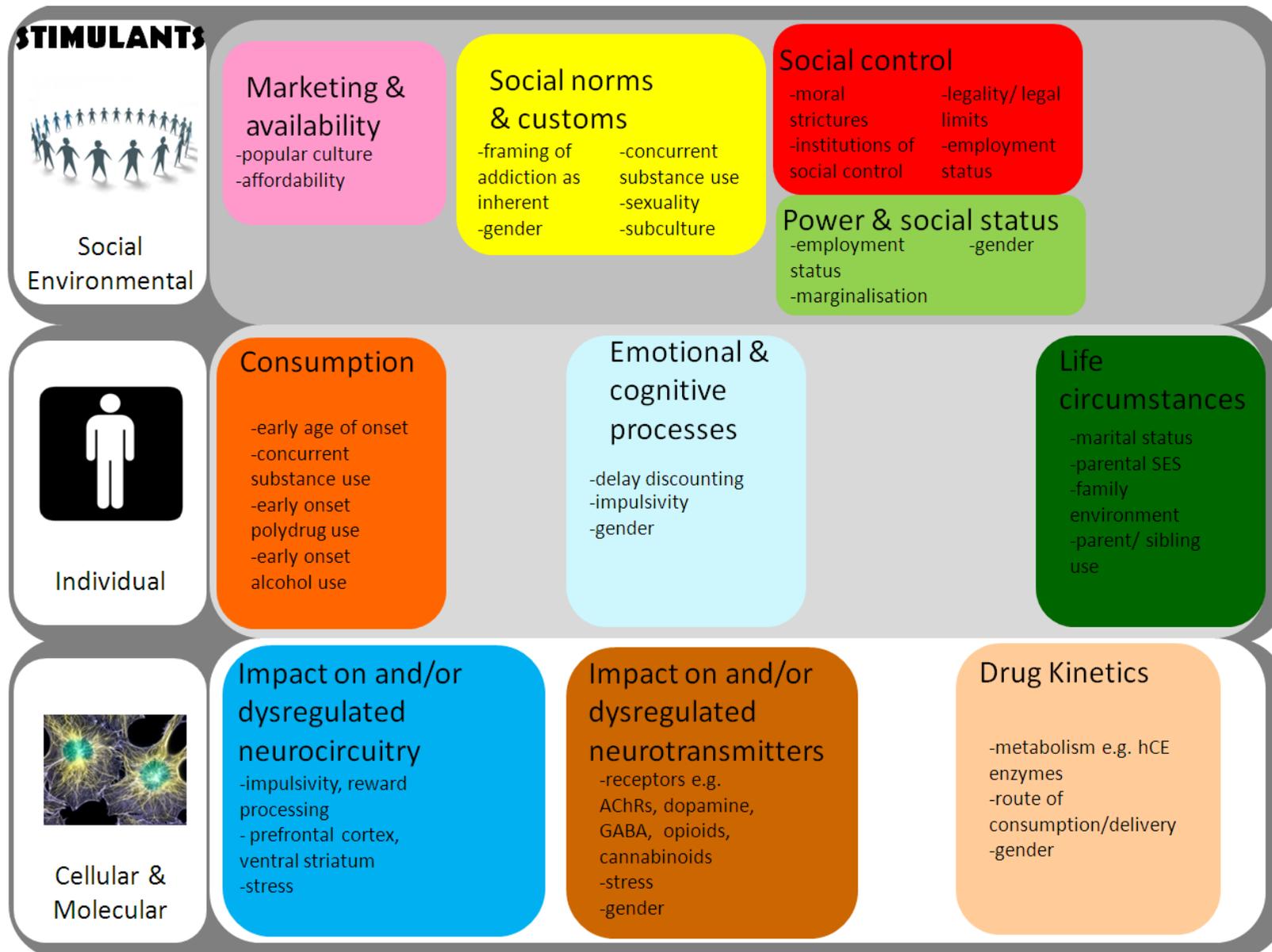




Figure 8: the opioids model

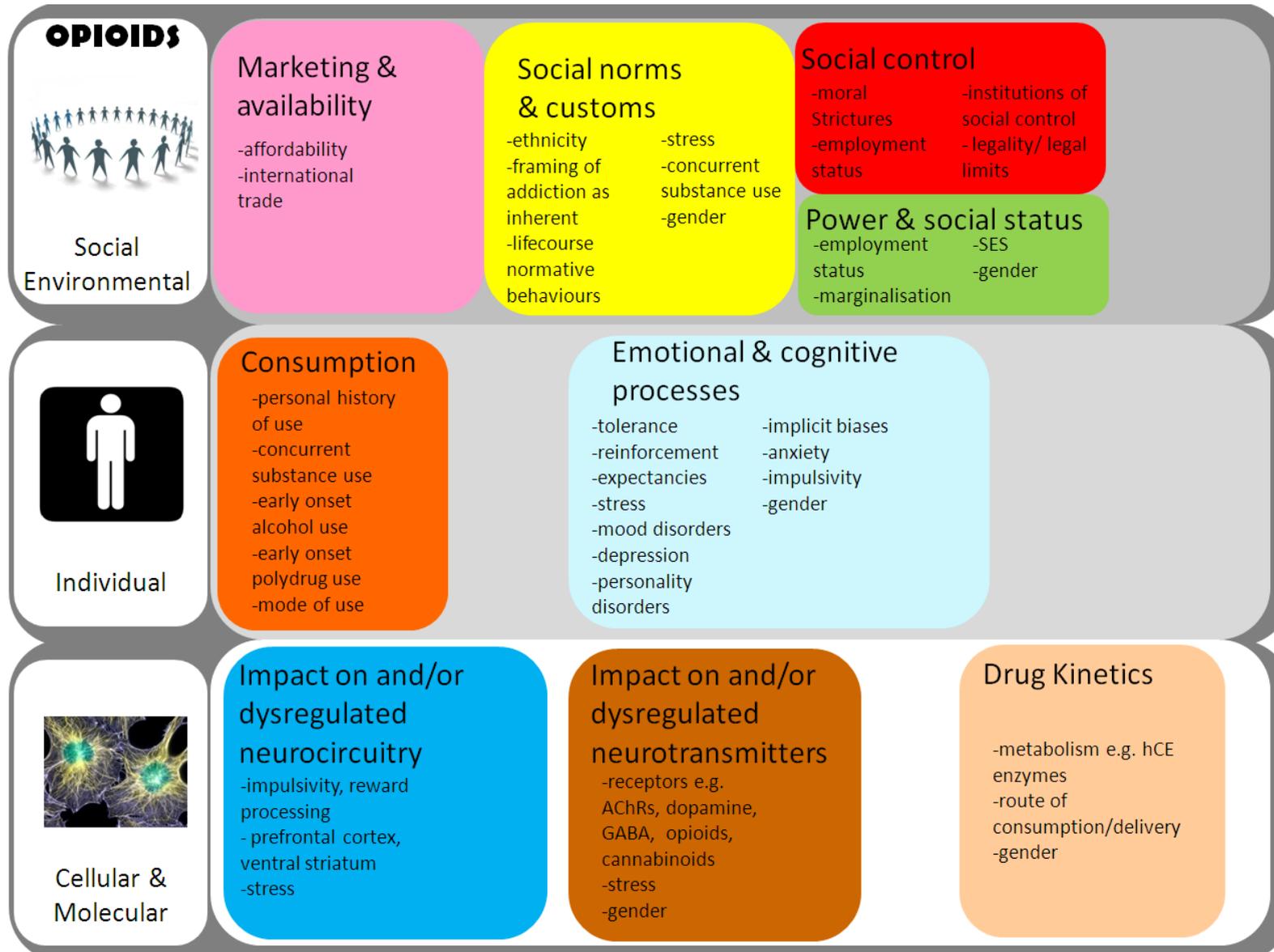




Figure 9: the 'club drugs' model

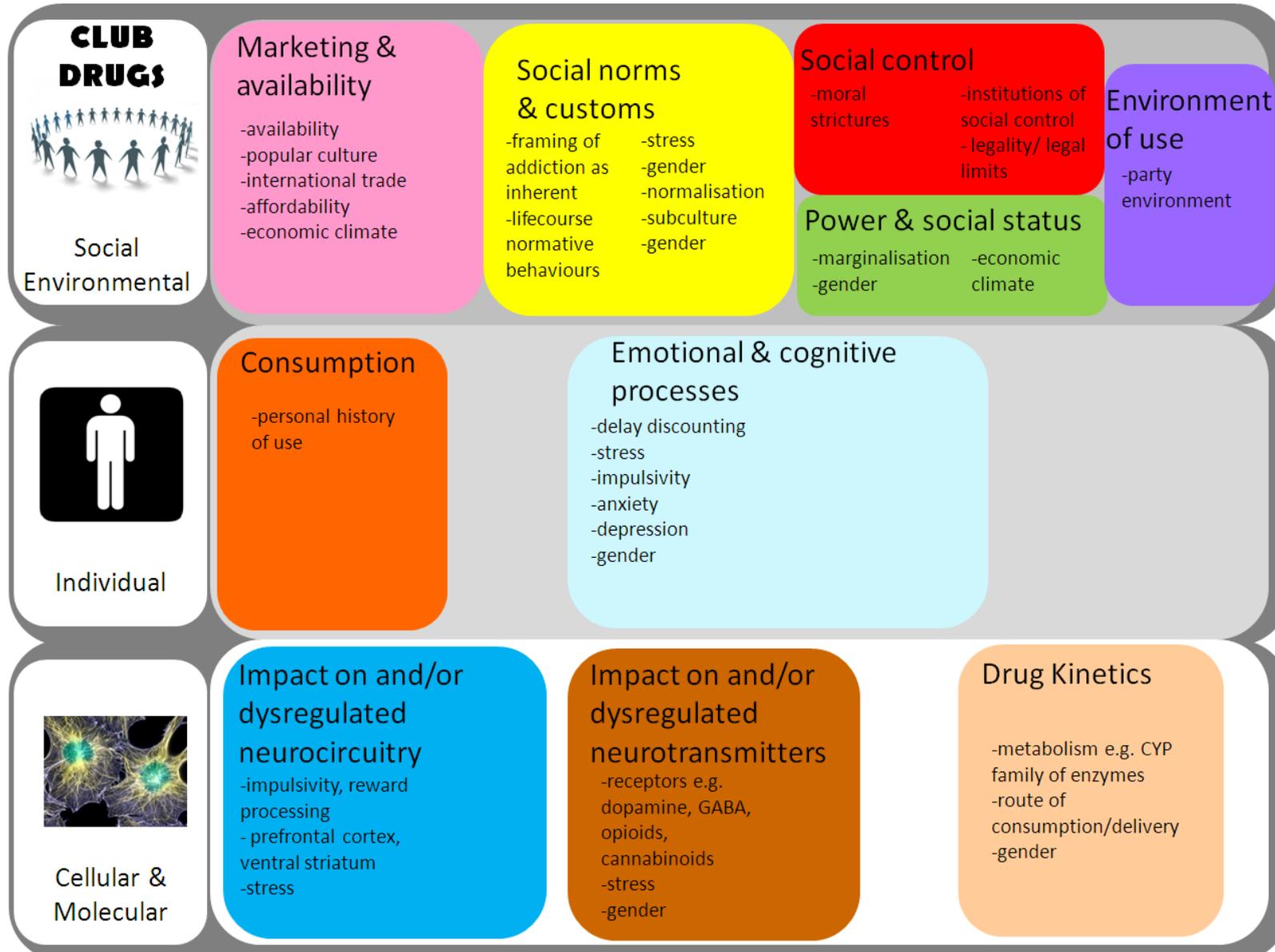
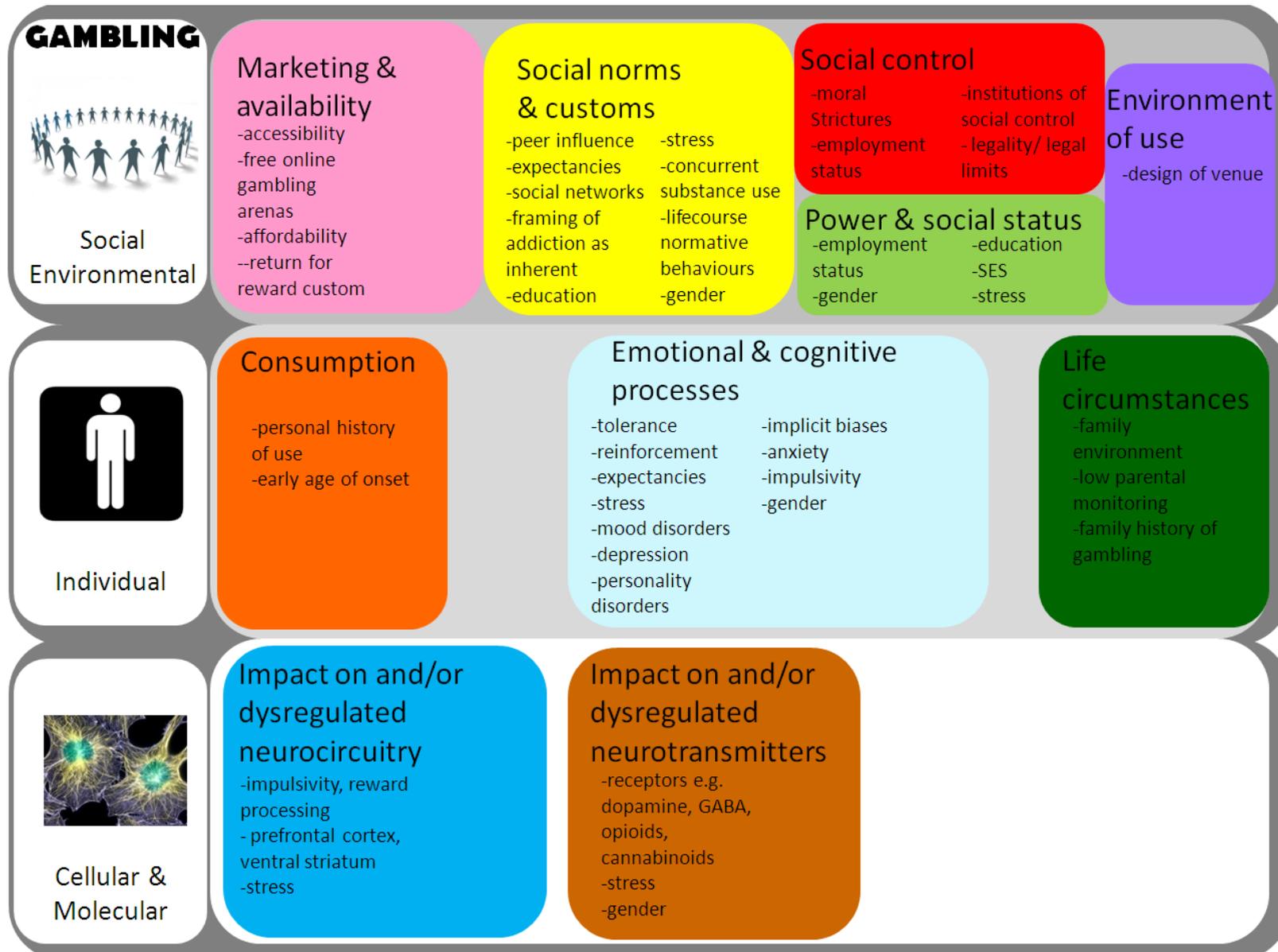




Figure 10: the gambling model





3.1.1 Marketing & Availability

Risky use as determined by marketing and availability factors is concerned with increasing population awareness of and desirability to use a substance or engage in behaviour, thus increasing risky use. For legal substances this is enabled through activities such as sports sponsorship, branding and price promotions (e.g. Figure 4, alcohol, p.26) (Hastings et al. 2008; Smith and Foxcroft, 2009; Wellman et al. 2006). As four of the seven models we have produced concern substances which are illegal in the majority of countries marketing via the traditional channels is illegal and so traditional marketing strategies and factors are not included in many of the maps (e.g. Figure 6, cannabis, p.29). Consequently, the illicit substances show a lower number of determinants within this theme compared to the models for alcohol, tobacco and gambling. The marketing of illicit substances occurs through other channels including popular culture, which raises awareness of substances and can contribute to the appeal of consumption.

Financial factors are important for both legal and illegal substances and gambling. The availability and affordability of these behaviours is a determinant of risky use, with increasing availability and affordability resulting in increased risky use (e.g. Figure 10, gambling, p.33) (Caulkins and Nicosia, 2010). Across all substances, with the exception of gambling, international trade is a determinant of risky use. This determinant represents both trade through legal and illegal channels, with the latter in particular involving a number of risks to the individual and society (Wallace, 2012). Furthermore, high levels of international trade can increase availability, perpetuating awareness and risky use.

3.1.2 Social norms and customs

Each society has a set of cultural and social practices that are considered normative within that society. For example, drinking alcohol is normal in the UK, but not in Saudi Arabia where the consumption of alcohol is illegal. Thus, society has a set of expectations around how individuals and groups within that society should behave. For example, within the model we present a determinant called life course normative behaviours, which indicates those behaviours that society perceives to be acceptable and typically expressed by individuals at different ages. An example of a lifecourse normative behaviour might include experimentation with illicit substances during adolescence and reduction of substance use in early adulthood (Meng et al. 2013; Skog, 1985).

Different societal groups hold their own expectancies and associations in terms of substance use, such as ethnic groups, for example, White and African Americans have been found to have different injecting practices in their opioid use (Figure 8, opioids, p.31) (Adrian, 2002; Skog, 1985) and



different subcultures such as the rave scene where the commonality of trance music is associated with the use of club drugs (Figure 9, club drugs, p.32) (Measham et al. 1994). In these terms, an individual's social networks and associations, as well as the society in which they live their everyday lives, may determine their risky substance use or gambling.

3.1.3 Social control

Society controls addictive behaviours through a number of interrelated channels. For example, an explicit form of social control is legislation to ban the consumption of certain substances or control the age at which consumption is accepted. However, social control is also exerted more implicitly through social institutions, such as religion, which provide suggestions for how people should live without legislating certain forms of behaviour (Becker, 1963; Room, 2011). Such moral strictures subtly moderate behaviour, so that individuals who behave in a manner that is perceived to be unacceptable in certain contexts might experience exclusion from particular social groups, for example the use of a legal substance despite its legal status within the wider society (Figure 4, alcohol, p.26). Across all of our models the legality of the behaviour determines risky use (Figure 11, non-substance specific model, p.42), both through the risks of punitive sanctions from engaging in illegal behaviours either through the illegal nature of the substance or through engagement in activities which hold age limits whilst underage and increasing the drive of an individual to engage in a behaviour for the fact that it is illegal and thus poses a risk that some wish to experience (Grube and Stewart, 2004; Room, 2011).

3.1.4 Power and social status

Another theme that the experts identified within the model was power and social status. This includes determinants such as employment, SES and education, which contribute to the status of an individual within society relative to others in that society (for example Figure 4, alcohol, p. 26). If an individual holds a position of high power then traditionally they have increased access to a range of resources, perhaps including substances of use and this may increase the likelihood of them engaging in risky use. Conversely, if an individual holds a low social status then they may engage in risky substance use or gambling as a coping strategy to deal with their position and the associated restrictions imposed upon them by their marginalisation from society. Traditionally males within society held positions of higher power than females, and as such engaged in increased levels of substance use and gambling. However, as gender equality increases within society these roles are changing, resulting in increased substance use and gambling among females (Bloomfield et al. 2006; Kuntsche et al. 2006; Makela et al. 2006; Meng et al. 2013; Pearson, 1996).



3.1.5 Environment of use

The environment in which behaviour is carried out may determine an individual's risky use. For example, clustering seating around a bar within a venue has been shown to increase alcohol consumption (Hughes et al. 2011) and the lack of natural daylight within casinos has been shown to keep gamblers playing for longer periods as they are unaware of time passing through natural light changes (for example, Figure 10, gambling, p.33). Smoking within enclosed spaces is associated with increased risks as an increased level of toxicant is breathed in by the smoker, also risks are posed to non-smokers within the environment (Figure 5, tobacco, p.28). As a result of this effect smoking within confined spaces has been made illegal across Europe. Living in an urban environment was identified as a determinant of risky cannabis use, as this increased the likelihood of increased availability (Figure 5, cannabis, p.29), whilst we did not find evidence to support the importance on environment of use for risky use of stimulants and opioids, perhaps because illicit substances are more difficult to research.

3.1.6 Consumption

Different patterns of consumption of a substance or of gambling may result in the transition of an individual from non-risky use to risky use. An individual's personal history of use increases their familiarity with the behaviour, making it seem more normal and thus reducing the perceived risk of increasing use (e.g. Figure 6, cannabis, p. 29) (Becker, 1963). Many substances have a demonstrable link to early age of onset of a behaviour and risky use (Chen et al. 2005; Englund et al. 2008; Fergusson et al. 2006; Nigg et al. 2006; Tyas and Pederson, 1998). This is in part through the lack of risk awareness of those of young age, the adoption of behaviours as habits and also as those that engage with such behaviours at a young age may be more likely to engage in more risky use naturally. Early onset of alcohol use, nicotine use and for stimulants and opioids early onset of polydrug use also increase the likelihood of risky use of substances (see Figures 4-10, pp.26, 28-33). This works through a number of mechanisms including the complementarity of drugs, the expansion of drug-related social networks, the normalisation of substance use behaviour through exposure and membership of a subculture or the adoption of a deviant identity (which may cement subculture membership) (Becker, 1963; Caulkins and Nicosia, 2010; Goode and Ben-Yehuda, 1994; Goode, 2004; MacDonald, 2004; Measham et al. 1994).

3.1.7 Emotional and cognitive processes

This theme relates to conscious and subconscious decision making processes. Impaired emotional or cognitive processes may result in decisions being taken incorrect or the missing information. Missing



or incorrect information may result from individual biases that influence the decision to engage, or not, in risky substance use or gambling behaviours. Encompassed within this theme are tolerance and reinforcement, elements of the rational addiction model (Figure 4, alcohol, p. 26) (MacDonald, 2004). This states that substance users make conscious decisions to engage with risky behaviours, however these choices are often made as a result of thought patterns such as delay discounting where immediate rewards are given greater value over larger rewards where there is a time delay to receiving them and cue reactivity where images associated with substance use or gambling increase the craving and appetite of the individual to engage in the behaviour (MacDonald, 2004; Winkielman et al. 2005). Externalising disorders, such as ADHD, increase the likelihood of engaging in risky substance use often through the same impulsive pathways (Elkins et al. 2006; King et al. 2004).

Compared with legal substances, our understanding of the influence of emotional and cognitive processes on the risky use of illicit drugs is less well developed, as illustrated by the relatively few determinants presented in this theme within the illicit substance models (e.g. Figure 7, stimulants, p.30). An exception is impulsivity, which recurs across multiple models in relation to risky behaviours. Within this theme we also present a number of mood disorders, such as anxiety, depression and neuroticism, which have been identified as determinants of the transition to risky use for alcohol, opioids, club drugs and gambling. These mood disorders may increase the likelihood of engaging with risky substance use and gambling as coping strategies (Huizink et al. 2006; Serena et al. 2004).

3.1.8 Life circumstances

Life circumstances may work to increase the likelihood of an individual engaging with risky substance use or gambling. For example, substance use may be used within a coping strategy, for example to manage chronic pain or PTSD (Figure 6, cannabis, p.30) (Cogle et al. 2011; Ware et al. 2003). The relationship between marital status and risky substance use or gambling is complex. For example, a change in marital status from married to separated/divorced/widowed may result in an increase in free time to use substance, fewer restrictions on use, or the use of substances as a coping mechanism. On the other hand, if the partner or spouse was a drinking/drug/gambling partner then this change in marital status may result in a decrease in risky use. Family and friend use of a substance may serve to normalise risky behaviours (El Marroun et al. 2008; Korhonen et al. 2009; Strandberg-Larsen et al. 2008). Permissive parenting of adolescents for risky alcohol use and low parental monitoring for risky gambling allows increased access to these risky behaviours, and if adolescents feel that they are not restricted they may engage more with these behaviours (Figure



10, gambling, p.33) (Barnes et al. 2002). No determinants were listed in this theme for the substances of club drugs and opioids (Figures 8 & 9, p.31-32), once again suggesting a lack of research into these illicit substances.

3.1.9 Impact on and/or dysregulated neurocircuitry

Engaging with substance use or gambling may alter an individual's neurocircuitry, which may lead to increased future use and potentially risky use. The mechanism by which these determinants work is through the reward pathways and the reward centre of the brain in the ventral striatum. The reward pathways and reward centre of the brain are activated by engagement with addictive substances and gambling, with use resulting in increased craving and the desire to engage repeatedly in such activities. Furthermore, stress pathways within the brain are activated following substance use and gambling as the changes they cause in brain circuits take time to return to previous levels through homeostatic mechanisms (Robinson and Berridge, 1993). In the case of risky alcohol use the additional determinant of a family history of drinking problems is listed, (Figure 4, alcohol, p.26) which may give baseline differences in neurocircuitry and liking of alcohol which would increase an individual's likelihood of using alcohol in a risky manner (Dalley et al. 2007; Dalley et al. 2011).

3.1.10 Impact on and/or dysregulated neurotransmitters

The levels of different neurotransmitters and receptors within the brain are carefully balanced to allow correct function. The use of addictive substances and gambling can change baseline levels as the brain adapts to the chemical changes that the different substances impose upon the brain (Di Chiara and Imperato, 1988; Robinson and Berridge, 1993; van Ree, 1979). Some individuals may have an inherent bias towards substance use and gambling as a result of different baseline levels of neurotransmitters, such as low levels of dopamine receptors. When individuals with low levels of dopamine engage with substances or gamble, their dopamine levels are increased, helping them to function at a much higher rate than without substance use or gambling (e.g. Figure 10, gambling, p.33) (Dalley et al. 2007; Dalley et al. 2011). Following substance use or gambling the levels of neurotransmitters and receptors is altered within the brain (Volkow et al. 1999), which may increase the likelihood of an individual engaging in repeated substance use or gambling in an attempt to overcome these imbalances (Robinson and Berridge, 1993). Men and women may have different enzyme activity and different enzyme levels within the brain's pathways which may increase their likelihood of engaging with substance use or gambling (Figure 5, tobacco, p.28), such as increased AChR, which are active in tobacco smoking, in men compared to women (Cosgrove et al. 2012; Esterlis et al. 2013).



3.1.11 Drug Kinetics

Different enzymes have different metabolic rates within the body to process the different substances. For example, a version of the ALDH2 gene, which is present in people of East Asian origin, is defective and results in the build-up of a toxic intermediate in alcohol metabolism (Figure 4, alcohol, p.26) (Ball, 2004; Edenberg and Foroud, 2006; Gizer et al. 2011; Kim, 2009; Kuo et al. 2008; Reich et al. 1998). This gives rise to flushing and feelings of dizziness in people who carry this gene. The CYP family of enzymes are important in smoking of tobacco and cannabis as they metabolise nicotine and increase the liking of such substances (e.g. Figure 5, tobacco, p.28) (Lee et al. 2010). Equally, the CE enzymes metabolise stimulants and opioids and different enzymatic rates may increase or decrease the effects and therefore the likelihood of an individual repeatedly engaging with, or increasing their use of, these substances (Kamendulis et al. 1996). The route of drug delivery and mode of use is important in metabolism as smoking is known to deliver a rapid 'hit', as does injection of drugs, as these rapidly enter the bloodstream, whereas drinking alcohol has a much slower effect. This can be both more dangerous in that an individual may ingest a larger amount of the substance prior to its effects being felt and so may overdose without knowledge, or safer as the large 'hits' delivered by injection may be too rapid for the body's systems to cope with. No determinants are listed for the kinetics of gambling in terms of metabolic changes at the biological level, as this is not an ingested substance.

3.2 Determinants common to multiple substances

Across all of the substance specific models that we have presented above, there exist a number of determinants that are common to all forms of risky substance use and risky gambling. Figure 11 illustrates those determinants that are present in all of the risky addictive behaviours we have analysed (p.42).

It is evident from the model that the majority of the determinants at the individual level do not apply to the risky use of all the substances and/or gambling. Both the themes of 'Consumption' and 'Life circumstances' are absent within Figure 11 as no determinants have been found to be relevant across all the behaviours of interest. Impulsivity is the only individual level determinant for which we found evidence relating it to risky substance use and gambling. However, given that impulsivity itself is a multi-dimensional construct (Blaszczynski and Nower, 2002; Dick et al. 2010), it is plausible that this, at least in part, explains why impulsivity remains within the common determinants model.

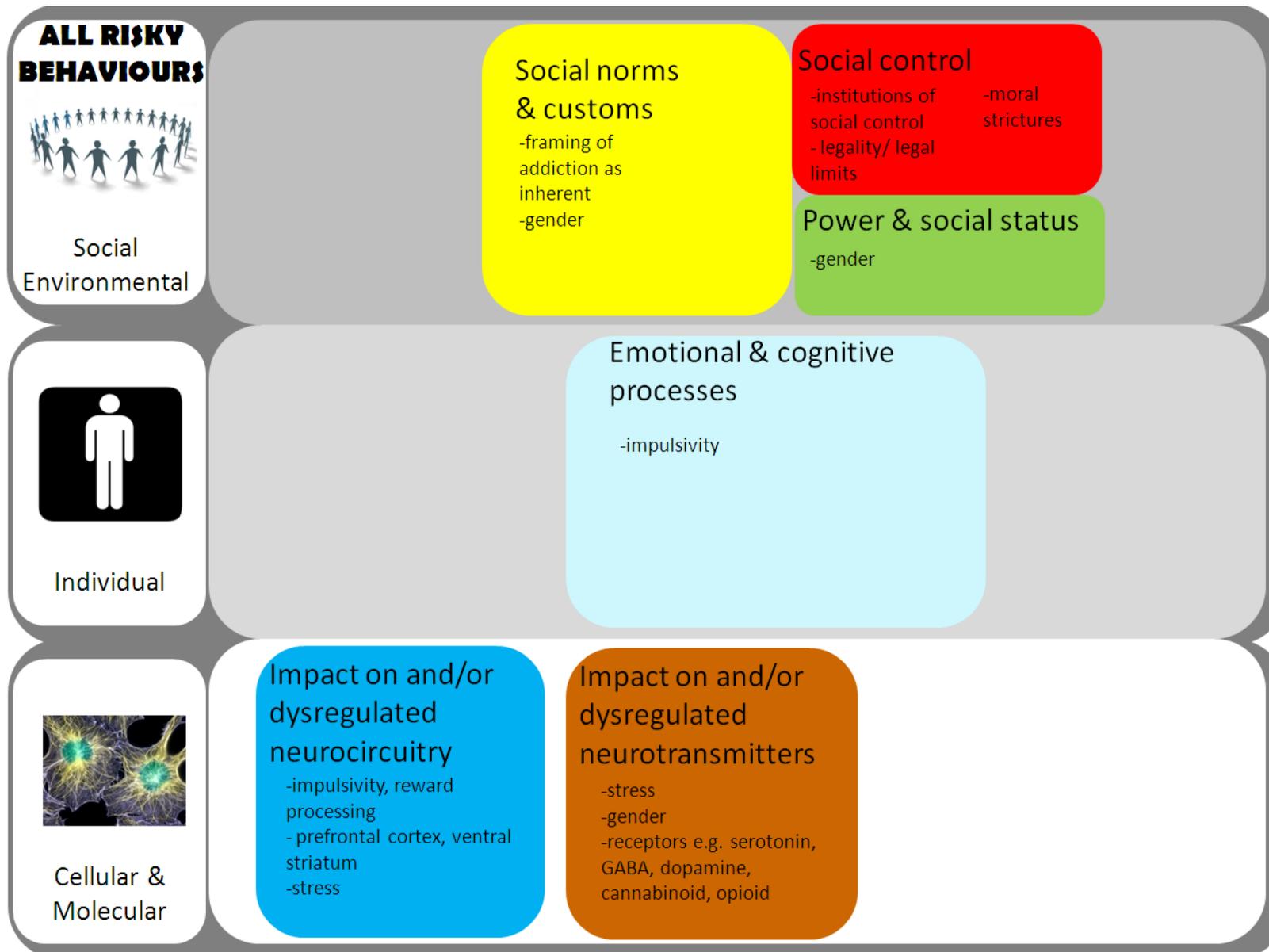


Indeed, many of the studies included within our work assess different elements of the impulsivity construct through different methods, or do not specifically state which elements of impulsivity are included within their research (Barnes et al. 2002; Dick et al. 2010; Gorwood, 2001; Gorwood et al. 2012; Grant and Potenza, 2011; Hamidovic et al. 2009; Hur and Bouchard, 1997; Koob and Volkow, 2010; Koopmans et al. 1995; Kreek et al. 2005; Magid et al. 2007; Patkar et al. 2002; Urcelay and Dalley, 2012; Verdejo-Garcia et al. 2008). It is important for future research to separate out the different elements of this trait and determine which are relevant to each of the different risky substance use and gambling behaviours. We feel however, that given the evidence around the impulsivity trait is raised as a determinant of risky substance use of all substances and risky gambling, a number of elements within this construct are likely to be important influences of the transition to risky use.

At the cellular and molecular level the theme 'Drug kinetics' is absent in Figure 11 (p.41). We perceive that this is because drug kinetics are not relevant to gambling, as this activity does not require the ingestion of a substance and to date no metabolic changes at the biological level resulting purely from engaging in this activity have been reported. The majority of the factors within the themes of 'Impact on and/or dysregulated neurocircuitry' and 'Impact on and/or dysregulated neurotransmitters' are relevant across all the risky substance use and gambling models. This demonstrates that the majority of the substances interact on common neurological pathways and transmitters, such as the reward pathway of the ventral striatum, where excess dopamine is released in response to substance use and results in feelings of pleasure and reward to the user (Dalley et al. 2007; Dalley et al. 2011; Di Chiara and Imperato, 1988; Nestler, 2000; Robinson and Berridge, 1993; van Ree, 1979; Volkow et al. 1999). This commonality in neurological responses to risky substance use and gambling also reflects our lack of understanding of the detail of these mechanisms at this level and the difficulties in addressing risky use within the currently available biological research models, with further research required to elucidate the exact action and mechanisms involved for each of the risky behaviours in question.



Figure 11: determinants common to multiple substances





The determinants at the social environmental level which are relevant to the risky use of all substances and gambling are those of the theme ‘Social control’, as all the substances and gambling are controlled to some extent, either through age limits or prohibition (Grube and Stewart, 2004; Room, 1974; Room, 2004a; Room, 2004b; Room, 2011). As the majority of the determinants listed within this theme are common across all the substance and gambling models for risky use, perhaps the manner in which substances are controlled within society is an easy target for policy interventions.

A further determinant present in all the models at the social environmental level is that of gender, which is present within the two themes of ‘Social norms and customs’ and ‘Power and social status’. Different societies hold different views of gender roles and rites of passage in terms of substance use and closely related are roles and ideas of power and status of each of the different genders within society. For example, it was considered the norm for males to drink large quantities of alcohol but frowned upon for females, whilst this relationship also gave more power to those of male gender (Bloomfield et al. 2006; Kuntsche et al. 2006; Makela et al. 2006; Meng et al. 2013; Pearson, 1996).

The final determinant relevant to all risky substance use and risky gambling is that of the framing of addiction as inherent, which is an element of ‘Social norms and customs’. This determinant denotes the current societal view of addicts as something one simply is or is not and that there is no pathway between these two types. As a result those who do engage in substance use and gambling but are not addicts feel able to increase their levels of usage, as they are unable to become addicts and so are behaving in a perceived ‘safe’ manner (Jellinek, 1952; Room, 1974).

The determinants which are common to all risky substance use and gambling are often those that refer to larger complex theories which allow the inclusion of multiple behaviours and substances, though they may infer important future research and policy strategies.

3.3 Multidisciplinarity within the model

Research within the addiction field has long been fractured, with knowledge from across the disciplines being brought together all too rarely. It has been compared to ‘The tale of the elephant and the blind men’, where each man touches and describes one part of the animal, but none can describe the whole beast. ALICE RAP seeks to advance the synergy within the contributing disciplines in the field of addiction research, and our logic models bring to light areas of interest for such



multidisciplinary work, which can improve our current understanding, highlight new solutions to problems and present productive avenues for further research.

In Section 2.5.5 (p.18) we highlighted the challenges encountered in developing a multidisciplinary model of risky substance use and gambling. One key challenge was to develop a model that best illustrated the state of knowledge to our audience. In presenting the model clustered around themes, we have masked some of the additional learning around the multidisciplinary nature of research of the determinants of risky substance use and gambling. As such, here we present an alternative version of the model that is targeted towards researchers and policy makers with an interest in our learning around the multidisciplinary nature of research around risky substance use and gambling.

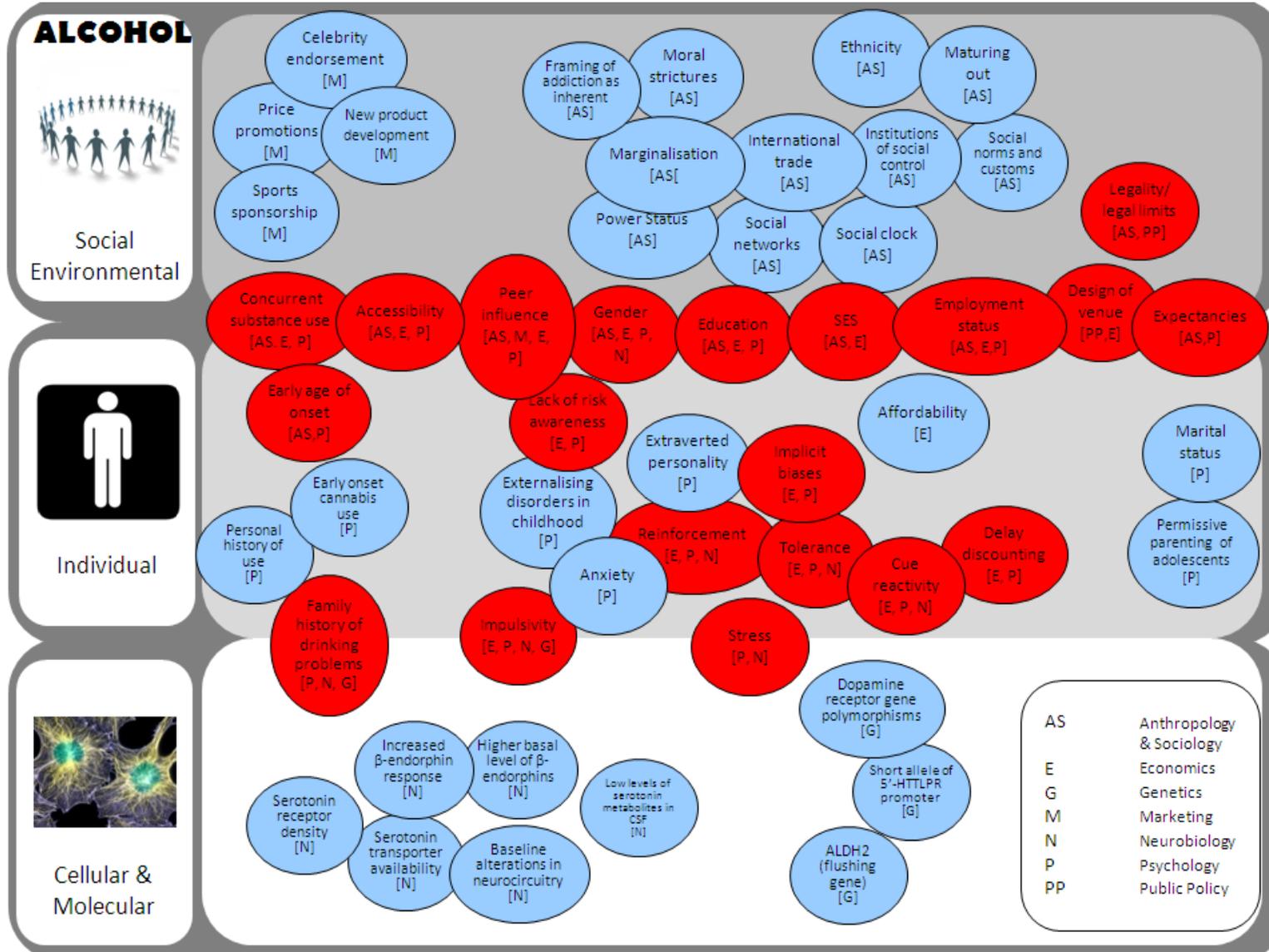
3.3.1 Example: the multidisciplinary nature of alcohol research

Figure 12 (p.44) presents a variation on the alcohol model described in Section 3.1 (p.26) (for another example see Appendix 2: tobacco model with multidisciplinary emphasis, p.84). The same determinants are illustrated within both models, but rather than clustering determinants into broader themes, each individual determinant is a stand-alone bubble in Figure 12. The model is two-toned; the lighter, blue circles indicate determinants that are only researched by a single discipline whilst the darker, red circles show determinants that are researched within two or more disciplines. Within each circle, the square brackets indicate the disciplines that have contributed to research on that determinant.

The model illustrates that around 20 determinants are researched within at least two disciplines, whilst a further 23 are researched by a single discipline. The majority of those determinants that are researched by multiple disciplines cross the boundary between two levels of analysis, for example the individual level and social environmental level. Whilst a number of determinants are researched by two or more disciplines, multidisciplinary research into these determinants is rare. Early in our work we identified some relatively isolated multidisciplinary papers within the addiction field; work by West (2013) 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. However, during discussions with our discipline experts both preceding and during a two-day meeting in December 2013, the absence of multidisciplinary work on these determinants was noted.



Figure 12: alcohol model with multidisciplinary emphasis





Case studies 1 and 2: risky alcohol use

Case study 1: Steve

Steve is a sixty six year old retired teacher living in a small village. He reports being in good health, although he does have type-2 diabetes which he struggles to control. He eats well, exercises moderately and considers himself to be a relatively low-level drinker. With the exception of six years served in the armed forces in his early 20s, he is confident that he has been a low-level drinker all of this life. He is conscious not to drink to excess because his brother struggled for many years with an alcohol addiction and now suffers from liver disease. Since finishing work last year he enjoys spending time with his wife, gardening and going out for meals with friends. Every Friday he drives to meet old work colleagues for lunch. He usually drinks three pints of beer over the course of two hours before driving home. He enjoys good wine and usually drinks a bottle over dinner at home with his wife three or four times a week. They used to only drink at the weekend, but now that Steve doesn't have to get up early for work, he can drink on weekdays too. He is a member of a local wine club and is pleased that he can learn about nice wines that can be bought at relatively low prices from supermarkets. He doesn't feel he is a risky drinker, after all, he believes he follows the government guidelines on drinking, and he certainly doesn't drink anywhere near the amount his brother used to cause his liver disease!





Case study 2: Maggie

Maggie is a twenty four year old assistant manager working in a high street shop. She left school at sixteen and has worked in the retail sector since then. In her spare time she likes to socialise with friends; she is often the centre of attention and is energised by being around others. She started smoking at a young age and currently smokes around 10 cigarettes a day, except when out drinking when her tobacco consumption doubles. Maggie and her friends particularly like to go out drinking and dancing at the weekend when they often have drinking competitions or play drinking games. Only very occasionally does she drink alcohol during the working week. Maggie enjoys the taste of alcohol and finds that it helps her to relax and unwind after a busy week at work; she often has a particularly heavy drinking weekend if work has been particularly stressful. Maggie did not drink much as a teenager, but her parents would often give her some beer when she went to parties with friends. She knows that she will have to curb her weekend binge drinking at some point, but any potential health problems seem so far away that she is happy to carry on having fun for now.

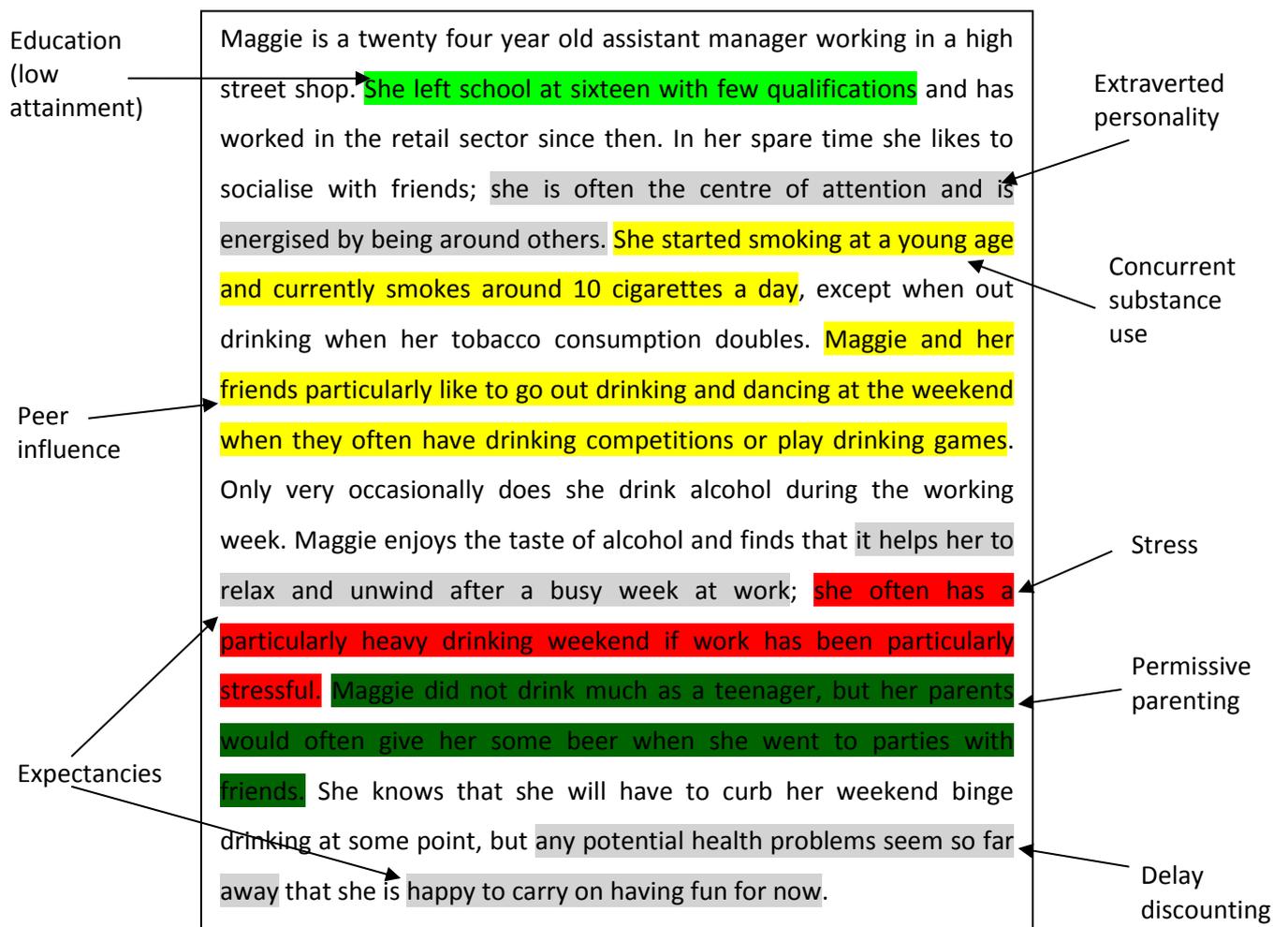
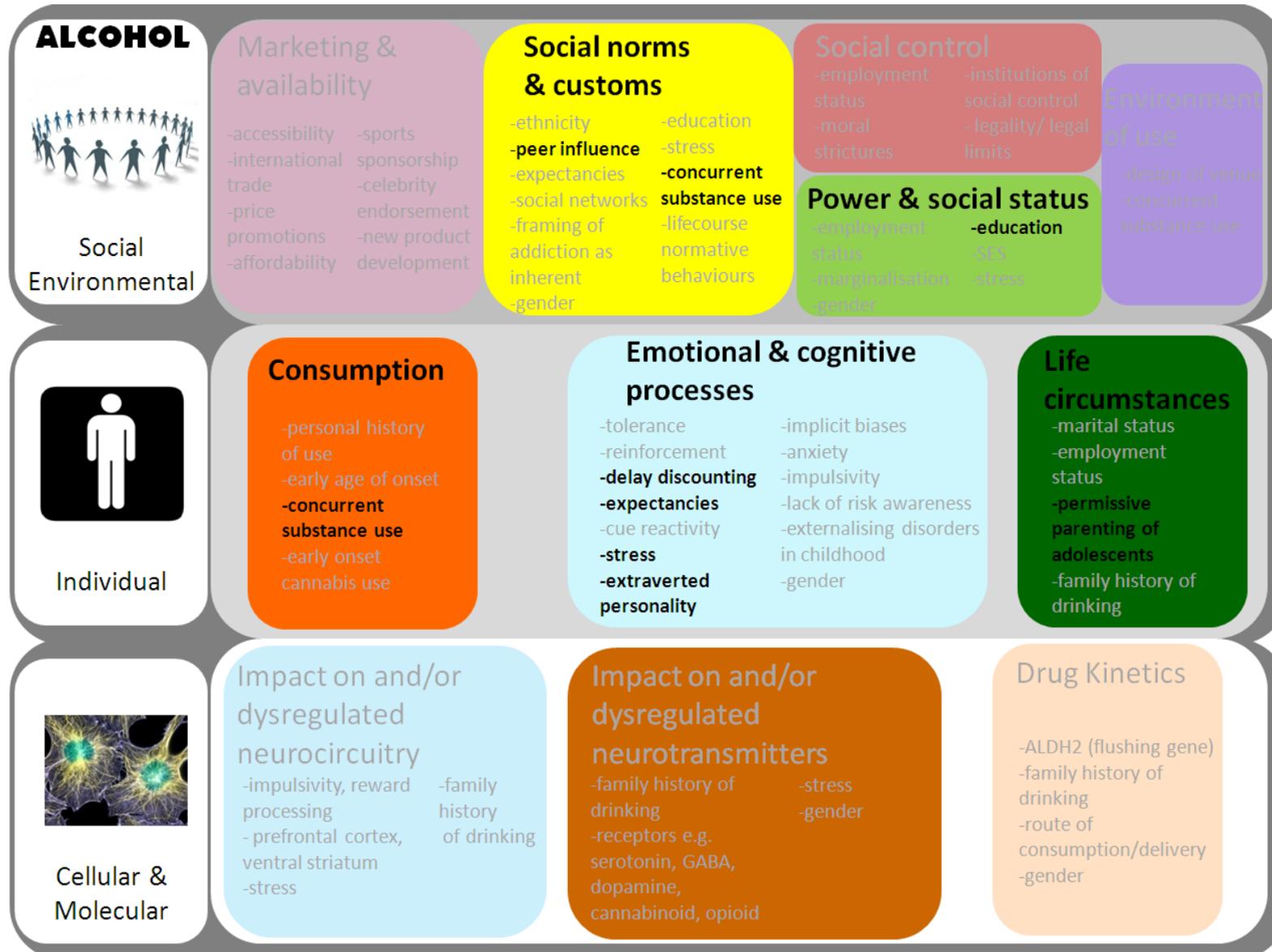




Figure 14: case study 2 - Maggie





Case studies 3 and 4: risky cannabis use

Case study 3: Rachael

Rachael is an unemployed young mother of two. She is 22 years old and lives with her partner and their two young children on a council estate in the small town in which she was raised. She does not drink alcohol as she does not like the taste, but she smokes about 20 cigarettes a day and has done for nearly ten years, though she cut down whilst she was pregnant with both her children. Rachael left school at 16 when she became pregnant with her first child. She worked as a care worker in a nursing home for six months prior to having her first child and has not worked since. Day to day she spends her time caring for her children, spending long periods of time alone with them, which she finds quite boring and lonely. She smokes cannabis in the evening with her partner to relax and at the weekends with their friends to feel young and carefree. They do not tend to go out often to socialise, preferring to invite friends to their house, as it is cheaper and more convenient with the children. Her first experience of cannabis was with school friends at the age of 13. She does not feel her level of cannabis use is in any way dangerous because most of her friends smoke cannabis without suffering any ill effects.

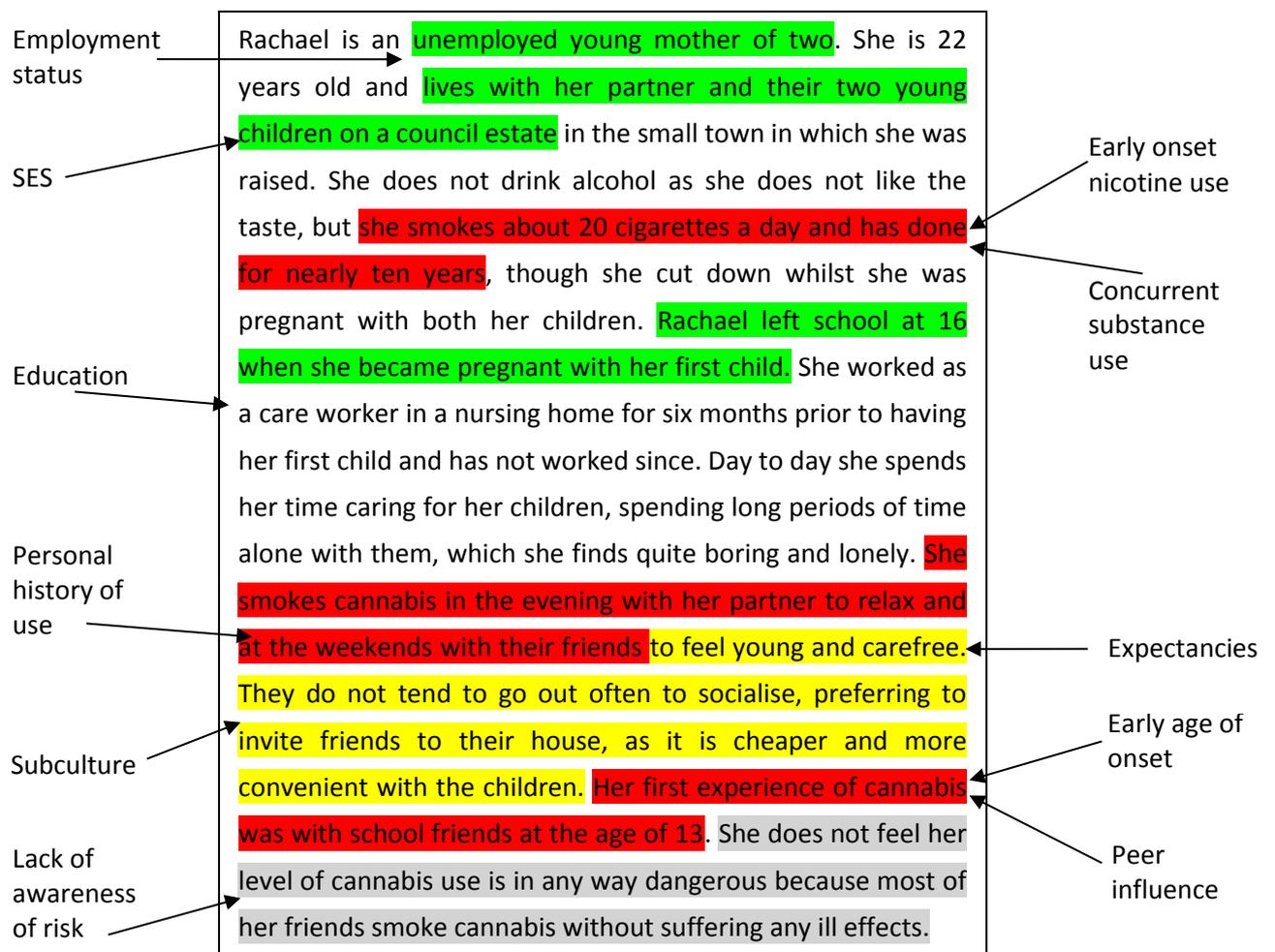
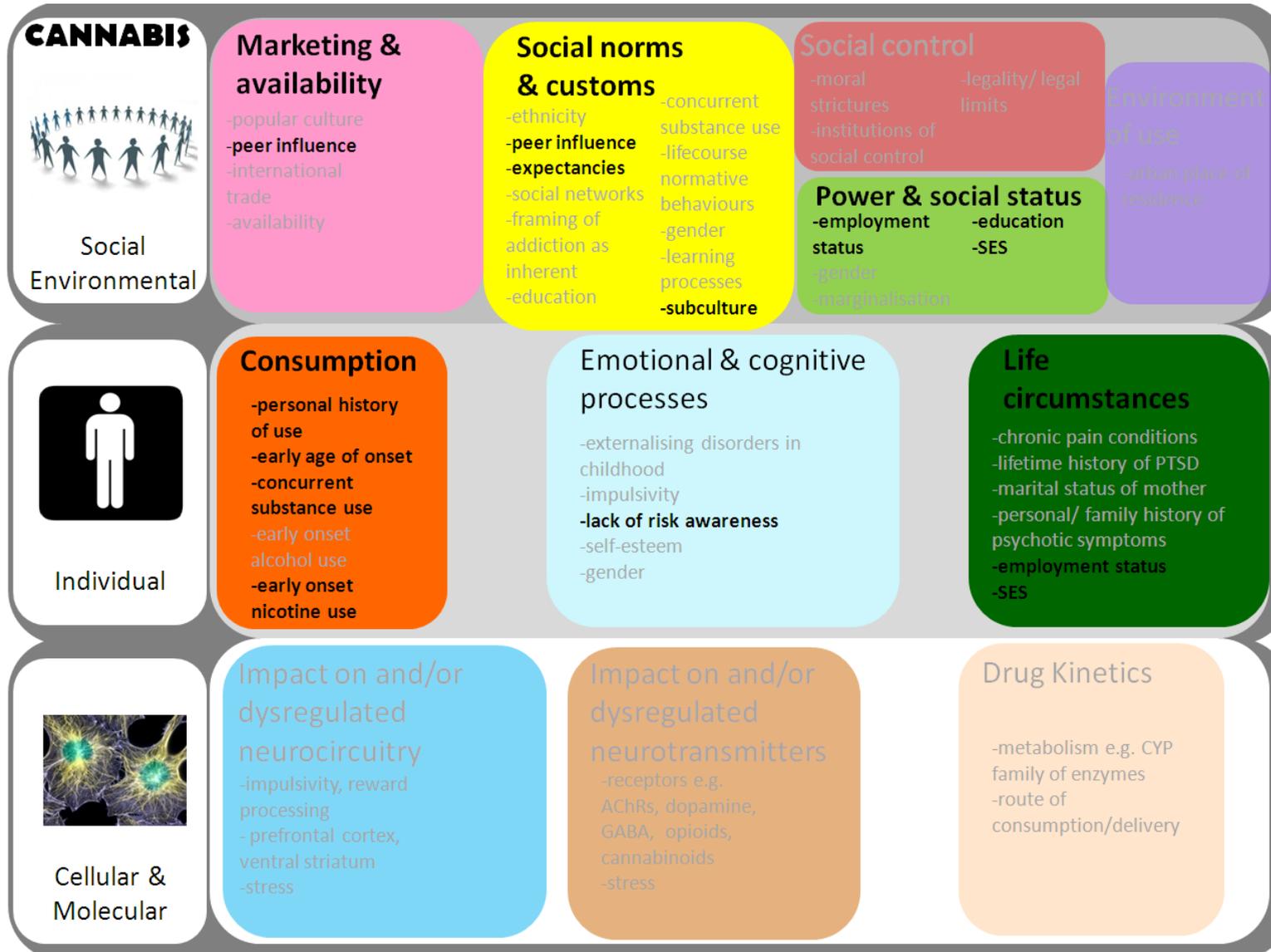




Figure 15: case study 3 - Rachael





Case study 4: Jack

Jack is a high achieving second-year student, studying chemistry at university. He lives in a student house with three friends from his course. As a teenager, Jack was quite reclusive; he struggled to make friends because he suffered from low self-esteem. His parents got divorced when he was fifteen and he began to drink alcohol quite heavily as a way to escape his difficult home life. When he started university he moved from his small home town to a large city to live in student accommodation; he enjoys the variety of activities now available to him compared to where he grew up. Jack has made some really good friends at university, they live together and enjoy hosting house parties for their friends. They drink alcohol and smoke cannabis together three to four nights a week. Jack first smoked cannabis in his first week of university when he was just getting to know these friends; he'd never used cannabis before but it was offered and he acted on a whim. Two years later smoking cannabis has become something of a habit. A guy on his course sells weed so it's really easy to get hold of at any time. Jack isn't concerned about his drinking or cannabis use, after all, he's at university and he'll grow out of it once he graduates next year.

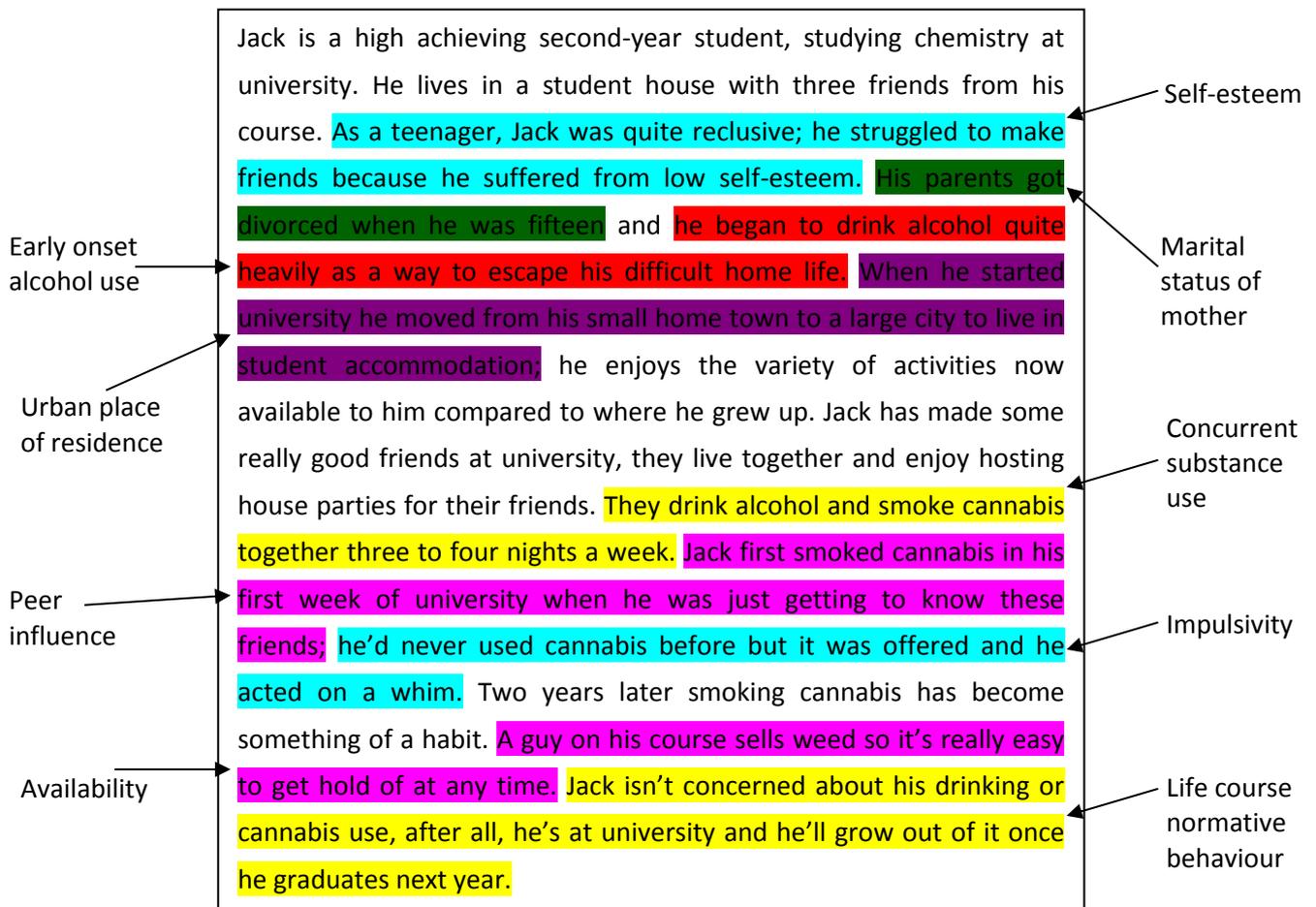
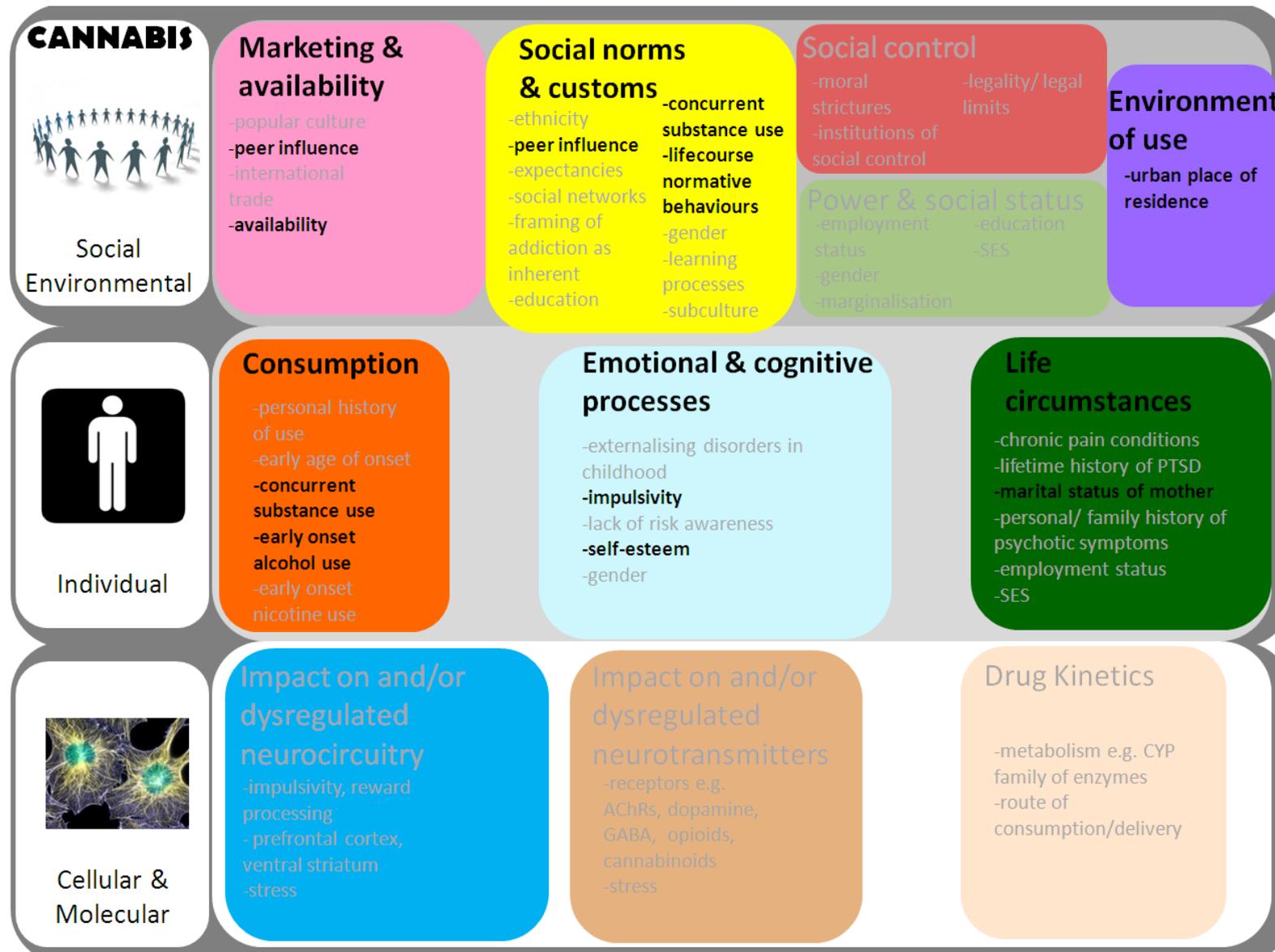




Figure 16: Case study 4 - Jack





3.5 Transition probabilities

3.5.1. Sample description

From the first wave (baseline to T2) we included all 14 to 22 year olds (686 women and 753 men). 71.8 % of those participants reported a lifetime comorbidity of any mental disorder. From the second wave (T2 to T3) we included all 23 to 28 year olds (427 women and 423 men). In this subsample of participants 62.2% reported lifetime comorbidity. For more details on the number of individuals in different subgroups see Table 3. As Table 3 shows, version B led to lower N in the risky use category since version A applied lower limits of mean daily consumption for risky use than Version B. Furthermore, version B led to higher figures in the category of harmful use since this included patterns of consumption as well as alcohol use disorders instead of just alcohol use disorders as in version A.

Table 3: Number of persons included into the calculations, stratified by age, gender, and comorbidity. The values are derived from version A (version B). Figures for version B are only displayed when differing from version A.

	Females		Males		Total
	No comorbidity	Comorbidity	No comorbidity	Comorbidity	
Age group 14-17					
Total		260	120	223	676
Abstinent	45	123	62	89	319
User	24	102	40	90 (91)	256 (257)
Risky user	2	13 (12)	6	9 (7)	30 (27)
Harmful user	2	22 (23)	12	35 (36)	71 (73)
Age group 18-22					
Total	188	557	337	434	1516
Abstinent	62	163	67	49	341
User	107 (111)	298 (308)	193 (198)	216 (221)	814 (838)
Risky user	13 (8)	60 (38)	40 (27)	61 (46)	174 (119)
Harmful user	6 (7)	36 (48)	37 (45)	108 (118)	187 (218)
Age group 23-28					
Total	112	413	232	305	1062
Abstinent	32	101	25	38	196
User	63 (66)	227 (237)	150 (154)	154 (159)	594 (616)
Risky user	14 (8)	61 (42)	30 (15)	53 (35)	158 (100)
Harmful user	3 (6)	24 (33)	27 (38)	60 (73)	114 (150)



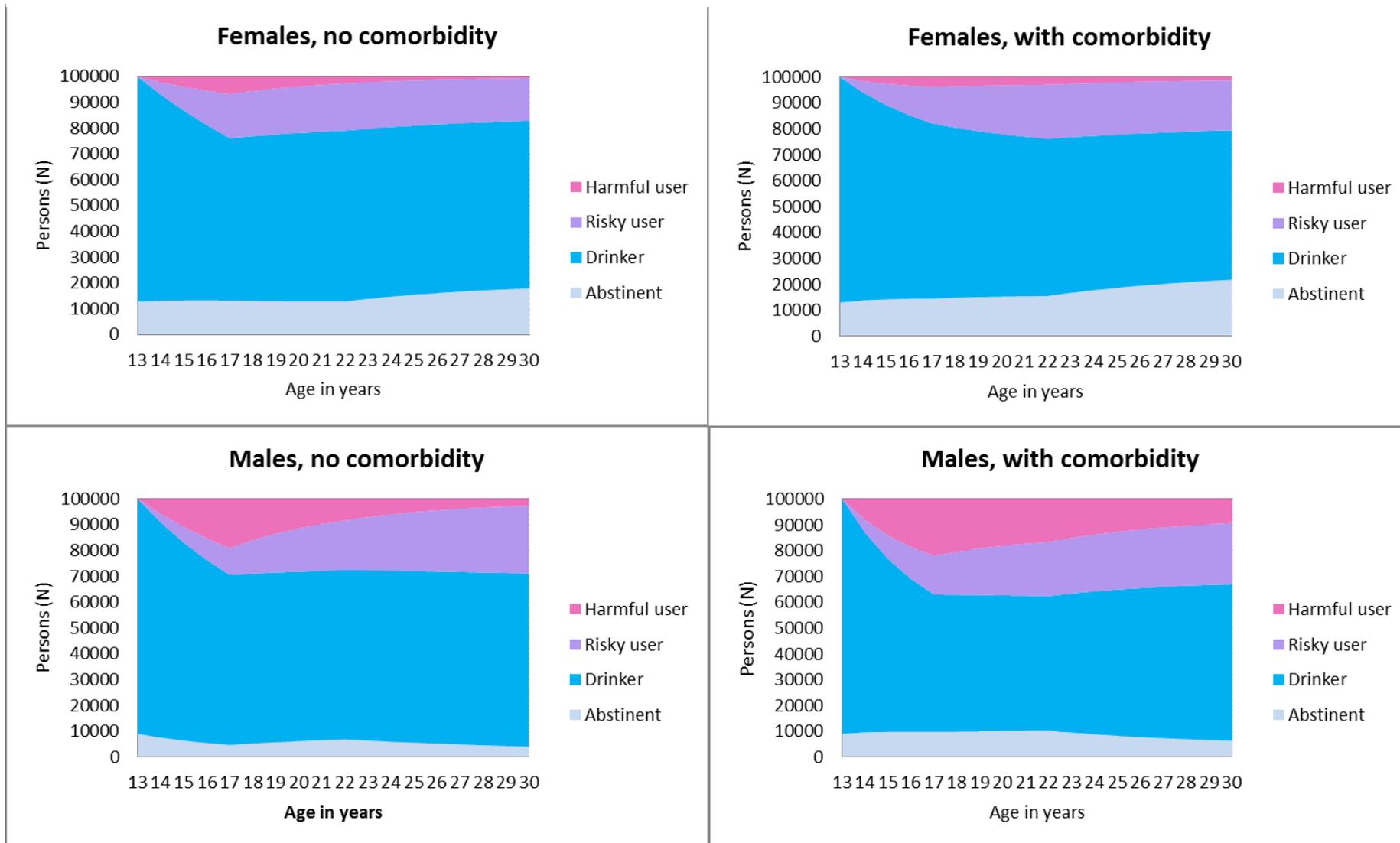
3.5.2 Transition probabilities and simulations

Based on the derived transition probabilities, simulations were calculated for ages 13 to 30 on a fictitious sample of 100,000 individuals. The simulations display the expected prevalence of each use category based on the age-, gender-, and comorbidity-specific transition probabilities.

Overall, the results show that a considerable proportion of 25 to 37% of male 17 to 30 year olds are either risky or harmful users varying by age, status of comorbidity, and version of operationalization. For females the same figures are 15 to 25%. Among men, harmful use peaks around the age 16-17 years with a prevalence of 20 to 25%. Among women prevalence were much lower with between 2 and 6.5% of the women aged 17 being harmful users. Overall the proportion of harmful users shows a decrease with increasing age, while the proportion of risky and harmful users together remains stable. At age 30 between 3 and 17.5% of males are harmful users; this is dependent upon the variant of operationalization and comorbidity. Women aged 30 show prevalence of harmful use of 0.5 to 5%. Independent of comorbidity and variant of operationalisation females show higher rates of abstinence and lower rates of harmful use than men. Furthermore, across simulations, comorbidity is associated with higher rates of harmful use in men. The results show that neither the variant of operationalization nor the smoothing processes change the whole picture considerably. Figure 17 displays example simulations for males and females with and without lifetime comorbidity based on crude annual rates from version A.



Figure 17: Simulations for males and females with and without lifetime comorbidity based on crude annual rates from Version A.



4. DISCUSSION

4.1 Substance and gambling models

4.1.1 Key findings

The models presented here for addictive substances and gambling demonstrate for the first time many of the different key determinants of risky behaviours across numerous disciplines which contribute to addiction research. It is evident from the models that the majority of the determinants of risky use of all substances and gambling lie at the social environmental level of analysis, suggesting that the environment of an individual is critical in determining engagement with addictive substances and behaviours.

We have grouped these determinants into key themes, which provide easy ways to understand the mechanisms by which these determinants may function and consequently infer possible policy responses and interventions. It is obvious from the number of different themes and determinants across all the models that the problem of risky substance use and gambling is complex in nature and is determined by a greater number of factors than the individual's own characteristics; involving environmental, personal and molecular factors for each of the risky behaviours analysed here. Indeed, the number of determinants and themes contributing to risky behaviour from the social environmental level of analysis is greater than that of inherent determinants, demonstrating clearly the key influential role of the environment on risky use. Though this is in part due to the difficulties in studying this stage of behaviour in the currently available biological systems, this lack of determinants of risky substance use or gambling at the molecular and cellular level demonstrates a clear need to focus policy on the best currently available evidence from the other levels of analysis relating to the individual and societal factors.

The presentation of the identified determinants of risky substance use and gambling within these models highlights the lack of known determinants for the illegal substances compared to alcohol and tobacco. This lack of research evidence concerning the risky substance use of opioids, stimulants and club drugs is possibly associated with their illegal nature, which makes them more difficult to study, yet points to the need for an increased research focus within this area, in order to aid in the understanding of the use of such substances.

We have presented a version of the model which displays those determinants common to the risky use of all the substances examined here and gambling. This model demonstrates that risky use is influenced by determinants at all of the different levels of analysis from the molecular to the social environmental, and that some of the basis of such behaviours may be common across all substances and gambling. These common determinants may serve as initial focus points for the development of policy strategies which are

effective in tackling risky use of all substances and gambling. Additionally, this version of the model highlights the fractured nature of the addiction research field in that use of many of the substances are studied separately by different research groups and different terminology and theories used by each of the groups may prevent unification of a total hypothesis of risky use across all the substances and gambling.

We have shown which disciplines have contributed evidence to support each of the included determinants for alcohol and tobacco, and thus highlighted key patterns within the research, such as the lack of research at the molecular and cellular level associated with risky use. In presenting the determinants in terms of their contributing disciplines we establish focus points for future multidisciplinary research around determinants to which multiple disciplines already contribute. This multidisciplinary research is essential in order to gain a complete and accurate understanding of the development of addictive behaviours, and will hopefully open up new avenues to pursue in terms of solutions.

Finally, we have presented here example case studies of individual's engaging in risky use. These examples illustrate the complexities involved in why an individual may engage in risky substance use or risky gambling. These examples also serve to demonstrate how some of the different determinants identified for each of the different risky behaviours can converge within an individual's circumstances to influence their use of such substances or gambling. Additionally, the use of these case studies highlights that not all the identified determinants contained within each of the models may function simultaneously within an individual's circumstances, indeed this is most unlikely to be the case, yet may operate within different individuals and different circumstances to increase the likelihood of risky use at different times.

We believe that the models presented here and our interpretations of these show for the first time the breadth of influences upon risky substance use and risky gambling, whilst highlighting where the majority of these determinants may lie and allowing the inference of future effective research and policy strategies.

4.1.2 Limitations

Our research carries a number of limitations resulting from both the evidence available to use from previous research publications and our study design.

It must be acknowledged that this range of models is specific to the range of disciplines which have contributed to work area 3 of ALICE RAP and the time frame within which it has been generated. Were this model to have been informed by a different panel of experts in different disciplines, for example biochemistry, law or history, the model would undoubtedly contain different determinants. Further, our

expert panel from across all the disciplines involved showed a bias towards alcohol research. Consequently, our model of the determinants of alcohol use shows a greater number of determinants than that of tobacco or gambling. Were the research bias in our expert panel weighted differently then perhaps the models presented here would display a different level of understanding of the different risky behaviours examined. Similarly, if this model were to be generated in a decade's time again the determinants considered important would be different than those highlighted here; as addiction studies move forward key theories and determinants will change in light of new evidence. However, it is important to not only assess our current position of knowledge within the field, of which these models provide an overview for factors contributing to risky substance use or gambling, but also to provide workable models for future research to build upon. Our models highlight current knowledge gaps specific to life stages and addictive behaviours, multidisciplinary research within the addiction field somewhere. Within our models we have presented key determinants around which different discipline experts can collaborate to enhance our understanding.

An obvious omission from our models is the relationships that exist between the determinants, either as additive or counteractive factors. The determinants show some relationship to one another by the level of analysis at which they have been included in the model, (whether they are in the molecular and cellular, individual or social environmental rings in the model) and through the themes within which they have been grouped, but specific relationships have not been demonstrated here. After consideration of the available research pertaining to risky substance use or gambling it was concluded that there existed a lack of evidence for many of the possible relationships hypothesised between the listed determinants, and that with such little supporting evidence to include these relationships may appear misleading. Some of the relationships, which were felt to be important, are however outlined in the text of the companion report (Lees et al. 2012).

During the process of our work we did attempt to address the relative importance of each of the determinants identified to the progression of the transition from non-use or use to risky use of a substance or gambling. However, due to the level of complexity and the breadth of issues included within this work, the distinct nature of many of the research studies into the different determinants, as well as the working practices of some of the disciplines such as anthropology and sociology being incompatible with such quantitative methods, this was considered to be beyond the scope of this study. We do however, recommend that this work be analysed in future studies and appreciate the important illuminations such findings would bring to this work.

A further challenge we have encountered within our work is that the concept of risky use is not widely used within the literature, and thus obtaining evidence specifically pertaining to this behavioural transition has

been difficult. Much of the published literature uses alternative definitions, with a greater focus upon the later stages of substance use and gambling, addiction and cessation.

Within our work we have included studies from a number of disciplines that vary according to their definitions of what they regard as risky use levels, concurrent substance use patterns and age groups examined. For example, substance use at an early age may be defined by one study as below 16 years of age yet another may refer to early use as below 25 years of age. Further to this many of the studies do not specifically define the terms they are using, such as the multi-dimensional concept of impulsivity. In the interest of bringing together so many different disciplines we have had to include all of these studies using such terms as use levels and age groupings as stated by the research authors, which may result in less accurate determinants by age or substance. We propose that future research within the addiction field defines these concepts prior to beginning research for the purposes of clarification and unification of research findings across the disciplines and research field.

Furthermore, the published research literature concerned with risky substance use and risky gambling has a focus on the risk of youth engaging with such activities, and there appears to be an absence within the literature of studies examining different age populations within society, particularly the elderly. These findings would contribute significantly to our models, as the determinants of engagement with risky use by adolescents are unlikely to be the same for different age populations, and thus targeting risky use in alternative populations requires further research in these areas to develop our understanding and allow the generation of evidence-based policy interventions.

All the studies cited across the disciplines in our review of the evidence on determinants of risky substance use and risky gambling reported at least one significant effect of a determinant on risky use. This suggests a publication bias is in operation, whereby journals publish significant results and reject null findings. The magnitude of this 'file drawer' effect are impossible to determine, and thus the determinants listed within the models presented here must be interpreted with caution.

Finally, due to the level of work bringing together all the disciplines from across the sciences displayed here we have chosen to reduce the factors that we analysed in order to both simplify the presentation and increase engagement with our work. Consequently, within this work we have only analysed risk as a negative concept, without looking at the possible positive connotations of engaging with risky use both to society and the individual, and we have neglected to examine determinants that may act as protective factors preventing the engagement of an individual with risky substance use or risky gambling.

To generate logic models which are clear and accessible enough for policy makers to engage with, yet display the full complexity of determinants contributed from all the research disciplines involved in work area 3 of ALICE RAP, and can be used as testable models to further hypotheses, we felt posed too many requirements. Rather than attempting to generate models which comply with all these requirements for all audiences, whilst risking alienating all users, we have provided logic models which demonstrate the key determinants resulting from our work, which can be used to link determinants in future research, highlight possible areas for multidisciplinary collaboration and can be adapted and built upon as the research field progresses.

4.2 Transition probabilities

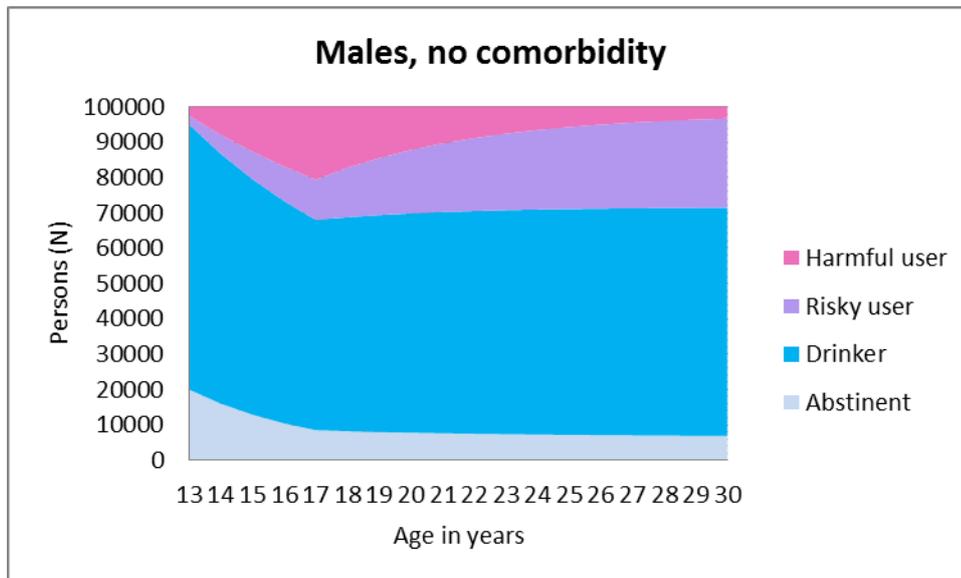
The modelling of prevalence of four different drinking patterns shows that a considerable proportion of adolescents and young adults from a European country fall into risky and harmful categories of use. Our results thereby indicate an extent of both risky and harmful use of alcohol, which is relevant to and should be addressed by public health measures. Furthermore, we see that harmful patterns of use are decreasing with age even in the limited age span observed. Several factors, such as ‘maturing out’ (O’Malley, 2004), public health policy, therapy or other interventions (Martineau et al. 2013), can be hypothesised to influence the observed reduction. Research has shown that public policy relevant factors, such as early availability of alcohol or alcohol advertisement influence trajectories of alcohol consumption patterns (Casswell et al. 2002). It is of central importance to understand and emphasize these factors. Given the rather low rates of treatment (Alonso et al. 2004), we speculate that natural remission processes play a crucial role here (Lopez-Quintero et al. 2011; Grella and Stein, 2013).

4.2.1 Methodological limitations

We did not have enough cases to reliably calculate all single transitions. Errors in measurement and uncertainty, i.e. confidence intervals, were not taken into account. This may have led to unrepresentative transition probabilities, particularly within the younger age groups examined. Nevertheless, the results are quite stable across the different variants of operationalization as well as before and after smoothing, indicating a relative robustness of our results.

Due to the design of the main underlying study, which had measurement points only after several years, we had to calculate transition probabilities in age groups instead of calculating transitions for each year of age separately. Therefore one has to keep in mind that the peak at age 17 may be impacted by the specific age categories we selected (based on the legal drinking age). Different cut-offs for age groupings might have led to a slightly different shape.

Figure 18 Model using the starting values 20% abstinent, 75% user, 2.5% risky user and 2.5% harmful user for age 13 on males without lifetime comorbidity.



The same applies to the starting prevalence upon which we based our model. We did not have an adequate estimator for prevalence of abstinence, use, risky use, and harmful use of 13 year olds in Germany. Applying a different set of starting values would have shifted the results slightly as shown in Figure 18. We had to calculate transition probabilities on overlapping populations, so the estimations are not independent. Transition probabilities for the oldest age group rely on the same individuals as those for the young and the middle age group. Transitions for the young and the middle age group are based on an exhaustive set of individuals. Also, we do not have any information from the main study on how transition probabilities change with increasing age above 30. Therefore another cross sectional, representative study investigating an older cohort is required to complete this dataset.

In terms of the operationalisations it would be more desirable to use universally used thresholds for risky and harmful use such as used by the European Medicines Agency (European Medicines Agency, 2010) based on earlier work from the World Health Organization ((World Health Organization, 2001), see also the proposal of Rehm, 2013)). Concerning mean daily consumption we may have to break down a continuum into distinct categories, which will always be to a certain extent arbitrary. Nevertheless it would increase comparability of research results. It is possible that certain differential effects concerning frequency and quantity are superimposed by the combined measure of mean daily consumption. As Casswell et al. (2002) showed for a different set of factors, trajectories and their respective influential factors depend on the aspect of use examined (frequency vs. quantity). From a health perspective it does make a difference if someone drinks 60g of pure alcohol once a week or 10g six times a week. For example, if someone consumes

60g of alcohol on one day of the weekend at age 19 and changes their pattern of use to 10g of alcohol on six days a week by age 23, this change in riskiness would not be reflected in mean daily consumption. The operationalisations underlying the report took this aspect of more differentiated concepts of risky and harmful use into account by including frequency of binge drinking. Future research could advance this approach by defining risky and harmful use with respect to specific patterns of use beyond mean daily consumption.

4.2.2 Generalisability

How do these results from a Bavarian, German sample apply to other regions within Europe and across the world? Across Europe marked differences in the drinking cultures with respect to beverages consumed, patterns of use, and acceptance of use are observable: historically southern European countries are wine drinking cultures with high frequency of consumption embedded in everyday life (e.g. drinking with meals in daytime). Central Western and Western European regions showed similar patterns with beer being the most frequently consumed beverage and less drinking with meals. Northern European and Central-Eastern and Eastern European countries historically showed patterns of irregular heavy drinking (e.g. drinking to intoxication) (Rehm et al. 2012). These differences across Europe are diminishing. Beer is now the most-consumed beverage, followed by wine. Daily use of alcohol at lunch as well as dinner has strongly declined in all countries. However, there are also further important similarities: the mean level of consumption in Europe is about double the global average, across all European countries lifetime abstention rates are low (Rehm et al. 2012), and men show higher values in almost all indicators of use (World Health Organization, 2011). Furthermore, the age of initiation is quite young, especially when compared to low- and middle-income countries (Degenhardt et al. 2008; Gururaj et al. 2011). These inner-European similarities suggest some generalisability of our results, even if limited. These prevalence numbers stem from current WHO efforts for the 2014 Global Status Report on Alcohol and Health, where all published literature on alcohol use disorders had been systematically reviewed and then modelled to impute for countries with no data based on alcohol consumption, the number of abstainers, and Gross Domestic Product based on purchasing power parity per capita (GDP PPP).

Worldwide, per capita consumption, ages of onset and abstention rates vary much more between countries than in Europe (Rehm et al. 2003; Rehm et al. 2009; Degenhardt and Hall, 2012; Shield et al. 2013). Generally, drinking cultures are widely influenced by the sociocultural context, including norms, the social function of drinking, gender roles and religion as well as the economic status of one country (Shield et al. 2011; Gordon et al. 2012). So in a global context the generalisability of our transition probabilities is not given, mainly because of vast differences in drinking cultures and ages of initiation. Presumably, a 25 year-old Indian man initiating alcohol use would have quite different transition probabilities for risky or harmful

patterns of use than a 15 year old Bavarian boy. Beyond the different cultural context, the totally different life situation, combined with different psychosocial and bio-developmental maturation processes will produce large differences and a different course of consumption can be assumed.

This implies that we need two things: first of all we need separate country- or region-specific calculations of transition probabilities and second we need to investigate those factors that make the difference in detail. In this manner we may be able to derive useful public health measures to decrease the transition probabilities into harmful or risky patterns and support transitions into less risky patterns of use or abstinence.

4.2.3 Outlook

In our future research it will be necessary to include the measurement error and confidence intervals in our calculations, using similar Monte Carlo simulations as has been used for the 2010 Global Burden of Disease estimate (Gmel et al. 2011). Furthermore, extending the work to adults over age 30 would be desirable. Generally worldwide country-specific transition models would give useful information on the on-going country-, age-, and gender-specific processes, and would increase our knowledge of transition probabilities. The current effort is based on one country (Germany). All research investigating such transitions should consider calculating annual rates, independent of the survey-specific delay between two points of observation. This would be a step towards better comparability of research results across studies. Finally, we should link the work of our transition probabilities to the WHO/GBD work on prevalence. The age-specific prevalence estimates can be seen as end results of the transition processes for each age category. This would require more modelling efforts to ensure that the estimated parameters from one tradition of modelling correspond to another. Part of the problem is the scarcity of data: while there are a multitude of cross-sectional surveys on alcohol consumption and related problems, longitudinal studies are scarce, and thus systematic research on the duration of use and remission in Europe is almost impossible. Future research should focus on longitudinal and more in depth analyses of fewer cohorts, rather than adding to the large number of prevalence studies, which are of questionable value for scientific progress.

Modelling such processes as carried out within this report will always be afflicted with error and uncertainty of estimation. Nevertheless it is a useful instrument to depict the on-going processes. Much higher accuracy in the investigation of individual and group specific developments would require completely new methods. It is for example imaginable to assess individual information based on apps for smart phones documenting daily or weekly alcohol consumption much more precisely and with less bias with respect to memory effects. This information could be combined with information on important life events documented in the same program or on e.g. something like a Facebook account. Such methodology will undoubtedly confront us with a multitude of new problems and biases as self-selection bias of participants for such methodology.

This is the first systematic modelling of transition probabilities; we see our work as a beginning rather than as conclusive and hope that the feedback which we will receive for this report will impact positively upon improvements in the knowledge of this area.

4.3 Consequences for EU research, clinical practice and health policy

The findings of our work have major implications for future EU research, clinical practice and EU member state health and broader social policy.

4.3.1 Consequences for EU research

One of the major findings of our research on the determinants of risky substance use and gambling was the lack of differentiation, within existing research, between the transition to risky behaviour and the transition to harmful behaviour (including addiction). Instead, most studies analyse critical factors for addiction or for umbrella terms like “problem behaviour”. However, this differentiation is highly relevant in order to be able to focus on very early development of problem behaviour, rather than waiting for the development of more severe, addiction-related negative consequences to have occurred. To use a public health analogy, we need to differentiate between risky and harmful use so that we can use our knowledge on the determinants of risky substance use and gambling to build a fence at the top of the cliff to prevent people from falling off, rather than providing an ambulance at the bottom once they have already experienced harm. Focusing on the prevention of risky substance use and gambling would facilitate early identification and intervention around critical behaviours and therefore avoid the costly waiting for long-term negative consequences of addictive disorders.

In addition to this key implication for EU research, we have identified a number of wide ranging gaps in the current literature and suggest nine actions for EU research:

- 1) To distinguish between the aetiology of risky substance use and risky gambling in research calls and increase the number of calls for research that focuses specifically on risky behaviour.
- 2) To promote the involvement of multidisciplinary research groups in the study of addictive behaviours. Our experiences of the past two years have clearly demonstrated the need for interdisciplinary research teams. To date, almost all available findings are derived from the work of individual disciplines (such as anthropology or psychology) and it is incredibly challenging to find a shared language to analyse and describe commonly relevant determinants. A growth in the

prevalence of multidisciplinary research teams can only help us to further our knowledge and understanding in this complex field.

- 3) To focus on the relevance and interaction of environmental, individual and biological related determinants together. There is clear evidence that these three broad areas each contribute to the transition to risky behaviour, although social environmental factors play the biggest role in the transition to risky behaviour. However, knowledge on the specific impact of these three areas and interactions between them is limited.
- 4) To promote research on the determinants of risky behaviour across the life span. Much of research currently available research on the determinants of risky behaviour is related to adolescence and young adults. We know that risky behaviour can also occur in later life but evidence to further our understanding of the determinants of risky substance use and gambling in older adulthood is scarce.
- 5) To support research on the impact of measures to reduce social environmental determinants (including policy impacts) for risky behaviour. There is a lack of research on effective measures to address the determinants of risky substance use and gambling on this level, including substance use and gambling related policy as well as general health policy around the prevalence and severity of risky behaviour.
- 6) To promote research on early identification and modification of individual vulnerability related determinants. Individual vulnerability develops and changes over the lifetime, from conception to death, and is determined by complex interactions of genetic, psychological, early family influence and environmental factors. There is a lack of research to early identify relevant patterns of vulnerability for risky behaviour and to find effective measures for modification.
- 7) To promote longitudinal cohort studies on the onset and cause of risky behaviour as such data would help us to better understand the dynamics of change in individual behaviour. Currently most research is based on cross-sectional studies, which do not permit us to derive conclusions for long-term behavioural processes.
- 8) To engage in better understanding the positives and negatives of potentially risky behaviour. Risky behaviour has two facets: on the one hand it can cause acute (e.g. drunk driving) or chronic (e.g. addiction) negative consequences, but on the other hand it can be considered a necessary component of the transition from adolescence to adulthood. Adolescents have to overcome the

protective regulations of childhood, finding their own way in life by seizing different opportunities that arise, e.g. experimenting with alcohol or gambling, in order to test and identify their limits for low risk behaviour across the life course. At present there is no research that enables us to compare such “positive” and “negative” consequences of risky behaviour and so guidance is on how to develop balanced educational or other preventive actions.

- 9) To promote research on the development of individual perceptions for risky behaviour. There is evidence that the development of a sense for risk does not develop until an individual is in their early twenties. However, at present we do not have enough knowledge on this process to be able to engage with the concept of an underdeveloped “sense for riskiness” in adolescence.

4.3.2 Consequences for clinical practice

Before we discuss the consequences for clinical practice from our research, it is important to stress that the research included in our review was most often drawn from samples of the general population rather than clinical populations. Therefore we do not see any consequences for clinical practice in the traditional understanding of medical or psychotherapeutic interventions for patients. However, there is a need for the early identification of subjects who are at risk of risky substance use or gambling because they experience a number of the determinants of risky behaviour identified in our work. Such individuals might benefit from education and individual support, such as alcohol brief interventions. In certain cases, such individual support might cross the boundary into therapeutic interventions, especially in severe cases of risky behaviour or where the risky behaviour becomes harmful over the course of time. Thus, our only implication for clinical practice is:

- 1) To detect and modify early determinants of individual vulnerability for risky behaviour in critical phases of life, especially for children, adolescents, young adults and older people. Our research shows that, at present, the focus is on the treatment of severe expressions of risky behaviour and therefore there is a lost opportunity to intervene early to modify possible risky developments.

4.3.3 Consequences for health and broader social policy

To date, the focus of health policy has been on the prevention of harmful behaviour, with no separation between the prevention of risky and harmful behaviour. In this context, our research group highlights the need to promote a public discussion on the advantages and disadvantages of early detection and modification of risky behaviour. “Risky” here is a statistical term in the sense that an individual displaying the behaviour is at higher risk of experiencing negative consequences than an individual who does not display a particular determinant. A focus on the prevention of risky behaviour may result in a situation where

interventions are delivered to many individuals who might never experience any negative consequences. However, it is the intention of such primary prevention approaches that we prevent a significant minority of individuals from developing risky use and going on to experience harm in the future. There is a question here to be raised around the role of the state in health promotion, and how far we should go to prevent the risk of harm to the population. Unwanted public or society control has to be discussed and measures have to be found to avoid a situation of total public control, or ‘nanny state’.

Considering this, we have identified four policy implications of our research for the EU:

- 1) There needs to be a separation between the public policy and action on the prevention of risky use from the prevention of harmful use. This separation is important, as it will facilitate a focus on reversing the early development of risky behaviour.
- 2) Within the prevention of risky use, to acknowledge and treat separately the following components of risky use: (a) the modification of environmental determinants and (b) the early detection and modification of individual vulnerability related determinants. This separation is particularly important, as the target for modifying environmental determinants are groups or segments of society, whereas the target of interventions around vulnerability-related determinants are individuals. Both need different approaches and strategies.
- 3) To encourage research around “positive” risky behaviours. We discussed above how “positive” risky behaviour can be a natural part of the development from adolescent to adult. The promotion of testing risks and one’s own limits with licit substances is of high relevance for society and the individual and we should engage in public debates around this.
- 4) Whilst much work can be done within health policy to reduce the development of risky substance use and gambling, it is evident from our models that many of the determinants lie beyond the scope of health policy makers, for example within areas of policy such as education and employment. Thus, the final policy implication of our work is that policy makers must work cross-departmentally to address the full range of the social determinants of the transition to risky substance use and gambling.

5. CONCLUSIONS

The major conclusions arising from this work are:

- The influence the environment of an individual plays in the development of problems of risky substance use and risky gambling is greater than and more acutely understood than that of individual characteristics and molecular factors.
- The determinants underlying the transition from non-use/ use to risky use or substances or gambling are complex in nature and span factors from the molecular and cellular through the individual to the environment.
- Specific determinants are common to the development of all risky behaviours, and these include determinants from the molecular and cellular, individual and social environmental levels of analysis.
- In order to address problems of risky substance use and gambling society as a whole must work to overcome key issues, for example the balance of power and social status, through tackling factors such as marginalisation.
- An increased research focus on this early stage in the development of addiction is required to increase understanding and produce effective strategies for the prevention of future harm to individuals and society by allowing the development of such addictive trajectories.
- Increased levels of multidisciplinary research within this field are necessary to fill knowledge gaps and highlight possible effective future strategies in dealing with problems of risky use.
- Clarification of multi-dimensional concepts, age boundaries and usage patterns within published research is essential to allow the unification of future research findings.

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APPENDIX 1: GLOSSARY OF DETERMINANTS

This glossary includes all the determinants that occur within the model for each different substance and gambling. A number of determinants (listed first below) are not defined because they were deemed self-explanatory:

- Marital status
- Chronic pain conditions
- Drinking in pregnancy
- Drinking in lactation
- Family history of drinking problems
- Family history of gambling
- Family history of drug use
- Free online gambling arenas
- Increased frequency of use
- Increased volume of use
- Marital status
- Parent/sibling substance use
- Personal/family history of psychotic symptoms
- Personal history of use
- Smoking during pregnancy
- Urban place of residence
- Tax increases

Accessibility – the extent to which people are able to find an individual or business selling a given product, with high accessibility referring to a state in which it is easy to gain access to a product.

Affordability – the state of being cheap enough for people to be able to buy, with high affordability referring to a price at which many people can afford to buy a product.

Agency – the capacity of a person (or other entity) to act in an environment.

Institutions of social control – powerful bodies that regulate group and individual behaviour leading to conformity to the rules of a given social situation; for example family, religion, government, media and education.

ALDH2 – Aldehyde dehydrogenase 2, an enzyme involved in alcohol metabolism. Approximately 50% of Orientals lack a functional form of this enzyme, which leads to flushing, nausea etc when drinking alcohol and may result a greater susceptibility to many types of cancer.

Anxiety – ranges from a normal emotion to an unpleasant state of inner turmoil, often accompanied by nervous behaviour (such as pacing) and it is a subjectively unpleasant feeling . There are a range of anxiety disorders including social anxiety, panic disorder etc

Availability – the extent to which something is easily obtainable and ready for use. Availability and accessibility are often used interchangeably.

Baseline alterations in neurocircuitry – Neurocircuitry refers to the connections and relationships between different areas of the brain that are involved in a particular function.

Baseline refers to the state of neurocircuitry prior to any substance use or gambling.

Branding – the process involved in creating a unique name and image for a product in the consumers' mind. Branding aims to establish a significant and differentiated presence in the market that attracts and retains loyal customers (such as mild or menthol cigarettes).

Celebrity endorsement – a form of brand or advertising campaign that involves a well known person using their fame to help promote a product or service, for example television advertisements or launch event appearances.

Concurrent substance use – simultaneous use of two or more psychoactive substances, including alcohol and nicotine.

Cue reactivity – physiological and subjective reactions to presentations of drug-related stimuli (such as cigarettes or bottles of alcohol) or being in an environment associated with drug use.

Delay discounting – represents ability to resist taking an immediate smaller reward and wait for a larger reward.

Depression – ranges from a normal emotion to a severe unremitting constant feeling of sadness and lack of interest, affecting how a person feels, behaves and thinks and at its most severe, depressive disorder with suicidal ideation is a medical emergency.

Design of venue – for example designing bar/club layout to minimise violence.

Dopamine receptor gene polymorphisms – different forms of the dopamine receptor genes that may confer susceptibility to the risky use of substances or gambling .

Early age onset – engaging in substance or gambling use prior to the age of 17.

Early onset alcohol use – engaging in alcohol use prior to the age of 17 (although many neurobiology studies consider early age of onset to be under 25 years).

Early onset cannabis use – engaging in cannabis use prior to the age of 17.

Early onset polydrug use – engaging in polydrug use prior to the age of 17.

Economic climate – a general characterization of the overall mood of the global or a regional economy, which captures the status of the stock market, the perception of the economy by consumers and the availability of jobs and credit.

Education – the process of receiving or giving systematic instruction, especially at a school or university.

Employment status – describes an individual's state of employment; self-employed, employed, unemployed, retired, student.

Ethnicity – a socially defined category of people who identify with each other based on a shared characteristic such as a shared ancestry, history, ideology, or cultural heritage.

Expectancies – the state of thinking or hoping that something, especially something good, will happen as a result of performing a given behaviour.

Extraverted personality – extraversion is manifested in outgoing, talkative, energetic behaviour.

Family environment – the social-environmental characteristics of family, including family structure (e.g. single parent versus two-parent households).

Framing of addiction as inherent – The distinction between individuals who can handle their behaviour and those cannot. This dissociates users into two groups of ‘addicts’ and ‘normal’ users, where normal use is perceived as use without risk.

Gender – the range of physical, biological, mental and behavioural characteristics pertaining to, and differentiating between, masculinity and femininity.

Healthcare services – the availability and accessibility of healthcare services that seek to manage potentially risky substance use.

Higher basal β -endorphin level - naturally higher levels of β -endorphins (opioids in the brain) found within the brain confer an increased alcohol preference.

Implicit bias – is prejudice or partiality that that we carry without awareness or conscious direction.

Impulsivity – a multi-factorial construct that involves a tendency to act on a whim, displaying behaviour characterized by little or no forethought, reflection, or consideration of the consequences.

Increased β -endorphin response – following substance use the levels of β -endorphins released are higher in individuals susceptible to risky use.

International trade – the exchange of capital, goods and services across international borders or territories.

IQ – the intelligence quotient is a score derived from one of several standardized tests designed to assess intelligence.

Lack of risk awareness – the individual has a limited awareness of the risks associated with engaging in a behaviour.

Learning processes – the ways in which people learn, for example through verbal and problem solving elements.

Legal limits/legality – the legal status of a substance or behaviour within a society, including the age at which consumption of a particular substance becomes legal. For example, in certain

countries alcohol is prohibited whilst in others it is legal to drink above a certain age (e.g. 18 or 21 years).

Lifetime history of PTSD – A lifetime history of post-traumatic stress disorder, a particular type of anxiety disorder following a significantly traumatic event.

Loss aversion – is the tendency to strongly prefer avoiding losses to acquiring gains.

Low activity level – the situation in which an individual engages in only limited amounts of physical activity or exercise.

Low levels of serotonin metabolites in CSF – low levels of the serotonin break down product 5-hydroxyindoleacetic found within the cerebrospinal fluid of an individual.

Low levels of D2/D3 receptor – reduced availability of dopamine receptors (targets), D2 and D3, within specific brain regions contributes to increased impulsivity and susceptibility to risky use of some substances or gambling in some individuals.

Low parental monitoring – a low level of knowledge about the activities, whereabouts, and companions of one's children.

Marginalisation – the social process of becoming or being made marginal that can apply to an individual or group within a larger society.

Maturing out – a process that is believed to result when people reach their twenties or thirties and take on the roles and responsibilities of adulthood, such as marriage and having children.

Mode of use – the different ways in which a user can take particular substances, including drinking, smoking, snorting and injecting.

Mood disorders – a disorder characterized by the elevation or lowering of a person's mood, such as depression or bipolar disorder (mania and depression).

Moral strictures – rules or limits relating to morality.

Neuroticism – a personality trait characterized by anxiety, moodiness, worry, envy and jealousy.

New product development – the development of new products that are targeted to different segments of a population, for example Alcopops.

Normalisation – the process by which an activity or behaviour becomes common, and therefore is seen to be relatively normal, within in a given society.

Parental SES – the influence of socio-economic status of parents (see SES below for a definition).

- Peer influence** – the pressure that a peer group, observers or individual exerts that encourages others to change their attitudes, values, or behaviours to conform to group norms.
- Permissive parenting** – is parenting that is characterized by parents who are responsive to their children, but lack rules and discipline.
- Personality disorders** – a deeply ingrained and maladaptive pattern of behaviour of a specified kind, typically apparent by the time of adolescence, causing long-term difficulties in personal relationships or in functioning in society.
- Plastic glasses** – a safety measure introduced to drinking establishments, replacing glass containers with plastic, to prevent incidences of violence involving broken glass.
- Popular culture** – the influence of popular culture on the acceptability of substance use and user expectations of use, for example with substance use portrayed as fun as fashionable.
- Power status** – the level of power an individual holds in society and over the circumstances in which they find themselves. Those in positions of low SES are often relatively powerless.
- Price promotions** – offers on a purchase price making products more affordable, for example ‘buy one get one free’ and ‘25% off if you buy 6 bottle’ deals.
- Public Health Recommendations** – advice given to the population aimed at improving public health, such as drinking guidelines or dietary guidance.
- Reinforcement** – an event, circumstance, or condition that increases the likelihood that a given response will recur in a situation like that in which the reinforcing condition originally occurred.
- Rewards for return custom** – incentivising repeat custom by providing a reward for loyalty.
- Schizophrenia** – a mental disorder characterized by a breakdown of thought processes and by a deficit of typical emotional responses. Common symptoms are delusions, auditory hallucinations, disorganized thinking and a lack of emotional intelligence.
- Secondary deviance** – the internalisation of deviant identity through integration into self-concept.
- Security staff training** – training of security staff to better manage encounters with drunk or high individuals.
- Serotonin receptor density** – A higher density of serotonin receptors within specific regions of the brain are associated with an increased preference for alcohol in some rats.
- Self esteem** – a reflection of a person's overall emotional evaluation of his or her own worth. It is a judgment of oneself as well as an attitude toward the self, encompassing beliefs and emotions.

Sensation seeking – a personality trait defined by the search for experiences and feelings, that are "varied, novel, complex and intense", and by the readiness to "take physical, social, legal, and financial risks for the sake of such experiences."

Serotonin transporter availability – An increased serotonin transporter availability in specific brain regions is associated with increased alcohol intake in primates.

SES – an economic and sociological combined total measure of a person's work experience and of an individual's or family's economic and social position in relation to others, based on income, education, and occupation.

Sexuality – a broad area of study related to an individual's sex, gender identity and expression, and sexual orientation.

Short allele of 5'-HTTLPR promoter – a variant or polymorphism in the short allele of the serotonin transporter promoter may be associated with increased risky substance use or gambling.

Sink estates – council housing estates characterised by high levels of economic and social deprivation.

Lifecourse normative behaviours – the culturally prescribed timeline for accomplishing life tasks in adulthood (varies by culture and time); for example, having your first job, getting married, having children & retiring.

Social networks – a social structure made up of a set of social actors (such as individuals or organizations) and a set of the dyadic ties between those actors.

Social norms and customs – group-held beliefs about how members should behave in a given context; informal understandings that govern society's behaviours. *Customs* infer to the behaviours and mannerism of a given people.

Sports sponsorship – support for sporting events through the provision of products or services in return for product advertising at sports events.

Stress – a state of mental or emotional strain or tension resulting from adverse or demanding circumstances.

Subculture – a group of people within a culture that differentiates themselves from the larger culture to which they belong.

Tolerance – the need to take more of a drug to get the same effect.

Youth – the period of life when one is young, often referring to the time between childhood and adulthood.

APPENDIX 2: TOBACCO MODEL WITH MULTIDISCIPLINARY EMPHASIS

