Addiction and Lifestyles in Contemporary Europe – Reframing Addictions Project

ALICE RAP (2011-2016)

Project no. 266813

FINAL PUBLISHABLE SUMMARY REPORT

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1. Executive summary

1.1 BIOLOGY AND ADDICTIONS

There are many reasons why societies are concerned about alcohol, nicotine, and other psychoactive drugs (hereafter, drugs). One obvious and important reason is because these drugs interfere with our biology and functioning.

Years of life lost due to drugs

There are many ways to document and describe this interference. One way is to use years of life lost (YLL), which also acts as a surrogate indicator of broader impact on functioning and well-being. YLLs are calculated by subtracting the actual age at death from the life expectancy given that age; if somebody dies aged 65 years, and the life expectancy for people his or her age is 80 years, then YLLs would amount to 15 years. In the European Union in 2013, illegal drug use was responsible for 1.4 million YLL (1.8% of all YLL), alcohol for 6.1 million years of YLL (8.2% of all YLL) and tobacco for 13.6 million YLL (18.2% of all YLL).

Quantitative risk assessment

Another way to describe the interference of drugs on our biology and functioning is to use quantitative risk assessment. For example, the Margin of Exposure (MOE) for any drug gives an indication of whether individuals are exposed to (or use) a drug at a lower level of risk or not. Margins of exposure compare the ratio of a toxic dose of a drug (usually the benchmark dose BMDL10, the lowest dose which is 95% certain to cause no more than a 10% negative outcome incidence) with the dose consumed. A MOE of 100 means that the drug is being consumed at one hundredth of the toxic dose; a MOE of 1 means that the drug is being consumed at the toxic dose. Thus, the higher the MOE, the lower the level of risk. MOE for drugs can be calculated taking into account a range of hazard outcomes in health and other well-being domains, as long as suitable dose-response data are available (which is not the case for most drugs). Therefore, analyses to date are primarily restricted to lethal outcomes based on animal studies, which also act as a surrogate indicator of broader impact on functioning and well-being. Results for European adults find that for individual European users, nicotine has a margin of exposure of 7.5 (95% CI 2.7 to 14.0), heroin 2.2 (95% CI 0.5 to 8.2) and alcohol 1.3 (95% CI 0.6 to 2.7). It is important to note that the MOE as described here applies where the harm from the drug is inherent in the drug itself; it does not account for the harms that arise from drug delivery systems, for example, smoked tobacco. The low MOE for alcohol (and thus high risk) is due to the high exposure levels of alcohol use by European adults.

Evolutionary drivers of drug use

It is often considered that one of the reasons that there is so much harm from drugs is that exposure to them is an evolutionary novelty. The evidence suggests otherwise: drugs are not evolutionary novelties. In the story of life over the last 400 million years, one of the developments has been the battle between plants and the animals that eat them. Of many defence mechanisms, plants produce secondary metabolites, including cannabis, cocaine, morphine and nicotine, potent neurotoxins that evolved because they punished and deterred consumption by plant-eating animals. Thus, from the evolutionary ecological perspective, we find selection for drugs that discourage consumption of the plant (i.e. punishment of the consumer). We do not find selection for drugs that encourage consumption of the plant (i.e. rewarding the consumer), which is the inferred outcome based on the neurobiological and behavioural psychological theory of reward and reinforcement. Counterbalancing the development of plant neurotoxins, animals have evolved to counter-exploit the use of drugs including buffering against nutritional and energetic constraints on signalling in the central nervous system and exploiting the anti-helminthic properties of many drugs. Present day examples of pharmacophagy are seen with Congo basin hunter gatherers, amongst whom the

quantity of cannabis and nicotine consumed is titrated against intestinal worm burden - the higher the intake, the lower the worm burden. Moreover, when treated with the anti-worm drug, abendazole, the number of nicotine-containing cigarettes smoked is reduced.

In another example, the presence of ethanol within ripe fruit suggests low-level but chronic dietary exposure for all fruit-eating animals, with volatilized alcohols from fruit potentially serving in olfactory localization of nutritional resources. The same seems to apply to humans, since our ape ancestors gained a digestive dehydrogenase enzyme capable of metabolizing ethanol near the time that they began using the forest floor, about 10 million years ago. The alcohol dehydrogenases in our more ancient and arboreal ancestors did not efficiently oxidize ethanol. This change suggests that exposure to dietary sources of ethanol increased in hominids during the early stages of our adaptation to a terrestrial lifestyle. Because fruit collected from the forest floor is expected to contain higher concentrations of fermenting yeast and ethanol than similar fruits hanging on trees, this transition may also be the first time our ancestors were exposed to (and adapted to) substantial amounts of dietary ethanol.

Heavy use over time as explanatory variable

The evolutionary evidence suggests that humans have evolved to seek out and extract cholinergic agents from plants in order to combat invertebrate parasites such as helminths. This does not imply that humans evolved to specifically consume, for example tobacco, or that tobacco use is beneficial in the modern world. What is different in the modern world is novel availability. With alcohol, the evolutionary evidence implies that the genomes of modern humans began adapting at least 10 million years ago to dietary ethanol present in fermenting fruit— a source of ethanol that is remarkably similar in concentration and form (i.e., with food) to the low levels of ethanol consumption that might reduce the risk of ischaemic events. Again, what is different in the modern world is novel availability through fermentative technology enabling humans to consume beverages (devoid of food bulk) with higher ethanol content than fruit fermenting in the wild.

It is the sustained use of drugs over time, and, in particular, heavy use over time that leads to harm. In fact, the evidence suggests we can go further in noting that heavy use over time explains the consequences of what are called ‘addiction’ or ‘substance use disorders’, with heavy use causing end organ damage that results in more heavy use. The term ‘substance use disorder’, is often used as shorthand to identify individuals who might benefit from advice or treatment, but as a condition itself, ‘substance use disorder’ is a medical artefact for which biology provides no support, since ‘substance use disorder’ itself occurs in all grades of severity, with no natural distinction between ‘health’ and ‘disease’.

Take one example, alcohol consumption. Chronic disease risk is a continuous exponential relationship with consumption. Alcohol consumption is close to log-normally distributed in populations, skewed towards heavy drinking. There is no natural cut-point above which "alcohol use disorder" or “alcohol dependence” definitively exists and below which, it does not. Unmanaged heavy drinking can be associated with even further heavy drinking, often culminating in a more difficult to manage state due to end organ brain damage, with the brain damage a consequence of the heavy drinking. "Alcohol use disorder" or “alcohol dependence” are defined as a score on a checklist of symptoms, and there is a smooth line exponential relationship between levels of alcohol consumption and the score on the checklist. Heavy drinking is a cause of the items on the checklist, including compulsion to drink more which is a consequence of brain damage, itself caused by heavy drinking. Thus “alcohol use disorder” is a diagnostic artefact and no more is needed to consider what is called “alcohol use disorder” other than heavy use over time. This does not imply that heavy use over time is the only cause of harm - there are other biological and contextual factors, for example,

alcohol dehydrogenase polymorphisms and income levels, which can impact harm independent of levels of alcohol consumption.

There is on-going discussion as to whether or not sugar is an 'addictive' substance in the same bucket as alcohol and other drugs. Moving out of the addiction frame to the heavy use over time frame provides an alternative insight to this. As with alcohol (and, high blood pressure), chronic disease risk associated with plasma glucose levels is a continuous exponential relationship. The distribution of blood glucose levels is close to log-normally distributed in populations, skewed towards high levels. There is no natural cut-point above which diabetes definitively exists and below which, it does not. Similar to the alcohol model (heavy use of alcohol over time results in brain damage, which leads to further heavy use of alcohol over time), there is evidence that heavy use of sugar over time damages hippocampal function, which leads to further heavy use of sugar over time. Thus, in the heavy use over time frame, sugar can be placed in the same bucket as alcohol and other drugs.

1.2 PREVENTION AND TREATMENT

Prevention

A combination of three factors, biological (e.g., genes), individual (e.g., knowledge and skills – health literacy) and the environment (e.g., social norms) drive heavy drug use, with components from all three factors (for example, alcohol dehydrogenase at the molecular level, income at the individual level, and stigma at the environmental level) exacerbating harm, independent of the level of use. One of the implications of the biological approach is that, given the active and functional relationship we have with drugs, it is not surprising that exposure to drugs facilitated by low affordability (high availability and low price) and commercial communications result in heavy use over time. Advertising increases use for both novice users and heavy users, operating at the level of measurable brain responses. Given the drivers acting across all three factors (biological, individual and environmental), it is little wonder that prevention amongst youth has not had the impacts that we would like. This is also due, to a large part, to insufficient resourcing for prevention, insufficient research and appraisal of impact of preventive activities, and insufficient implementation of evidence-based effective programmes. One solution to help rectify these deficiencies is to create a central, transparent and evidence-based approval process for behavioural interventions, a European Prevention Agency.

Treatment

No matter what prevention or policies are put into place, some people will always run into problems with heavy drug use over time and will need and benefit from treatment. Unfortunately, there are three problems here. First, the gap between need and treatment is large. Using United States data, for example, less than 1 in 5 of individuals with a lifetime 'diagnosis of alcohol use disorder' have ever received treatment and less than 1 in 4 of individuals with a lifetime 'diagnosis of drug use disorder' have ever received treatment. Second, considerable marginalization and stigmatization happen in the path to treatment, and these are often exacerbated by treatment. And, third, even if people get into treatment, pharmacotherapy for heavy use of alcohol and drugs is generally under developed and underperforming for impact.

Drug delivery systems

Harm from drugs also results from modes of drug delivery, as in the case of nicotine. Whilst nicotine itself is not a harm free drug, over the last one hundred years, the harm has largely derived from its mode of delivery - smoked tobacco. Technological developments have now led to electronic nicotine delivery systems (ENDS) (e-cigarettes) as widespread alternative delivery systems to smoked tobacco, with best estimates showing e-cigarettes to be 95% less harmful to health than smoked

cigarettes. Margins of exposure analyses of ENDS find that tobacco-specific toxicants and trace nicotine impurities are below levels likely to cause harm, suggesting that at least, from this perspective, e-cigarettes are likely to be less harmful than smoked tobacco. MOE analyses find that it is nicotine that is the toxic drug in e-cigarettes. Nicotine levels can be set, regulated and monitored. Concern has been raised that ENDS are additive or gateway products to smoked tobacco, rather than replacement products. However, the evidence does not support this.

1.3 GOVERNANCE

Governance

Governance can be considered as the processes and structures of public policy decision making and management that engage people across the boundaries of public agencies, levels of government, and/or the public, private and civic spheres in order to carry out a public purpose that could not otherwise be accomplished. An analysis of 28 European countries finds that only one-quarter of countries can be considered as having a comprehensive policy for all drugs, within a broad societal well-being approach. For almost all European countries, there are opportunities for improving governance both for legal and illegal drugs, while pursuing a societal well-being goal.

Missed opportunities

There are a number of reasons for the un-achieved governance opportunities. First, it is not generally clear what is being governed. Concepts of addiction have varied enormously over both time and place within Europe, with considerable heterogeneity between drugs (alcohol, tobacco and illegal drugs) and levels of governance (international, national and local). Using heavy use over time as the frame for action would simplify and facilitate convergence of our approaches to drug governance as we move forward across different jurisdictions. Second, a panoply of stakeholders is active in addictions governance, and the relationship between evidence and policy will be driven by the stakeholder group which has power and influence at the time - and this will also vary by time and place. Third, concepts and power are reflected in and further driven by variations in media constructs, which also vary over time and place. And, fourth, corporate power through multiple channels of influence can hinder inadequate governance - there are insufficient and inadequate rules of the game in place to ensure level playing fields for discussions across all actors. There is no simple solution for moving forward. However, three opportunities present themselves.

Well-being

First, societal well-being, as captured, for example, by OECD, provides a frame for improved governance. Well-being has various dimensions, including quality of life (health, education and skills, social connections, civic engagement, and personal security), material conditions (income, employment and housing) and sustainability over time. Drugs and drug-related harms are affected by and affect all of these dimensions. Well-being analyses find that, whilst some drug policies may reduce health harms, they often come at the expense of adverse side effects including criminalization, social stigma and social exclusion, all of which also independently exacerbate health harms. A well-being frame calls for whole-of-society approaches that avoid criminalization due to drug use.

Whole-of-government and whole-of-society approaches

Drug governance strategies need to be comprehensive, combining legal and illegal substances. Strategies should manage drugs as a whole, with a focus on well-being, and the impact of harm addressed independently of the drug. Approaches should be anticipative rather than reactionary, with regulation embedded within international coordination. The structures to support the strategy should be based on coordinated networked governance, with complex organizational structures and

stakeholder involvement. Silos need to be broken inside of government, bringing together health, social welfare, justice, well-being and international treaties. Regional and local public policies can create policy communities and networks for responses, within an overall common strategy. The creation of new organizational structures to manage new drugs should be avoided.

When managing the private sector, the leading role in determining the strategy of public drug policy should be in public sector hands to enhance societal well-being. An evolved co-production system needs to include means of avoiding co-option by both industry and non-governmental organizations dependent on public budgets. Transparency, and checks and balances should be ensured as the drivers to increase evidence-based impact in decision-making. The relation with stakeholders should establish the rules of the game regarding which phase of the policy cycle and which typologies of stakeholders can provide a contribution for the public good, simultaneously to their own interests. Drug governance, in particular, needs to address marketing, which includes all the actions undertaken by producers of drugs to persuade consumers to buy and consume more, including creating and facilitating opportunities, eliciting and shaping social cognitions, and activating and using automatic responses through distribution, pricing, product design, as well as advertising. There are existing models of how to control marketing effectively for public health, the most notable being the Framework Convention on Tobacco Control, an international treaty whose articles include controls on the advertising, display, packaging and design of tobacco products.

The potential of civil society organizations to influence drug policies and preventive actions has been very strong historically. The work required for civil society organizations to claim their own role and to profile themselves, and, often, to defend their views on effective action in relation to business actors is a tough task. Civil society organizations have more chances for success in parliamentary representative processes than through executive channels, but this requires effective coalition building, something yet to be fully achieved.

Accountability

Structural drivers of harm from drug use include biological attributes and functions, population size and structure, and levels of wealth and income disparities within jurisdictions. Core drivers refer to the processes, mechanisms, and characteristics that influence harm, sometimes through the structural drivers, and sometimes not. Core drivers of harm include drug potency and drug exposure levels, the technological developments that might influence these, and social influences and attitudes, including social stigma and social exclusion. Included in the policy drivers level are measures that reduce drug exposure, actions that promote research and development to reduce drug potency, measures that maximize co-benefits and minimize adverse side-effects of policies and actions, incentives for healthy individual behaviour, and legislation aimed at managing markets, such as the definition and enforcement of rules of engagement of the private sector. Policies and measures affect the core drivers of harm. The structural and core drivers may, in turn, influence policies and measures.

Placed conceptually at the centre of the drivers is the Health Footprint, the accounting system for identifying the determinants of drug-related harm and the management tool to evaluate opportunities by the public and private sectors and civil society to reduce harm. Modelled on the carbon footprint, the health footprint can be defined as a measure of the total amount of drug-attributable disability adjusted life years (DALYs) of a specific population, sector or action of interest, defined by specific spatial (e.g., jurisdiction) and temporal (e.g. year) boundaries. The Health Footprint can measure the impact of a range of structural and core drivers of impaired health and the policies and measures that impact upon them. The Health Footprint, thus, accounts for who and what causes the harm done by drugs. Drug-related health footprints could become standard components of annual reporting by relevant public and private sector bodies.

2. Summary description of project content and main objectives

Introduction:
Addictions are an extensive feature of contemporary societies, bringing considerable concerns. As their number has increased over the last decades, they have become a focus of social, economic and political attention, sometimes polarising societies and politics. The changing nature of work and of private life, the evolution of consumption patterns, values, attitudes and beliefs of contemporary societies have all changed the place and challenges of addictions to present European society. ALICE RAP (Addictions and Lifestyles in Contemporary Europe: Reframing Addictions Project) is a trans-disciplinary EU project which aims to help policy makers "re- think and re-shape" current and future approaches to the huge human and economic costs of addictions and lifestyles in Europe. ALICE RAP aims to critically examine and analyse currently fragmented research and strengthen scientific evidence to inform a new dynamic platform for public and political dialogue and debate on current and alternative approaches to addictions.

Summary:
ALICE RAP's trans-disciplinary research programme included a wide range of coordinated quantitative and qualitative disciplines stretching across the humanities and social sciences and the biological and medical sciences, with expertise in addiction studies, anthropology, cognitive science, criminology, demography, economics, education, engineering, epidemiology, evolutionary biology, foresight management, history, journalism, law, mathematics, media, neurobiology, political science, psychiatry, psychology, psychotherapy, public health, public management, social marketing, social policy, social psychology, sociology, technology, and toxicology. Whilst capitalizing on existing research, ALICE RAP has overcome previously under resourced and fragmented research in addiction sciences, and has provided a critical mass of European researchers, contributing to a European research space in addictions.

Main Objective:
Through integrated trans-disciplinary research, to study a wide range of factors through a foresight approach to provide an improved knowledge base for policies and to inform a redesign of effective addictions governance.

Vision Statement:
Promote well-being through a synthesis of knowledge to redesign European policy and practice to better address the challenges posed by substance use and addictive behaviours.

Mission Statement:
Advance synergy among sciences that address substance use and addictive behaviours, through a five-year programme of European trans-disciplinary research.

3 Description of the main scientific and technical results

The ALICE RAP project (http://www.alicerap.eu/) was a €10 million, five year (2011-2016) action co-financed by the FP7 programme of the European Union to study the place of addictions and lifestyles in contemporary Europe. One thousand months of scientific endeavour by 67 scientific institutions from 24 European countries covering over thirty scientific disciplines ranging from anthropology to toxicology have analysed the biological, economic, historical, medical, political and social factors behind addictive drugs and behaviours. The goal of the project was to do much more than just study the place of addictions in contemporary Europe, but, rather, reach a reframing of our understanding of addictions – elucidating where our concepts and beliefs about addictions come from, how we use them, and with what consequences for societies and individuals. With this reframing, we propose a redesign of addictions governance.

In our work, we have built on two main strengths - our multi-disciplinarity, and our ability to network across topics and disciplines. Our disciplines stretch across the humanities and social sciences and the biological and medical sciences, with expertise in addiction studies, anthropology, cognitive science, criminology, demography, economics, education, engineering, epidemiology, evolutionary biology, foresight management, history, journalism, law, mathematics, media, neurobiology, political science, psychiatry, psychology, psychotherapy, public health, public management, social marketing, social policy, social psychology, sociology, technology, and toxicology.

The strength of our networking during the third year of the five-year project is illustrated in Figure 1. Between end of the first year, and the third year of the project, network density had increased by 20%, and the number of isolated participants had decreased by nearly two-fifths.

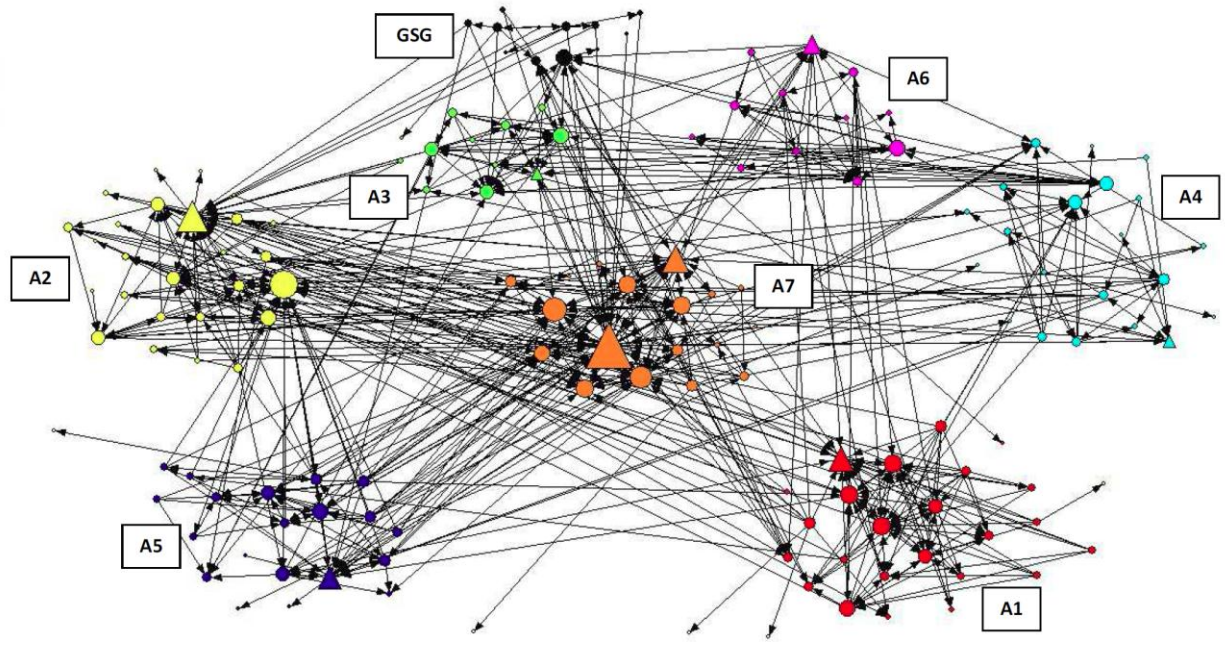

Figure 1. Network diagram of ALICE RAP scientists during the third year of the five year project.
Legend - The 'As' represent different areas of work, with groups of scientists: A1, Culture and History of addictions; A2, Epidemiology of addictions; A3, Determinants of addictions; A4, Business of addictions; A5, Governance of addictions; A 6, Youth and addictions; A7, Project coordination, evaluation and dissemination; GSG, Global Scientific Advisory Group.
Source: http://www.alicerap.eu/resources/documents/doc_download/225-wp20-alice-rap-network-evaluation-report-2nd-wave.html.

Over the course of the project, ALICE RAP has produced over five million words in its scientific reports (www.alicerap.eu/resources/documents/cat_view/1-alice-rap-project-documents/7-reports.html). On top of that, there have been more than 160 scientific publications in peer-reviewed journals, journal supplements, and books (www.alicerap.eu/resources/documents/cat_view/2-alice-rap-scientific-publications.html), culminating in a series of six books on the governance of addictive substances and behaviours, published by Oxford University Press (Ysa et al. 2014; Anderson et al. 2015; Hellman et al. 2016; Gell et al. 2016; Miller et al. 2016; Anderson et al. 2016). The content of this summary is driven not only by the immense scientific output of ALICE RAP, but also by the intense formal and informal conversations that took place during the estimated 1,000 hours that some or all of the 180 scientists met together whilst working on ALICE RAP. The summary follows three main headings, biology and addictions, prevention and treatment, and governance.

3.1 Biology and addictions

There are many reasons why societies are concerned about alcohol, nicotine, and other psychoactive drugs (hereafter, drugs). One obvious and important reason is because these drugs interfere with human biology and functioning.

Years of life lost due to drugs

Taking drugs alone, in the European Union in 2010, illegal drug use was responsible for 0.5 million years of life lost due to premature mortality (0.7% of all YLL - **Y**ears of **L**ife **L**ost due to premature mortality) and 2 million **D**isability-**A**djusted **L**ife **Y**ears lost (1.4% of all DALYs lost) (see Table 1). YLLs are calculated by subtracting the actual age at death from the life expectancy given that age; if somebody died aged 65 years, and the life expectancy for people his or her age would be 80 years, then YLLs would amount to 15 years. DALYs are a measure which combines years of life lost due to premature mortality with years of life lost due to disability with disability rated for severity between perfect health (0) and death (1). Alcohol consumption contributed to the burden of disease to a greater extent than illegal drug use but less than tobacco use with 5.9 million years of YLL (7.9% of all YLL) and 7.5 million DALYs lost (5.3% of all DALYs lost). Tobacco use in the EU contributed the most to the burden of disease of all drugs, and was responsible for 13.8 million YLL (18.5% of all YLL) and 16.2 million DALYs lost (11.4% of all DALYs lost). The burdens caused by illegal drug use, alcohol, and tobacco in the EU were greater among men than among women, with alcohol and drug burdens incurring at much younger ages than tobacco; for all drugs, the burden of disease in the EU was proportionally larger than the global burden, which is not surprising, as the prevalence of use and heavy use is larger in the EU than the rest of the world.

Due to this high disease burden, the European Union incurs substantial social costs, in the magnitude of several hundred billion Euros per year. These costs are not limited to the health care sector, but comprise the legal sector (police, court, prison), the workplace (productivity losses via absenteeism, presenteeism, disability and mortality), and the family. Social cost studies are limited as not all burdens can be quantified in monetary terms such as pain and suffering, so-called intangible costs , resulting from drugs, which add to their burden to European societies. It is heavy use that makes up the substantial part of the burden and the costs of drug use.

Table 1 **Burden of illegal drug use, alcohol consumption and tobacco use in the EU in 2010**

Risk factor	Sex	YLLs (1000s)	YLLs per 100,000	% of all YLLs	DALYs (1000s)	DALYs per 100,000	% of all DALYs
Illicit drug use	Men	435.9	178	1.0%	1,453.6	593	1.9%
	Women	109.2	43	0.4%	554.4	216	0.8%
	Total	545.2	109	0.7%	2,008.0	400	1.4%
Alcohol consumption	Men	4,543.5	1,854	10.3%	6,020.6	2,457	7.9%
	Women	1,380.0	538	4.5%	1,508.0	588	2.2%
	Total	5,923.5	1,181	7.9%	7,528.6	1,501	5.3%
Tobacco use	Men	10,318.6	4,211	23.3%	11,725.2	4,785	15.4%
	Women	3,514.4	1,369	11.4%	4,535.5	1,767	6.8%
	Total	13,832.9	2,757	18.5%	16,260.8	3,241	11.4%

Source: own calculations based on revised estimates from the Institute for Health Metrics and Evaluation.

Quantitative risk assessment

Another way to describe the interference of drugs on our biology and functioning is to use quantitative risk assessment. For example, the Margin of Exposure (MOE) for any drug gives an indication of whether individuals are exposed to (or use) a drug at a lower level of risk or not. Margins of exposure compare the ratio of a toxic dose of a drug with the dose consumed. A MOE of 100 means that the drug is being consumed at one hundredth of the toxic dose; a MOE of 1 means that the drug is being consumed at the toxic dose. Thus, the higher the MOE, the lower the level of risk. MOE for drugs can be calculated taking into account a range of hazard outcomes in health and other well-being domains, as long as suitable dose-response data are available (which is not the case for most drugs). Therefore, analyses to date are primarily restricted to lethal outcomes based on animal studies, which also act as a surrogate indicator of broader impact on functioning and well-being.

One way to the toxic dose, used by toxicologists and those who assess safety of consumed products is the Benchmark Dose (BMD). BMD10 is the benchmark dose in which an adverse event (commonly death) occurs in 10% of subjects (commonly animals) given a one off dose of the drug. BMD10 is normally calculated from LD_{50} (Lethal Dose), the amount of a material, given all at once, which causes the death of 50% (one half) of a group of test animals, by dividing LD_{50} by 10.2. BMD10 is expressed as a mean with 95% confidence interval. The 'L' in BMDL10 indicates that the chosen value is the lower level of the 95% confidence interval. The lower dose is taken for precautionary reasons. Thus BMDL10 is the dose at the lower level of the 95% confidence interval at which 10% of animals taking that dose in one go die.

The BMDL10 has been estimated for a range of drugs and is summarized in Table 2. For a 70kg adult, the BMDL10 works out at 0.14 grams for heroin, 0.21 grams for nicotine and 37.3 grams for alcohol.

Table 2. Average BMDL10 for a range of drugs [mg/kg body weight]. Source: Lachenmeier et al. 2015.

Drug	Average BMDL10 extrapolated from LD50 [mg/kg body weight]
Heroin	2
Cocaine	2
Nicotine	3
Amphetamine	7
Methadone	8
Methamphetamine	8
Diazepam	27
MDMA	32
THC	56
Alcohol	531

Exposures have been calculated for daily doses amongst European adult users and are summarized Table 3.

Table 3 Estimates of daily drug exposure amongst European adults. Source: Lachenmeier et al. 2015.

Drug	Range of individual daily dosage (low, high) [mg]
Heroin	5-300
Cocaine	20-100
Nicotine	1.65-1.89 mg/cig. 10-20 cigs./smoker/day
Amphetamine	5-50
Methadone	10-40
Methamphetamine	5-150
Diazepam	5-40
MDMA	50-700
THC	10-60
Alcohol	13.6 g-54.4 g (1-4 standard drinks)

Knowing both the potency through the benchmark dose and the exposure estimated from surveys, the margin of exposure (MOE) can be calculated as follows:

$$\text{Margin of Exposure (MOE)} = \frac{\text{Benchmark Dose}}{\text{Exposure}}$$

The MOE is the ratio of the benchmark dose divided by the exposure dose. Toxicology-based risk assessment uses different MOE thresholds as guidelines, depending on whether the benchmark dose is derived from animal or human studies. For example, for carcinogens in food products, when derived from animal studies, MOEs should be higher than 10,000, whereas when derived from human studies they should be higher than 1,000. Differing MOEs are often set for differing health outcomes, with lower MOEs for non-cancer outcomes, compared with cancer outcomes.

According to the typical interpretation of MOEs derived from animal experiments (i.e. as in Table 4.1), MOE < 10 is judged to pose "high risk", while MOE < 100 are judged as "risk". MOEs above 100 are often judged as acceptable because the value of 100 corresponds to the default 100-fold uncertainty factor, which has been historically used in regulatory toxicology. The factor of 100 is based on scientific judgement and represents the product of two separate 10-fold factors that allow for interspecies differences and human variability. When the toxicological endpoint is based on human data and not on animal experiments as has been done for alcohol in relation to liver cirrhosis, MOEs above 10 would be judged acceptable and MOEs below 1 as "high risk". Results for European adults are summarized in Figure 2. It is important to note that the MOE as described here applies where the harm from the drug is inherent in the drug itself; it does not account for the harms that arise from drug delivery systems, for example, smoked tobacco. The low MOE for alcohol (and thus high risk) is due to the high exposure levels of alcohol use by European adults. For individual European users, nicotine has a margin of exposure of 7.5 (95% CI 2.7 to 14.0), heroin 2.2 (95% CI 0.5 to 8.2) and alcohol 1.3 (95% CI 0.6 to 2.7). In other words, nicotine users are using the drug at a level of 7.5 times the benchmark dose, heroin users twice and alcohol users just over the benchmark dose. That alcohol has a lower MOE (and thus more risky) than heroin is simply due to the high dose that individual alcohol users take on average.

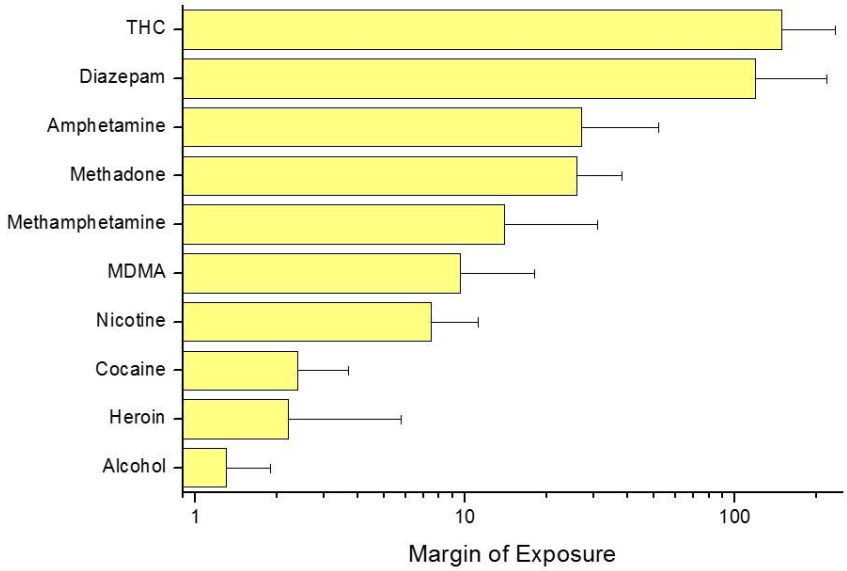

Figure 2 Margin of exposure for daily drug use estimated using probabilistic analysis. Source: Lachenmeier & Rehm (2015).

Drug policies could thus be evaluated for their impact on MOE, with a target that all policies should achieve MOEs of 100 or 10, depending on the BMDL10 data source (animal or human). Policies could achieve their result by either reducing exposure or the potency of the consumed product through technological development of less potent drugs or less amount of the drug in the standard ingestion unit.

Drug delivery systems

Harm from drugs also results from modes of drug delivery, as in the case of nicotine. Whilst nicotine itself is not a harm free drug, over the last one hundred years, the harm has largely derived from its mode of delivery - smoked tobacco. Technological developments have now led to electronic nicotine delivery systems (ENDS) (E-cigarettes) as widespread alternative delivery systems to smoked tobacco, with best estimates showing e-cigarettes to be 95% less harmful to health than smoked cigarettes. Margins of exposure analyses of ENDS find that tobacco-specific toxicants and trace nicotine impurities are below levels likely to cause harm, suggesting that at least, from this perspective, e-cigarettes are likely to be less harmful than smoked tobacco. MOE analyses find that it is nicotine that is the toxic drug in e-cigarettes. Nicotine levels can be set, regulated and monitored. Concern has been raised that ENDS are additive or gateway products to smoked tobacco, rather than replacement products. However, the evidence does not support this. A recent report from the UK Royal College of Physicians (2016) found that E-cigarettes, marketed as consumer products, are proving much more popular than NRT as a substitute and competitor for tobacco cigarettes, and appear to be effective when used by smokers as an aid to quitting smoking. The report noted that E-cigarettes are not currently made to medicines standards and are probably more hazardous than nicotine replacement products, but technological developments and improved production standards could reduce any long-term hazard of e-cigarettes. The report concluded that there is a need for regulation to reduce direct and indirect adverse effects of e-cigarette use, but this regulation should not be allowed significantly to inhibit the development and use of harm-reduction products by smokers.

Evolutionary drivers of drug use

It is often considered that one of the reasons that there is so much harm from drugs is that exposure to them is an evolutionary novelty. The evidence suggests otherwise: drugs are not evolutionary novelties.

There is archaeological and anthropological evidence of ubiquitous use of drugs throughout human pre-history, including nicotine from tobacco and pituri plants, cocaine from coca plants, arecoline from betel nut and ephedrine from khat. Biological evidence also points to a long-time co-evolutionary relationship of these neurotoxins between plants and animals. Most plant species have evolved defensive strategies that punish herbivores that feed on them. Amongst these strategies are psychoactive plant-based drugs that have evolved to interfere with signalling in the central and peripheral nervous systems. These drugs interfere with neurotransmitter synthesis, storage, release, binding and re-uptake; receptor activation and function; and, key enzymes involved in signal transduction.

In the story of life over the last 400 million years, one of the developments has been the battle between plants and the animals that eat them. Of many defence mechanisms, plants produce secondary metabolites, including cannabis, cocaine, morphine and nicotine, potent neurotoxins that evolved because they punished and deterred consumption by plant-eating animals. Thus, from the evolutionary ecological perspective, we find selection for drugs that discourage consumption of the plant (i.e. punishment of the consumer). We do not find selection for drugs that encourage consumption of the plant (i.e. rewarding the consumer), which is the inferred outcome based on the neurobiological and behavioural psychological theory of reward and reinforcement.

Counterbalancing the development of plant neurotoxins, animals have evolved to counter-exploit the use of drugs including buffering against nutritional and energetic constraints on signalling in the central nervous system and exploiting the anti-helminthic properties of many drugs. Present day examples of pharmacophagy are seen with Congo basin hunter gatherers, amongst whom the quantity of cannabis and nicotine consumed is titrated against intestinal worm burden - the higher the intake, the lower the worm burden. Moreover, when treated with the anti-worm drug, abendazole, the number of nicotine-containing cigarettes smoked is reduced.

In another example, the presence of ethanol within ripe fruit suggests low-level but chronic dietary exposure for all fruit-eating animals, with volatilized alcohols from fruit potentially serving in olfactory localization of nutritional resources. The same seems to apply to humans, since our ape ancestors gained a digestive dehydrogenase enzyme capable of metabolizing ethanol near the time that they began using the forest floor, about 10 million years ago. The alcohol dehydrogenases in our more ancient and arboreal ancestors did not efficiently oxidize ethanol. This change suggests that exposure to dietary sources of ethanol increased in hominids during the early stages of our adaptation to a terrestrial lifestyle. Because fruit collected from the forest floor is expected to contain higher concentrations of fermenting yeast and ethanol than similar fruits hanging on trees, this transition may also be the first time our ancestors were exposed to (and adapted to) substantial amounts of dietary ethanol.

The evolutionary evidence suggests that humans have evolved to seek out and extract cholinergic agents from plants in order to combat invertebrate parasites such as helminths. This does not imply that humans evolved to specifically consume, for example tobacco, or that tobacco use is beneficial in the modern world. What is different in the modern world is novel availability. With alcohol, the evolutionary evidence implies that the genomes of modern humans began adapting at least 10 million years ago to dietary ethanol present in fermenting fruit— a source of ethanol that is remarkably similar in concentration and form (i.e., with food) to the low levels of ethanol consumption that might reduce the risk of ischaemic events. Again, what is different in the modern world is novel availability through fermentative technology enabling humans to consume beverages (devoid of food bulk) with higher ethanol content than fruit fermenting in the wild.

Heavy use over time

It is the sustained use of drugs over time, and, in particular, heavy use over time that leads to harm. In fact, the evidence suggests we can go further in noting that heavy use over time explains the consequences of what are called ‘addiction’ or ‘substance use disorders’, with heavy use causing end organ damage that results in more heavy use. The term ‘substance use disorder’, is often used as shorthand to identify individuals who might benefit from advice or treatment, but as a condition itself, ‘substance use disorder’ is a medical artefact for which biology provides no support, since ‘substance use disorder’ itself occurs in all grades of severity, with no natural distinction between ‘health’ and ‘disease’.

Take one example, alcohol consumption. Chronic disease risk is a continuous exponential relationship with consumption. Alcohol consumption is close to log-normally distributed in populations, skewed towards heavy drinking. There is no natural cut-point above which "alcohol use disorder" or “alcohol dependence” definitively exists and below which, it does not.

Unmanaged heavy drinking can be associated with even further heavy drinking, often culminating in a more difficult to manage state due to end organ brain damage, with the brain damage a consequence of the heavy drinking. "Alcohol use disorder" or “alcohol dependence” are defined as a score on a checklist of symptoms, and there is a smooth line exponential relationship between levels of alcohol consumption and the score on the checklist. Heavy drinking is a cause of the items on the

checklist, including compulsion to drink more which is a consequence of brain damage, itself caused by heavy drinking. Thus “alcohol use disorder” is a diagnostic artefact and no more is needed to consider what is called “alcohol use disorder” other than heavy use over time. This does not imply that heavy use over time is the only cause of harm - there are other biological and contextual factors, for example, alcohol dehydrogenase polymorphisms and income levels, which can impact harm independent of levels of alcohol consumption.

From a public health perspective, heavy drinking has been shown to be responsible for the vast majority of alcohol-attributable harm in Europe. The dose-response curves are mostly exponential, leading to the implication that the same reduction in level of consumption (e.g., 40 grams per day) leads to considerably more pronounced reductions in mortality and hospitalizations if it is taken off from a higher level of consumption than from a lower level of consumption. For public health, it is vital to reduce consumption, especially at high levels of consumption, even if these people do not qualify for alcohol dependence or alcohol use disorders. Similarly, it is important to reduce high levels of consumption, even if the people who reduce do not change their status as having an alcohol dependence or alcohol use disorder based on the diagnostic criteria of the current medical systems. Heavy drinking over time clearly is the more meaningful criterion with respect to health consequences compared to a diagnosis of alcohol dependence or alcohol use disorders.

Similar arguments could be made for cannabis). Heavy cannabis use over time has been linked to a number of health effects such as altered brain development, cognitive impairment, chronic bronchitis, psychosis and schizophrenia and lung cancer and single occasion heavy use has been linked to acute effects such as motor vehicle and other injury), independently of whether the criteria for cannabis use disorders were fulfilled or not. A definition based solely on heavy use criteria would also facilitate concentration on the public health aspects of cannabis use, independently of its legal situation, where too often one is confronted with the false dichotomy of equating policy option preferences with presumed presence or absence of consequences (i.e., “cannabis should be legalized because it is a benign substance” vs. “cannabis is linked to considerable health harm, and thus should be prohibited”.

There is ongoing discussion as to whether or not sugar is an ‘addictive’ substance in the same bucket as alcohol and other drugs. Moving out of the addiction frame to the heavy use over time frame provides an alternative insight to this. As with alcohol (and, high blood pressure), chronic disease risk associated with plasma glucose levels is a continuous exponential relationship. The distribution of blood glucose levels is close to log-normally distributed in populations, skewed towards high levels. There is no natural cut-point above which diabetes definitively exists and below which, it does not. Similar to the alcohol model (heavy use of alcohol over time results in brain damage, which leads to further heavy use of alcohol over time), there is evidence that heavy use of sugar over time damages hippocampal function, which leads to further heavy use of sugar over time. Thus, in the heavy use over time frame, sugar can be placed in the same bucket as alcohol and other drugs.

3.2 Prevention and Treatment

Prevention

A combination of three factors, biological (e.g., genes), individual (e.g., knowledge and skills – health literacy) and the environment (e.g., social norms) drive heavy drug use. In addition, components from all three factors (for example, alcohol dehydrogenase at the molecular level, income at the individual level, and stigma at the environmental level) exacerbating harm, independent of the level of use.

Molecular level

As an example, a genetic variant in a gene (ADH1B rs1229984) affects an enzyme that metabolizes alcohol in the body, and is associated with lower levels of alcohol consumption and risks of heavy drinking. Since variants in the ADH1B gene lead to increased levels of the carcinogen acetaldehyde, heavy drinkers who carry the variant have increased risk of gastrointestinal cancers. However, at the same time, there is evidence that variants in the gene can protect against cardiovascular disease. A large study of 260,000 European individuals compared the cardiovascular health outcomes of people with the genetic variant gene to those without. One in 14 Europeans carry the altered gene. Across all levels of alcohol consumption, drinkers with the variant consumed, on average, 17% less alcohol than drinkers without the variant.

Compared with drinkers who did not have the gene variant, drinkers who had the gene variant were less likely to have high blood pressure, coronary heart disease and ischaemic stroke. The analyses called into question alcohol's impact in reducing the risk of coronary heart diseases. From the J-shaped association between alcohol consumption and risk of coronary heart disease seen in observational studies, one would expect that for drinkers below the nadir (20 grams of alcohol a day), a reduction of 17.2% in alcohol consumption corresponding to rs1229984 A-allele carriage would lead to a small increase in the risk of coronary heart disease, whereas for those with alcohol consumption above the nadir, a similar reduction in alcohol consumption would lead to a decrease in coronary heart disease risk. Contrary to these expectations, individuals drinking below the nadir with a genetic predisposition to consume less alcohol had lower odds of developing coronary heart disease at all categories of alcohol consumption.

Income

As sociodemographic status improves in lower income countries, so do years lived with disability increase from mental and substance use disorders. Between and within countries people with lower incomes suffer more from the harm done by drugs than people with higher incomes. For example, as GDP increases, per capita adult alcohol consumption increases, at least up to a GDP of USPPP$10,000, largely driven by abstainers starting to drink. For the same amount of alcohol consumed, people who live in lower income regions of the world have higher alcohol-related deaths and DALYs than people who live in higher income regions of the world. The same applies within countries; for the same amount of alcohol consumed, people with lower incomes have higher alcohol-related deaths than people with higher incomes. Similarly, smoking prevalence is expected to increase in low income countries, and, within countries, poorer people tend to smoke more than richer people and are more likely to die from smoking than richer people.

Stigma and social exclusion

Social influences and attitudes are drivers of drug-related harm. Humans are hard-wired social animals. We are unusual in that we form longstanding, non-reproductive unions with unrelated individuals – friends. Cooperation is a defining feature of these friendships. We also learn from and influence each other, leading to an exceptional reliance on cultural transmission. We form social networks which have a significant effect on individual behaviours, such as tobacco use, alcohol intake obesity, loneliness, and cooperative social behaviour. With alcohol, for each additional heavy drinker in his or her network, the likelihood that an individual drinks heavily in the future increases by 18% and decreases the likelihood of abstaining by 7%. Each additional abstainer in the network significantly reduces the likelihood that an individual principal drinks heavily in the future by 10% and increases the likelihood of abstaining by 22%. The opposite consequence of social networks is social exclusion. Also hard-wired, possibly to avoid poor social exchange partners and risk of contact with communicable pathogens, are drivers of stigma and social isolation, themselves independent risk factors for poorer health.

In addition to threats posed by negative societal reactions, societal norms may influence societal responses to drugs, and the harm experienced from them. Drugs can be highly moralised and are often subject to prohibitory or strict regulatory frameworks which vary from place to place and from time to time. Engagement with drugs can convey strong social meaning and may lead to stigma, which can be particularly focused on the marginalised 'misusers' as opposed to the supposedly more responsible mainstream users. This can lead to punitive societal responses which are potentially harmful to well-being in themselves and, conversely, a lack of intervention into mainstream behaviour which allows harms to occur unchecked. For example, if caught using drugs in a country with a zero tolerance approach to illegal drugs, individuals may be subject to criminal sanctions with potential negative implications for quality of life and material living conditions (see Stoll & Anderson 2015). Countries may also change drug laws or law enforcements' response to drug use over time, perhaps resulting in the reclassification of a drug or a law enforcement crackdown, with implications for the experience of harm for those individuals continuing to use particular drugs.

Drug control policy also frames and influences drug users' health, for example through laws around the provision or lack of access to clean needles and syringes. Lack of access to clean needles is one example of how it may not be drug use in itself that causes health problems, but a lack of services that societies offer to drug users that would enable people to take drugs in less harmful ways. The extent to which harm reduction is pursued as a policy objective in a given society thus influences the experience of negative well-being consequences resulting from the use of a drug.

Policies and programmes

One of the implications of the biological approach is that, given the active and functional relationship we have with drugs, it is not surprising that exposure to drugs facilitated by low affordability (high availability and low price) and commercial communications result in heavy use over time. Advertising increases use for both novice users and heavy users, operating at the level of measurable brain responses. Given the drivers acting across all three factors (biological, individual and environmental), it is little wonder that prevention has not had the impacts that we would like. This is also due, to a large part, to insufficient resourcing for prevention, insufficient research and appraisal of impact of preventive activities, and insufficient implementation of evidence-based effective programmes. One solution to help rectify these deficiencies is to create a central, transparent and evidence-based approval process for behavioural interventions, a European Prevention Agency.

Treatment

No matter what prevention or policies are put into place, some people will always run into problems with heavy drug use over time and will need and benefit from treatment. Unfortunately, there are three problems here. First, the gap between need and treatment is large. Using United States data, for example, less than 1 in 5 of individuals with a lifetime 'diagnosis of alcohol use disorder' have ever received treatment and less than 1 in 4 of individuals with a lifetime 'diagnosis of drug use disorder' have ever received treatment. Second, considerable marginalization and stigmatization happen in the path to treatment, and these are often exacerbated by treatment. And, third, even if people get into treatment, pharmacotherapy for heavy use of alcohol and drugs is generally under developed and underperforming for impact.

In the case of tobacco, the most common addiction, only 7% of smokers who tried to quit sought support from a health professional. It may be argued that some of them did not want any support, but given the low success rates and the scarcity of treatments provided at a primary health care level, a simpler explanation is that treatment and advice are not offered to those in need. On top of this, even pharmacological options like nicotine replacement therapy are offered at very expensive prices (especially when compared to the price of nicotine in the cigarettes.

In the case of alcohol, data show that alcohol use disorder is the least-treated mental disorder in Europe, with 92% of those in need not receiving any treatment. In the USA the treatment gap is also high: 3 out of 4 USA citizens with alcohol related problems will not receive any formal treatment. Identification of alcohol dependence is sometimes difficult, but even when correctly identified, this may not lead to action. In a recent European study three out of four patients identified by their GP as meeting criteria for alcohol dependence, did not receive any treatment nor advice to reduce their drinking. For a complete picture, we must add the fact that there is a time gap of around 10 years between the establishment of dependence and attendance for treatment.

According to the EMCDDA, over one million EU citizens receive treatment for addiction to illegal drugs in a given year. Estimates of the population in need are difficult to make since reliable data on the prevalence of addictive disorders across the EU are not available. An EU diabetic citizen should probably expect similar treatments and standards of care in most of the EU countries, but this would not be the case if this citizen suffers a substance use disorder. Diversity here also means inequality. In some countries (or regions) specialized treatment is offered within mental health facilities, while in other countries they are completely independent. Funding bodies are also diverse, and when they are different from the Health Department this tends to create difficulties to promote a seamless treatment and to facilitate coordination among professionals. Diversity is also reflected in the available clinical guidelines. Data collected by the EMCDDA show that 17 EU countries do not have harm reduction guidelines and, further, 50% of the guidelines are not evidence based, and often not in concordance with the evidence based 2009 WHO guidelines on the treatment of opioid dependence (which include opioid substitution treatment among other options).

A major problem is that services are not integrated, and the average primary-care practitioner, e.g., family doctors, psychologist, nurse or teacher are not required as part of their core training to develop skills in detecting or intervening with substance use disorders, keeping treatment in this field as highly specialised, unregulated, and limited to those with the most severe need.

3.3 Governance

Governance

Governance can be considered as the processes and structures of public policy decision making and management that engage people across the boundaries of public agencies, levels of government, and/or the public, private and civic spheres in order to carry out a public purpose that could not otherwise be accomplished.

Nineteen key policy characteristics have been used to cluster 28 European countries into four different groups (see Table 4). Some of the grouped countries may seem strange to the reader, especially if they have traditional models in mind, but the addiction field poses some challenges and complexities, and contextual factors (geopolitics), culture and traditions, among others, that have a high impact in their governance.

Model 1: Trend-setters in illegal substances

The first model is determined by its strategy for illegal substances, which, apart from taking into account prevention and treatment, gives much importance to harm reduction policies. A distinctive characteristic of this model is the fact that the clustered countries decriminalize possession of illegal substances (i.e. a shift from repression to regulation and from criminal to administrative law). Furthermore, they have relatively weaker policies for alcohol and tobacco. Model 1 includes Continental and Mediterranean welfare states, and all these countries have developed well-being oriented policies by placing the Ministry of Health as the responsible institution. This results in their

giving much weight to harm reduction policies, decriminalizing possession of illegal substances, proactively developing policies aimed at coping with drug-related problems, embracing a health-oriented rather than a security oriented approach and protecting the public and society in general instead of the individual. However, when it comes to evidence-based regulation of legal substances, Model 1 states still have not introduced measures related to production, distribution, age limits, taxes and advertising and marketing, which still are not as developed as in other states.

Model 2: Regulation of legal substances

Countries in this second model, regulation of legal substances, do not focus on decriminalization, but implement evidence-regulations aimed at reducing the levels of alcohol and tobacco consumption, and enhancing societal well-being. It is worth noting that all Model 2 countries have developed evidence and research-based regulations aimed at reducing the levels of legal substances' consumption, prevent heavy use over time and improve the overall well-being of the population. These countries have complex structures to dealing with drugs, i.e. they devolve implementation to decentralized structures, involve non-profit organizations in the decision-making and have a sound trajectory dealing with drugs. In fact, this model gathers countries with different welfare states traditions, Nordic, Anglo-Saxon and Continental countries. It is worth noting here that the Nordic and the Anglo-Saxon countries are pioneers in evidence-based research.

Table 4 Models of governance of addictions in Europe

Model	Characteristics	Countries
1 Trend-setters in illegal substances	These countries combine a well-being and relational management strategy with a comprehensive structure.	Belgium, Czech Republic, Germany, Italy, Luxemburg, Netherlands, Portugal and Spain
2 Regulation of legal substances	These countries have strict regulation on legal substances (tobacco and alcohol).	Finland, France, Ireland, Norway, Sweden and the United Kingdom
3 Transitioning model	This group gather the most divergent countries of the sample. They do not follow a clear trend.	Austria, Bulgaria, Cyprus, Denmark, Poland and Slovenia
4 Traditional approach	Countries within this cluster still have not embraced the three trends. They have a 'safety and disease' strategy combined with a 'substance-based structure'.	Estonia, Greece, Hungary, Latvia, Lithuania, Malta, Romania and Slovakia

Source: Ysa et al. (2014)

Model 3: Transitioning model

In this model are the most divergent and most peculiar group of countries: Austria, Bulgaria, Cyprus, Denmark, Poland and Slovenia. Those are countries in transition regarding the governance of addictions, from this model to the other three. These countries are characterized by placing the Ministry of Health as the main responsible institution and foster treatment, prevention and harm reduction above supply reduction measures. Moreover, these countries have been clustered together for not having a set of characteristics: decriminalization of possession, injection rooms, tobacco control, and public-health aims. Regarding structure, these countries do not tackle legal and illegal substances together; hence they focus on the substances rather than on addictions. Furthermore, none of the countries involve non-profit and private organisations in the decision-making process.

Model 4: Traditional approach

In model 4, are primarily central and eastern European countries that have become EU member states during the first decade of the 2000s, the only exceptions in this respect are Greece and Malta. These countries have been classified as having a 'safety and disease' strategy combined with a 'substance-based' structure. All these countries except for Greece give the responsibility to manage drug and addiction policies to the Prime Minister, the Ministry of Interior, the Ministry of Justice or the Ministry Social Affairs. These countries are entrance points for illegal substances and for smuggling alcohol and tobacco, which, to some extent, could justify the supply reduction approach. There is little involvement of private and non-profit stakeholders in the decision-making process and regional administrations are involved neither in the policy-making nor in the implementation process. We must not forget that these countries have been recently become members of the EU and still are incorporating most of the guidelines and the 'well-being and relational management' strategy promoted by this institution.

Thus, an analysis of 28 European countries finds that only one-quarter of countries can be considered as having a comprehensive policy for all drugs, within a broad societal well-being approach. For almost all European countries, there are opportunities for improving governance both for legal and illegal drugs, while pursuing a societal well-being goal.

Missed opportunities

There are a number of reasons for the un-achieved governance opportunities. First, it is not generally clear what is being governed. Concepts of addiction have varied enormously over both time and place within Europe, with considerable heterogeneity between drugs (alcohol, tobacco and illegal drugs) and levels of governance (international, national and local). Using heavy use over time as the frame for action would simplify and facilitate convergence of our approaches to drug governance as we move forward across different jurisdictions. Second, a panoply of stakeholders is active in addictions governance, and the relationship between evidence and policy will be driven by the stakeholder group which has power and influence at the time - and this will also vary by time and place. Third, concepts and power are reflected in and further driven by variations in media constructs, which also vary over time and place. And, fourth, corporate power through multiple channels of influence can hinder inadequate governance - there are insufficient and inadequate rules of the game in place to ensure level playing fields for discussions across all actors. There is no simple solution for moving forward. However, three opportunities present themselves.

Well-being

First, societal well-being, as captured, for example, by OECD (Figure 3) provides a frame for improved governance. Well-being has various dimensions, including quality of life (health, education and skills, social connections, civic engagement, and personal security), material conditions (income, employment and housing) and sustainability over time. Drugs and drug-related harms are affected by and affect all of these dimensions. Well-being analyses find that, whilst some drug policies may reduce health harms, they often come at the expense of adverse side effects including criminalization, social stigma and social exclusion, all of which also independently exacerbate health harms. A well-being frame calls for whole-of-society approaches that avoid criminalization due to drug use.

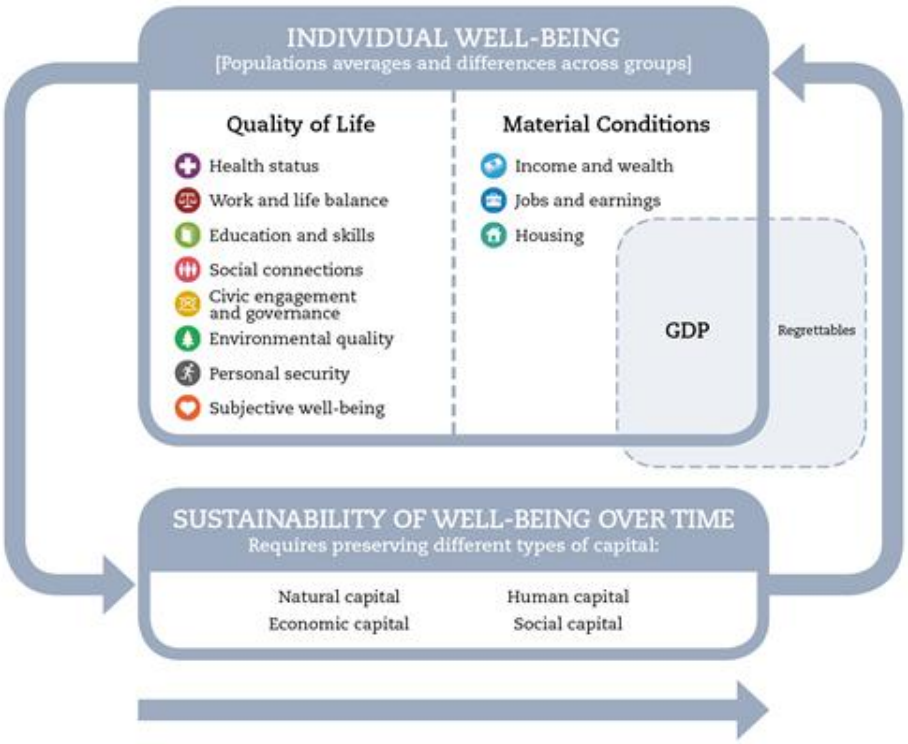

Figure 3 OECD societal well-being frame. Source: OECD (2015).

Whole-of-government and whole-of-society approaches

Drug governance strategies need to be comprehensive, combining legal and illegal substances. Strategies should manage drugs as a whole, with a focus on well-being, and the impact of harm addressed independently of the drug. Approaches should be anticipative rather than reactionary, with regulation embedded within international coordination. The structures to support the strategy should be based on coordinated networked governance, with complex organizational structures and stakeholder involvement. Silos need to be broken inside of government, bringing together health, social welfare, justice, well-being and international treaties. Regional and local public policies can create policy communities and networks for responses, within an overall common strategy. The creation of new organizational structures to manage new drugs should be avoided.

When managing the private sector, the leading role in determining the strategy of public drug policy should be in public sector hands to enhance societal well-being. An evolved co-production system needs to include means of avoiding co-option by both industry and non-governmental organizations dependent on public budgets. Transparency, and checks and balances should be ensured as the drivers to increase evidence-based impact in decision-making. The relation with stakeholders should establish the rules of the game regarding which phase of the policy cycle and which typologies of stakeholders can provide a contribution for the public good, simultaneously to their own interests.

Drug governance, in particular, needs to address marketing, which includes all the actions undertaken by producers of drugs to persuade consumers to buy and consume more, including creating and facilitating opportunities, eliciting and shaping social cognitions, and activating and using automatic responses through distribution, pricing, product design, as well as advertising. There are existing models of how to control marketing effectively for public health, the most notable being the Framework Convention on Tobacco Control, an international treaty whose articles include controls on the advertising, display, packaging and design of tobacco products.

Accountability

Structural drivers of harm from drug use include biological attributes and functions, population size and structure, and levels of wealth and income disparities within jurisdictions (Figure 4). Core drivers refer to the processes, mechanisms, and characteristics that influence harm, sometimes through the structural drivers, and sometimes not. Core drivers of harm include drug potency and drug exposure levels, the technological developments that might influence these, and social influences and attitudes, including social stigma and social exclusion. Included in the policy drivers level are measures that reduce drug exposure, actions that promote research and development to reduce drug potency, measures that maximize co-benefits and minimize adverse side-effects of policies and actions, incentives for healthy individual behaviour, and legislation aimed at managing markets, such as the definition and enforcement of rules of engagement of the private sector. Policies and measures affect the core drivers of harm. The structural and core drivers may, in turn, influence policies and measures.

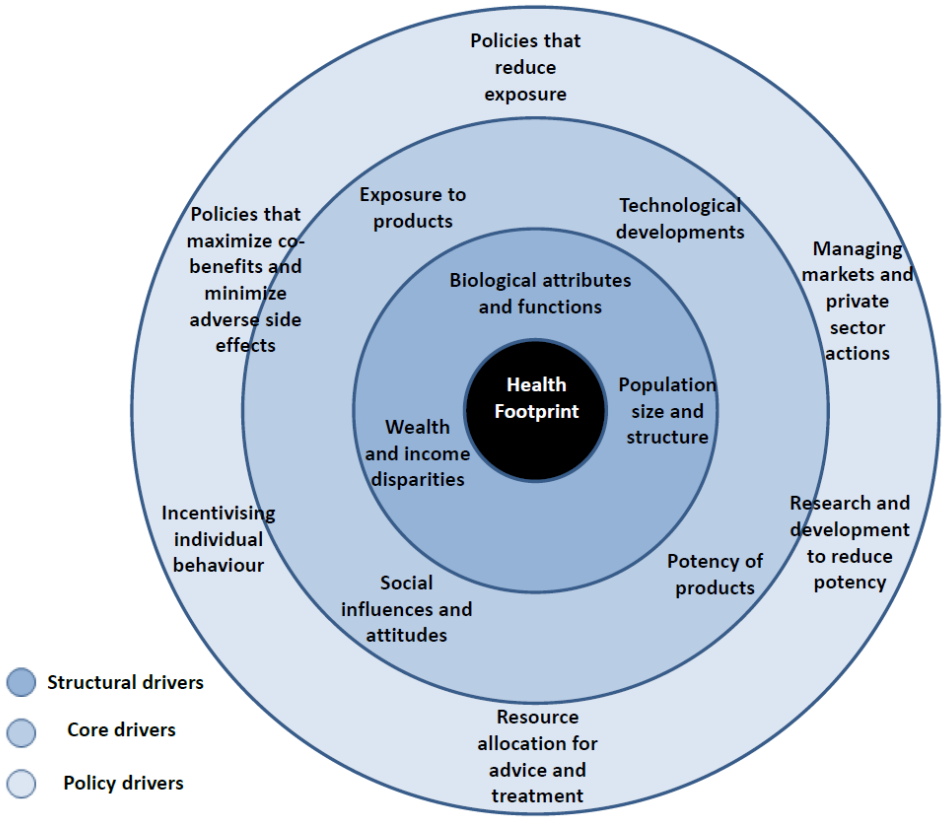

Figure 4 Drivers of harm done by drugs and addictive behaviour. Source: Anderson et al. (2016).

At the centre of the interconnections of Figure 4 is the Health Footprint, the accounting system for identifying the determinants of drug-related health and the management tool to evaluate opportunities by the public and private sectors and civil society to reduce harm.

Footprints were developed in the ecological field as a measure of human demand on ecosystems. They have since developed in a range of areas including water footprints that measure water utilization, and carbon footprints that apportion greenhouse gas emissions (normally carbon dioxide, CO_2 and methane, CH_4) to a certain activity, product or population. The central reason for estimating a carbon footprint is to help reduce the risk of climate change through enabling targeted and effective reductions of greenhouse gas emissions. We define the health footprint as a measure of the total amount of risk factor attributable disability adjusted life years (DALYs) of a defined

population, sector or action within the spatial (e.g., jurisdiction) and temporal boundary (e.g. stated year, such as 2012) of the population, sector or action of interest. It can be calculated using standard risk factor related DALY methodologies of the Global Burden of Disease Study and of the World Health Organization.

Nations, regions, cities - Jurisdictions at differing levels, supranational, national, regional and city level, can influence drug exposure through the policies and programmes implemented or not. For example, the introduction of smoke free public places as happened in the 2000s led to reductions in smoking, harm to the smoker and harm to those surrounding the smoker. Reducing taxes on alcohol, as happened in Finland in 2004, led to an increase in alcohol consumption, alcohol-related deaths and health inequalities, which subsequently reversed, when taxes were increased in 2008.

Jurisdictional entities can be ranked according to their overall health footprint, in order to identify the countries that contribute most to drug attributable ill-health and premature death and, therefore, where best health gain could be achieved for groupings of countries as a whole. This could be supplemented with health footprint estimates per capita, to ensure that targeted country approaches can be implemented so as to reduce health inequalities between countries. Apportioning health footprints by country and by per capita will enable jurisdictions to facilitate policy planning, to consider the need for strengthened policy for a particular population (e.g., those with younger versus older populations, those with gender disparities or those with specific genetic profiles), and to monitor the outcomes of policies and programmes over time. Table 5 gives an example ranking European Union countries by an alcohol-attributable health footprint for the population up to age 65 years. To improve European Union health as a whole, with associated productivity gains (OECD 2015), Europe-wide policy could target the top five contributing countries (Germany, France, United Kingdom, Poland and Romania), considering how to reduce these countries' alcohol-attributable footprint to the level (= DALY rate) of Italy. Were this to be achieved, European Union alcohol-attributable DALYs could be reduced from 4.8 million to 2.7 million.

Jurisdictional footprints could be developed to what might be termed 'policy attributable health footprints' which estimate the health footprint between current policy and ideal health policy. This would address the question: 'were the country to implement strengthened or new policies compared to present policies, what would be the improvement in the health footprint?'. Conversely, failure to implement the evidence-based policy apportions accountability for the failure.

Sectors A range of sectors are involved in drug-related risk factors that the health footprint encompasses. Sectors include producer organizations, retail organizations, such as large supermarket chains, and service provider companies such as the advertising and marketing industries. There is considerable overlap between sectors, and estimates will need to determine appropriate boundaries for health footprint calculations. For the sector and company calculations, a counterfactual scenario could be constructed in which a hypothetical situation is taken for comparison where the products and services to evaluate do not exist. For example, Table 6 estimates the health footprint of a major beer producer. For the year 2012, it is estimated to have contributed 3.34 million alcohol-attributable DALYs, 3.4% of all alcohol-attributable DALYs, and 0.13% of all DALYs. The company could choose to commit to reducing its health footprint by 10% to 3 million alcohol-attributable DALYs over the next five years. One way to achieve this is by removing alcohol from the market through lower alcohol concentration products.

The Health Footprint, thus, accounts for who and what causes the harm done by drugs. Drug-related health footprints could become standard components of annual reporting by relevant public and private sector bodies.

Table 5 Ranking of European Union countries by alcohol health footprint (own calculations)

	Total DALYs (2004)	DALYs / 100,000 women	DALYs / 100,000 men
Malta	1,222	63	537
Cyprus	2,173	no net harm	632
Luxembourg	4,278	366	1,573
Slovenia	29,739	464	2,487
Ireland	33,781	353	1,292
Estonia	43,790	860	6,006
Denmark	49,615	368	1,533
Finland	62,002	347	2,099
Greece	62,296	209	894
Belgium	69,468	330	1,045
Sweden	73,963	392	1,313
Austria	74,993	324	1,508
Bulgaria	77,400	239	1,763
Latvia	80,890	1,035	6,254
Slovakia	101,221	429	3,438
Netherlands	108,256	252	1,129
Lithuania	113,236	788	6,146
Portugal	120,922	490	1,847
Czech Republic	136,523	348	2,318
Italy	179,757	146	457
Hungary	264,255	767	4,649
Spain	268,247	274	954
Romania	484,007	907	3,734
Poland	521,557	380	2,425
United Kingdom	543,377	374	1,501
France	597,597	359	1,694
Germany	704,462	259	1,483
European Union	4,809,027	343	1,649

Table 6 Health footprint of a major beer producer

Regions	Production in 2012 in thousand hectolitres	attributable DALYs*
North America	125,129	749,338
Latin America North	126,189	1,645,115
Latin America South	34,292	428,060
Western Europe	2,931	15,113
Central and Eastern Europe	2,278	48,776
Asia Pacific	57,667	411,601
Global export and holding	7,030	41,869
Globally	402,631	3,339,873
	0.13 % of all DALYs, 3.4% of all alcohol-attributable DALYs	

* based on 2010 GBD DALY values for regions (combined with adult alcohol *per capita* consumption data for 2010 from WHO Global Information System for Alcohol and Health)

4. The potential impact of the ALICE RAP project, with main dissemination activities and exploitation of results

4.1 Potential impact

ALICE RAP proposes reducing the harm done by addictions through advocating a redesign of addictions governance based on the following twleve approaches:

1. 'Heavy use over time' is proposed as the replacement descriptor for concepts and terms such as 'addiction' or 'dependence'. Heavy use over time is the primary determinant and predictor of the health and social sequelae normally captured by terms such as 'addiction' and 'dependence'. Heavy use over time is a more accurate description; it recognizes that use and harm exist within continua with no natural cut-off points; and it could help to reduce the stigma associated with dichotomous labelling (e.g. addict versus non-addict). Heavy use over time is responsible for the changes in the brain and other physiological characteristics of addictive disorders; is responsible for intoxication, and for the loss of control characterizing current definitions of addiction; is responsible for the main social consequences of using addictive products, such as problems in fulfilling social roles; is responsible for the majority of burden of disease and mortality attributable to using addictive products; and, as a descriptor, overcomes many of the historical, cultural and political uncertainties and current problems with definitions and operationalization, which vary a great deal between different countries. Transitions into and out of heavy use over time are determined by an interplay of molecular, individual and societal factors.
2. Policies should acknowledge and aim at reducing the social stigma linked to using addictive drugs and products. Heavy use of drugs and other addictive products are some of the most stigmatized behaviours over time and place. As a powerful social force, stigmatization functions as a barrier to the normalization of advice and treatment for addictive drugs and behaviours that should meet the same standards of care and service provision as for any other chronic condition, such as diabetes or high blood pressure. Further, stigmatization maintains structural inequalities in society. A European coordinated and continued action, involving public, non-governmental and private sectors, should be mobilized for a cultural transformation that reduces the stigma associated with addictive drugs and behaviours and their treatment.
3. Policies should be based on a sound understanding of evolutionary behaviour. Ecological analyses find humans have evolved to be active and functional, rather than passive and vulnerable with respect to the drugs that they take. Many drugs are plant neurotoxins, and ethanol results from fermenting sugar in fruit. Humans have evolved to counter-exploit these drugs for advantage. This has at least two implications: first, policies that prohibit the use of drugs are likely to fail because people have a biological predisposition to seek these chemicals; and, second, in modern society, drug potency and related drug delivery systems are a core drivers of harm, with potency largely determined by producer organisations operating in inadequately managed markets.
4. Policies should be assessed for their impact on a range of societal well-being outcomes beyond physical and mental health. At the international level, the OECD societal well-being frame has proven a useful concept for assessing the un-intended and un-accounted harm caused by policies. Well-being analyses find that, whilst some drug and gambling policies reduce health harms and bring co-benefits, they can simultaneously have adverse side-effects, including criminalization and related violence, and social stigma and social exclusion, which detract from individual and societal well-being. To minimize these adverse side-effects, drug and gambling policies should account for overall contexts and dimensions of well-being, for example through relational management strategies. This means policies should be built on a comprehensive

structure that involves different stakeholders and processes. Policies should, for instance, balance decriminalization of illegal substances with innovative harm reduction policies; and, effectively regulate legal drugs, such as tobacco and alcohol, and legal behaviours, such as gambling. Regulation, not an unfettered free market at one extreme, or prohibition with its attendant criminalisation at the other extreme, should be the centre of drug and gambling policies.

5. Policies should be informed and monitored by quantitative risk assessment. Quantitative risk assessment is widely applied in other fields for prioritization of risk management actions. For example, the Margin of Exposure (MOE) for any substance gives an indication of whether individuals or populations are exposed to (or use) a substance at an acceptable level of risk or not. The methodology can be applied to any legal or illegal drug, enabling comparisons of MOE between drugs, which can indicate which drug requires a policy shift or amendment. Margins of exposure compare the ratio of a toxic dose of a drug (usually the benchmark dose BMDL10, the lowest dose which is 95% certain to cause no more than a 10% negative outcome incidence) with the dose consumed. A MOE of 100 means that the drug is being consumed at one hundredth of the toxic dose; a MOE of 1 means that the drug is being consumed at the toxic dose – thus, the higher the MOE, the lower the level of risk. MOE for drugs can be calculated taking into account a range of hazard outcomes, in health and other well-being domains, so far as suitable dose-response data are available (which is not the case for most drugs). Therefore, analyses to date are primarily restricted to lethal outcomes based on animal studies. These initial analyses suggested that most efforts should go to alcohol, tobacco, cocaine and heroin. With this quantitative risk assessment, drug policies could aim for a MOE of no less than 10 for individual daily consumption of voluntarily consumed drugs. It is important to note that the MOE as described here applies where the harm from the drug is inherent in the drug itself; it does not account for the harms that arise from drug delivery systems, for example, smoked tobacco.

6. Policies should be judged for their impact in reducing heavy use. In general, the risk of harm from addictive drugs and behaviours increases with the dose of the drug taken, or the time involved with the behaviour, along a continuum of risk. The shapes of risk curves vary, depending on the drug, the behaviours and the harm being measured, between linear risk curves and curvilinear risk curves, where risk increases disproportionally faster at higher doses. The preponderance of curvilinear risk curves leads to the findings that the majority of individual and societal addictive-related harms results from heavy use; thus, the same reduction in heavier use brings greater individual and societal benefit than the same reduction in lighter use. This means that policies and actions, including individually directed advice and treatment programmes, will bring greater health gain when they focus on reducing heavier drug use than when they reduce lighter drug use.

7. Drug policies should recognise the vulnerability of the adolescent brain, particularly with respect to decision making abilities. Adolescence is a time of enormous biological and social change accompanied by increased risk taking. During adolescence, the brain undergoes profound structural change until at least about 25 years of age. During this time, young people have a well-developed reward system but they have a more flexible engagement of the executive control centre than when fully adult, meaning that young people's skills in controlling impulses and planning behaviour are still being developed. Adolescent brain development, itself, might be impaired by drug use, which, in turn, renders a young person who uses drugs at greater risk of longer term drug use. Drug policies should not penalise or stigmatise underage people who use drugs. Youth should be engaged in the development and implementation of drug policies. Youth-informed policies should focus on reducing early onset or heavy use and reducing the use of high potency or unregulated harmful substances. Policies and actions should aim to reduce risk, build resilience, and promote physical and mental health. Drug policies focussed on youth need to be embedded in whole-of-society and whole-of-government youth development policies that aim

for security of education, employment and full civic engagement. Policies that restrict access to these basic rights for underage people who use drugs are expensive and can lead to greater risk of drug use and harmful use due to secondary effects of social exclusion.

8. Policies should ensure that the gaps between those who need advice and treatment and those who receive it are overcome. United Nations Sustainable Development Goal 3 aims to ensure healthy lives and promote well-being for all ages, (http://www.un.org/sustainabledevelopment/sustainable-development-goals/) with target 3.5, strengthening the prevention and treatment of substance use problems, including narcotic drug use and harmful use of alcohol. A core indicator to monitor achievement of the goal is coverage of treatment interventions (pharmacological, psychosocial and rehabilitation and after care services) for substance use disorders. Presently, there is an unacceptable treatment gap for drugs and addictive behaviours that leads to loss of life and undermines societal well-being. Across Europe, fewer than 1 in 10 people who would benefit from treatment of alcohol use disorder receive any treatment. In the United States, for example, only 13.5% of adults who would benefit from treatment of drug use disorder during the previous twelve months have received treatment. Further, there are also many lost years between the commencement of substance use disorders and receipt of treatment, often referred to as the 'decade of harm'. Closing the treatment gap would bring health gains, reduce preventable deaths and disability, improve social inclusion, reduce stigma, and can have a positive impact in lessening the human and economic costs due to processing drug users through the criminal justice system.

9. Drug policies should ensure that programmes designed to prevent harm are assessed for their cost-effectiveness by agencies similar to those that assess pharmacological treatments. Programmes and actions designed to promote health and healthy lifestyles, and to prevent health problems and illnesses can improve individual and societal health and well-being, and give a good return on investment. Yet, many current prevention programmes are poorly evaluated or not evaluated at all. Some programmes actually do harm and should be withdrawn. Through mapping and systematic reviews of reviews, there is little evidence to support the majority of prevention approaches currently adopted and delivered by many European countries to address drug problems. By contrast, prevention efforts can lead to substantial reductions in drug-related harm when evidence-based programmes are implemented. Although some countries have bodies that review the impact of prevention and lifestyle programmes, the existence of such institutions is not consistent or widespread across Europe. In contrast, all countries have mechanisms in place to assess the safety and effectiveness of pharmacological treatments. At the European level, the European Medicines Agency (http://www.ema.europa.eu/ema/) is responsible for the scientific evaluation of medicines developed by pharmaceutical companies for use in the European Union. Modelled on the European Medicines Agency, prevention and health promotion programmes could be approved by national agencies or a European Prevention Agency, specifically set up for the purpose, and covering all health topics.

10. Smart policies require whole-of-government and whole-of-society approaches. The whole-of-government, or joined-up government, approach represents the diffusion of governance vertically across levels of government and areas of governance as well as horizontally throughout sectors, institutions and professions. This approach requires building trust, a common ethic, a cohesive culture and new thinking and skills throughout all parts of government. The approach includes cabinet committees, interministerial or interagency units, intergovernmental councils, task forces, lead agency assignments, cross-sectoral programmes and projects and mechanisms for overseeing policies and convincing agencies to work together. Whole-of-society approaches involve collaborative governance that emphasizes coordination through normative values and building trust and ownership among various actors in society. The whole-of society approach goes beyond institutions, and influences and mobilizes local and

global culture and mass media, and all relevant public and private policy sectors, such as agriculture, education, transport, media and entertainment, justice, and urban design in reducing harmful drug use and behaviour. Whole of government and whole of society approaches need to address the structural factors of poverty and marginalization that are independent determinants of harm over and above the addictive drugs and behaviours themselves.

11. Government policy-making for addictive drugs and behaviours should be free of the undue influence of relevant private producer companies. The potency of business influence on policy-making is too high, and can lead to a weakening of policy at the expense of health. Private producer companies generally wield a great deal of economic, political and organizational power in the policy arena, often fostering common policy interests that are not conducive to health. There are many structural factors to counter private sector influence, one of which includes redesign of governance systems that shift away from the present short-term, fast-scale economic and political systems in favour of longer time-scale systems that promote sustainable health and well-being. Whole-of-government and whole-of-society approaches to drug policy should define the relation with private sector stakeholders and establish the rules of the game for stakeholder engagement in the policy cycle through accountability for the common good, where private sector stakeholders contribute to the public health good, simultaneously to their own interests. In order to ensure societal well-being is enhanced, rather than in the hands of commercial interests, the leading role in determining the strategy of public policy for drugs should be in public sector hands. Transparency systems, controls on the revolving door and enhanced conflict of interest policies should be put in place in government, science, civil society and the media as drivers to increase the impact of evidence-based information on decision-making. One approach for producer companies to reduce harm is to change the potency of their products (for example, reducing alcohol concentration of existing products) and the toxicity of their drug-delivery systems (for example cigarette companies shifting to electronic nicotine delivery devices). Shifts towards less harmful products could be incentivized by smart government tax policies.

12. A health footprint can be used as an accountability tool to apportion the harm to health and premature death imposed by the different drivers of addictive drug use and behaviours. Structural drivers of harm from the use of addictive products and behaviours include biological attributes and functions, population size and structure, and levels of wealth and income disparities within jurisdictions (see figure). Core drivers refer to the processes, mechanisms, and characteristics that influence harm, sometimes through the structural drivers, and sometimes not. Core drivers of harm include drug potency and drug exposure levels, the technological developments that might influence these, and social influences and attitudes, including social stigma and social exclusion. Included in the policy drivers level are measures that reduce drug exposure, actions that promote research and development to reduce drug potency, measures that maximize co-benefits and minimize adverse side-effects of policies and actions, incentives for healthy individual behaviour, and legislation aimed at managing markets, such as the definition and enforcement of rules of engagement of the private sector. Policies and measures affect the core drivers of harm. The structural and core drivers may, in turn, influence policies and measures. Placed at the centre of the drivers is the Health Footprint, the accounting system for identifying the determinants of drug and addictive behaviour-related harm and the management tool to evaluate opportunities by the public and private sectors and civil society to reduce harm. Modelled on the carbon footprint, the health footprint can be defined as a measure of the total amount of risk factor attributable disability adjusted life years (DALYs) of a specific population, sector or action of interest, defined by specific spatial (e.g., jurisdiction) and temporal (e.g. stated year, such as 2014) boundaries. The Health Footprint can measure the impact of a range of structural and core drivers of impaired health and the policies and measures that impact upon them. The Health Footprint, thus, accounts for who and what causes the harm

done by drugs and addictive behaviours. Drug and addictive behaviour-related health footprints could become standard components of annual reporting by relevant public and private sector bodies.

4.2 Main dissemination activities and exploitation of results

The ALICE RAP project established a clear yet flexible strategy for disseminating and exploiting its findings, promoting them among all relevant stakeholders, as well as to the general population; with a set of interlinked communication tools and activities that have been developed and used throughout the life of the project.

Over 220 dissemination activities (presentations, interviews, press releases, articles in the popular press, videos) were carried out (averaging one every 8 days of the project lifetime), either at scientific events or targeted at a political or wider audience. These were aimed at sharing AR aims, progress of work, specific findings, overviews and policy recommendations with relevant stakeholders.

Online communication and dissemination activities

- The **ALICE RAP Website** (http://www.alicerap.eu/) has been developed to make accessible all products and information related to the project, with a constantly updated home page, highlighting the latest developments in the project and key outputs; and sections relating to the project work and partners, a wide range of resources, related projects and events, the ALICE RAP blog and contact details. The final key whole-project outputs (the ALICE RAP policy frame, AR Policy Paper Series, Science Findings, OUP Future challenges book series and A-Debate science summary,) are especially highlighted, whilst maintaining access to the rest of the products from areas and work packages.

  Between the first and third years of ALICE RAP, the Website tripled the volume of traffic that it received, achieving over 12,000 sessions from around 9,000 unique visitors per year, and this was maintained through the last 2 years of the project. By the end of the project, several project documents had been downloaded over 5,000 times, such as AR Policy Papers on Gambling (7,449 downloads); cannabis (6,472 downloads); or Prescription opioids (7,173 downloads). The ALICE RAP e-book had been downloaded 4536 at the time of writing. Of the 35 detailed technical documents made public (deliverables and milestone reports), over a third have been downloaded more than 1000 times and 4 of these have more than 2000 hits.

- **Online social media** accounts were set up for the project in its first year and have grown steadily over ALICE RAP's lifetime. All project developments are announced and disseminated through twitter and Facebook; and news and comment on developments in the fields of addiction science, public health research and drugs policy are also passed on and received via these. The project twitter account has nearly 330 followers and posts on Facebook have reached over 1,422 people.

  Throughout the course of ALICE RAP, a collection of **videos** has been built up, comprising short interviews with the AR scientists, highlighting, presenting and explaining key elements of the research, findings or implications; as well as video accounts of the main public events held by the project (the 2014 Cannabis debate in Amsterdam and the 2016 A-Debate in Barcelona). These have been placed on the YouTube accounts of the project or communication partner WHCA, and embedded/linked to the relevant pages of the ALICE RAP website.

ALICE RAP Policy Frame

- The cumulative work of ALICE RAP has been synthesised into the **ALICE RAP Policy Frame to reduce the harm done by addictive drugs and behaviours** by the project leaders and

coordinating team, which has been revised according to comments and suggestions from the steering group of the project. The resulting 12-point ALICE RAP policy frame covers the main scientific outcomes of the project with relevance to policy, and is aimed at informing a redesign of the governance approaches to reduce the individual and societal harm done by addictive drugs and behaviour.

AR Policy Papers

- The **AR policy papers series** is a collection of concise documents, between 10-30 pages in length, which summarise the scientific knowledge and evidence for consideration for a public policy readership. Six AR policy papers were developed over the course of ALICE RAP, using iterative consensus procedures and in consultation with the network of ALICE RAP partners:

    1. Alcohol – the neglected addiction (2012)
    2. Gambling: two sides of the same coin (2013)
    3. Novel psychoactive substances (2013)
    4. Prescription opioids and Public Health (2013)
    5. Cannabis: from prohibition to regulation – when the music changes, so does the dance (2014)
    6. Addiction in the family (2016)

    By the end of the project, translations have been made of several of the papers in the series, including a Catalan translation of the policy paper on alcohol – disseminated by the Catalan department of health; and Czech translations of two of the series (alcohol and gambling), which have been disseminated widely to relevant professionals (political and clinical) through the bulletin of the Czech National Monitoring Centre for Drugs and Addiction (Zaostřeno).

Science Findings

- Having detected the need for a highly accessible and attractive format in which to present and communicate the large number of wide-ranging research outcomes from the different ALICE RAP work packages, the **ALICE RAP Science Findings** were developed. Each of the 55 ALICE RAP Science Findings gives a simple account or mini-report of the main results coming out of one of the many different lines of ALICE RAP research, written by the AR scientists themselves, following a standard format with references and electronic links to further reading and the more detailed ALICE RAP deliverable reports. The series of mini-reports has been grouped and ordered within a structure of 6 clusters, based loosely on the six future challenges series (see below), as well as being searchable for keywords and scientists in the corresponding Science Findings section of the AR Resources, and downloadable as a single volume.

    By May 2016, just three months since their publication in mid-February, all Science Findings had each been downloaded over 200 times, with the following topping the list: Accountability tool (322 hits), Policies for the young (274 hits), Popular images (272), Addiction policy scales (266 hits), Governance practices (262 hits), Toxicology MOE (260 hits) and Online bingo (257 hits).

Future Challenges Book Series (OUP)

- The **ALICE RAP Future Challenges Series** is a coordinated and integrated series of 6 books, of around 200 pages each, to be brought out by the publisher **Oxford University Press (OUP)**, with the aim of drawing the scientific findings of the project together and presenting them in a narrative and engaging format to inform the relevant stakeholders in strengthening the governance of addictions. The Authors/editors and titles in the series are:
    1. Ysa T, Colom J, Albareda A, Ramon A, Carrión M, Segura L (2014). Governance of Addictions: European Public Policies. Oxford: OUP
    2. Anderson P, Rehm J and Room R (eds.) (2015). Impact of Addictive Substances and Behaviours on Individual and Societal Well-being. Oxford: OUP

3. Gell L, Bühringer G, McLeod J, Forberger S, Holmes J, Lingford-Hughes A, Meier P (2016). What Determines Harm from Addictive Substances and Behaviours? Oxford: OUP
4. Hellman M, Berridge V, Duke K, Mold A (eds.) (2016). Concepts of Addictive Substances and Behaviours across Time and Place. Oxford: OUP
5. Miller D, Harkins C, Montague B, Schloegl M (2016, In press). Impact of Market Forces on Addictive Substances and Behaviours. Oxford: OUP
6. Anderson P, Braddick F, Conrod P, Gual A, Hellman M, Matrai S, Miller D, Nutt D, Rehm J, Reynolds J, Ysa T (2016, In press). The New Governance of Addictive Substances and Behaviours. Oxford: OUP

ALICE RAP e-book

- A seventh book was originally planned to be published as part of the OUP series of ALICE RAP books. However, in streamlining the series at the publisher's request, the editorial team decided to publish instead the contents of this book as the ALICE RAP eBook - Reframing addictions: policies, processes and pressures, with the added advantage of reaching a much broader audience. This eBook brings together ten essays on the policies, processes and pressures influencing the governance of addictions in Europe, with the aim of providing thought-provoking reflections that have arisen from the work of ALICE RAP, either directly or through the discussions and ideas generated by ALICE RAP scientists. The e-book was launched in November 2014 and has been downloaded over 4500 times before the end of the project.

Decision Makers' Dialogues

- Six **Decision Makers' Dialogues** have been successfully organised, enabling exchange with key stakeholders from a variety of government levels (national –England, Latvia-, European, International), including an end-of-project debate held on-site and on-line.

  The first decision makers' policy dialogue was convened in February 2012 with officials from a range of UK government departments on pricing policy options for alcohol, in advance of the publication of the most recent UK alcohol strategy.

  A second decision makers' dialogue took place in Brussels in November 2013 and put together researchers of the multiple disciplines involved in the study of addictions in the frame of ALICE RAP with policy makers from the different EC Directorates related to addictions and Public Health.

  A third ALICE RAP decision makers' dialogue was held in June 2015 with officials from World Health Organization. An open lunch time seminar took place with 40 WHO staff and interns in attendance; followed by a closed meeting with 12 WHO officials from the Programme on Substance Abuse, the WHO Expert Committee on Drugs and the HIV/AIDS programme.

  Two invited briefing sessions with policy makers in the context of the Latvian EU presidency comprise the fourth ALICE RAP decision makers' dialogue: two AR scientists – Jürgen Rehm and Petra Meier – delivered a presentation to the Latvian Parliament on policy options impacting on the price of alcoholic beverages in March 2015; and AR Latvian project partner, Aleksandrs Aleksandrovs, contributed to development of the healthcare framework and strategy for the period of 2014–2020.

  Fifth, ALICE RAP scientists were invited to share project results and implications with EU policy actors in the contexts of two topic-specific European Commission-led initiatives: The Expert Group on Gambling lead by DG GROW; and the European Council Horizontal Drugs Group, led by DG HOME.

  The sixth, and final, decision makers' dialogue event took the form of an on-site and on-line debate (the A-Debate) to present and discuss key research findings coming out of the project, their policy implications and the science with the greatest potential to contribute to smart and

evidence-based global drugs policy; involving addiction scientists, policy actors from national and international organisations related to drug policy and expert civil society actors in the fields of drug policy, public health and treatment.

Further attempts were also made to hold events in connection with the 59th CND meeting and UNGASS 2016 on drugs. The proceedings of the 2-day event can be seen in the videos on the A-Debate web-page.

A-Debate Science Summary

- The science presented at the on-site and on-line A-Debate event was summarised in a concise public document – **the A-Debate Science Summary** – which was revised and amended according to the discussions that took place over the course of the A-Debate. The information in the 9-page science summary is grouped into 3 sub-headings:
  1. Biology and addictions – encompassing the years of life lost due to drugs, quantitative risk assessment, Evolutionary drivers of drug use, and heavy use over time as explanatory variable
  2. Prevention and Treatment – looking at prevention, treatment (and stigma) and drug delivery systems
  3. Governance – comprising drug policy approaches, missed opportunities due to the failure to take into account variance over place and time and the inequalities in power and influence, well-being as framework for governance, whole-of-government and whole-of-society approaches, and accountability.

Scientific publications

- Over 85 articles have been published (before the end of the project) in scientific peer-reviewed journals, based on the work of ALICE RAP, as well as 75 chapters published in edited books, with more final publications currently in preparation. These can be seen and searched in the scientific publications section of the resources library.

Scientific presentations

- Over 130 scientific presentations on ALICE RAP research have been made at conferences, symposia, workshops and meetings on the local, national and international levels. Key presentations on overarching project themes can be found on the presentations section of the AR website.

  One key area of work in the communications plan has been the collaboration of AR with SICAD and EMCDDA to encourage maximum diffusion of AR science through the **Lisbon Addictions conference** (22-25 September 2015), including holding the final plenary meeting as an open pre-conference satellite symposium, running a parallel session and presenting numerous individual paper abstracts within the conference programme: 1 key note plenary presentation, 26 oral interventions in parallel sessions and symposiums, and 5 rapid communications – 13% of all conference interventions. Details of all ALICE RAP scientists' interventions at the Lisbon Addictions conference can be seen in a purpose-designed flyer.

Bulletins

- The aim of the **ALICE RAP Bulletin** was to provide a short and accessible account of some scientific aspects of the project, while it was on-going, to increase communication within and without the ALICE RAP Consortium. As well as the main article, the bulletins also contained sections dedicated to networking activities, alerts for forthcoming relevant events or deadlines and references for further reading. In total, 10 editions of the AR Bulletin have been produced, over the first 4 years of the project. In the final year, the Science Findings replaced the bulletins as a more complete and comprehensive means to disseminate the science of ALICE RAP in a concise and accessible manner.

Press activity

- Regular press releases and press conferences were held over the course of ALICE RAP, starting in the first year of the project. Project partners from different countries held press events or disseminated press notes to launch the project in 2012, including a press briefing event on addictions at the Science Media Centre in London. Press releases were also developed to coincide with the publication of AR policy papers on alcohol and cannabis and a Guardian article was published to accompany the open debate on cannabis policy in Amsterdam. A press release was also circulated internationally on the prize awarded to the ALICE RAP Heavy use over time article by the EMCDDA.

  A final communication activity targeting the mainstream media and specialised media channels in parallel was carried out as part of the preparations for the A-Debate. A press release on one of the principle initiatives proposed by the project (a health addiction footprint) was sent out to coincide with the opening of the A-Debate to targeted journalists identified by the AR partners.

  All ALICE RAP press releases can be seen here.

4.3 Address of project public website and relevant contact details

The ALICE RAP public website is available at www.alicerap.eu. Project leaders Dr. Peter Anderson and Dr. Antoni Gual, and members of the Coordinating team can be contacted at the following addresses:

PROJECT LEADERS:
Peter Anderson - peteranderson.mail@gmail.com
Antoni Gual - tgual@clinic.ub.es

OTHER MEMBERS OF THE COORDINATING TEAM:
Silvia Matrai (Project manager) - smatrai@clinic.ub.es
Jillian Reynolds (Scientific Officer) - reynolds@clinic.ub.es
Fleur Braddick (Science Communications Officer) - fmbooth@clinic.ub.es

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