

## Substance use in young people 1



# The increasing global health priority of substance use in young people

Louisa Degenhardt, Emily Stockings, George Patton, Wayne D Hall, Michael Lynskey

Substance use in young people (aged 10–24 years) might disrupt key periods of transition that occur as the adolescent brain undergoes cognitive and emotional development, and key psychosocial transitions are made. Adolescence is the peak time for initiation of substance use, with tobacco and alcohol usually preceding the use of illicit drugs. Substantial variation is noted between countries in the levels, types, and sequences of substance use in young people, indicating that a young person's use of substances depends on their social context, drug availability, and their personal characteristics. The Global Burden of Disease (GBD) 2013 study suggests that the burden attributable to substance use increases substantially in adolescence and young adulthood. In young men aged 20–24 years, alcohol and illicit substance use are responsible for 14% of total health burden. Alcohol causes most health burden in eastern Europe, and illicit drug burden is higher in the USA, Canada, Australia, New Zealand, and western Europe. Large gaps exist in epidemiological data about the extent of drug use worldwide and much of what we know about the natural history of substance use comes from cohort studies in high-income countries undertaken decades ago, which hinders effective global policy responses. In view of the global epidemiological transitions from diseases of poverty to non-communicable diseases, the burden of disease and health risks among adolescents and young adults is likely to change substantially, in ways that will no doubt see substance use playing an increasingly large part.

## Introduction

Different cultures have used different substances to experience their intoxicating, euphoric, disinhibiting, or relaxing effects for thousands of years. Until industrialisation for production of beer and spirits, mostly in the mid to late 18th century in Europe, use of substances was constrained by their restricted and often seasonal availability. Nowadays, alcohol and tobacco are legally and readily available to adults in most countries. These are typically not legally available to young people below a specific age; however, the minimum ages and the extent to which they are enforced varies substantially across countries.<sup>1</sup> Illicit drugs are defined as those drugs whose non-medical use has been prohibited by international drug control treaties because of the belief that they pose an unacceptable risk to the health of adult users.<sup>2,3</sup> These include plant-based substances (eg, heroin, cocaine, and cannabis) and synthetic substances, such as amphetamine-type stimulants and pharmaceutical opioids (eg, oxycodone, buprenorphine, and methadone). In this Series paper we focus on use of alcohol, tobacco, and illicit drugs (panel 1).

Substance use in young people (defined in this paper as aged 10–24 years; panel 1) has been the cause of increasing concern to parents, friends, communities, and policy makers. This concern underlines the fact that adolescence and early adulthood are key periods of transition. Substantial changes occur in the adolescent brain, including great cognitive and emotional development.<sup>4</sup> Some have suggested that this period might, in itself, be a crucial time of susceptibility for the development of substance dependence.<sup>5</sup> This period is also one in which key psychosocial transitions are typically made: completing

education, transitioning to employment, forming sexual relationships, and transitioning to marriage and parenthood. Use of substances during these years is of concern to the extent that it might impair these transitions.<sup>10</sup>

Increasing attention has been given to substance use in young people across communities, countries, and global organisations. Young people were particularly noted in WHO's global strategy on alcohol,<sup>11</sup> which was endorsed in 2010 by consensus at the 63rd session of the World Health Assembly (Geneva, May 17–21). WHO's Framework Convention on Tobacco Control,<sup>12</sup> which has 168 signatories, noted that access to tobacco by young people was an issue. For both the alcohol and tobacco strategies, numerous policy levers are available to prevent and reduce use and harms, the strongest of which involves legislation to restrict the availability, use, and sales of these substances.<sup>1</sup> However, there is concern that low-income and middle-income countries do not have the capacity to implement these<sup>13</sup> in the face of promotional activities by the alcohol and tobacco industries.

In April, 2016, the UN General Assembly will convene a Special Session to review progress made against the 2009 Political Declaration and Plan of Action<sup>14</sup> to address illicit drug use and harms globally. A particular focus will be upon young people. The policy levers available for illicit substances are much more restricted than for alcohol and tobacco since their non-medical use is illegal. UN Member States' efforts are often centred upon policing supply and consumption, whereas efforts to reduce demand for illicit substances typically focus upon prevention. There is less focus on harm reduction and treatment of illicit substance use and dependence in young people.

*Lancet Psychiatry* 2016;  
3: 251–64

Published Online  
February 18, 2016  
[http://dx.doi.org/10.1016/S2215-0366\(15\)00508-8](http://dx.doi.org/10.1016/S2215-0366(15)00508-8)

This is the first in a *Series* of three papers about substance use in young people

National Drug and Alcohol Research Centre, University of New South Wales Australia (UNSW), Sydney, NSW, Australia

(Prof L Degenhardt PhD, E Stockings PhD); Centre for Adolescent Health, Murdoch Children's Research Institute, Melbourne, VIC, Australia (Prof G Patton PhD); Centre for Youth Substance Abuse Research, University of Queensland, Brisbane, QLD, Australia (Prof W D Hall PhD); and National Addiction Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK (Prof W D Hall, Prof M Lynskey PhD)

Correspondence to:  
Prof Louisa Degenhardt,  
National Drug and Alcohol Research Centre, University of New South Wales Australia (UNSW), Sydney, NSW 2052, Australia  
[l.degenhardt@unsw.edu.au](mailto:l.degenhardt@unsw.edu.au)

### Panel 1: Definitions

**Adolescent:** people aged 10–19 years (according to UNICEF, WHO, and UN Population Fund [UNFPA]).\*

**Young people:** people aged 10–24 years (according to UNICEF, WHO, and UNFPA).\*

**Youth:** people aged 15–24 years (by UNICEF, WHO, UNFPA, and UN Secretariat), or 15–32 years (by UN Habitat [youth fund]).\*

**Child:** people aged <18 years (UNICEF, on the basis of the Convention on Rights of the Child).\*

**Alcohol:** a psychoactive substance that has both intoxicating and relaxing effects. It has been used widely in many cultures for thousands of years.

**Tobacco:** a green leafy plant, the leaves of which are dried, ground, and used in various ways. The most common use is via smoking in a cigarette, but it can also be smoked in a pipe or cigar, chewed, or sniffed (called snuff or snus). There are thousands of chemicals in cigarettes. Inhibition of monoamine oxidase activity by compounds in tobacco smoke has been suggested to combine with nicotine (thought to be the most important compound for psychoactive effects) to increase the addictive properties of smoking.<sup>4</sup>

**Cannabis:** a generic term for preparations (eg, marijuana, hashish, and hash oil) derived from the *Cannabis sativa* plant, which contain many cannabinoids. Tetrahydrocannabinol is thought to be mainly responsible for the psychoactive effects of cannabis, producing euphoria and relaxation, heightening the senses, and increasing sociability.

**Amphetamine-type stimulants:** synthetic sympathomimetic amines with powerful stimulant effects on the CNS. The most common types used are methamphetamine, amphetamine, and methylenedioxymethamphetamine.

**Cocaine:** an alkaloid derived from the coca plant that is a powerful CNS stimulant.

**Opioids:** derivatives from the opium poppy (eg, heroin and morphine) and their synthetic analogues (eg, oxycodone, methadone, and fentanyl). Opioids relieve pain and produce a feeling of euphoria.

**Novel psychoactive substances or so-called legal highs:** many different kinds of substances that include a range of stimulants (ie, cathinones or piperazines, which are usually in powder or tablet form) and synthetic cannabinoids (which are usually smoked). These are receiving increased attention but are used much less often than are other illicit substances.

**Lifetime use:** use at least once in a person's lifetime. Most commonly measured in community and school surveys of young people; does not provide information about recency of use or any features of risky use for young persons (eg, frequency, amount, or route of administration).

**Past year use:** use at least once in the past year; in younger age groups, this is very similar to lifetime use.

**Past month use:** use at least once in the past month; indication of use that is likely to be more regular, and very recent.

**Injecting drug use:** consumption of drugs via injection (typically intravenous). Injection of drugs by a young person places them at high risk of problematic use and the transmission of HIV and hepatitis C virus.

**Binge use (or heavy episodic use):** can refer to consumption of a specific number of standard alcoholic drinks (eg,  $\geq 5$  drinks containing 10 g of alcohol) or a large amount of a substance; or can refer to sustained use of a substance during a period of time (eg, 24–48 h). Is a measure that assesses large amounts of substances used on single occasions that identify young people at higher risk of experiencing harms of intoxication (eg, injury and assault).

**Heavy use:** either large use in a specific use episode, or frequent use. Often used interchangeably with regular use, typically use is at least once a week or every day.

**Problem use:** use identified as associated with experience of problems (eg, interpersonal problems) without reaching a diagnostic threshold. However, the word “problem” can be taken to mean different things to different people.

**Dependent use:** frequent use of a substance resulting in impaired control over substance use, as shown by a strong desire to take the substance; impaired control over use; tolerance to effects and withdrawal syndrome on ceasing or reducing use; and continued use despite social and health difficulties. Criteria to define dependent use are largely developed from adults,<sup>5</sup> some criteria might not be particularly strong indicators of problems (eg, development of tolerance to the effects of alcohol with increasing exposure might be expected<sup>5</sup>). In studies of substance use disorders in young people, issues have been identified with respect to use of standardised interviews developed for adults.<sup>6</sup>

\*Information from the UN Department of Economic and Social Affairs.<sup>7</sup>

This is the first in a Series of three papers that discusses substance use in young people. We will present data about the epidemiology of substance use and health burden in young people; discuss key issues associated with substance use in young people, particularly the stage in the life course for patterns of

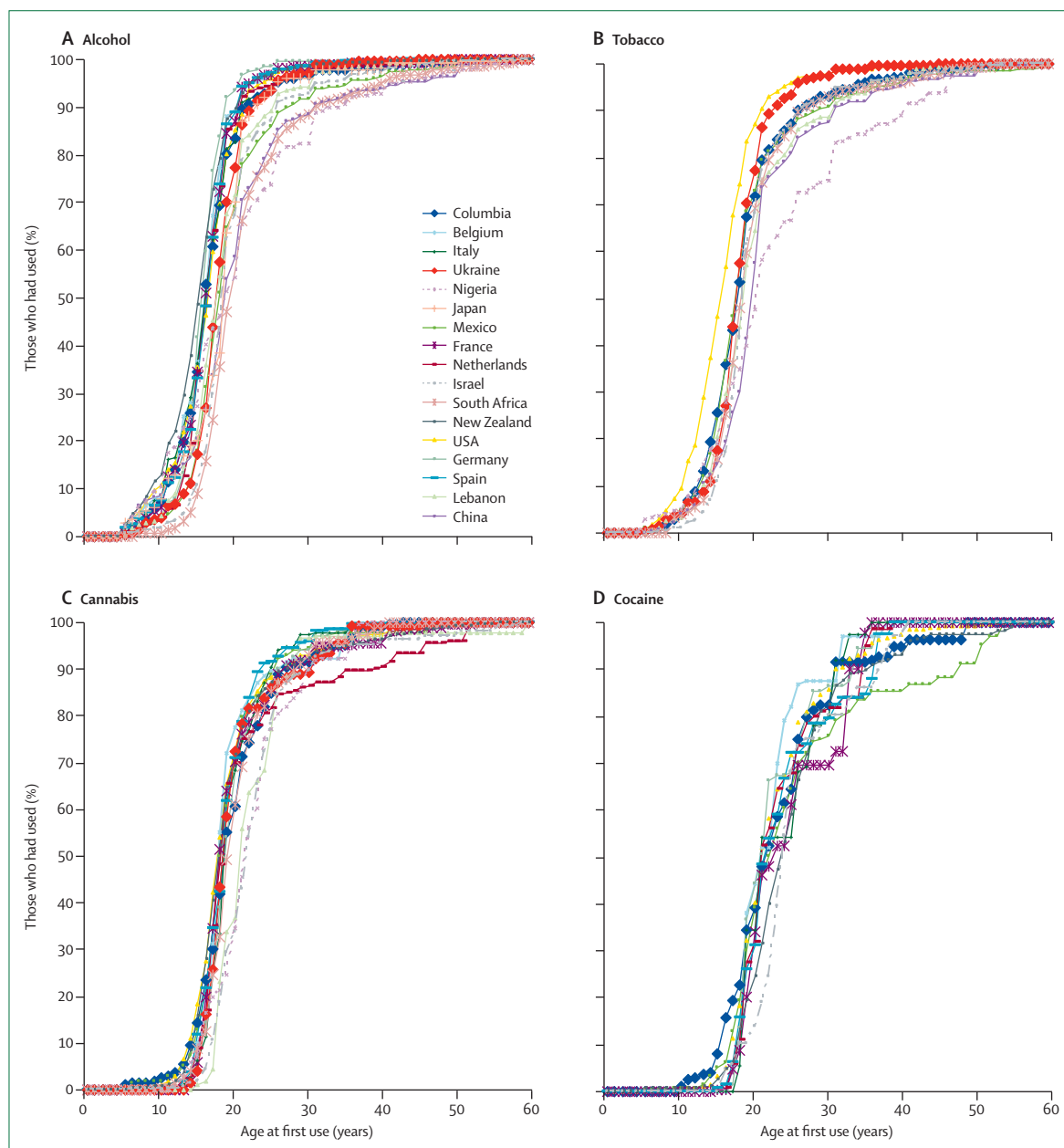
substance use, persistence of use and progression to dependent use, and differences in use between sexes; identify several at-risk populations of young people; and discuss emerging trends in the availability, contexts of use, and resulting effects of substance use in young people.

## What is the extent of substance use in young people?

### When does substance use begin?

Adolescence is the peak period during which substance use first occurs. This finding is consistently reported in surveys of drug use in young people and young adults. Levels and frequency of use begin to increase in mid-adolescence and peak in very early adulthood, as reported in long-running US cohorts.<sup>15</sup>

The age of onset in prospective cohorts is similar in high-income countries.<sup>16</sup> Figure 1 shows the age-of-onset curves for use of substance use in people using specific substances in the World Mental Health Surveys (WMHS), cross-nationally.<sup>16</sup> Among those who have used substances, the age-of-onset curves were strikingly similar across countries. For alcohol, median age of onset was 16–19 years for all countries, except South Africa (20 years), and the same age for tobacco in all countries,



**Figure 1: Age of onset of substance use by people who had used each substance, by country**

Reproduced from Degenhardt and colleagues,<sup>16</sup> by permission of Degenhardt and colleagues. If lines are not presented for an individual country, either no assessment was done for the age of onset of that substance, or fewer than 30 people reported having used the substance.

except Nigeria (21 years) and China (20 years). Median age of onset of illicit substance use was slightly older in all countries (cannabis median age of onset 18–19 years; cocaine median age of onset 21–24 years).<sup>16</sup>

The age range for initiation was also consistent across countries in the WMHS.<sup>16</sup> Half of people who had ever used alcohol began between ages of 14 years and 21 years. The IQR of age-of-onset distributions was typically 15–21 years for tobacco, 16–22 years for cannabis, and 19–28 years for cocaine.

Many policy makers have argued that delaying the onset of substance use is important to reduce the risk of developing problematic use of that substance later in life.<sup>17</sup> However, in 2014 a systematic review<sup>18</sup> reported an absence

of high quality prospective research on alcohol. Only five prospective cohort studies, undertaken in the USA and Norway, met the review's inclusion criteria, and their findings were mixed on associations between age of onset of alcohol use and later problematic alcohol use.<sup>18</sup> Studies that did note an association typically reported elimination or substantial attenuation of the association once confounding factors were included.<sup>18</sup> Delaying of the age of onset might still be an important strategy to reduce risks associated with acute intoxication and other health and social harms associated with early-onset alcohol consumption.<sup>10</sup>

### Is there a consistent order in initiation of substance use?

Studies in countries with quite high prevalence of cannabis use have often reported a typical temporal order of drug initiation: alcohol and tobacco first, followed by cannabis and then other illicit drugs. Early initiators and regular users of any of these drugs are most likely to progress to use the next drug in the sequence. This pattern, which persists after control for confounders,<sup>19–21</sup> has led to some drugs being labelled so-called gateway drugs (eg, cannabis as a gateway drug for the use of other illicit drugs). However, this pattern is not consistent across all countries.<sup>22</sup> Use of other illicit drugs is more common than cannabis in some countries (eg, Japan), and the association between initiation of alcohol, tobacco, cannabis, and other illicit drug use is stronger in some countries (eg, the USA) than others (eg, the Netherlands).<sup>22</sup>

These variations in patterns of drug use initiation between countries and cultures suggest that a young person's entry into illicit drug use might be representative of their social context, illicit drug availability, and their personal characteristics and social settings that facilitate or deter drug use. This conclusion is supported by the range of social and contextual factors associated with the initiation of substance use (table 1).

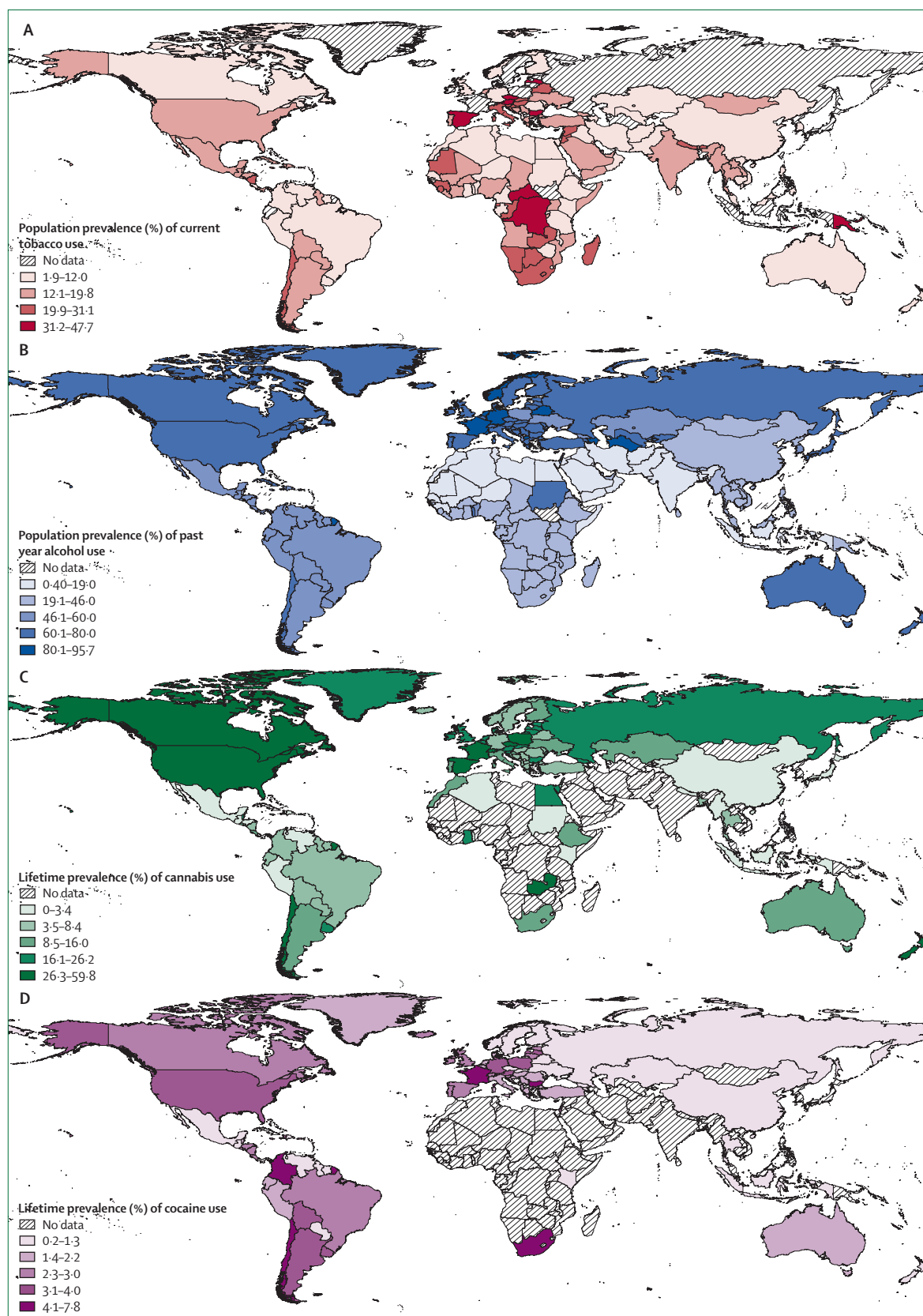
### Geographical variation

Figure 2 presents the latest data reported by UN agencies that monitor tobacco, alcohol, and cannabis use by young people (WHO<sup>25,26,51</sup> and the UN Office on Drugs and Crime;<sup>27</sup> appendix). Substantial cross-national variation is visible in the levels of substance use reported by UN Member States (figure 2). Tobacco use is most common in western Europe and African countries; levels of past year alcohol use and of recent heavy episodic alcohol use are high in eastern Europe, Australasia, western Europe, and North America; and lifetime cannabis use is high in Australasia, North America, and several countries in western Europe.

Large subnational variations are shown in substance use, particularly of illicit drugs where availability is often concentrated in large cities. Even in particular geographical areas, substantial variations are noted in levels of use in young people who differ by sociodemographical characteristics that increase or decrease their risk of substance use (table 1).

	Association
<b>Contextual factors</b>	
Laws and taxation <sup>23,26</sup>	↓ *
Availability <sup>23,27–30</sup>	↑
Positive norms about substance use <sup>23,31</sup>	↑
<b>Fixed markers of risk</b>	
Structural	
Low socioeconomic status <sup>23,32,33</sup>	↑
Neighbourhood environment <sup>23</sup>	↑
Of a racial or ethnic minority <sup>23</sup>	↑ †
Familial	
Low parental education attainment <sup>23</sup>	↑
Parental conflict or separation <sup>23,34,35</sup>	↑
Parental psychopathology <sup>23</sup>	↑
Family history of substance use <sup>23,36–39</sup>	↑
Potential genetic risk factors <sup>23,40–44</sup>	↑
Individual	
Men <sup>23,34</sup>	↑
Prenatal or post-natal exposure to substances <sup>23</sup>	↑
Personal income <sup>23</sup>	↑
<b>Individual and interpersonal factors</b>	
Abuse or neglect <sup>23</sup>	↑
Stressful life events <sup>23</sup>	↑
Poor family relations <sup>23,37</sup>	↑
Family management (eg, guidelines and monitoring) <sup>23,45</sup>	↓
Internalising behaviours <sup>23,34</sup>	↑
Externalising behaviours <sup>23,34,36,43,44,46</sup>	↑
Substance use expectancies <sup>23</sup>	↑
Favourable attitudes <sup>23</sup>	↑
Peer use, norms about substance use <sup>23,47,48</sup>	↑
Leaving home at a young age <sup>23</sup>	↑
Adolescent employment <sup>23</sup>	↑
Low educational attainment <sup>23,49,50</sup>	↑
Becoming pregnant <sup>23</sup>	↓
Married or in a stable relationship <sup>23</sup>	↓
Data are from Stone and colleagues. <sup>23</sup> ↑ = increase in risk. ↓ = decrease in risk.	
*The evidence referred to applies to alcohol and tobacco; scarce evidence is available about the effects of laws on illicit drug use in young people. <sup>1</sup> †Varies substantially by country and by racial or ethnic group.	
<b>Table 1: Risk and protective factors for substance use in young people</b>	

See Online for appendix



**Figure 2: Prevalence of substance use in young people**

Prevalence of current tobacco use (A), past year alcohol use in young people aged 15–19 years in 2010 (B), and prevalence of lifetime cannabis (C) and cocaine (D) use. Data are from WHO's Report on the Global Tobacco Epidemic 2013 (A),<sup>26</sup> WHO's Global Information System on Alcohol and Health (B),<sup>26</sup> and the UN Office on Drugs and Crime's 2015 World Drug Report (C and D).<sup>27</sup> Substantial differences are noted in countries and substances in the age ranges included, years of data collection, coverage of the survey, and available details of the studies' methodology (appendix). Prevalence of lifetime amphetamine and opioid use is shown in the appendix.



Data reported to UN agencies by Member States have several limitations. First, these include variations in the year of collection, age ranges of people covered, use of subnational surveys, and the definitions of substance use (panel 2). One of the greatest issues, however, is the little information available about survey sampling, fidelity of assessment, and how consistent measurements are within countries, across years, and across countries. Finally, there are large gaps in the data available in some countries on the extent of substance use in young people (panel 2).<sup>52</sup>

WHO's WMHS initiative analysed data from 17 countries about the prevalence of substance use at ages 15 years and 21 years (in people aged 22–29 years at the time of surveying) and the age of onset of substance use (appendix).<sup>16</sup> Substantial differences were reported in substance use in young people between countries (appendix). Most young adults in the Americas, Europe, Japan, and New Zealand had used alcohol by age 21 years, with smaller proportions having used alcohol in the Middle East, Africa, and China by the same age. Use by age 15 years was lower, but had a similar country pattern.<sup>16</sup>

#### Panel 2: Limitations of cross-national data about substance use in young people

Large gaps exist in the data reported to UN agencies about substance use in young people (an issue in many areas of global reporting on the health and wellbeing of young people<sup>52</sup>). The appendix has details about UN data collections.

Some of the key difficulties facing the development of an accurate and timely picture of national, regional, and global substance use in young people include:

- incomplete reporting of data by Member States to UN agencies responsible for collating these data;
- differences across countries in the years of data collection, sampling frames (eg, school vs community), coverage (eg, subnational vs national), and method of assessment;
- reliance on school surveys, meaning that young people not in school are not questioned (which can be a large proportion of young people in the later years of education);
- less emphasis to obtain accurate estimates of prevalence of less common or more stigmatised patterns of substance use (typically more regular, risky, or problematic patterns of use), which need the use of indirect prevalence estimation methods rather than surveys;<sup>53</sup>
- a reliance on measurements of lifetime or past year use with few estimates of the proportion of young people who might be engaging in more regular or dependent patterns of use, which are arguably the patterns of greater concern;
- differences in the measures of use assessed;
- little monitoring, in most countries, of levels and trends in substance use by at-risk groups of young people, who might begin using new substances sooner than most young people or be at greater risk of experiencing harms;
- differences in the age ranges assessed (eg, many estimates for tobacco use are for 13–17 year olds, but some refer to those aged 10–19 years, 15–16 years, and so on);
- differences in the fidelity of surveys to the study design;
- few repeat measures of use across years in most countries, which would permit a more evidence-based assessment of trends over time in use by young people.

#### Differences between men and women

Drug use is consistently more common in men than women<sup>16,25,27,51,54</sup> (appendix). These differences might partly represent sex differences in the opportunities to use substances in North American<sup>55–58</sup> and Latin American<sup>59–62</sup> countries, in which men have greater opportunities to try substances than women do.<sup>55–62</sup> The WMHS<sup>63</sup> reported large variations between countries in sex differences in the opportunity to use drugs and in progression to use.<sup>63</sup> In some countries, differences between sexes were small at both stages (particularly for alcohol) whereas in other countries they were apparent at both stages; and in the remainder, men had a much higher chance of being offered substances (particularly illicit drugs) than women, accounting for sex differences in use. In no country were alcohol or drugs more available for women or were women more likely than men to take up the opportunity to use substances.

#### Substance use patterns

##### Regularity and quantity of use

We need to be clear about what we mean by substance use (panel 1). In adolescents, use of substances is typically sporadic, often experimental and opportunistic, with many young people taking advantage of opportunities to use substances and experiencing both the desired and the less positive effects. As adulthood approaches, an increasing number of young people have income from employment and increased independence in the ways in which they spend their time. Some young people begin to use drugs more frequently than before. A small number of young people progress to regular use and a subset of these develop dependent use, typically during young adulthood. Further details about different patterns of substance use are listed in panel 1.

A fairly consistent picture has emerged from prospective cohort studies,<sup>9,54,64</sup> and modelling of epidemiological data,<sup>65–67</sup> in which substance use begins in adolescence and peaks in young adulthood (age 20–24 years). Clear differences are noted between substances in whether use continues, ceases, or progresses to problematic or dependent use. In an early and highly valued study charting substance use through childhood, adolescence, and young adulthood, Chen and Kandel<sup>15</sup> showed that the use of most substances peaked in late adolescence and early adulthood. Sharp decreases were reported in monthly cannabis use from the mid-20s and more gradual decreases in the use of other illicit drugs. By contrast, much smaller reductions were noted in monthly use of alcohol and tobacco by the late 20s.<sup>15</sup> When the focus was on people who had used substances at least ten times in their lifetime, the proportion of tobacco users who used every day increased as the cohort aged. This proportion remained stable from about 20 years of age for alcohol users, but decreased from the mid-20s for cannabis users.<sup>15</sup> The decrease in daily cannabis use particularly has been associated with changes in social roles as young

people enter relationships, marry, have children, undertake further education, and enter the workforce. A failure to make these transitions is associated with persistent use of cannabis.<sup>54</sup>

The natural history of other types of illicit drug dependence has been less well studied than cannabis in prospective cohorts, largely because of their much lower prevalence of use. A study<sup>22</sup> of initiation of use and progression to dependence in 17 WMHS countries noted that drug dependence was more likely to develop in those with a more extensive substance use history (use of more substances and earlier onset of use) and a history of externalising and internalising disorders before the age of 15 years. Similar findings have emerged from cohort studies in high-income countries in which early involvement with substances and mental health problems increased the risk of problematic substance use.<sup>68</sup>

Cohort studies of people who use less common illicit drugs (eg, cocaine and heroin) often include adult users seeking treatment for dependence or entering the criminal justice system. Little examination of these types of illicit drug use has been undertaken in representative cohorts of young people. This evidence suggests that a small number of people will no longer meet criteria for dependence a year after receiving a dependence diagnosis.<sup>69</sup>

### Effect of changes in social roles and transitions

All of the evidence we have reviewed so far was historical. Data for the initiation, trajectory, persistence, and progress of substance use are, in many cases, from cohorts of young people first interviewed several decades ago. Since that time, massive changes have occurred in the types of substances used, levels of use, and age of onset of use across many countries.<sup>10</sup> Simultaneously, large shifts have also occurred in social features of adolescence and young adulthood in high-income countries. In many low-income and middle-income countries, the social position of women is changing, with increasing autonomy and participation in education and employment. In many countries, marriage and parenthood occur at older ages than was previously the case. The acquisition of adult roles is delayed in many high-income countries. The effect that these shifts have on the initiation and persistence of substance use is not yet known.<sup>10</sup> However, delays in transitions to adult roles and responsibilities will be likely to allow substance use to persist, increasing the opportunity to develop problematic or dependent use and increasing the length of time that young people are exposed to the risks of drug-related health and social harms.<sup>10</sup>

### Risk and protective factors

Many studies examining risk and protective factors for substance use in young people have been cross-sectional. This design makes it difficult to identify which factors might play a causal role in development of risky patterns

of substance use. Nonetheless, a growing number of studies, mostly in high-income countries,<sup>70–72</sup> have used prospective cohort study designs to disentangle the potential causes of the initiation and progression to regular substance use in young people. The most informative of these studies identified risk factors for and pathways into regular alcohol, tobacco, and cannabis use in high-income countries. Few studies have examined whether risk factors for drug dependence differ between countries,<sup>22</sup> but, so far, similar risk factors seem to predict early cannabis use in high-income and low-income and middle-income countries.<sup>70</sup>

Risk and protective factors for adolescent substance use can be grouped in various ways. We use the classification in one systematic review<sup>23</sup> that characterised risk and protective factors as contextual risk factors, fixed markers of risk, and individual and interpersonal risk factors (table 1). These types of risk factors have different implications for population-level and individual targeted prevention interventions.<sup>1</sup>

First, the major contextual factors that affect the likelihood of use are the availability of the substance (eg, the density of outlets selling tobacco<sup>73</sup> or alcohol,<sup>28</sup> and the availability of illicit drugs<sup>29,30</sup>) and social norms that are tolerant of substance use.<sup>31</sup>

Second, fixed risk markers include being a man,<sup>23,34</sup> parental and sibling substance use,<sup>36,39</sup> and potential genetic factors,<sup>40–42</sup> all of which increase an adolescent's risk of use. Additionally, parental conflict increases the likelihood of a young person using substances.<sup>22,34,35</sup> People from socially disadvantaged backgrounds have an increased likelihood to use illicit drugs,<sup>32</sup> but structural risk factors such as poverty, social, and cultural factors have been assessed in few studies.

Finally, individual and interpersonal risk factors include novelty<sup>43</sup> and sensation seeking,<sup>44</sup> oppositional behaviour and conduct disorder in childhood,<sup>46,47</sup> poor school performance, low commitment to education, and leaving school early (ie, before mandatory education is completed).<sup>49,50</sup> Family factors associated with an increased risk of drug use during adolescence include: parenting styles, poor quality of parent–child interaction, and parent–child relationships.<sup>37,72</sup> Affiliation with antisocial and drug-using peers is one of the strongest predictors of adolescent substance use,<sup>47,48</sup> independent of other risk factors.<sup>50,71</sup>

Many risk factors frequently co-occur. Young people who initiate substance use at an early age have often been exposed to social and family disadvantages, and come from families with marital difficulties and a history of parental substance use. They are also often impulsive, have performed poorly at school, and are affiliated with delinquent peers. Young people with many of these risk factors often start alcohol, tobacco, and illicit drug use at an early age and develop problematic drug use.<sup>47</sup>

Particular groups of young people exist who might also be at an increased risk of substance use, substance use problems, or adverse resulting effects of use (panel 3).

**Panel 3: Populations of young people at risk for substance use and associated problems**

UN organisations have identified most at-risk populations for becoming infected with HIV.<sup>74</sup> We adopted a similar logic to identify at-risk groups of young people who might: be at an increased risk of engaging in early-onset substance use; have increased levels of risky or problematic patterns of substance use if they have started using; and be at an increased risk of experiencing adverse effects of use once they initiate use.

**Young people with mental health problems**

- About 10–20% of children and adolescents,<sup>75</sup> and an even greater proportion of young adults,<sup>76</sup> are estimated to have at least one mental health problem in a year.
- Young people with common mental disorders (eg, depression or anxiety) have substantially higher rates of substance use, dependence, and harms than those without such disorders.<sup>77,78</sup> Common mental disorders typically precede substance use disorders in young people.<sup>79</sup>
- Young people with psychosis are at an increased risk of substance use. Research has suggested that in young people susceptible to psychotic disorders, substance use is associated with subclinical psychotic symptoms<sup>80</sup> and perhaps transition to first-onset psychosis.<sup>81,82</sup>
- For young people with previous mental health problems, substance use might worsen or trigger a recurrence of symptoms.<sup>83</sup> Evidence suggests that once young people with mental health problems start using substances, they might be at a greater risk of progressing to problematic or dependent use.<sup>84,85</sup>

**Young people who identify as lesbian, gay, bisexual, transgender, and questioning (LGBTQ), or same-sex attracted**

- A 2011 UK survey<sup>86</sup> estimated that 2.7% of young people aged 16–24 years identified as lesbian, gay or bisexual; an Australian study<sup>87</sup> noted that 6% of young people aged 16–18 years reported same-sex attraction.
- LGBTQ young people have high rates of substance use and associated problems.<sup>88,89</sup> A systematic review noted that although all substances were more likely to be used by LGBTQ young people, the strongest associations of sexual orientation in young people were typically with less common patterns of drug use (eg, cocaine or injecting drug use) and problem use.<sup>88</sup>
- A systematic review noted that substance use in LGBTQ young people was associated with victimisation, negative experiences of disclosure of their sexuality, and a lack of supportive environment.<sup>89</sup>

**Young offenders**

- About 1.4% of adolescents were convicted of a criminal offence in Australia in 2007–08; 0.4 per 1000 adolescents were detained in juvenile detention.<sup>90</sup>
- Prevalence of substance use disorders is greatly increased in young people in contact with the criminal justice system.<sup>91–93</sup>
- Debates surround whether substance use and crime are causally linked.<sup>10</sup>

**Indigenous young people**

- Substance use in indigenous young people has been reported to be high in many populations—eg, Native Americans<sup>94</sup> and Maori<sup>95</sup> and indigenous young people in the Arctic<sup>96</sup> and Australia.<sup>97</sup>
- The types of substance use both within and across communities of indigenous young people are varied. Alcohol has often been a substance of particular concern in indigenous communities.
- Indigenous young people are in many cases susceptible to misuse because of social and economic disadvantage and high unemployment, homelessness, incarceration, and familial disruption.<sup>97,98</sup>

(Continues on next page)

**Health burden**

The Global Burden of Disease (GBD) studies estimated the health burden of injuries and diseases by combining years of life lost due to disability<sup>104</sup> and years of life lost due to early mortality<sup>105</sup> into a metric called disability-adjusted life-years (DALYs).<sup>106</sup> WHO estimated that in 2004, the biggest contributors to health burden in 10–24 year olds were mental and substance use disorders (19% of DALYs), injuries (both unintentional and intentional; 12% of DALYs), and HIV, tuberculosis, and lower respiratory infections (8.2% of DALYs).<sup>107</sup>

The latest iteration of GBD study estimated the burden of disease attributable to tobacco, alcohol, and illicit drug use in its comparative risk assessment exercise, in which these substances were deemed risk factors.<sup>108</sup> A restricted number of harms were included in these estimates in the case of illicit drugs<sup>109</sup> because of limitations on the evidence on causality (in paper two of this Series, Hall and colleagues<sup>10</sup> discuss the evidence for a causal role of substance use in various adverse health and social outcomes). These estimates are made with epidemiological data for exposures (eg, substance use) and information about the association with health outcomes, and by modelling national, regional, and global estimates of how much each risk factor contributes to disease burden (table 2; appendix).

Tobacco use is attributable to no estimated disease burden in 2013 (DALY) in the age groups 10–24 years (appendix). This result is because tobacco smoking causes little harm until much later in adult life, when extended use is responsible for a substantial proportion of global health burden in the total (adult) population.<sup>108</sup> Alcohol use is the largest cause of disease burden in young adults and in older age groups, particularly for young men aged 20–24 years in whom it accounts for 10% of all disease burden. The intervention literature on responses to substance use in young people (as reviewed in paper three in this Series by Stockings and colleagues<sup>11</sup>) also has been most researched for alcohol use.

The burden attributable to alcohol and illicit drug use is greater for men than women, because more men consume these substances (appendix).<sup>108</sup> For men aged 20–24 years, alcohol and illicit drug use together were responsible for 14% of total global disease burden.

Attributable burden has large regional variations (table 2). In young people, alcohol has a much larger effect on health in eastern Europe, whereas illicit drug burden is higher in the USA, Canada, Australia, New Zealand, and western Europe.

**Emerging trends that might affect substance use**

Broadly speaking, two factors are changing the context of substance use in young people. The first concerns changes in availability of substances, reflecting marketing activities in some regions (eg, alcohol and tobacco in low-income and middle-income countries), increased sales of



e-cigarettes in others, and the use of the internet to supply illicit substances. The second concerns changes in the regulatory environment, both for licit and illicit substances. As alcohol and tobacco become increasingly marketed to young people in low-income and middle-income countries, some governments might struggle to use the policy mechanisms that effectively reduce alcohol and tobacco use in young people in high-income countries.<sup>1</sup> Some countries are considering changes in the legal control of cannabis. This amendment could lead to changes in substance use in young people and provide governments with new policy levers to reduce use and harm.<sup>1</sup>

The consumption of alcohol and tobacco by young people is increasing in some low-income and middle-income countries.<sup>25,51</sup> Cigarette smoking has substantially increased in China and the Middle East, and there is concern about possible increases in Africa.<sup>110</sup> Alcohol consumption is thought to have increased in China and India.<sup>51</sup>

One issue associated with these shifts is the way in which alcohol and tobacco are available and sold. A large proportion of alcohol consumption in these regions is unrecorded, meaning that alcohol is produced and sold outside of government control and therefore untaxed. This unrecorded production could partly be from traditional methods of alcohol production but could also represent illicit production or smuggling across country borders.<sup>51</sup> As a result, the traditional policy levers of taxation, control of outlets, and legal minimum age for consumption are not available to governments for these substances.<sup>51,110</sup> Other issues include the restricted capacity of low-income and middle-income countries to deal with the alcohol and tobacco industries and with those who trade in illicit products. These policy levers can be very effective in reducing consumption of these substances by young people.<sup>1</sup>

### Manufacture of amphetamine-type stimulants and new psychoactive substances, and changes in use of e-cigarettes and legal status of cannabis

Amphetamine-type stimulants are the second most widely used group of illicit drugs after cannabis.<sup>109</sup> Added to these are an increasing number of new psychoactive substances (NPSs). NPSs mimic the stimulant effects of amphetamines, cannabinoids, and other drugs but are not under domestic or international control by the 1961 or 1972 UN Conventions on Narcotic Drugs.<sup>111</sup> Of those experimenting with NPSs, young people are over-represented, although these substances are more typically used by experienced drug consumers. NPSs have been identified in 96 countries worldwide; the largest variety has been reported in Europe and North America.<sup>112</sup> More than twice as many NPSs have been reported as there are substances currently controlled under the UN Conventions.<sup>112</sup> Stockings and colleagues<sup>1</sup> discuss regulatory responses to these substances.

(Panel 3 continued from previous page)

#### Young people who are homeless

- In Australia, 1.3% of young people aged 12–24 years are estimated to be homeless.<sup>99</sup>
- Young people who are homeless typically do not have support during a crucial time of transition to adulthood. Homelessness might be the result of trauma, neglect, or marginalisation.<sup>100</sup>
- High rates of substance use among homeless youth have been consistently reported worldwide, and in young people of very different cultures and ethnic origin.<sup>100,101</sup> Among those with substance use problems, high risks of infectious disease (via injecting drug use), sexually transmitted infections, and mental health problems are also reported.<sup>101</sup>
- Restricted access to health and social services and support<sup>102</sup> can compound the problems that young homeless people with substance use problems might experience.<sup>100</sup>

#### Young people who inject drugs

- Almost no data are available about the extent of injecting drug use in young people (particularly those aged <18 years), but adolescents could be a large proportion of people who inject drugs.<sup>103</sup>
- Types of drugs injected vary; opioids are often one of the major drugs injected by this group, and opioid dependence is an increasing public health concern worldwide.<sup>66</sup>
- Great differences exist between younger and older people who inject drugs, including the extent of injecting risk behaviour.<sup>103</sup> The first 1–2 years of an individual's injecting drug use is often the peak of risk for first exposure to HIV and hepatitis C virus.<sup>10</sup>
- Young people with previous serious substance dependence and injecting drug use often have a range of other large health, social, and welfare needs.
- Young people who inject drugs might face particular barriers in accessing services for their substance use.<sup>1</sup>

Regulation of e-cigarettes, which have been advocated for their potential as a tobacco harm reduction strategy in people already smoking, is greatly debated.<sup>113–116</sup> Increases in use in young people<sup>117</sup> have led to concern that e-cigarettes might act as a gateway to tobacco smoking and undermine the success of tobacco control policies by normalising tobacco smoking again; although, currently little research supports this concern.

Several countries are considering or have changed the legal status of medical and non-medical cannabis use. Opponents of medical cannabis laws argue that legalisation will increase adolescent cannabis use by increasing access to cannabis, increasing the social acceptability of its use, and reducing its perceived risks.<sup>118,119</sup> The potential effect of allowing the medical use of cannabis has been examined in the USA, where nearly half of states have legalised its medical use. Data from the US Monitoring the Future Surveys on cannabis use among adolescents between 1991 and 2014 compared changes in rates of past month cannabis use in the 21 states that legalised medical cannabis use with states that had not.<sup>120</sup> The analysis controlled for social, economic, and demographical differences between the states and schools. The survey reported that states that permitted medical cannabis use had higher rates of 30 day cannabis use before they changed their laws than states that did not (15.9% vs 13.3%). However, no

	Age 10–14 years				Age 15–19 years				Age 20–24 years			
	Men		Women		Men		Women		Men		Women	
	Alcohol use	Illicit drug use	Alcohol use	Illicit drug use	Alcohol use	Illicit drug use	Alcohol use	Illicit drug use	Alcohol use	Illicit drug use	Alcohol use	Illicit drug use
Asia												
Pacific (high income)	36 (0.6%)	5 (0.1%)	19 (0.3%)	4 (0.1%)	738 (9.5%)	226 (2.9%)	249 (3.2%)	174 (2.2%)	1293 (12.8%)	537 (5.3%)	410 (4.2%)	336 (3.4%)
Central	85 (0.9%)	7 (0.1%)	40 (0.5%)	4 (0.1%)	1199 (8.8%)	324 (2.4%)	372 (3.6%)	201 (2.0%)	2523 (13.0%)	626 (3.2%)	568 (4.4%)	300 (2.3%)
East	89 (1.2%)	7 (0.1%)	59 (0.9%)	5 (0.1%)	1096 (0.5%)	304 (2.9%)	253 (3.4%)	207 (2.8%)	1658 (12.6%)	484 (3.7%)	287 (3.1%)	291 (3.1%)
South	40 (0.3%)	4 (0%)	26 (0.2%)	3 (0%)	774 (4.5%)	142 (0.8%)	208 (1.2%)	153 (0.8%)	1579 (7.2%)	268 (1.2%)	328 (1.5%)	228 (1.1%)
Southeast	66 (0.7%)	11 (0.1%)	29 (0.4%)	7 (0.1%)	957 (7.0%)	687 (5.0%)	182 (1.9%)	376 (3.8%)	1552 (8.4%)	1105 (6.0%)	223 (1.8%)	549 (4.5%)
Australasia‡	60 (0.8%)	15 (0.2%)	36 (0.5%)	12 (0.1%)	1168 (10.2%)	846 (7.3%)	431 (3.8%)	574 (5.0%)	1677 (11.7%)	1566 (10.8%)	483 (3.6%)	833 (6.2%)
Caribbean	115 (1.1%)	6 (0.1%)	61 (0.6%)	4 (0%)	1165 (8.4%)	354 (2.5%)	384 (3.2%)	222 (1.8%)	2053 (11.4%)	568 (3.1%)	561 (3.5%)	325 (2.0%)
Europe												
Central	55 (0.7%)	6 (0.1%)	38 (0.6%)	4 (0.1%)	1008 (10.1%)	287 (2.8%)	305 (3.7%)	156 (1.9%)	1821 (14.1%)	477 (3.7%)	305 (3.2%)	217 (2.3%)
East	113 (1.5%)	6 (0.1%)	81 (1.1%)	4 (0%)	2274 (18.6%)	400 (3.3%)	820 (8.3%)	187 (1.9%)	5460 (26.4%)	1011 (4.9%)	1245 (10.0%)	348 (2.8%)
West	58 (0.8%)	8 (0.1%)	30 (0.4%)	6 (0.1%)	1079 (10.7%)	509 (5.0%)	323 (3.2%)	270 (2.7%)	1774 (14.0%)	946 (7.5%)	408 (3.4%)	407 (3.4%)
Latin America												
Andean	137 (1.4%)	5 (0%)	72 (0.8%)	3 (0%)	1389 (10.2%)	301 (2.2%)	356 (3.1%)	233 (2.0%)	2641 (14.5%)	455 (2.5%)	459 (3.4%)	276 (2.0%)
Central	144 (1.6%)	5 (0%)	62 (0.8%)	3 (0%)	2216 (13.4%)	289 (1.7%)	434 (4.0%)	189 (1.7%)	3832 (16.5%)	493 (2.1%)	512 (4.0%)	281 (2.2%)
South	96 (1.2%)	8 (0.1%)	57 (0.7%)	8 (0.1%)	1653 (12.7%)	809 (6.2%)	410 (3.9%)	395 (3.7%)	2666 (16.4%)	1208 (7.4%)	514 (4.3%)	541 (4.5%)
Tropical‡	170 (1.8%)	5 (0.1%)	84 (0.9%)	3 (0%)	3030 (16.8%)	378 (2.1%)	538 (4.7%)	239 (2.1%)	4689 (20.5%)	542 (2.4%)	612 (4.7%)	315 (2.4%)
North Africa and the Middle East	29 (0.3%)	4 (0%)	14 (0.2%)	3 (0%)	320 (2.4%)	421 (3.1%)	92 (0.8%)	205 (1.8%)	517 (3.3%)	843 (5.3%)	114 (0.9%)	329 (2.5%)
North America (high income)	81 (1.1%)	10 (0.1%)	49 (0.6%)	7 (0.1%)	1883 (14.8%)	799 (6.3%)	675 (5.9%)	411 (3.6%)	2782 (16.7%)	1499 (9.0%)	772 (5.6%)	720 (5.2%)
Oceania‡	64 (0.5%)	11 (0.1%)	26 (0.2%)	6 (0.1%)	918 (5.1%)	412 (2.3%)	260 (1.6%)	228 (1.4%)	2046 (7.6%)	624 (2.3%)	395 (1.9%)	349 (1.7%)
Sub-Saharan Africa												
Central	96 (0.5%)	5 (0%)	56 (0.3%)	3 (0%)	1207 (5.5%)	305 (1.4%)	423 (2.0%)	163 (0.8%)	2509 (8.2%)	577 (1.9%)	782 (2.6%)	265 (0.9%)
East	81 (0.5%)	5 (0%)	41 (0.3%)	3 (0%)	903 (4.8%)	278 (1.5%)	306 (1.8%)	187 (1.1%)	2061 (7.9%)	503 (1.9%)	694 (2.4%)	324 (1.1%)
South	102 (0.6%)	6 (0%)	42 (0.3%)	3 (0%)	2085 (10.1%)	498 (2.4%)	503 (2.7%)	354 (1.9%)	5716 (17.1%)	914 (2.7%)	1597 (4.3%)	653 (1.7%)
West	178 (1.1%)	4 (0%)	85 (0.6%)	3 (0%)	1234 (6.9%)	457 (2.6%)	490 (2.6%)	181 (0.9%)	2332 (9.8%)	911 (3.8%)	910 (3.1%)	304 (1.0%)
Global	78 (0.7%)	6 (0%)	42 (0.4%)	4 (0%)	1098 (7.4%)	350 (2.4%)	298 (2.2%)	219 (1.6%)	1992 (10.5%)	630 (3.3%)	438 (2.6%)	337 (2.0%)

Data are n (%). No burden is attributable to tobacco use between the ages of 10 years and 24 years. Data are from the Global Burden of Disease Study 2013.<sup>100</sup> DALYs=disability-adjusted life-years; combines disease burden due to premature mortality (years of life lost) with that due to disability (years of life lived with disability). \*Number of DALYs attributed to alcohol or illicit drug use per 100 000 men or women in that age group; but there is much uncertainty with respect to these figures, 95% uncertainty intervals have been modelled in the appendix. †Percentage of all DALYs in that age or sex group that were attributed to either alcohol or illicit drug use. ‡Countries included in these regions are according to the 2015 Global Burden of Disease Geographies (appendix).

**Table 2: Health burden attributable to alcohol and illicit drug use in people by region in 2013, DALYs per 100 000 people\* (% total DALYs†)**

changes were reported in adolescent cannabis use in states before and after medical cannabis use was legalised (before: 16.3% vs after: 15.5%). In fact, a reduction was noted in the states that permitted medical use in rates of cannabis use in 8th grade students (aged 13–14 years),<sup>120</sup> suggesting that availability for medical use did not lead to increased non-medical use by young people in these US States.

### Concerns about the internet as a potential source of illicit substances

The internet has become an increasingly important part of everyday life for young people. It is used to exchange information about the types, effects, and ways to use substances.<sup>121</sup> However, there is increasing concern that it might also be used to sell illicit substances. Substances can be sold on the surface web (indexed websites accessible via search engines, with illicit drugs sold as being not for human consumption), but an increasing amount of substances are being sold via the so-called dark web<sup>122</sup> (domains that are only accessible through anonymised connections).<sup>123</sup> Surveillance of websites selling substances on dark web marketplaces has shown an increasing number of retailers selling legally available and illicit substances in these markets.<sup>122</sup> The much publicised closure of the Silk Road (one of the more well known dark web marketplaces) by the US Federal Bureau of Investigation in 2013 saw many of the operators shift to other internet marketplaces.<sup>122</sup>

The extent to which the internet will become a dominant source for substances is unclear. For example, studies suggest that the internet is a minor source for pharmaceutical opioids.<sup>124</sup> Although the internet started out as a major source of NPSs, legislation in many jurisdictions now imposes similar penalties for importation of NPSs as for other illicit substances. Data also suggests that dark web markets are used mainly to purchase traditional illicit substances rather than NPSs.<sup>122</sup>

### Conclusions

Our capacity to respond appropriately to substance use in adolescents is limited by the scarcity of evidence about the nature and extent of harms,<sup>10</sup> extent of substance use, and shape of this problem. In this Series paper we focused on the nature of substance use. Without good coverage of high-quality data for the extent of substance use and the harms associated with it, policy responses will be poorly targeted and potentially might fail to address the most commonly used substances or the biggest causes of health burden. To improve policy responses, the amount, quality, regularity, and consistency of data about substance use in young people need to urgently increase. These should include not only the general population of young people but also at-risk or sentinel groups of young people who might begin involvement of problematic patterns of

#### Search strategy and selection criteria

We searched Project Cork bibliographies, PubMed Clinical Queries, Scopus, MEDLINE, MEDLINE-in-process, Embase, and PsycINFO for reviews that examined the epidemiology of substance use in young people and of associated health and social consequences published between Jan 1, 1990, and April 23, 2015. The appendix has the full list of search terms used, including “substance”, “adolescent”, and “health”. We also reviewed several major international sources of data and information about substance use in young people: UN’s Office on Drugs and Crime’s 2015 Annual World Drug Report; WHO’s Global Information System on Alcohol and Health from which WHO’s Global Status Report on Alcohol and Health 2014 was compiled; and WHO’s Report on the Global Tobacco Epidemic, 2013.

We also used information from published analyses of data from WHO’s World Mental Health Survey initiative, which includes data for substance misuse from representative community surveys of the population assessed with a standardised survey in more than 30 countries. We also report some results from the 2013 Global Burden of Disease Study’s modelled estimates of health burden attributable due to tobacco, alcohol, and illicit drugs, arising from the comparative risk assessment exercise.

substance use, or types of substance use earlier than their peers, and in whom baseline risks of harm are already increased.

#### Contributors

All authors had initial discussions about the content of the paper. LD led the review, drafting, and revision of the manuscript. ES assisted with the literature searches and created figure 2. All authors contributed to the critical review of the paper, provided substantial comments, and approved the final version of the manuscript for publication.

#### Declaration of interests

We declare no competing interests.

#### Acknowledgments

We thank Mary Kumvaj for her assistance with literature searches and thank Janni Leung and Alize Ferrari for providing data from Global Burden of Disease Study 2013. We thank Sarah Larney, Elizabeth Whittaker, Anthony Shakeshaft, and Joe Van Buskirk for their assistance with identifying material and providing feedback on sections of this Series paper and Leoni Degenhardt for providing comments on an early draft of this paper. LD is supported by an Australian National Health and Medical Research Council (NHMRC) principal research fellowship (1041472). GP is supported by an NHMRC senior principal research fellowship (1019887). ES was supported by the NHMRC Centre of Research Excellence in Mental Health Systems Improvement (CREMSI; 1041131). The National Drug and Alcohol Research Centre at University of New South Wales Australia (Sydney, Australia) is supported by funding from the Australian Government under the Substance Misuse Prevention and Service Improvements Grant Fund. No funder had any role in the conceptualisation or completion of this Series paper.

#### References

- 1 Stockings E, Hall WD, Lynskey M, et al. Substance use in young people 3. Prevention, early intervention, harm reduction, and treatment of substance use in young people. *Lancet Psych* 2016; published online Feb 18. [http://dx.doi.org/10.1016/S2215-0366\(16\)00002-X](http://dx.doi.org/10.1016/S2215-0366(16)00002-X).

- 2 Babor TF, Caulkins JP, Edwards G, et al, eds. Drug policy and the public good. Oxford: Oxford University Press, 2010.
- 3 McAllister WB, ed. Drug diplomacy in the twentieth century. London: Routledge, 2000.
- 4 Guillem K, Vouillac C, Azar MR, et al. Monoamine oxidase inhibition dramatically increases the motivation to self-administer nicotine in rats. *J Neurosci* 2005; **25**: 8593–600.
- 5 Martin CS, Winters KC. Diagnosis and assessment of alcohol use disorders among adolescents. *Alcohol Health Res World* 1998; **22**: 95–105.
- 6 Chung T, Martin CS. What were they thinking? Adolescents' interpretations of DSM-IV alcohol dependence symptom queries and implications for diagnostic validity. *Drug Alcohol Depend* 2005; **80**: 191–200.
- 7 United Nations Department of Economic and Social Affairs. Definition of youth. <http://www.un.org/esa/socdev/documents/youth/fact-sheets/youth-definition.pdf> (accessed Jan 4, 2016).
- 8 Patton GC, Viner R. Pubertal transitions in health. *Lancet* 2007; **369**: 1130–39.
- 9 Chambers RA, Taylor JR, Potenza MN. Developmental neurocircuitry of motivation in adolescence: a critical period of addiction vulnerability. *Am J Psychiatry* 2003; **160**: 1041–52.
- 10 Hall WD, Patton G, Stockings E, et al. Substance use in young people 2. Why young people's substance use matters for global health. *Lancet Psych* 2016; published online Feb 18. [http://dx.doi.org/10.1016/S2215-0366\(16\)S2215-0366\(16\)00013-4](http://dx.doi.org/10.1016/S2215-0366(16)S2215-0366(16)00013-4).
- 11 WHO. Global strategy to reduce the harmful use of alcohol. Geneva: World Health Organization, 2010.
- 12 WHO. WHO framework convention on tobacco control. Geneva: World Health Organization, 2005.
- 13 WHO. WHO report on the global tobacco epidemic 2015: raising taxes on tobacco. Geneva: World Health Organization, 2015.
- 14 United Nations. Political declaration and plan of action on international cooperation towards an integrated and balanced strategy to counter the world drug problem. High-level segment commission on narcotic drugs; Vienna; March 11–12, 2009. New York: United Nations, 2009.
- 15 Chen K, Kandel DB. The natural history of drug use from adolescence to the mid-thirties in a general population sample. *Am J Public Health* 1995; **85**: 41–47.
- 16 Degenhardt L, Chiu WT, Sampson N, et al. Toward a global view of alcohol, tobacco, cannabis, and cocaine use: findings from the WHO World Mental Health Surveys. *PLoS Med* 2008; **5**: e141.
- 17 Donaldson L. Guidance on the consumption of alcohol by children and young people: from Sir Liam Donaldson, Chief Medical Officer for England. London: England Department of Health, 2009.
- 18 Maimaris W, McCambridge J. Age of first drinking and adult alcohol problems: systematic review of prospective cohort studies. *J Epidemiol Community Health* 2014; **68**: 268–74.
- 19 Kandel DB, Yamaguchi K, Klein LC. Testing the gateway hypothesis. *Addiction* 2006; **101**: 470–72.
- 20 Hall WD, Lynskey M. Is cannabis a gateway drug? Testing hypotheses about the relationship between cannabis use and the use of other illicit drugs. *Drug Alcohol Rev* 2005; **24**: 39–48.
- 21 Hall W, Degenhardt L. Adverse health effects of non-medical cannabis use. *Lancet* 2009; **374**: 1383–91.
- 22 Degenhardt L, Dierker L, Chiu WT, et al. Evaluating the drug use “gateway” theory using cross-national data: consistency and associations of the order of initiation of drug use among participants in the WHO World Mental Health Surveys. *Drug Alcohol Depend* 2010; **108**: 84–97.
- 23 Stone AL, Becker LG, Huber AM, Catalano RF. Review of risk and protective factors of substance use and problem use in emerging adulthood. *Addict Behav* 2012; **37**: 747–75.
- 24 Nelson JP. Binge drinking and alcohol prices: a systematic review of age-related results from econometric studies, natural experiments and field studies. *Health Econ Rev* 2015; **5**: 6.
- 25 WHO. WHO report on the global tobacco epidemic 2013: enforcing bans on tobacco advertising, promotion and sponsorship. Geneva: World Health Organization, 2013.
- 26 WHO. Global health observatory data: global information system on alcohol and health (GISAH). <http://www.who.int/gho/alcohol/en/> (accessed Jan 4, 2016).
- 27 United Nations Office on Drugs and Crime. World Drug Report 2015. Vienna: United Nations, 2015.
- 28 Weitzman ER, Folkman A, Folkman MP, Wechsler H. The relationship of alcohol outlet density to heavy and frequent drinking and drinking-related problems among college students at eight universities. *Health Place* 2003; **9**: 1–6.
- 29 Degenhardt L, Day C, Dietze P, et al. Effects of a sustained heroin shortage in three Australian States. *Addiction* 2005; **100**: 908–20.
- 30 Degenhardt L, Day C, Conroy E, Gilmour S, Hall W. Age differentials in the impacts of reduced heroin: effects of a “heroin shortage” in NSW, Australia. *Drug Alcohol Depend* 2005; **79**: 397–404.
- 31 Lascala E, Friesthler B, Gruenwald PJ. Population ecologies of drug use, drinking and related problems. In: Stockwell T, Gruenwald P, Toubmourou J, Loxley W, eds. Preventing harmful substance use: the evidence base for policy and practice. Chichester: John Wiley & Sons, 2005.
- 32 Daniel JZ, Hickman M, Macleod J, et al. Is socioeconomic status in early life associated with drug use? A systematic review of the evidence. *Drug Alcohol Rev* 2009; **28**: 142–53.
- 33 Wiles NJ, Lingford-Hughes A, Daniel J, et al. Socio-economic status in childhood and later alcohol use: a systematic review. *Addiction* 2007; **102**: 1546–63.
- 34 Fergusson DM, Horwood LJ, Lynskey MT. Parental separation, adolescent psychopathology, and problem behaviors. *J Am Acad Child Adolesc Psychiatry* 1994; **33**: 1122–31.
- 35 Flewelling RL, Bauman KE. Family structure as a predictor of initial substance use and sexual intercourse during early adolescence. *J Marriage Fam* 1990; **52**: 171–81.
- 36 Lynskey MT, Fergusson DM, Horwood LJ. The effect of parental alcohol problems on rates of adolescent psychiatric disorders. *Addiction* 1994; **89**: 1277–86.
- 37 Cohen DA, Richardson J, LaBree L. Parenting behaviors and the onset of smoking and alcohol use: a longitudinal study. *Pediatrics* 1994; **94**: 368–75.
- 38 Needle RH, Su S, Doherty WJ. Divorce, remarriage, and adolescent substance use: a prospective longitudinal study. *J Marriage Fam* 1990; **52**: 157–69.
- 39 Leonardi-Bee J, Jere ML, Britton J. Exposure to parental and sibling smoking and the risk of smoking uptake in childhood and adolescence: a systematic review and meta-analysis. *Thorax* 2011; **66**: 847–55.
- 40 Lynskey MT, Agrawal A, Heath AC. Genetically informative research on adolescent substance use: methods, findings, and challenges. *J Am Acad Child Adolesc Psychiatry* 2010; **49**: 1202–14.
- 41 Agrawal A, Lynskey MT. Are there genetic influences on addiction: evidence from family, adoption and twin studies. *Addiction* 2008; **103**: 1069–81.
- 42 Hines LA, Morley KI, Mackie C, Lynskey M. Genetic and environmental interplay in adolescent substance use disorders. *Curr Addict Rep* 2015; **2**: 122–29.
- 43 Cannon DS, Clark LA, Leeka JK, Keefe CK. A reanalysis of the Tridimensional Personality Questionnaire (TPQ) and its relation to Cloninger's type 2 alcoholism. *Psychol Assess* 1993; **5**: 62–66.
- 44 Lipkus IM, Barefoot JC, Williams RB, Siegler IC. Personality measures as predictors of smoking initiation and cessation in the UNC Alumni Heart Study. *Health Psychol* 1994; **13**: 149–55.
- 45 Lac A, Crano WD. Monitoring matters: meta-analytic review reveals the reliable linkage of parental monitoring with adolescent marijuana use. *Perspect Psychol Sci* 2009; **4**: 578–86.
- 46 Lynskey MT, Fergusson DM. Childhood conduct problems, attention deficit behaviors, and adolescent alcohol, tobacco, and illicit drug use. *J Abnorm Child Psychol* 1995; **23**: 281–302.
- 47 Fergusson DM, Boden JM, Horwood LJ. The developmental antecedents of illicit drug use: evidence from a 25-year longitudinal study. *Drug Alcohol Depend* 2008; **96**: 165–77.
- 48 Kandel DB, Andrews K. Processes of adolescent socialization by parents and peers. *Int J Addict* 1987; **22**: 319–42.
- 49 Townsend L, Flisher AJ, King G. A systematic review of the relationship between high school dropout and substance use. *Clin Child Fam Psychol Rev* 2007; **10**: 295–317.
- 50 Lynskey M, Hall W. The effects of adolescent cannabis use on educational attainment: a review. *Addiction* 2000; **95**: 1621–30.



- 51 WHO. Global status report on alcohol and health 2014. Geneva: World Health Organization, 2014.
- 52 Patton GC, Coffey C, Cappa C, et al. Health of the world's adolescents: a synthesis of internationally comparable data. *Lancet* 2012; **379**: 1665–75.
- 53 Hickman M, Taylor C, Chatterjee A, et al. Estimating the prevalence of problematic drug use: a review of methods and their application. *Bull Narcot* 2002; **LIV**: 15–32.
- 54 Bachman JG, Wadsworth KN, O'Malley P, Johnston L, Schulenberg J. Smoking, drinking and drug use in young adulthood: the impacts of new freedoms and responsibilities. National Criminal Justice System 1997: abstr NCJ 176728.
- 55 Van Etten ML, Anthony JC. Comparative epidemiology of initial drug opportunities and transitions to first use: marijuana, cocaine, hallucinogens and heroin. *Drug Alcohol Depend* 1999; **54**: 117–25.
- 56 Van Etten ML, Anthony JC. Male-female differences in transitions from first drug opportunity to first use: searching for subgroup variation by age, race, region, and urban status. *J Womens Health Gen Based Med* 2001; **10**: 797–804.
- 57 Van Etten ML, Neumark YD, Anthony JC. Initial opportunity to use marijuana and the transition to first use: United States, 1979–1994. *Drug Alcohol Depend* 1997; **49**: 1–7.
- 58 Van Etten ML, Neumark YD, Anthony JC. Male-female differences in the earliest stages of drug involvement. *Addiction* 1999; **94**: 1413–19.
- 59 Benjet C, Borges G, Medina-Mora ME, et al. Drug use opportunities and the transition to drug use among adolescents from the Mexico City metropolitan area. *Drug Alcohol Depend* 2007; **90**: 128–34.
- 60 Chen CY, Dormitzer CM, Bejarano J, Anthony JC. Religiosity and the earliest stages of adolescent drug involvement in seven countries of Latin America. *Am J Epidemiol* 2004; **159**: 1180–88.
- 61 Delva J, Van Etten ML, González GB, et al. First opportunities to try drugs and the transition to first drug use: evidence from a national school survey in Panama. *Subst Use Misuse* 1999; **34**: 1451–67.
- 62 Wagner FA, Gonzalez-Forteza C, Aguilera RM, Ramos-Lira LE, Medina-Mora ME, Anthony JC. Prevalence of illegal drugs in terms of snuff consumption in a sample of students in Mexico. *Salud Ment* 2003; **26**: 1402–12 (in Spanish).
- 63 Wells JE, Haro JM, Karam E, et al. Cross-national comparisons of sex differences in opportunities to use alcohol or drugs, and the transitions to use. *Subst Use Misuse* 2011; **46**: 1169–78.
- 64 Swift W, Coffey C, Carlin JB, Degenhardt L, Patton GC. Adolescent cannabis users at 24 years: trajectories to regular weekly use and dependence in young adulthood. *Addiction* 2008; **103**: 1361–70.
- 65 Degenhardt L, Baxter AJ, Lee YY, et al. The global epidemiology and burden of psychostimulant dependence: findings from the Global Burden of Disease study 2010. *Drug Alcohol Depend* 2014; **137**: 36–47.
- 66 Degenhardt L, Charlson F, Mathers B, et al. The global epidemiology and burden of disease attributable to opioid dependence: results from the global burden of disease study 2010. *Addiction* 2014; **109**: 1320–33.
- 67 Degenhardt L, Ferrari AJ, Calabria B, et al. The global epidemiology and contribution of cannabis use and dependence to the global burden of disease: results from the GBD 2010 study. *PLoS One* 2013; **8**: e76635.
- 68 Toumbourou JW, Stockwell T, Neighbors C, Marlatt GA, Sturge J, Rehm J. Interventions to reduce harm associated with adolescent substance use. *Lancet* 2007; **369**: 1391–401.
- 69 Calabria B, Degenhardt L, Briegleb C, et al. Systematic review of prospective studies investigating “remission” from amphetamine, cannabis, cocaine or opioid dependence. *Addict Behav* 2010; **35**: 741–49.
- 70 Hall W, Degenhardt L. Prevalence and correlates of cannabis use in developed and developing countries. *Curr Opin Psychiatry* 2007; **20**: 393–97.
- 71 Hawkins JD, Catalano RF, Miller JY. Risk and protective factors for alcohol and other drug problems in adolescence and early adulthood: implications for substance abuse prevention. *Psychol Bull* 1992; **112**: 64–105.
- 72 Cablova L, Pazderkova K, Miovsky M. Parenting styles and alcohol use among children and adolescents: a systematic review. *Drugs Educ Prev Policy* 2014; **21**: 1–13.
- 73 Marashi-Pour S, Cretikos M, Lyons C, Rose N, Jalaludin B, Smith J. The association between the density of retail tobacco outlets, individual smoking status, neighbourhood socioeconomic status and school locations in New South Wales, Australia. *Spat Spatio-Temporal Epidemiol* 2015; **12**: 1–7.
- 74 UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance. Guidelines on surveillance among populations most at risk for HIV. Geneva: World Health Organization, 2011.
- 75 Kielsing C, Baker-Henningham H, Belfer M, et al. Child and adolescent mental health worldwide: evidence for action. *Lancet* 2011; **378**: 1515–25.
- 76 Patel V, Flisher AJ, Hetrick S, McGorry P. Mental health of young people: a global public-health challenge. *Lancet* 2007; **369**: 1302–13.
- 77 Gomes ST, Frota MV, Aguiar MBP, Nogueira MB. Substance abuse and depression in adolescents. *Neuropsychiatr Enfance Adolesc* 2012; **60**: S243.
- 78 Lamps CA, Sood AB, Sood R. Youth with substance abuse and comorbid mental health disorders. *Curr Psychiatry Rep* 2008; **10**: 265–71.
- 79 O'Neil KA, Conner BT, Kendall PC. Internalizing disorders and substance use disorders in youth: comorbidity, risk, temporal order, and implications for intervention. *Clin Psychol Rev* 2011; **31**: 104–12.
- 80 van der Meer FJ, Velthorst E, Meijer CJ, Machielsen MW, de Haan L. Cannabis use in patients at clinical high risk of psychosis: impact on prodromal symptoms and transition to psychosis. *Curr Pharm Des* 2012; **18**: 5036–44.
- 81 Large M, Sharma S, Compton MT, Slade T, Nielssen O. Cannabis use and earlier onset of psychosis: a systematic meta-analysis. *Arch Gen Psychiatry* 2011; **68**: 555–61.
- 82 Cannon TD, Cadenhead K, Cornblatt B, et al. Prediction of psychosis in youth at high clinical risk: a multisite longitudinal study in North America. *Arch Gen Psychiatry* 2008; **65**: 28–37.
- 83 Yui K, Goto K, Ikemoto S, Nishijima K, Yoshino T, Ishiguro T. Susceptibility to subsequent episodes of spontaneous recurrence of methamphetamine psychosis. *Drug Alcohol Depend* 2001; **64**: 133–42.
- 84 Dierker LC, Avenevoli S, Merikangas KR, Flaherty BP, Stolar M. Association between psychiatric disorders and the progression of tobacco use behaviors. *J Am Acad Child Adolesc Psychiatry* 2001; **40**: 1159–67.
- 85 Boys A, Farrell M, Taylor C, et al. Psychiatric morbidity and substance use in young people aged 13–15 years: results from the Child and Adolescent Survey of Mental Health. *Br J Psychiatry* 2003; **182**: 509–17.
- 86 UK Office for National Statistics. Integrated Household Survey (IHS) April 2011 to March 2012: experimental statistics. Newport: UK Office for National Statistics, 2011.
- 87 Smith AMA, Lindsay J, Rosenthal DA. Same-sex attraction, drug injection and binge drinking among Australian adolescents. *Aust N Z J Public Health* 1999; **23**: 643–46.
- 88 Marshal MP, Friedman MS, Stall R, et al. Sexual orientation and adolescent substance use: a meta-analysis and methodological review. *Addiction* 2008; **103**: 546–56.
- 89 Goldbach JT, Tanner-Smith EE, Bagwell M, Dunlap S. Minority stress and substance use in sexual minority adolescents: a meta-analysis. *Prev Sci* 2014; **15**: 350–63.
- 90 Richards K, Lyneham M. Juveniles in detention in Australia, 1981–2008. Monitoring report no.12. Canberra: Australian Institute of Criminology; 2010.
- 91 Teplin LA, Elkington KS, McClelland GM, Abram KM, Mericle AA, Washburn JJ. Major mental disorders, substance use disorders, comorbidity, and HIV-AIDS risk behaviors in juvenile detainees. *Psychiatr Serv* 2005; **56**: 823–28.
- 92 Vermeiren R, Jaspers I, Moffitt T. Mental health problems in juvenile justice populations. *Child Adolesc Psychiatr Clin N Am* 2006; **15**: 333–51.
- 93 Lader D, Singleton N, Meltzer H. Psychiatric morbidity among young offenders in England and Wales. *Int Rev Psychiatry* 2003; **15**: 144–47.
- 94 Mail PD, Johnson S. Boozing, sniffing, and toking: an overview of the past, present, and future of substance use by American Indians. *Am Indian Alsk Native Ment Health Res* 1993; **5**: 1–33.



- 95 Lanumata T, Thomson G. Unequal risks, unmet needs: the tobacco burden for Pacific peoples in New Zealand. *N Z Med J* 2009; **122**: 39–53.
- 96 Lehti V, Niemelä S, Hoven C, Mandell D, Sourander A. Mental health, substance use and suicidal behaviour among young indigenous people in the Arctic: a systematic review. *Soc Sci Med* 2009; **69**: 1194–203.
- 97 Zubrick S, Silburn S, Lawrence D, et al. The Western Australian Aboriginal Child Health Survey: volume 2—the social and emotional wellbeing of Aboriginal children and young people. Perth: Curtin University of Technology and Telethon Institute for Child Health Research, 2005.
- 98 Jorm AF, Bourchier SJ, Cvetkovski S, Stewart G. Mental health of Indigenous Australians: a review of findings from community surveys. *Med J Aust* 2012; **196**: 118–21.
- 99 Homelessness Australia. Homelessness statistics. 2015. <http://www.homelessnessaustralia.org.au/index.php/about-homelessness/homeless-statistics> (accessed Sept 17, 2015).
- 100 Edidin JP, Ganim Z, Hunter SJ, Karnik NS. The mental and physical health of homeless youth: a literature review. *Child Psychiatry Hum Dev* 2012; **43**: 354–75.
- 101 Embleton L, Mwangi A, Vreeman R, Ayuku D, Braitstein P. The epidemiology of substance use among street children in resource-constrained settings: a systematic review and meta-analysis. *Addiction* 2013; **108**: 1722–33.
- 102 United Nations. Human Rights. Commission on Human Rights 61st Session. Report of the Special Rapporteur on adequate housing as a component of the right to an adequate standard of living, Miloon Kothari. New York: United Nations Human Rights; 2005.
- 103 Barratt D, Hunt N, Stoicescu C. Injecting drug use among under-18s: a snapshot of available data. London: Harm Reduction International, 2013.
- 104 Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries for 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; **386**: 743–800.
- 105 Murray CJL, Ortblad KF, Guinovart C, et al. Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014; **384**: 1005–70.
- 106 Murray CJL, Barber RM, Foreman KJ, et al, and the GBD 2013 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life years (DALYs) for 306 diseases and injuries and healthy life expectancy (HALE) for 188 countries, 1990–2013: quantifying the epidemiological transition. *Lancet* 2015; **386**: 2145–91.
- 107 Gore FM, Bloem P, Patton GC, et al. Global burden of disease in young people aged 10–24 years: a systematic analysis. *Lancet* 2011; **377**: 2093–102.
- 108 Forouzanfar MH, Alexander L, Anderson HR, et al, and the GBD 2013 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015; **386**: 2287–323.
- 109 Degenhardt L, Whiteford H, Ferrari AJ, et al. Global burden of disease attributable to illicit drug use and dependence: findings from the Global Burden of Disease Study 2010 study. *Lancet* 2013; **382**: 1564–74.
- 110 Eriksen M, Mackay J, Ross H. The tobacco atlas, fourth edition. Atlanta, GA; New York, NY: American Cancer Society and World Lung Foundation, 2012.
- 111 United Nations. Single convention on narcotic drugs, 1961, as amended by the 1972 protocol, 1961. 1972. <https://www.unodc.org/unodc/en/treaties/single-convention.html> (accessed Jan 4, 2016).
- 112 United Nations Office on Drugs and Crime. Global SMART update volume 14. Legal responses to NPS: multiple approaches to a multi-faceted problem. Vienna: United Nations Office on Drugs and Crime, 2015.
- 113 McNeill A, Brose LS, Calder R, Hitchman SC, Hajek P, McRobbie H. E-cigarettes: an evidence update, 2015. Public Health England. <https://www.gov.uk/government/publications/e-cigarettes-an-evidence-update> (accessed Jan 4, 2016).
- 114 McKee M, Capewell S. Evidence about electronic cigarettes: a foundation built on rock or sand? *BMJ* 2015; **351**: h4863.
- 115 Fairchild AL, Bayer R, Colgrove J. The renormalization of smoking? E-cigarettes and the tobacco “endgame”. *N Engl J Med* 2014; **370**: 293–95.
- 116 McNeill A, Brose LS, Calder R, Hitchman SC, Hajek P, McRobbie H. Ann McNeill and colleagues reply to Martin McKee and Simon Capewell. *BMJ* 2015; **351**: h5010.
- 117 Goniewicz ML, Gawron M, Nadolska J, Balwicki L, Sobczak A. Rise in electronic cigarette use among adolescents in Poland. *J Adolesc Health* 2014; **55**: 713–15.
- 118 Cerdá M, Wall M, Keyes KM, Galea S, Hasin D. Medical marijuana laws in 50 states: investigating the relationship between state legalization of medical marijuana and marijuana use, abuse and dependence. *Drug Alcohol Depend* 2012; **120**: 22–27.
- 119 Lynne-Landsman SD, Livingston MD, Wagenaar AC. Effects of state medical marijuana laws on adolescent marijuana use. *Am J Public Health* 2013; **103**: 1500–06.
- 120 Hasin DS, Wall M, Keyes KM, et al. Medical marijuana laws and adolescent marijuana use in the USA from 1991 to 2014: results from annual, repeated cross-sectional surveys. *Lancet Psychiatry* 2015; **2**: 601–08.
- 121 Soussan C, Kjellgren A. Harm reduction and knowledge exchange—a qualitative analysis of drug-related Internet discussion forums. *Harm Reduct J* 2014; **11**: 25.
- 122 Van Buskirk J, Roxburgh A, Farrell M, Burns L. The closure of the Silk Road: what has this meant for online drug trading? *Addiction* 2014; **109**: 517–18.
- 123 Barratt MJ. Silk road: ebay for drugs. *Addiction* 2012; **107**: 683.
- 124 Inciardi JA, Surratt HL, Cicero TJ, et al. Prescription drugs purchased through the internet: who are the end users? *Drug Alcohol Depend* 2010; **110**: 21–29.