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Review

Meth/amphetamine use and associated HIV: Implications for global policy and public health

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ABSTRACT

Amphetamine type stimulants (ATS) have become the focus of increasing attention worldwide. There are understandable concerns over potential harms including the transmission of HIV. However, there have been no previous global reviews of the extent to which these drugs are injected or levels of HIV among users. A comprehensive search of the international peer-reviewed and grey literature was undertaken. Multiple electronic databases were searched and documents and datasets were provided by UN agencies and key experts from around the world in response to requests for information on the epidemiology of use. Amphetamine or methamphetamine (meth/amphetamine, M/A) use was documented in 110 countries, and injection in 60 of those. Use may be more prevalent in East and South East Asia, North America, South Africa, New Zealand, Australia and a number of European countries. In countries where the crystalline form is available, evidence suggests users are more likely to smoke or inject the drug; in such countries, higher levels of dependence may be occurring. Equivocal evidence exists as to whether people who inject M/A are at differing risk of HIV infection than other drug injectors; few countries document HIV prevalence/incidence among M/A injectors. High risk sexual behaviour among M/A users may contribute to increased risk of HIV infection, but available evidence is not sufficient to determine if the association is causal. A range of possible responses to M/A use and harm are discussed, ranging from supply and precursor control, to demand and harm reduction. Evidence suggests that complex issues surround M/A, requiring novel and sophisticated approaches, which have not yet been met with sufficient investment of time or resources to address them. Significant levels of M/A in many countries require a response to reduce harms that in many cases remain poorly understood. More active models of engagement with M/A users and provision of services that meet their specific needs are required.

Introduction

Amphetamines are the second most commonly used illicit drug type worldwide, after cannabis (United Nations Office on Drugs and Crime, 2009). They are central nervous system (CNS) stimulants that were first synthesised more than a century ago. Initially used for medical applications, they are currently produced by legal and illegal manufacturers; multiple forms of amphetamines exist, but methamphetamine and amphetamine (M/A) are reportedly the most common amphetamine type stimulants (ATS) used globally (United Nations Office on Drugs and Crime, 2007b).

M/A both increase the release of dopamine, noradrenalin, adrenaline and serotonin (Seiden, Sobol, & Ricaurte, 1993; World

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Health Organization, 2004), stimulate the central nervous system, and have a range of effects including increased energy, feelings of euphoria, decreased appetite, and elevated blood pressure, heart rate, and other physiological effects. In this report, we use the term "meth/amphetamine" (M/A) as a general term given the varying forms used, the fact that most users are not aware of the difference, and the general applicability of research findings to both.

Despite increasing use and incidence of harms, there has been no previous global review of the epidemiology of M/A use, injection, human immunodeficiency virus (HIV) and possible responses. This review seeks to address this gap. We focus here upon M/A (and exclude 3,4-methylenedioxymethamphetamine (MDMA) – commonly known as "ecstasy").

We searched Medline, EMBASE and PubMed citation indexes for articles published in English between 1997 and 2007 that addressed the epidemiology of M/A use, injection, associations with HIV and interventions. Search terms are outlined in Appendix A. Grey literature on M/A use was sought using online grey literature databases, library databases and general online searches (see Appendix B and the online report by (Calabria et al., 2008)). Additional material was identified by members of the Reference Group to the UN on HIV and Injecting Drug Use.

Meth/amphetamine manufacture and trafficking

The manufacture, availability and consumption of M/A are dynamic(United Nations Office on Drugs and Crime, 2007a, 2009). In contrast to the production requirements for heroin and cocaine, M/A can be manufactured in almost any geographic location, under more clandestine conditions and for comparatively less cost.

M/A labs are increasingly being concentrated in areas where capacity to respond to manufacture and supply, and respond to problematic use, is severely limited (United Nations Office on Drugs and Crime, 2008a). Currently, the largest M/A manufacture areas are in the Middle East, South East Asia (particularly Myanmar, China and the Philippines) and North America (Mexico). Drug trafficking organisations might be increasing ATS manufacture in other areas including Central America, the Middle East and possibly Africa (United Nations Office on Drugs and Crime, 2009).

The context of meth/amphetamine use

M/A use occurs in a range of contexts, and for a variety of purposes. Both recreational and occupational reasons may determine initial use and use may occur in public settings (e.g. nightclubs), private parties, work environments or sites of sexual interactions, which probably differ across countries or regions (Fig. 1).

M/A is used recreationally to experience its effects of increased sociability, loss of inhibitions, a sense of escape, or to enhance sexual encounters (Diaz, Heckert, & Sanchez, 2005; Halkitis, Fischgrund, & Parsons, 2005; McKirnan, Vanable, Ostrow, & Hope, 2001; Ross, Mattison, & Franklin, 2003). M/A is sometimes used in occupational settings to sustain long work hours and to increase energy and productivity. Examples include: jade-mine workers in Myanmar, sex workers in Cambodia (Chouvy & Meissonnier, 2004), truck drivers (Malta et al., 2006; Nascimento, Nascimento, & Silva, 2006) and airforce pilots (Emonson & Vanderbeek, 1995).

In high income countries, users typically have a history of other drug use and may use drugs in combination with M/A (e.g. (Darke & Hall, 1995). Where use is concentrated among some occupational groups, other drug use may be less extensive, and/or involve concomitant use of one or two other drugs (e.g. alcohol use among truck drivers in Brazil (Malta et al., 2006)).

Routes of administration and development of dependence

Dependence typically develops after a period of sustained regular use; daily use is particularly risky (Gossop, Griffiths, Powis, & Strang, 1992; Hall & Hando, 1994), but weekly users are still at risk of dependence (Lee, 2004). Dependence has been associated with mental health, physical, occupational, relationship, financial and legal problems (Joe-Laidler & Morgan, 1997; Kurtz, 2005; London et al., 2004; Morgan & Beck, 1997; Zweben et al., 2004).

Injection and smoking of M/A provide greater bioavailability, faster onset of action and higher peak effects than snorting or swallowing, and are also likely to increase risk of dependence (Volkow, Fowler, Wang, & Swanson, 2004). Some users who begin using M/A through other routes switch to injecting (Darke, Cohen, Ross, Hando, & Hall, 1994); this switch may be precipitated by dependence (Chamla, Chamla, Dabin, Delin, & Rennes, 2006; Matsumoto et al., 2002; Neaigus et al., 2001; Swift, Maher, & Sunjic, 1999). As M/A smoking becomes more established in some populations, transition to injection may increase, particularly if it is viewed as socially acceptable (Neaigus et al., 2001; Swift et al., 1999).

Dependence risks may differ across different M/A forms (Cho & Melega, 2002; Matsumoto et al., 2002; McKetin, Kelly, & McLaren, 2006). The crystalline form of methamphetamine is more potent than powder (Chesher, 1993), is generally higher in purity (Maxwell, 2005; Stafford et al., 2005), is more commonly smoked or injected than other forms, and, as a consequence, may possess a higher dependence potential. There are limited data currently available on the forms of M/A used in many countries (Degenhardt et al., 2007; UNODC, 2009).

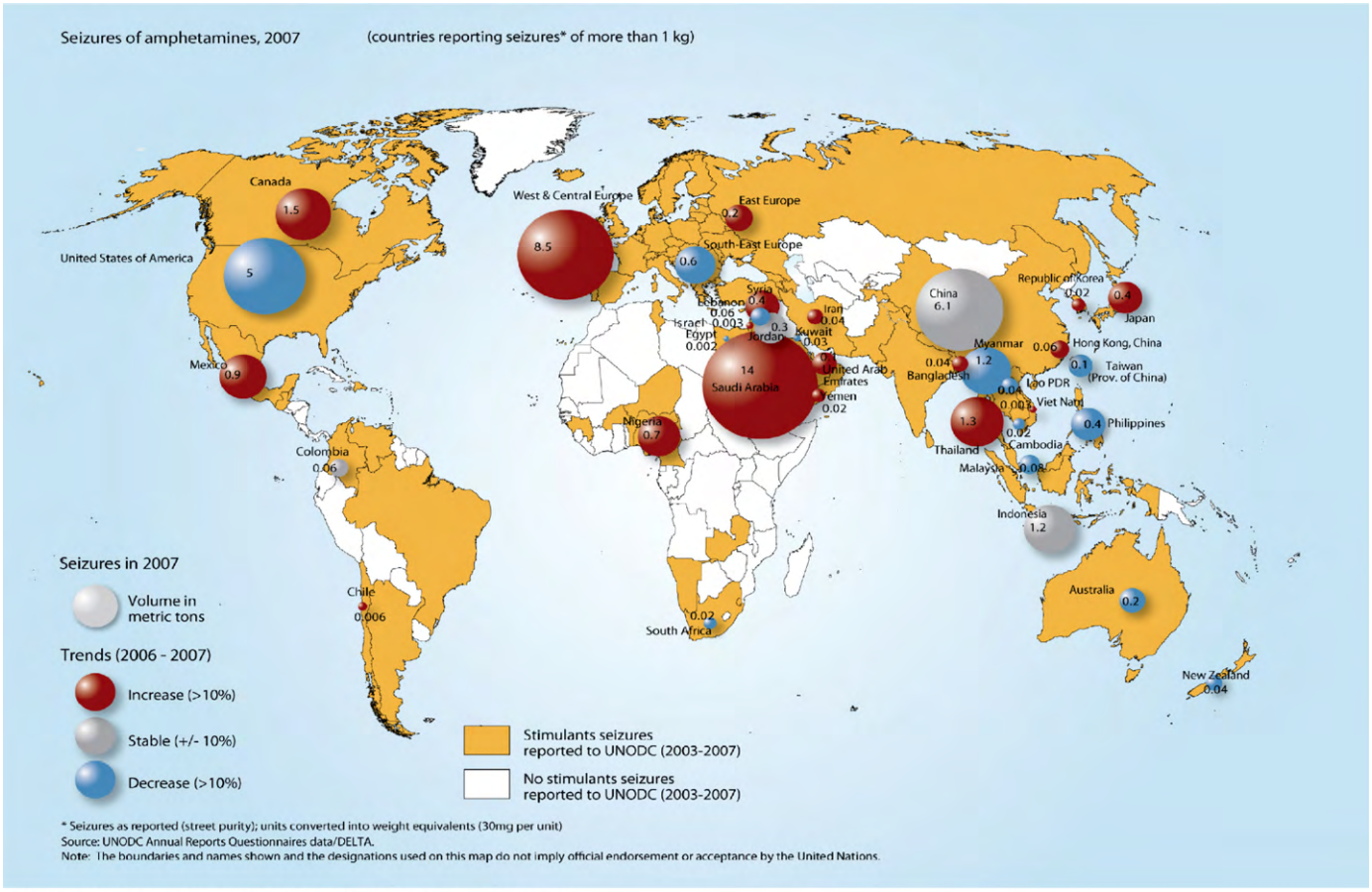
HIV risk and meth/amphetamine use and injection

Injecting drug users (IDUs) account for approximately 10% of HIV infections globally; 30% outside of Africa (UNAIDS, 2006a). It has been estimated that between 0.8 and 6.6 million IDUs globally are infected with HIV (Mathers et al., 2008).

M/A injectors are at risk of HIV and other infections, such as viral hepatitis and bacterial infections, through unsafe injecting practices. M/A injectors may be more likely than those injecting other drugs to engage in risky injecting practices (Degenhardt et al., 2007). Risk is elevated by re-use of equipment, hurried injecting, and frenetic injecting when on "binges" (Degenhardt et al., 2007).

Conflicting findings surround the association of M/A injection and HIV infection, because of concurrent sexual HIV risks (Degenhardt et al., 2007). Among Australian men who have sex with men (MSM), sexual risk was a significant predictor of HIV infection but M/A use was not an independent predictor (Kippax et al., 1998); while among female sex workers in Mexico, *both* non-injection use of M/A use and injection of stimulants were independently associated with HIV infection (Patterson et al., 2008). Among IDUs in Russia, M/A injection was independently associated with HIV seroconversion (Kozlov et al., 2006). There are clearly important and varying predictors across different populations of M/A users in different regions but too little work has been conducted to disentangle the effects of injection versus sexual risks (Drumright, Patterson, & Strathdee, 2006).

M/A use is associated with high risk sexual risk behaviours that can heighten the risk of acquiring sexually transmitted infections (STIs) such as Chlamydia, gonorrhoea and syphilis, which also serve as cofactors of HIV transmission (Kral et al., 2001; Wasserheit, 1992). M/A has been linked to sexual risk with multiple groups including: MSM, sex workers (SW), men who purchase sex, heterosexuals and occupational groups (such as truck drivers) (for more details of studies see Degenhardt et al., 2007). M/A is *not* unique in being a drug that is linked to sexual risk: amyl nitrite, alcohol and numerous other drugs can also disinhibit users and have been



Source: Reproduced with permission from UNODC's *World Drug Report* 2009

Fig. 1. Meth/amphetamine seizures in 2007. Source: Reproduced with permission from UNODC's *World Drug Report* 2009.

associated with STI and HIV transmission (e.g. Halkitis, Parsons, & Stirratt, 2001).

Patterns of methamphetamine use and injection around the world

M/A use was reported in 110 countries/territories, and injection in 60 (see Fig. 2). M/A use and harm appears more prevalent in Asia, the Western U.S., Mexico, South Africa, New Zealand, Australia and several European countries. This section briefly summarises this evidence, which is listed country-by-country in Tables 2–10 (for a more detailed discussion of this evidence see (Degenhardt et al., 2007)).

Eastern Europe and Central Asia

Both problematic use and injection of M/A are prevalent in Eastern Europe (Table 2). In many countries, significant home-made manufacture of amphetamines has occurred for decades, which have varied over time and across countries (Grund et al., 2009). These have included *Vint* and *jeff* (whose active ingredients are methamphetamine and methcathinone, respectively), and more recently in the **Ukraine**, *boltushka* (Chintalova-Dallas, Case, Kitsenko, & Lazzarini, 2009). Meth/amphetamine ("pervitin") is an established – and increasing – problem in the **Czech Republic** (EMCDDA, 2005y; Zabransky, 2007). In 2005, 0.3% of the population were estimated to be meth/amphetamine dependent, with higher rates among younger females, and the drug mentioned in 58% of drug treatment episodes (Zabransky, 2007).

In **Belarus**, there is evidence that the availability of M/A is increasing (Lelevich, Kozlovsky, Vinitskaya, & Maksimchuk, 2006). At the end of 2005, 3.7% of "registered [drug] users" were using M/A, with IDU the dominant route; 3% of all IDUs were M/A injectors (Lelevich et al., 2006).

Poland is experiencing increased problems related to M/A. It is commonly detected in poisoning cases, is the second most common drug noted in possession offences, and treatment episodes are also increasing (EMCDDA, 2005r). In multiple other Eastern European countries including **Latvia**, **Lithuania** and **Slovakia**, M/A use has been reported as an increasing problem but data are much more limited. Injection of M/A was reported to be an issue in Slovakia, and treatment numbers are increasing (EMCDDA, 2005u). A significant problem has been noted in **Hungary**, with 9% of treatment entrants being for meth/amphetamine use (EMCDDA, 2005i). Low levels of M/A use in the general population were reported in **Uzbekistan** (0.01%) but no data on M/A use could be obtained for any other countries in Central Asia.

East and South-East Asia

M/A manufacture and use has been a notable trend in East and South-East Asia in the past decade (Ahmad, 2003; Farrell, Marsden, Ali, & Ling, 2002; UNODC, 2009; United Nations Office on Drugs and Crime, 2007) (Table 3).

In **Thailand**, M/A ("yaba") is typically found in crystal and pill forms (United Nations Office on Drugs and Crime, 2007) and is mentioned in the majority of treatment admissions in the country; 16% of IDUs use the drug(United Nations Office on Drugs and Crime, 2007). There may be geographic differences: 1% of the

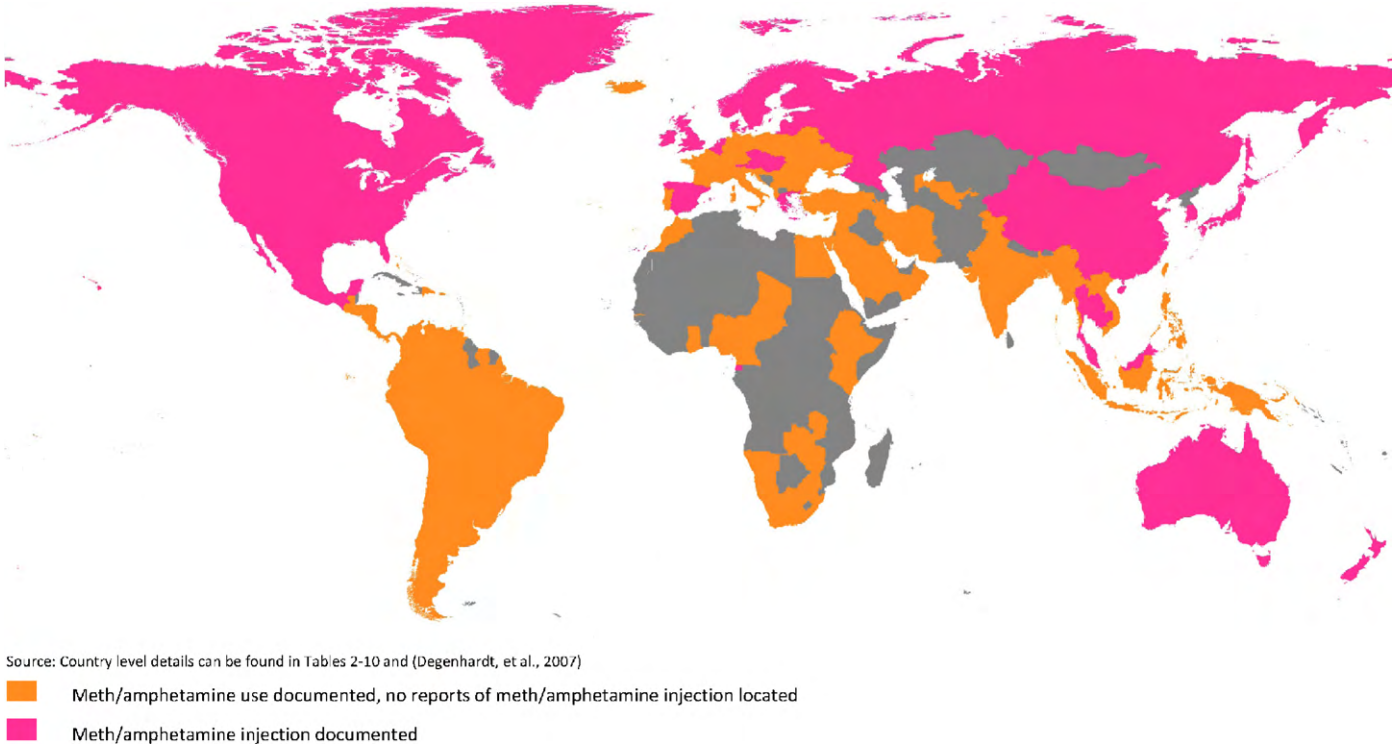


Fig. 2. Locations of meth/amphetamine use and injection. Source: Country level details can be found in Tables 2–10 and (Degenhardt et al., 2007) Meth/amphetamine use documented, no reports of meth/amphetamine injection located Meth/amphetamine injection documented No reports of meth/amphetamine use or injection located.

entire Bangkok population were M/A dependent in 2001 (Bohning, Suppawattanabodee, Kusolvisitku, & Viwatwongkasem, 2004). A 2004 study found that among IDUs in Bangkok, 49% had injected M/A – and this group was highly unlikely to have entered treatment (Wattanaa et al., 2007). Among IDU in Bangkok with a prison history, independent risk factors for HIV infection included M/A injection before detention, sharing needles in cells, tattooing in prison, and borrowing needles post-release (Buavirat et al., 2003). In contrast, M/A users in northern Thailand were a much younger and different population from opium/heroin users, with higher rates of sexual activity and chlamydia infection (Beyrer et al., 2004) but lower rates of initiation to injection (Cheng et al., 2006; Jittiwutikarn et al., 2006).

In **Viet Nam**, swallowing appears to be the most common route of administration of M/A, which is largely available in pill form (United Nations Office on Drugs and Crime, 2007). In 2004, 88% of drug treatment entrants were IDUs (United Nations Office on Drugs and Crime, 2007).

Japan has an established history of problematic use of M/A despite having an apparently very low general population prevalence of use (United Nations Office on Drugs and Crime, 2007b). Population estimates of use may be much higher than official estimates. The crystalline form is thought to be the most common, and injecting is a major route (United Nations Office on Drugs and Crime, 2007). One study found that 7% of adolescents in drug treatment had problems with the drug (Miura, Fujiki, Shibata, & Ishikawa, 2006); a study of adults found 67% of M/A treatment entrants were injecting (Matsumoto et al., 2002).

In **China**, evidence of increased use exists, particularly in the north east of the country (National Surveillance Center on Drug Abuse, 2006; United Nations Office on Drugs and Crime, 2007). In 2005, 14% of "first registered addicts" were M/A, MDMA or ketamine users; 11% were injecting and 22% smoking (National Surveillance Center on Drug Abuse, 2006). M/A use also appears more frequently in locations associated with riskier injecting practices such as temporary dwellings or "non-fixed places" (National Surveillance Center on Drug Abuse, 2006).

In the **Republic of Korea**, as in **the Philippines,** two-thirds of treatment entrants in 2004 were using M/A (Tsay, 2006; United Nations Office on Drugs and Crime, 2007); in 2006 over half of all treatment episodes in **Singapore** (United Nations Office on Drugs and Crime, 2007) and one-third in **Taiwan** were for M/A. One study identified increased injection in **the Philippines,** however, with reports of M/A being mixed with Nubain© (Nalbuphine Hydrochloride), a mixed opioid agonist-antagonist (Dangerous Drugs Board, 2005).

In **Cambodia**, there is evidence that M/A problems are increasing, particularly related to the crystal form (United Nations Office on Drugs and Crime, 2007). Studies have documented high rates of M/A use among at-risk groups, with reports of injecting (United Nations Office on Drugs and Crime, 2007).

In other countries, data were more limited but there are some reports of increasing use in **Brunei Darussalam**, **Indonesia**, **Lao People's Democratic Republic**, and **Malaysia** (United Nations Office on Drugs and Crime, 2007). In most of these countries, smoking and/or injecting predominate(United Nations Office on Drugs and Crime, 2007).

South Asia

M/A use in South Asia appears to be limited (Table 4). Although it is one of the world's largest producers of pseudoephedrine, availability and use of M/A appears limited in **India**. Trafficking of pseudoephedrine from the north-east of India into Myanmar and transport of M/A back into India is believed to occur (Panda, 2006, 2001). M/A use (oral and smoking) has been reported to occur in **Bangladesh** (Hassan, 2005; Mitu, 2007; Rahman, 2006), with anecdotal reports that it is common among the middle class (personal communication, Tasnim Azim 2008).

In **Iran**, there have been seizures of crystal methamphetamine (Samii, 2005). Minimal M/A use has been reported even among "at-risk" groups (Ahmadi & Benrazavi, 2002a,b; Ahmadi, Fakoor, Pezeshkian, Khoshnood, & Malekpour, 2001; de Kort, Batra, Pasaribu, Vazirian, & Ul-Hassan, 2005).

Data is scarce but limited use is understood to occur in **Bhutan** (United Nations Office on Drugs and Crime, 2007; World Bank, 2006); this needs verification.

Caribbean

Very limited data were available on the epidemiology of meth/amphetamine use in the Caribbean (Table 5). The existing data available strongly suggest that use is negligible (Caribbean Drug Abuse Epidemiology and Surveillance System Project, 2003; Dormitzer et al., 2004). Injecting drug use in general is thought to be negligible in the Caribbean with the exception of **Bermuda** and the **Commonwealth of Puerto Rico** (Caribbean Epidemiology Centre, 2007; Hacker, Malta, Enriquez, & Bastos, 2005).

In the **Commonwealth of Puerto Rico** HIV prevalence is very high among IDUs generally (20–25%) (UNAIDS, 2006a). In a cohort study of male IDUs with AIDS, 29% used M/A (cocaine and heroin were much more commonly used) (Robles et al., 2006).

Latin America

There is a lack of data on M/A use and injection in Latin America (Table 6), probably explained by the importance of cocaine in most countries in the region. Two countries where M/A was an issue were **Mexico** and **Brazil**.

Brazilian studies have documented high levels of M/A use and sexual risk among truck drivers (Malta et al., 2006; Nascimento et al., 2006). Manufacture of meth/amphetamine has increased dramatically in **Mexico** in the past decade, and it reportedly producing up to 95% of M/A entering the US market (Brouwer et al., 2006). Domestic consumption is also increasing, particularly among at-risk groups (Strathdee et al., 2008) (Patterson et al., 2006), with increased treatment admissions for meth/amphetamine dependence, which accounted for 25% of all drug treatment episodes in 2003 (Maxwell et al., 2006). M/A smoking has increased among meth/amphetamine treatment entrants from 45% in 1997 to 71% in 2003, with around 2–3% injecting (Maxwell et al., 2006). M/A use is most common in north-western Mexico, which is known for trafficking (Brouwer et al., 2006), but is emerging in north-eastern Mexico (Case et al., 2008).

Australasia and the Pacific

In most countries in the region there was limited or no data on meth/amphetamine use (Nejo, 2003; Reid, Devaney, & Baldwin, 2006), and use was presumed negligible (Table 7). Exceptions are Australia, New Zealand, the United States territory of Guam, and Samoa.

In the **United States territory of Guam** and **Samoa**, M/A use has been of particular concern for some years. According to one study one in four Guam school students had been offered crystal methamphetamine in 1998 (Storr, Arria, Workman, & Anthony, 2004); half of drug treatment episodes were for M/A (US National Drug Intelligence Center, 2003).

In **Australia**, there appears to have been an increase in both importation and local manufacture of M/A over the past decade (Degenhardt et al., 2008; McKetin & McLaren, 2004; Topp et al., 2002). Increases in crystal methamphetamine use have occurred among sentinel groups of regular drug users. Frequent crystal M/A use among regular IDUs is associated with earlier initiation to injecting, greater injection risk (Degenhardt et al., 2008), psychotic symptoms (McKetin, McLaren, Lubman, & Hides, 2006) and dependence (McKetin et al., 2006a; O'Brien et al., 2007).

In **New Zealand**, similar increases have occurred in M/A use over the past decade. The use of "pure" or "P" (the local term for crystal M/A) has been linked to violent behaviour and significant community concern; in 2004, M/A accounted for 10% of drug treatment episodes (Adamson, Sellman, Deering, Robertson, & de Zwart, 2006). Use is common among sentinel groups of drug users, and is usually smoked. Injection of M/A is common among IDUs (70%) (Centre for Social and Health Outcomes Research and Evaluation, 2006).

Canada, United States and Western Europe

These regions were notable for the greater breadth and depth of data on the epidemiology of use and harm related to M/A compared to other regions (Table 8). M/A use is an established and perhaps growing problem in numerous countries.

In the **United States** M/A accounted for 10% of emergency department drug-related visits (Maxwell & Rutowski, 2008) and 9% of drug treatment episodes in 2005 (Office of Applied Studies, 2006) and is increasing (Maxwell et al., 2006). Smoking has emerged as a route of administration and there is evidence that where the crystal form of the drug is more widely available, problems related to M/A use are more severe (Maxwell & Rutowski, 2008). In many instances, problematic users come from rural areas, the attendant problems related to dependent use have placed a strain on services; rural meth/amphetamine treatment clients are both younger and more likely to be injecting the drug (37% vs. 21%) than urban clients (Grant et al., 2007). Of concern are the high prevalence of HCV and HIV among dependent users. Those injecting M/A are less likely than other IDUs to attend outreach services, but have higher rates of injecting risk (Braine, Des Jarlais, Goldblatt, Zadoretzky, & Turner, 2005), making the need for innovative programmes to reach this population vital.

In **Canada**, limited data suggest that problems related to this drug use are increasing in Western Canada, and are more concentrated among younger IDUs (Fairbairn et al., 2007; Wood, Stoltz, Montaner, & Kerr, 2006); between 2001 and 2005 it was an issue for one-quarter of adolescent drug treatment entrants in one clinic (Callaghan et al., 2007).

In **Germany**, treatment episodes for M/A use have increased over the past decade from 2% in 1994 to 10% of all first-time outpatient drug treatment episodes (and 4% of inpatient episodes) in 2004 (EMCDDA, 2005g). In **Denmark**, there is evidence that M/A problems may be increasing. In 2004, one quarter of first time drug treatment entrants were for M/A; there is increasing evidence of greater treatment need among young adults for this drug use (EMCDDA, 2005c). Concerns about increased problems related to M/A use were voiced in southern **Italy** by clinicians a decade ago (Reccia, Rocco, Lioniello, & Fichera, 1995) and a novel examination of metabolites in wastewater from Milan confirmed high levels of M/A use in that population (Castiglioni et al., 2006). Population surveys have suggested increasing use, concentrated among some populations of young people (Table 8).

Similarly, **the Netherlands** appears to have considerable use, but it is not reflected in treatment numbers or hospital admissions (EMCDDA, 2005p); injection is rare even among treatment populations, and most use is either by swallowing or snorting (EMCDDA, 2005p). Users presenting for treatment are significantly younger than other drug users (EMCDDA, 2005p).

Underestimation of drug use produced by household surveys is clearly demonstrated using data from **Finland**. The household survey estimate of *any* past year use – 0.6% – is effectively the

same as the estimate of *problematic* meth/amphetamine use produced using indirect prevalence estimation methods (0.4–0.6%) (EMCDDA, 2005e); rates are higher among younger age groups. Meth/amphetamine accounted for 26% of treatment episodes and was injected by 79% of patients in 2004 (EMCDDA, 2005e).

In **France**, the population prevalence of M/A use in the past year was only 0.2% (vs. 0.6% for **Finland**), but accounted for only 0.7% of new drug treatment episodes in 2003 (vs. 26%) (EMCDDA, 2005f).

In the **United Kingdom**, M/A use was recently reported as low and stable (EMCDDA, 2005z), with higher levels of use among some groups including MSM (Bolding, Hart, Sherr, & Elford, 2006). The data for some other countries also suggested limited use and problems, including **Greece**, **Malta**, **Ireland**, and **Iceland**. Limited or no data were available to assess the state of affairs in numerous countries including **Albania**, **Andorra**, **Monaco**, **Montenegro**, **Liechtenstein**, and **Macedonia**. As a general comment, many countries in Europe have relatively good availability of cocaine. It may well be the case that this serves to contain the availability and/or use of M/A (through user preferences, supply control on the part of drug distributors, or both).

Middle East and Northern Africa

There were few data on M/A use in this region (Table 9). Khat predominates in many countries (Al-Habori, 2005) – in **Yemen** 60% reportedly use the drug "frequently"(Kandela, 2000). Khat plant leaves (*Catha edulis forsk*) are chewed; they contain an active psychostimulant, Cathinone, which is similar to amphetamine in both structure and activity (Aden, Dimba, Ndolo, & Chindia, 2006; Al-Motarreb, Baker, & Broadley, 2002; Ihunwo, Kayanja, & Amadi-Ihunwo, 2004; Kalix, 1988).

M/A precursor chemicals are produced in the **United Arab Emirates** and seizures of M/A have been reported in **Cyprus** (Mita, 2002). Limited reports and hospital treatment data in **Saudi Arabia** suggest that use and problems are increasing in this country (AbuMadini, Rahim, Al-Zahrani, & Al-Johi, 2008; Allam, 2007; United Nations Office on Drugs and Crime, 2008a). No direct data could be obtained on M/A use in **Iraq**, but there have been media reports of heavy use among Iraqi military personnel (Hughes, 2005; Stryker Meyer, 2005). In **Lebanon**, there have been reports of M/A use concentrated among "high income" members of the population (Bureau for International Narcotics and Law Enforcement Affairs, 2004).

Sub-Saharan Africa

Data are notably absent here (Table 10), but M/A use is presumably negligible in most countries, with the exception of **South Africa**. In **South Africa**, M/A use is concentrated among young people, and increasing (Morris & Parry, 2006; Parry, Myers, & Pluddemann, 2004). It was used by 45% of drug treatment entrants in 2005, with 41% using daily, with smoking typical (90%) (Morris & Parry, 2006). HIV prevalence *in the general population* is 19%; rates are four times higher among girls than boys aged 15–24 years (UNAIDS, 2006b). Khat has been used widely in some countries, and associated with psychosis and risky sexual behaviour among students (Table 10).

Research issues and gaps

The paucity of data in many countries probably reflects a range of issues including: limited resources, concentration of drug use among small or difficult to reach groups, difficulty distinguishing between different forms of amphetamines in seizure and other routine data sources (United Nations Office on Drugs and Crime, 2008a), stigma regarding the research into and reporting of drug use, and/or limited research capacity. There are significant difficulties in the conduct of illicit drug research in developing countries (Westermeyer, 2004), but similar issues exist in those with a more established history of illicit drug research. There is a strong imperative for a concerted investment to produce better epidemiological data on M/A use and injection, and associations with HIV and HCV.

Several points deserve mention. First, household survey-derived estimates of past year M/A use are *very* poor indicators of the extent of problematic use, for multiple reasons that include the exclusion of at-risk groups (e.g. the homeless and those incarcerated and hospitalised) and underreporting, among other things (Hall et al., 2000). Indirect estimations using methods such as capture-recapture and multiplier-benchmark methods should be used instead[2] (Kraus et al., 2003). Second, data on types of drug use among at-risk groups should be routinely collected (including through the use of respondent-driven sampling methods), as they can suggest how commonly problematic use is occurring among these groups. Third, the proportion of drug treatment episodes where M/A is mentioned is a useful indicator. However, it is most certainly a lagging indicator (dependence takes time to develop) and crucially depends on the availability of treatment for M/A users. Most countries do not have routine drug treatment data collections, recording differs across countries,[3] and treatment systems geared to opioid users struggle to engage M/A users, so these data are likely to significantly underestimate treatment need. Fourth, we need better collection of data on route of administration and M/A forms, as these appear strongly linked to the extent of M/A problems. Qualitative data are needed to inform some of the contexts and risks in which users are engaging given how much is *not* known in many countries.

Current responses to meth/amphetamine

Interventions to address use of amphetamines tend to be incongruent with scale of the issue, in terms of the size of the population of ATS users, the potential for harm, the intersection of risk and at-risk groups and the knowledge gaps. Globally, drug interventions are typically modelled on those developed for alcohol and opioids. Earlier interventions have typically assumed knowledge gain will lead to behaviour change, and often fail to identify specific issues for young and older ATS users, the sex of users, and the context of use, and how they might be transferred from well developed economies to very poor, resource strapped settings where there may be a minimal and/or poorly trained workforce. There has also been a lack of focus upon policy, structural, programmatic and socio-cultural impacts. For a longer discussion of the responses to M/A use and harm, please see Degenhardt et al. (2007).

Summary of major interventions (see Degenhardt et al., 2007 for more detail).

Supply control

Attempts to control supply may limit availability in some countries if precursor control or other interventions disrupt manufacture of trafficking of meth/amphetamine, but they are unlikely to permanently reduce availability or use as long as demand for the drug continues to be strong. Interventions to reduce demand and harm related to meth/amphetamine use must also be implemented. Evidence also suggests that such interventions may serve to shift manufacture to new geographic areas and involving different precursors.

[2] http://www.emcdda.europa.eu/themes/key-indicators/pdu.

[3] Some countries report drug use among treatment entrants; others report the main drug of concern. Both statistics are useful and should be reported clearly.

It is unlikely that increases in the severity of penalties for *possession* of meth/amphetamine will substantially reduce consumption (based upon prior studies examining cannabis use), and there is a risk they may further disadvantage users who are detected by police, since they are likely to already be experiencing problems related to their drug use.

Demand reduction

There is at present no evidence of the effectiveness of agonist pharmacotherapies for meth/amphetamine dependence (Baker, Lee, & Jenner, 2004; Shearer, 2009).

Some evidence exists that behavioural interventions are effective in the treatment of meth/amphetamine dependence (Knapp, Soares, Farrel, & Lima, 2007; Rawson et al., 2004a; Rawson, Gonzales, & Brethen, 2002; Shearer, 2009).

Successful reduction of drug use among dependent users has been associated with reductions in sexual risk behaviours (Shoptaw & Frosch, 2000) and HIV risk behaviours (Patterson and Semple, 2003; Reback, Larkins, & Shoptaw, 2004).

Drug use related harm reduction

It is important that harm reduction measures reach occasional, recent, experimental and young IDUs (Howard, Hunt, & Arcuri, 2003). More active models of engagement with meth/amphetamine IDUs must be developed.

Provision of smoking equipment through NSPs should be considered as an additional harm reduction measure. Nonetheless the risks of smoking crystal methamphetamine need to be communicated to users in a balanced manner.

Investigation of alternative methods of service delivery including a greater emphasis upon peer models of information and engagement, and access through groups not explicitly drug-focused might prove useful, and might allow for both sex and injecting harm reduction interventions (Rose, Raymond, Kellogg, & McFarland, 2006).

In countries where Internet access is high, delivery of brief interventions and harm reduction information electronically may provide some benefit to those unwilling to present to drug treatment services. Further work in this area could be of immense value.

Sexual risk reduction

There is a clear public health imperative to introduce programmes to reduce sexual risk, and several important components are indicated (Semaan, Des Jarlais, & Malow, 2006). They are:

Education: accurate information about HIV transmission and how safer sex can reduce HIV transmission risk, with peers playing an important role in developing social norms.

Condoms: ready and discreet availability of condoms, publicly and free or at little cost.

Voluntary HIV counselling and testing: to increase knowledge of serostatus and facilitate safer sexual behaviour (Semaan et al., 2006).

HIV prevention and treatment

Interventions to address HIV among meth/amphetamine IDUs should be consistent with the UNAIDS *Comprehensive Package* for prevention and care of injecting drug users[1]: information, education and communication (IEC); full range of treatment options; implementation of harm reduction measures; voluntary confidential HIV counselling and testing; prevention of sexual transmission of HIV; access to primary heath care; access to ARV therapy; and promotion, protection and respect for human rights – and particularly anti-stigma and discrimination measures.

Persons presenting with meth/amphetamine dependence who are also HIV positive should be encouraged to address their drug use (Eramova, Matic, & Munz, 2006). Those actively using meth/amphetamine should be offered treatment for HIV; clinicians should offer treatment and provide good support to assist clients with adhering to medication (Eramova et al., 2006). WHO guidelines state that current meth/amphetamine users should receive HAART but should *not* be prescribed ritonavir or lopinavir/ritonavir (Eramova et al., 2006).

International drug policy: precursor control and drug law enforcement

In many if not most countries the first response to increased availability of MA by governments seems to be consideration of changes in the scheduling of precursors for its manufacture. There has for example been examination in the USA of the impact of domestic scheduling changes upon MA related harms (Cunningham & Liu, 2003, 2005), with some evidence of a reduction following increased restrictions. The effects of such changes have generally not been sustained, given that production appeared to move to neighbouring countries.

Of course, restrictions upon availability in a country often lead to a shift by manufacturers to obtaining precursor chemicals from alternative sources. Efforts to control M/A precursor supplies in one country or region may have the unintended consequence of displacing manufacturing, as was the case in the US (shifting to Mexico), and following the Thai "war on drugs" (United Nations Office on Drugs and Crime, 2008a,b, 2009). Attempts to control supply may limit availability, but they are unlikely to permanently reduce availability or use as long as demand for a drug continues to be strong. Interventions to reduce demand and harm related to M/A use must also be implemented.

There are few data regarding the impact of changing laws surrounding penalties for possession of small quantities of M/A. It is unlikely that increases in the severity of penalties for *possession* of M/A will substantially reduce consumption (based upon studies of cannabis use laws), and there is a risk they may further disadvantage users who are detected by police, since they are likely to already be experiencing problems related to their drug use. We could not locate any studies evaluating the benefits (or negative consequences) of more severe penalties for *supplying* illicit drugs.

Demand reduction

There is at present no evidence that agonist pharmacotherapies for M/A dependence are effective, with interest among M/A users apparently limited and perhaps effective only in highly selected groups (Grabowski, Shearer, Merrill, & Negus, 2004; Shearer, 2009). Some evidence exists from more developed countries that behavioural interventions are effective treatments for M/A dependence, particularly cognitive behavioural therapy, and contingency management. Manuals for such interventions have been developed (Baker et al., 2004; Rawson et al., 2004b) as have guidelines for general practitioners. Much more research is needed, however, into effective approaches, and how they may work in resource-poor settings.

Harm prevention and reduction

Globally, most harm reduction is focused upon injecting risk. Sex risk reduction is rarely a focus with drug users and other drug-related risk reduction – risk related to other routes of administration, or preventive approaches for drug-induced psychosis, for example, even less common. In addressing meth/amphetamine related harm, there is a need to change *what* is targeted: multiple patterns of risky use, sexual risk behaviours and other adverse consequences, harms among multiple at-risk groups, and in multiple settings. There is a need to change *when* it is targeted: early intervention and prevention. There is a need to change *how* it is targeted: different models of intervening and a multilevel community response are needed, since M/A users are not as well served by using existing models of intervention. HIV prevention is considered "marginalised" compared to HIV treatment and there are multiple obstacles to achieving effective prevention. Some have suggested that effective prevention requires

a multilevel approach driven by bottom-up wisdom, comprising structural, biomedical and behavioural approaches within a context of strategic, critical, and comprehensively planned and evaluated programmes and policies: it seems particularly pertinent with this population (Merson, O'Malley, Serwadda, & Apisuk, 2008).

NSPs have been shown to reduce injecting risk and HIV transmission – typically among primary opioid injectors. Current NSP models appear less effective at engaging M/A IDUs, perhaps as they may be perceived as primarily directed at heroin injectors. M/A injectors are less likely than heroin injectors to engage in drug treatment, or be in touch with HIV outreach services (Degenhardt et al., 2007); they are also more likely to stock up on needles rather than picking them up one at a time (Zule, Desmond, Morgan, & Joe, 1999), reducing the window of opportunity for intervention.

Recent evidence from developed countries suggests that both frequency of injection *and* injecting risk might be reduced if there is greater access to drug smoking equipment (Leonard et al., 2008; Pizzey & Hunt, 2008). Much greater research into this possibility is warranted; and alternative service delivery models with an emphasis upon peer engagement considered.

High risk sexual behaviours appear more common among M/A users, constituting a further potential route of HIV transmission. There is a clear public health imperative to ensure sufficient coverage of M/A users with programmes to reduce sexual risk including: provision of condoms, accurate information, and voluntary HIV counselling and testing. An additional issue concerns ways to address risk when M/A users knowingly taking part in sexual activities that place them at risk of HIV infection.

HIV treatment for M/A users

For M/A users who have contracted HIV, interventions should be consistent with the Joint United Nations Programme on HIV/AIDS (UNAIDS) *Comprehensive Package for prevention and care of IDUs*, which includes: access to primary health care; access to ARV therapy; and promotion, protection and respect for human rights – and particularly anti-stigma and discrimination measures.

Highly active antiretroviral therapy (HAART) should be available to M/A users living with HIV. Persons who are M/A dependent who are also HIV positive should be encouraged to address their M/A and other drug use (Eramova et al., 2006). Those actively using M/A should be offered treatment for HIV; clinicians should offer treatment and provide good support to assist clients with adhering to medication (Eramova et al., 2006). WHO guidelines state that current meth/amphetamine users should receive HAART but should *not* be prescribed ritonavir or lopinavir/ritonavir (Eramova et al., 2006).

Conclusions

M/A use has been identified in 110 countries and territories, and studies have linked use with increased risk of HIV through both sexual and injecting risk behaviours. Current evidence to interpret this association is far from adequate. Furthermore, we need a coordinated and truly global response: one that involves the collaboration of law enforcement, policymakers, health and civil society, but also one that can be effectively adapted in terms of specific interventions, to accommodate regional, sub-regional and cultural variations. M/A manufacturers have demonstrated a well-developed capacity to quickly re-locate their manufacture efforts, find alternative sources of precursors and trafficking routes, and creating (or being responsive to) new and emerging markets. The health response must be equally 'evidence-based' and readily able to adapt to new and emerging situations, and work across multiple sectors with multilevel interventions.

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The work of the Reference Group is guided by the Secretariat, which in 2007 was based at the National Drug and Alcohol Research Centre (NDARC), University of NSW, and comprised Dr Bradley Mathers, Professor Louisa Degenhardt, Professor Richard P. Mattick, Benjamin Phillips, Dr Alex Wodak and Associate Professor Kate Dolan.

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Conflict of interest statement

None.

Appendix A. Method

This study comprised a desk-based literature review of peer reviewed and grey literature. Searches of the electronic databases of Medline (via the OVID platform) and PubMed were conducted. Details of these searches are given below.

Details of the searches of the "grey" literature can be obtained from a report, published online, written by Calabria

et al. (2008), which contains details of all websites consulted: http://ndarc.med.unsw.edu.au/NDARCWeb.nsf/resources/TR+293-297/$file/TR.293.pdf.

The following online drug and alcohol databases and related online libraries were searched: The Australian National Drug and Alcohol Research Centre (NDARC) library; The Alcohol and other Drugs Council of Australia (ADCA); The CORK network catalogue; and the Asian Harm Reduction Network (AHRN). The online bibliography "Key to methamphetamine-related literature" (Hammer, 2006) of the NY State Department of Health was also consulted: http://www.nyhealth.gov/diseases/aids/harm_reduction/crystalmeth/docs/meth_literature_index.pdf.

Google searches were conducted on a country-by-country basis. In addition, UNODC and WHO country and regional offices were requested to provide any available and relevant material. Additional literature cited within the retrieved material was also consulted.

Material retrieved from these searches was deemed appropriate for inclusion in this review if it was an original research study, a commentary, a policy analysis, a review or report that described the following: the prevalence or incidence of methamphetamine use by injected and non-injected routes of administration; harms associated with methamphetamine use; HIV prevalence and risk behaviours of methamphetamine users; methamphetamine and HIV treatment and care; methamphetamine and production, trafficking and seizures of methamphetamine; treatment and policy addressing methamphetamine use or production. As a general principle, more recent literature was preferred over older data. In all estimates of prevalence, only the most recent data were included in tables.

For some of the grey literature material retrieved data on sample sizes, methodology, and/or the organisation conducting the research could not be identified. If a country has no estimate, it means that either no data was available, or it did not investigate methamphetamine. For such countries, using other estimates from the region may be the only way to make an approximation of drug use in that country.

Appendix B. Medline search strategy

The following keywords and "MeSH" terms (in **bold**) were used in the searches of the literature for each region:

Injecting drug use
IDU OR IDUs OR "injecting drug" OR "intravenous drug" OR "intravenous substance" OR "injecting substance" OR **exp substance abuse, intravenous**/

Drugs and drug use
heroin OR cocaine OR amphetamine$ OR methamphetamine$ OR opioid$ OR opium OR opiate OR drug abuse OR drug use$ OR drug misuse OR drug dependen$ OR substance abuse OR substance use$ OR substance misuse OR substance dependen$ OR addict$ OR exp **designer drugs/** OR **exp street drugs/** OR **exp Cocaine/** OR **exp crack cocaine/** OR **exp amphetamines/** OR **exp amphetamine/** OR **exp methamphetamine/** OR **exp Opium/** or **exp Heroin/** OR **exp substance-related disorders/** OR **exp amphetamine-related disorders/** OR **exp cocaine-related disorders/** OR **exp opioid-related disorders/** OR **exp heroin dependence/** OR **exp morphine dependence/** OR **exp psychoses, substance-induced/**

HIV/AIDS
OR HIV or AIDS OR HIV/AIDS OR "Human Immunodeficiency Virus" OR "Human Immune Deficiency Virus" OR "Acquired Immunodeficiency Syndrome" OR "Acquired Immune Deficiency Syndrome" OR **exp HIV/** OR **exp HIV-1/** OR **exp HIV-2/** OR **exp HIV infections/** OR **exp acquired immunodeficiency syndrome/** OR **HIV seropositivity/** OR **exp HIV seroprevalence/** OR **exp AIDS serodiagnosis/**

Amphetamine type stimulants
ATS OR "amphetamine type stimulant$" OR amphetamine$ OR methamphetamine OR deoxyephedrine OR desoxyephedrine OR Desoxyn OR madrine OR metamfetamine OR methamphetamine hydrochloride OR methylamphetamine OR n-methylamphetamine OR d-amphetamine OR dextroamphetamine sulphate OR dexamphetamine OR dexedrine OR dextro-amphetamine sulphate OR dextroamphetamine sulphate OR d-amphetamine sulphate OR stimulant$ OR **exp amphetamines/** OR **exp amphetamine/** OR **exp dextroamphetamine/** OR **exp p-chloroamphetamine/** OR **exp 2,5-dimethoxy-4-methylamphetamine/** OR **exp p-hydroxyamphetamine/** OR **exp iofetamine/** OR **exp methamphetamine/** OR **exp benzphetamine/** OR **exp phentermine/** OR **exp chlorphentermine/** OR **exp mephentermine/** OR **exp amphetamine-related disorders/**

Appendix C. PubMed Search Strategy

The following keywords and "MeSH" terms (in **bold**) were used in the searches of the literature for each region:

Injecting drug use
IDU OR IDUs OR "injecting drug" OR "intravenous drug" OR "intravenous substance" OR "substance abuse, intravenous" OR "**substance abuse, intravenous**" [MH]

Drug use
"Drug abuse" OR "drug use" OR "drug user" OR "drug users" OR "drug misuse" OR "drug dependence" OR "drug dependency" OR "drug dependent" OR "substance abuse" OR "substance use" OR "substance user" OR "substance users" OR "substance misuse" OR "substance dependence" OR "substance dependency" OR "substance dependent" OR addict OR addicts OR addiction OR "substance-related disorders" OR "amphetamine-related disorders" OR "cocaine-related disorders" OR "opioid-related disorders" OR "heroin dependence" OR "morphine dependence" OR "**substance-related disorders**" [MH] OR "**amphetamine-related disorders**" [MH] OR "**cocaine-related disorders**" [MH] OR "**opioid-related disorders**" [MH] OR "**heroin dependence**" [MH] OR "**morphine dependence**" [MH]

HIV/AIDS
HIV OR AIDS OR AIDS [sb] OR "HIV/AIDS" OR "Human Immunodeficiency Virus" OR "Acquired Immunodeficiency Syndrome" OR "HIV-1" OR "HIV-2" OR "HIV seropositivity" OR "HIV seroprevalence" OR "AIDS serodiagnosis" OR "HIV-1" [MH] OR "HIV-2" [MH] OR "HIV seropositivity" [MH] OR "HIV seroprevalence" [MH] OR "AIDS serodiagnosis" [MH]

Amphetamine type stimulants
ATS OR "amphetamine type stimulants" OR amphetamine OR amphetamine OR methamphetamine OR deoxyephedrine OR desoxyephedrine OR Desoxyn OR metamfetamine OR "methamphetamine hydrochloride" OR methylamphetamine OR "n-methylamphetamine" OR "d-amphetamine" OR "dextroamphetamine sulphate" OR dexamphetamine OR dexedrine OR "dextroamphetamine sulphate" OR "d-amphetamine sulphate" OR stimulant OR stimulants OR "P-chloroamphetamine" OR "2,5-dimethoxy-4-methylamphetamine" OR "P-hydroxyamphetamine" OR iofetamine OR methamphetamine OR benzphetamine OR phentermine OR chlorphentermine OR mephentermine OR "amphetamine-related disorders" OR "**P-chloroamphetamine**" [MH] OR "**2,5-dimethoxy-4-methylamphetamine**" [MH] OR "**P-hydroxyamphetamine**" [MH] OR **iofetamine** [MH] OR **methamphetamine** [MH] OR **benzphetamine** [MH] OR **phentermine** [MH] OR **chlorphentermine** [MH] OR **mephentermine** [MH] OR "**amphetamine-related disorders**" [MH]

Appendix D. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.drugpo.2009.11.007.

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