Chapter 7
The fast and furious — cocaine, amphetamines and harm reduction

Jean-Paul Grund, Philip Coffin, Marie Jauffret-Roustide, Minke Dijkstra, Dick de Bruin and Peter Blanken

'The role of the state is not to make people happy but to relieve avoidable suffering.'

(Sir Karl Popper, 1945)

Introduction

Cocaine and amphetamines ('stimulants') are distinct central nervous system stimulants with similar effects (Pleuvry, 2009; Holman, 1994). Cocaine is a crystalline tropane alkaloid extracted from coca leaves. Amphetamines are a subclass of phenylethylamines with primarily stimulant effects, including amphetamine, methamphetamine, methcathinone and cathinone and referred to as 'amphetamines' in this review (Holman, 1994). MDMA (3,4-methylenedioxy-N-methamphetamine or ecstasy) is a substituted amphetamine known for its entactogenic, psychedelic, and stimulant effects (Morgan, 2000). Stimulants can produce increased wakefulness, focus and confidence, elevated mood, feelings of power, and decreased fatigue and appetite; stimulants also produce nervousness or anxiety and, in some cases, psychosis and suicidal thoughts (Holman, 1994; EMCDDA, 2007f; Hildrey et al., 2009; Pates and Riley, 2009). Although there is little evidence that stimulants cause physical dependence, tolerance may develop upon repetitive use and withdrawal may cause discomfort and depression (EMCDDA, 2007f; Pates and Riley, 2009). Users may engage in 'coke or speed binges' alternated with periods of withdrawal and abstinence (Beek et al., 2001).

Epidemiology of stimulant use in the European Union

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA, 2009) estimates that at least 3.9 % of the total adult population (15–64 years) in European Union (EU) Member States has used cocaine at least once in their lifetime (lifetime prevalence, LTP), but variations in prevalence and patterns are found between countries, demographic and social groups, and specific settings. Higher levels of cocaine use are found in western and southern countries, notably Denmark, Spain, Italy, Ireland and the United Kingdom, with relatively low LTP in most other European countries, ranging from 0.1 % to 8.3 % (EMCDDA, 2009). Cocaine use is concentrated among young adults (15–34 years), with an average LTP of 5.3 %, and more so among young men, with an LTP over 10 % and last year prevalence (LYP) over 5 % in Denmark, Spain, and the United Kingdom (EMCDDA, 2007b). LYP for all EU adults is 1.3 %, ranging from 0 % to 3.1 % by country. LYP among young adults is 2.2 %, ranging from 0.1 % to 5.5 %. Last month prevalence (LMP) for all adults range from 0 % to 1.1 %, two-thirds of whom are young adults (EMCDDA, 2007f).

Cocaine use appears to have increased among young adults since the 1990s and, while prevalence is leveling off or decreasing in many countries (EMCDDA, 2007a), Denmark and Italy report considerable increases as recently as 2005 and Spain, France, Denmark, and the United Kingdom report rapid growth among adults aged 15–24 (EMCDDA, 2007d). Those countries with data on problem cocaine use include Spain, with 4.5 to 6 problem cocaine users per 1 000 adults in 2002, Italy with 2.9 to 4.1 per 1 000 adults in 2005, and England with 5.7 to 6.4 problem crack users per 1 000 adults in 2004/05 (EMCDDA, 2007c).

Cocaine use is elevated in specific social settings and subpopulations, such as nightlife participants with rates from 10 to 60 % (Cohen and Sas, 1993; Cohen and Sas, 1994; Decorte, 2001; EMCDDA, 2007d; Nabben et al., 2007; Grund et al., 2007b; Haasen et al., 2004), sex workers, homeless people, treatment participants and marginalised young adults (EMCDDA, 2007d; Haasen et al., 2004). Largely employed, socially integrated users mostly sniff cocaine and do so occasionally within rather well-defined leisure settings and periods (Prinzleve et al., 2004; Bellis et al., 2003; Cohen and Sas, 1994; Decorte, 2001), with some experiencing periods of often short-lived uncontrolled use (Cohen and Sas, 1994; Decorte, 2001), a finding consistent with laboratory studies in which experienced cocaine users regulate their use (Sughondhabirom et al., 2005). Marginalised users, on the other hand, very often smoke cocaine-base (crack) or inject cocaine, use more frequently and chaotically, and more often use heroin, benzodiazepines or alcohol, while also experiencing a wide array of social-economic and medical problems (Prinzleve et al., 2004; Beek, 2001; Hando et al., 1997).

LTP of amphetamines among EU adults is 3.3 %, ranging from 0.1 % to 11.9 %, with 0.6 % LYP. As with cocaine, more young adults use amphetamines, with 5 % LTP and 1.3 % LYP (EMCDDA, 2008). Amphetamines are more common in nightlife, in particular in specific dance scenes, such as Hardcore, Tekno or Goa (Nabben et al., 2007; Grund et al., 2007b). In contrast to cocaine, amphetamine use is higher in northern, central and eastern parts of the EU, particularly Sweden and Finland, with rising rates among young adults in Austria, Germany, Denmark and southern Italy (Degenhardt et al., 2009). Amphetamine injecting is a long-established problem in the Czech Republic and increasing in Slovakia and Hungary (where methamphetamine use and injection is common) (EMCDDA, 2008; Degenhardt et al., 2009; Griffiths et al., 2008) as well as Estonia and countries across the eastern borders, such as Ukraine, Belarus, Russia and Georgia (Degenhardt et al., 2009; Griffiths et al., 2008; Grund et al., 2009; Grund and Merkinaite, 2009) Users in former Soviet states often produce amphetamine-type stimulants at home (Borodkina et al., 2005; Grund, 2001; Heimer et al., 2007), creating an environment where injecting is common among recreational users, in contrast to western EU countries where a division between integrated (party) and marginalised users of amphetamine seems to exist, similar to that between cocaine snorters and smokers or injectors (Grund, 2001; Grund et al., 2009; Degenhard et al., 2009).

LTP of ecstasy among EU adults is about 3 %, ranging from 0.3 to 7.3 %, with 0.8 % LYP. Among young adults, LTP is 5.6 % and LYP is 1.8 % (EMCDDA, 2008). The geographic

diffusion of ecstasy is less clear than that of cocaine and amphetamines, but is associated with diffusion of the electronic dance music culture (House or Techno parties, raves, etc.). Ecstasy is almost exclusively taken orally, most users are well-integrated and few seek treatment barring other drug or alcohol problems (EMCDDA, 2008). Thus, although the potential for harm of ecstasy use is not fictional, the reported burden of harm is very low in the EU compared to those of cocaine and amphetamines. For this reason this review will largely focus on (problem) use of cocaine and amphetamines. Fletcher and colleagues (2010) provide an overview of newly emerging harm reduction interventions aimed at users of ecstasy, amphetamines and other drugs in recreational settings.

In this review we use the term 'stimulant(s)' when discussing cocaine and (meth)amphetamines in general terms. We will use 'cocaine' when discussing this substance in either its salt or base form. 'Smokable cocaine' or colloquial terms like 'crack' will only be used when indicated (as in 'crack pipes'). Note that the term 'crack' is associated with stigma among drug users and some prefer saying they smoke 'free-base', instead of crack. Likewise, we use 'amphetamines' as a much as possible, when discussing amphetamines in general terms and use either 'amphetamine', 'methamphetamine' or '(meth)cathinone' when referring to those specific substances.

Methodology

This review was primarily based on searches in the Medline database for relevant articles. Several search terms were used and generally limited papers to those addressing human subjects and those published after 1990. The overwhelming majority of articles addressed a small number of harms and standardised search terms were unable to identify numerous articles known by the authors to be relevant to risk management among stimulant users. For example, we searched PubMed on 12 October 2008 for clinical trials, metaanalyses, randomised controlled trials, reviews, and practice guidelines involving human subjects with the search terms (cocaine or psychostimulants or amphetamine or methamphetamine) and (health consequences or overdose or cardiac toxicity or HIV or HCV or pregnancy) published after 1990, resulting in 779 papers. After eliminating papers that were not relevant (such as animal studies or medical use of stimulants), there were 287 articles, of which 49 % referred to pregnancy, 21 % to infectious diseases, 10 % to cardiovascular disease, 5 % to neurologic disease, 5 % to other medical problems, 4 % to overdose. Several searches were replicated in World of Science and through university search engines but with few additional relevant papers identified, nor did including more specific search terms related to these topics. A number of articles were identified from authors' previous knowledge and included in the review. With regard to infectious disease, stimulant use and harm reduction, 196 articles were identified in English and French; after examining these articles and selecting a number of other articles, 91 references were included. Only a few peer reviewed publications addressed crack use and harm reduction, and most of these were grey. Mental health issues were investigated in a similar fashion, including a broad search, manual review of the publications, and inclusion of outside sources including published papers, reports, organisational materials, and other grey publications.

Adverse (health) consequences associated with use of stimulants

Key findings

Scientific literature is overwhelmingly weighted toward the harms of stimulants, with minimal literature on harm reduction interventions. Among the myriad of ill health effects associated with stimulants, some are mediated by mode of administration (such as infections, overdose, and pulmonary damage) while others are independent thereof (such as neurologic, cardiovascular and mental health problems). But the distinction between the two categories of stimulant-related harm is subtle and contingent on the broader risk environment. For example:

- Problem stimulant use is associated with poverty, unemployment, homelessness or unstable housing, lower socio-economic status, a variety of other social problems, as well as legal problems and incarceration.
- Adulterants and use of caustic chemicals in drug preparation are stipulated by market conditions beyond the control of individual users.
- Traditional harm reduction programmes may fail to reach problem stimulant users due to opiate-centred services and social barriers to young or female users.
- Innovative service development paired with critical evaluation is necessary in translating the successes of harm reduction for opiates to stimulants.
- There is an important and unmet need for services that enhance the ability of stimulant users to control their intake levels, chaotic behaviour and mental health problems, as well as limit pulmonary, cardiovascular and neurologic harms.
- Stimulant-related harms are aggravated by external factors, such as selected aspects of international drug legislation, policing and public policies in a process of 'contingent causality'.

The risks associated with stimulants include medical harms, such as infectious, cardiovascular, and neurologic and psychiatric morbidity, as well as risks to pregnancy, pulmonary and renal toxicity, overdose and other less common sequelae. Problem stimulant use is also associated with poverty, unemployment, homelessness or unstable housing, lower socio-economic status, a variety of other social problems, as well as legal problems and incarceration. Here we focus primarily on medical health consequences while briefly addressing mental health and other problems associated with stimulant use.

Blood-borne viruses

Transmission of blood-borne viruses is consistently associated with stimulant use (Mitchell et al., 2006), due primarily to high-frequency use and to increased risky sexual behaviors. HIV and hepatitis C (HCV) transmission among stimulant injectors has been associated with higher injecting frequency (Kral et al., 2001; Gibson et al., 2002) and needle sharing (Rotheram-Borus et al., 1999). Frequent cocaine injection is a factor in the failure of selected syringe exchange programmes to prevent HIV transmission (Wood et al., 2002). HCV rates are very high, even

among recent initiates to cocaine injection (Maher et al., 2007). In central and eastern Europe, home-produced stimulants such as methcathinone and cathinone are injected up to 10 times daily (Kozlov et al., 2006; Booth et al., 2008; Grund et al., 2009; Chintalova-Dallas et al., 2009) and are associated with increased sexual activity (Kozlov et al., 2006) as well as sharing of equipment in home drug preparation (Grund, 2001; Des Jarlais et al., 2002; Grund and Merkinaite, 2009; Balakireva et al., 2006). In comparison to heroin users, stimulant users are more likely to have unstable social situations, larger drug-using social networks, riskier injection practices (e.g. increased frequency, chaotic drug preparation, injecting in unstable settings) and increased sexual activity (De et al., 2007; Elkashef et al., 2008; Grund et al., 1991b; Kozlov et al., 2006; Chintalova-Dallas et al., 2009; Booth et al., 2008). HCV is also prevalent among non-injection stimulant users, with rates of 2.3–35.3 % among those who sniff or smoke stimulants (Scheinmann et al., 2007) and 2.3–81 % among crack smokers (Fischer et al., 2008; Jauffret-Roustide et al., 2008a; Tortu et al., 2001); many are unaware that they are infected (Roy et al., 2001; Kwiatkowski et al., 2002). Hepatitis B (HBV) infection has also been associated with injection and non-injection drug use (NIDU), although the availability of a vaccine has greatly reduced infection rates (Kottiri et al., 2005). Stimulant use is associated with infrequent condom use (Edlin et al., 1992), amphetamine use preceding sex (Koblin et al., 2006), risk behaviours among young gay men (Celentano et al., 2006), and trading sex for drugs or money (Serraino et al., 1991; Stevens et al., 1998; Tortu et al., 2000; Tortu et al., 2003).

Cocaine smoking is a distinct risk factor for blood-borne virus transmission (Pechansky et al., 2006; Haydon and Fischer, 2005; McCoy et al., 2004; Adimora et al., 2003; Edlin et al., 1994; Chiasson et al., 1991; Haverkos and Steel, 1991), even when adjusted for injection behaviour (Wolff et al., 2007; Osher et al., 2003; Nyamathi et al., 2002; Rosenblum et al., 2001; Roy et al., 2001; Jauffret-Roustide et al., 2006), primarily due to an association with risky sexual behaviour (Hagan et al., 2005; McCoy et al., 2004; Edlin et al., 1994; Lejuez et al., 2005; Campsmith et al., 2000; Gross et al., 2000; Perlman et al., 1999; Word and Bowser, 1997; Centers for Disease Control and Prevention, 1996; Seidman et al., 1994; Edlin et al., 1992), with HIV prevalence estimates from 7.5–23.0 % (Jauffret-Roustide et al., 2006; McCoy et al., 2004; Edlin et al., 1994; Kral et al., 1998; Gyarmathy et al., 2002). Sex work is more frequent among cocaine smokers compared to other drug users (Faruque et al., 1996; Edlin et al., 1994; Campsmith et al., 2000; Fischer et al., 2006; Mehrabadi et al., 2008) and women cocaine smokers are particularly vulnerable as they are exposed to multiple risks associated with both sexual and drug use behaviours, contingent on broader gender relations (Jauffret-Roustide et al., 2008b; Shannon et al., 2008; Maranda et al., 2004; Cotten-Oldenburg et al., 1999; Heffernan et al., 1996; McCoy and Miles, 1992; Balakireva et al., 2006). While sexual transmission of HIV among cocaine smokers is mainly through unprotected intercourse (Haverkos and Steel, 1991), other routes include oral sores and cracked lips from hot pipes in the setting of unprotected fellatio (Faruque et al., 1996; Theall et al., 2003). Recent studies of cocaine smoking and HCV transmission have noted the collective use of glass smoking utensils ('crack pipes' or 'stems') as a potential risk factor. HCV is present in gingival fluid (Suzuki et al., 2005), nasal secretions (McMahon et al., 2004), saliva (Hermida et al., 2002), and crack pipes (Fischer et al., 2008), the last of which are frequently made of glass, metal or other materials that can get extremely hot, have jagged edges, and may break between clenching jaws. Oral sores and burns on lips can result from using these pipes (Ward et al., 2000; Faruque et al., 1996; Porter and Bonilla, 1993) and

small blood droplets deposit on the stem of the pipe, possibly transmitting HCV to others with similar sores (Hagan et al., 2005). One study reported that up to 81 % of all cocaine smokers had shared their crack pipes in the previous month (Jauffret-Roustide et al., 2006).

Stimulant use may hasten progression of HIV disease, although data are conflicting. Cocaine use has been associated with poor anti-retroviral initiation and adherence (Brewer et al., 2007), complicated by the interaction of depression, particularly among women (Cook et al., 2007) whose crack use is strongly associated with poor outcomes of HIV disease (Cook et al., 2008). While current or past cocaine use is associated with less favorable laboratory parameters (T cell and viral load) among patients on HIV treatment, past amphetamine use is associated with more favorable parameters (Cofrancesco et al., 2008). Studies of HIV-positive and HIV-negative men who have sex with men demonstrate no change in T cell counts among subjects related to their use of cocaine or amphetamines (Chao et al., 2008), and studies among women showed no difference in CD4 count, viral load, or mortality (Thorpe et al., 2004). References are available to predict possible interactions of HIV medications with illicit drugs (Wynn et al., 2005), but the clinical implication of these interactions remains uncertain (Pal and Mitra, 2006). The hypothesis of a direct immunomodulatory effect of stimulants that could increase vulnerability to HIV and other infections remains unproven (Cabral, 2006).

Other infectious complications

Stimulants have been associated with increased incidence of many sexually transmitted diseases including syphilis, gonorrhea, and chancroid (Bauwens et al., 2002; Friedman et al., 2003; Ross et al., 1999; Ross et al., 2002; Sorvillo et al., 1998; Stoner et al., 2000; Thomas et al., 1996; Centers for Disease Control and Prevention, 1991 and 1993; Chirgwin et al., 1991; Finelli et al., 1993; Martin and DiCarlo, 1994; Oxman et al., 1996; Shuter et al., 1998; Williams and Ekundayo, 2001; Cleghorn et al., 1995), as well as various bacterial infections (Kerr et al., 2005) and tuberculosis (Malakmadze et al., 2005; McElroy et al., 2003). Cocaine use has been independently associated with human papillomavirus infection and progression to cervical lesions (Minkoff et al., 2008). Skin and soft tissue infections (SSTIs) affect 10–30 % of injecting drug users (IDUs) (Binswanger et al., 2000; Murphy et al., 2001; Ciccarone et al., 2001) and are associated with loss of venous access and reliance on intramuscular or subcutaneous injection (Ciccarone and Bourgeois, 2003; Lloyd-Smith et al., 2008; Binswanger et al., 2000). Injecting crack, vint or boltushka (home-made meth-cathinone) is particularly damaging to veins due to the uninformed and unskilled use of chemicals for preparation (Rhodes et al., 2006; Chintalova-Dallas et al., 2009). Jeff or boltushka is injected with large-bore needles that rapidly damage veins. The United Kingdom has recently seen a rise in groin injection, with an estimated 45 % of IDUs in English cities recently injecting into the femoral vein (Maliphant and Scott, 2005; Rhodes et al., 2006). Groin injection has been associated with public use of crack and speedballs and is now common among new initiates and housed IDUs, not just older and homeless users with no other venous access, suggesting a shift from 'risk boundary' to 'acceptable risk' (Rhodes et al., 2006; Rhodes et al., 2007). Cocaine injectors, including women, those with unstable housing, and those who require help injecting, are independently more likely to have SSTIs (Lloyd-Smith et al., 2008).

Shooting Jeff (homemade methcatinone), Pskov, Russia, 1999

Source: J-P. Grund.

Stimulants are also associated with skin lesions resulting from excessive scratching or picking. Most lesions are not due to delusions, apart from 'Coke Bugs' or 'Meth Mites', which result from the sensation that insects are crawling on or under the skin or that the drug is coming out of the skin. These are hallucinations from prolonged stimulant use and resulting sleep deprivation (Frieden, 2006; Beek et al., 2001; Lee, 2008). Known as delusional parasitosis, this behaviour is associated with MRSA, streptococcal, and polymicrobial SSTIs (Hinkle and Nancy, 2000; Frieden, 2006; Beek et al., 2001; Cohen et al., 2007). Other self-mutilation behaviours observed by outreach workers in Frankfurt include 'working on wounds with giant knives' (primarily males), cutting (primarily females), cigarette burns and excessive fingernail-biting (both sexes) (personal email communication, M. Nickolai, 30 September 2009).

Neurologic effects

Cocaine induces plasticity in the dopaminergic system largely responsible for drug craving, yet the principal neurologic effects of cocaine are related to its cardiovascular effects: strokes, hemorrhages and blood clots. Persistent vasoconstriction may lead to reduced brain perfusion and associated cognitive deficits that may or may not resolve with abstinence (Nnadi et al., 2005). Heavy methamphetamine use also induces dopaminergic plasticity, as well as reduced dopaminergic activity and neuropsychiatric deficits in memory, attention, and executive function (Ferris et al., 2008). Alterations in

brain structure and chemistry have been convincingly documented in heavy users of methamphetamine although the clinical implications of these data remain uncertain (Chang et al., 2007). Numerous studies of long-term prescribed amphetamines have failed to demonstrate lasting psychiatric or neurologic deficits, although few are of high quality (Vitiello, 2001). In Central and Eastern Europe, chemical residues of home stimulant production (including potassium permanganate, gasoline, toluene or tetrachlorethylene, sodium hydroxide, or hydrochloric acid) (Grund and Merkinaite, 2009) may have toxic effects and local clinicans have reported 'amphetamine-induced movement disorder' (see e.g. Downes and Whyte, 2005) and declines in cognitive function and memory similar to dementia (Volik, 2008; Chintalova-Dallas et al., 2009). Pseudoephedrine restrictions in the region may have resulted in use of more hazardous precursors such as phenylpropanolamine, associated with hemmorrhagic stroke (Horwitz et al., 2000), in production of cathinone (Chintalova-Dallas et al., 2009). In the setting of HIV, stimulants have been associated with more rapid progression of cognitive decline and recent data suggest that stimulants may contribute to HIV-related neuron cell death, particularly within the dopaminergic (Ferris et al., 2008) and hippocampal (Venkatesan et al., 2007) systems (Goodkin et al., 1998; Basso and Bornstein, 2000; Nath et al., 2002; Cadet and Krasnova, 2007; Ferris et al., 2008).

Cardiovascular effects

Cardiovascular toxicities of cocaine are well-established (Vandhuick et al., 2004). Cocaine results in adrenergic activation through effects on norepinephrine and clot formation through activation of platelets, resulting in increased cardiac oxygen demand, coronary artery spasm, and coronary artery thrombosis. 'Cocaine chest pain' is usually not a sign of cardiac ischemia, yet cocaine also increases the risk of true myocardial infarction, aortic dissection, coronary artery dissection, cardiomyopathy, and sudden cardiac death (Steinhauer and Caulfield, 2001; McCord et al., 2008). Injection of any drug is associated with endocarditis (Guerot et al., 2002). Cocaine-induced tachycardia and hypertension play a role in many of these sequelae (Tuncel et al., 2002), accounted for in part by direct reduction in vagal tone (Newlin et al., 2000). Injected cocaine causes a dose-dependent prolongation of the QT segment of the cardiac cycle, raising the risk of potentially fatal arrhythmias (Haigney et al., 2006), particularly among those with genetic predispositions for QT prolongation (Karch, 2005). Overdose of cocaine can result in fatal monomorphic ventricular tachycardia by blocking sodium channels (Bauman and DiDomenico, 2002). Dilated cardiomyopathy may be related to direct toxicity of cocaine through increased programmed death of heart muscle cells (Zhang et al., 1999). Furthermore, prolonged cocaine use accelerates atherosclerosis (Kloner et al., 1992) and accumulation of metabolites in cardiac tissue may have further detrimental effects (Schindler et al., 1995). Clinicians are reluctant to use beta blockers, a key agent in heart disease, to manage cocaine-related disease due to fear of producing unopposed activation of other adrenergic receptors with cocaine (Afonso et al., 2007). Use of alcohol and cocaine together leads to production of cocaethylene, which is believed to increase the cardiotoxic effects of both drugs (Kertesz et al., 2007), increases the tachycardia produced by cocaine, and may increase the tendency toward violent thoughts and threats (Farre et al.,

1997; Pennings et al., 2002). Amphetamines produce substantial increases in blood pressure and heart rate, more marked when the drugs are injected and somewhat buffered among those who also use marijuana (Fleury et al., 2008). Use of ecstasy, amphetamine, and cocaine in a club setting did not result in any excess body temperature compared to use of alcohol and/or cannabis alone; those drugs did, however, result in a relative increase in blood pressure (increase of 40mm Hg systolic) and heart rate (increase of 30 beats/minute) (Mas et al., 1999), perpetuating concerns about possible cardiovascular toxicities (Cole et al., 2005).

Pulmonary and other health effects

Novel interventions: reinventing the 'micro' risk environment

Interventions aimed at reducing harms of cocaine use focus on BBVs and thus on the micro risk environment of drug consumption, providing utensils and practical information for safer use.

Crack kit programmes offer kits that generally include a Pyrex tube, plastic tips, filters, condoms, lip balm, sterile compresses and chewing gum for salivation (Aidslaw, 2007). An evaluation of crack kit distribution in Ottawa (Leonard et al., 2006; Leonard et al., 2007) suggested that sharing of crack pipes decreased dramatically, while crack users reduced injecting and more often smoked cocaine. The Dutch Mainline Foundation offers cocaine information in flyers, on the Internet and on the streets, including a van-based 'health circuit' for cocaine smokers (Boekhout van Solinge, 2001) to check their lung capacity, blood pressure and heart rate. The van is supervised by a trained nurse, providing participatory interaction in which pulmonary and mental health harm reduction and self-regulation strategies are discussed through motivational interviewing techniques (Wittenberg, 2005). Mainline's website and flyers emphasise practical information for managing health risks and controlling cocaine use, including tips for managing coke bugs, the coke shuffle and the urge to scratch (e.g. http://www.cocaineinfo.nl/).

Crack kits are controversial and rarely funded. In Canada and some US cities, crack kits are distributed with regional funding (Small and Drucker, 2008), but some have closed after local opposition (Symington, 2007). At the same time, France is improving access to crack kits (Jauffret-Roustide et al., 2008a) with plans for community-based evaluations. Recent technological developments such as personal vaporisers, similar to E-cigarettes for tobacco smokers, might offer additional opportunities to reduce pulmonary and other bodily harm, as vaporisation and filtering could reduce the amount of combustion products inhaled while offering an acceptable alternative to crack pipes and perhaps even syringes.

Nonetheless, reactive harm reduction measures focused at the micro risk environment of cocaine use do little to mediate the influences in the drug's macro risk environment, upon which risk behaviour and drug related harms are contingent (Rhodes, 2009). This review identifies an important need to apply harm reduction thinking in proactive policymaking towards changing the 'contingent causation' of problem stimulant use with unhealthy drug and social policies and those that influence the public domain.

The most notable pulmonary complication of smoked cocaine, referred to as 'crack lung', is difficult to differentiate from several other associated and life-threatening restrictive, granulomatous, infectious, and hematologic pulmonary diseases and frequently requires open-lung biopsy to diagnose (Terra Filho et al., 2004; Wolff and O'Donnell, 2004). The vasoconstrictor effect of smoked cocaine can also lead to pulmonary hypertension with chronic use (Glauser and Queen, 2007). Asthma exacerbations and eosinophilic pneumonias are also described in relation to inhaled stimulants (Mayaud et al., 2001). Intranasal cocaine use is clearly associated with septal necrosis and perforation (Glauser and Queen, 2007). Use of tobacco is thought to worsen pulmonary outcomes among stimulant smokers or injectors (Wolff and O'Donnell, 2004).

Amphetamine use has been associated with dental disease, although there is dispute as to the degree of destruction that is related to direct toxicity versus diet and personal hygiene (Chi and Milgrom, 2008; Heng et al., 2008). Renal diseases related to stimulants include glomerulonephritites, largely believed to be associated with IDU and contaminants, and tubulointerstitial processes resulting from vasoconstrictive properties in the setting of pre-existing mild renal disease (Crowe et al., 2000; Jaffe and Kimmel, 2006). Uncommon complications include renal infarction and rhabdomyolisis. Concerns with ecstasy use include hyperthermia and rhabdomyolisis with associated renal failure (Hedetoft and Christensen, 1999). Fear of dehydration has led to consumption of large quantities of water that, in individuals without appropriate regulation of antidiuretic hormone, may lead to dilutional hyponatremia and, rarely, death (Crowe et al., 2000). Urinary retention due to bladder neck closure has also been associated with ecstasy use (Crowe et al., 2000). Gastroschesis, or slowed gastric processing of food, has been associated with use of stimulants (Draper et al., 2008), and cocaine use has been associated with intestinal ischemia, likely due to both vasoconstrictor and pro-thrombogenic effects (Glauser and Queen, 2007).

Overdose

Opioids remain the source of most overdose deaths globally, yet in regions such as New York City (Coffin et al., 2003) and Sao Paolo, Brazil (Mesquita et al., 2001), the high prevalence of cocaine use contributes, often in conjunction with opioids, to the majority of overdose deaths. Among cocaine body-packers, overdose can result from the rupture of a container and requires immediate laparotomy for chance of survival (Schaper et al., 2007). Extreme overdose on stimulants can result in profound hyperthermia, with subsequent risks for rhabdomyolisis, seizures, and death (Callaway and Clark, 1994). Overdose on ecstasy without concomitant use of other drugs is notably rare and difficult to define, but may be related to seritonin syndrome (see 'Neurologic effects') (Schifano, 2004). In a survey of all amphetamine-related deaths in Belgium, cardiopulmonary arrest and trauma were the most common direct causes of death, and drug metabolite levels were notably variable (De Letter et al., 2006). Cocaine use is intimately associated with opioid overdose, with combined use of the two drugs substantially increasing the risk of both nonfatal and fatal overdose (Ochoa et al., 2005; Coffin et al., 2003; Coffin et al., 2007). Furthermore, while overdose on opioids is far more likely among IDUs, the rates are closer among injection and non-injection cocaine users (Kaye and Darke, 2004).

Pregnancy and parenting

Stimulant use during pregnancy and parenting has been a major concern, particularly in the United States where fears about a future generation of 'crack babies' inspired legislation and prosecutions against women for stimulant use, marijuana use, or any acts that might be considered risky during pregnancy (Harris and Paltrow, 2003). Risk factors for bad outcomes among drug-using pregnant women include lack of prenatal care, prior premature delivery, and active cigarette smoking (Kuczkowski, 2007; Ness et al., 1999). Cocaine use during pregnancy is more likely than opiates, tobacco, and marijuana to be associated with fetal growth decrements (Schempf, 2007), and is associated with abruptio placenta and premature rupture of membranes; other concerns such as spontaneous abortion, preterm labour, behavioural or developmental disabilities, feeding disturbances, or withdrawal syndromes were confounded by other variables and often better attributed to maternal poverty (Addis et al., 2001). Developmental effects, based on studies utilising vast arrays of tools in an effort to elucidate decrements, remain in doubt by some investigators (Frank et al., 2001), are at most subtle with unclear clinical significance (Lester et al., 2003) and are mediated with educational programmes (Schiller and Allen, 2005). Childhood psychiatric correlates are mediated by psychosocial factors and diminish as children age (Williams and Ross, 2007). There is no risk of direct toxicity to a pregnancy at the time of conception from male cocaine use (Klemmt and Scialli, 2005). A thorough 2005 review of amphetamines and pregnancy found insufficient evidence to evaluate the developmental toxicity of therapeutic amphetamines, with two underpowered cohort studies showing no effect (Golub et al., 2005). Amphetamines have been associated with a 3.5 fold increased risk of fetal growth restriction, while tobacco use had a twofold increased risk (Smith et al., 2006). Early research has demonstrated an association between amphetamine-using mothers and poor perceived quality of life, increased substance use among family and friends, as well as ongoing legal problems (Derauf et al., 2007).

Mental health and social problems

High levels of psychiatric and social comorbidities, in addition to dependence and addiction, are found among chronic stimulant users (Hall et al., 1996; Baker et al., 2004; Darke et al., 2008; Sutcliffe et al., 2009). Chronic amphetamine use is associated with psychosis, usually transient during use or withdrawal but occasionally occuring for several years after discontinuation (Scott et al., 2007). Pre-existing psychotic symptoms can be greatly exacerbated by amphetamine initiation (Hall et al., 1996; Suttcliffe et al., 2009). Stimulant use is also associated with suicide, suicidal ideation, depression, post-traumatic stress disorder, and several personality disorders (Kertesz et al., 2006; Scott et al., 2007). Methamphetamine use has been associated with anti-social personality disorder as well as mania and bipolar mood disorder (Chen et al., 2003). Although methamphetamine has been associated with impulsive or violent behavior, no causal relationship has ever been established (Scott et al., 2007). Compared to cocaine, crack use is associated with higher levels of anxiety, depression paranoia, and psychosis, likely due to intensity of use, physical health, and concurrent social situation rather than route of administration per se (Haasen, 2005). There is a strong association between amphetamine use and attention-deficit hyperactivity disorder (ADHD), which is treated with

amphetamine-type medications, leading some investigators to suspect that indviduals with ADHD are drawn to amphetamine use (Jaffe et al., 2005; Scott et al., 2007).

Problem use of stimulants is also associated with social and family problems, including poor interpersonal relationships, child abuse or neglect, job loss, motor vehicle accidents, trading sex for money or drugs, criminal or violent behaviour and homicide (Daley et al., 2002), although convincing causal relationships have not been established. Problem stimulant users are more likely to be unemployed and experience poor coping skills, limited social support, and disorganised lifestyles (Scott et al., 2007), which may play a central role in behavioural problems. Furthermore, the criminal and stigmatised nature of stimulant use, while possibly deterring wider use, serves as a barrier for problem users to participate in productive society (Grabowski et al., 2004).

Harm reduction for stimulant users

Are stimulants too fast and too furious for harm reduction? A relatively new focus for harm reduction programmers, stimulants require rethinking many traditional strategies. Here we discuss the evidence for, and emerging interventions in, harm reduction for stimulant users. We start with a brief review of behavioural and pharmacologic treatment interventions for stimulant dependence and then focus on the stimulant-specific harms discussed in the previous section.

Behavioural and pharmacologic interventions for stimulant users

Challenges for harm reduction for stimulant users

Harm reduction for problem stimulant users is both crucial and feasible, but requires consideration of the unique characteristics of stimulant use. There are many obstacles, including:

- Frequent cocaine injection is a factor in the failure of selected syringe exchange programmes to prevent HIV transmission and in low treatment success and retention.
- Local studies among IDUs in English cities show show that up to 45 % report recent injecting into the femoral vein.
- Cocaine smoking is a growing risk factor for blood-borne virus transmission, due to associations with risky sex and collective use of smoking utensils.
- Female users are exposed to multiple risks associated with both sexual and drug use behaviours, which are contingent on broader gender relations.
- Despite shifts toward smoking drugs in many EU countries, public health efforts remain almost exclusively focused on IDUs.

Independent of mode of administration, stimulant and other drug users must enjoy the fundamental human right to health protection, as stipulated by Article 25 of the Universal Declaration of Human Rights.

Generally, the primary goal of treatment is viewed as inducing abstinence and preventing relapse ('cure'). If abstinence is not (yet) feasible, treatment should aim at reducing or at least stabilising substance use and its consequences ('care'). The ultimate stage of treatment should be lenitive and aim at alleviating suffering ('palliation'). At all stages, crisis intervention, treatment of intoxication and withdrawal, and improving health, psychological and social functioning are self-evident (Health Council of the Netherlands, 2002).

The first line of treatment for problem stimulant use is outpatient psychosocial intervention (American Psychiatric Association, 2007), most notably cognitive behaviour therapy (CBT), contingency management (CM) (Dutra et al., 2008), and motivational interviewing (MI) (Shearer, 2007; EMCDDA, 2007e). In CM a well-described target behaviour (e.g., medication compliance, clinic attendance, stimulant use abstinence, or any other verifiable behaviour) is rewarded whenever the behaviour is demonstrated (Dutra et al., 2008). CM is most effective when cash (as opposed to vouchers) and higher-value incentives are used, and although the effects diminish after the intervention is discontinued, effects of incentives have been demonstrated for up to 12 months thereafter (Lussier et al., 2006; Prendergast et al., 2006).

There is no proven effective pharmacological treatment for cocaine and stimulant use, in spite of the large number of studies on a broad array of pharmaceuticals (for reviews, see: De Lima et al., 2002; EMCDDA, 2007e; Pirona and Hedrich, 2009). More recently, the Cocaine Rapid Efficacy Screening Trial (CREST) tested 19 medications, of which three potentially effective compounds (cabergoline, reserpine and tiagabine) were moved forward to be tested in larger, confirmatory trials (Leiderman, 2005; Kampman et al., 2005). However, in recent larger trials neither tiagabine (Winhusen et al., 2007a) nor reserpine (Winhusen et al., 2007b) were effective in reducing cocaine use compared to placebo. Another approach is to develop a vaccine to prevent cocaine from crossing the blood–brain barrier; the current vaccine needs improvement (Martell et al., 2009) and there are many ethical issues to be addressed even once a vaccine has shown to be effective (see e.g. Hall and Carter, 2004).

More recently, there is growing interest in shifting the focus from abstinence to 'substitution treatment', based on the effectiveness of replacement therapy for nicotine and opiate dependence (Moeller et al., 2008; Shearer, 2008). The rationale for substitution treatment is to replace harmful stimulant drug use 'with safer, licit pharmaceutical drugs, avoiding contaminants and risks associated with hazardous routes of administration, such as injecting (blood-borne viral infections, overdose)' (Shearer, 2008, pp. 302–03). Ultimately, substitution treatment should result in a stabilisation of illicit drug use, thereby enabling the stimulant drug user to benefit from additional psychosocial interventions. Although the evidence to date for substitution treatment of stimulant use is scant (De Lima et al., 2002; Castells et al., 2007), dexamphetamine (SR) and modafinil seem promising candidates for further study. Llosa (1994) and Hurtado-Gumucio (2000) have also documented in non-controlled studies that coca tea, coca leaves and cocaine tablets could be effective in terms of craving, cocaine use and social functioning.

Interventions aimed at reducing adverse (health) consequences associated with stimulant use

Blood-borne viruses

Harm reduction for stimulant injectors relies heavily on the evidence for HIV prevention among heroin injectors (see e.g. Kimber et al., 2010), but demands consideration of the unique setting of stimulant injection. In particular, stimulant injection involves more frequent injection, increased sexual risk behaviours, chaotic injecting behaviour, home production, younger ages and more frequent treatment utilisation. Stimulant injectors should have easy access to large volumes of sterile injection equipment and means of sexual protection, requiring liberal exchange and distribution policies, extended opening hours and, where needed, outreach activities in injecting and sexual risk environments (Beek et al., 2001; Des Jarlais et al., 2009). Proper injection kits should include a range of materials based on local assessment of drug use patterns and the social situation of injectors. One-for-one syringe exchange policies, still in place in various needle and syringe programmes (NSPs) in the EU and Eastern Europe, should be avoided due to the high frequency of stimulant injection.

Harm reduction materials

Collage: Jean-Paul Grund. Source images: Exchange Supplies.

Harm reduction kits for injecting drug users may include needles and syringes, disinfectants, alcohol pads, ascorbic or citric acid, filters, single-use cookers, plasters and antibiotic ointments, as well as educational materials. Sometimes other specific (e.g. for home preparation in CEE) or generic (such as vitamins or food) items are included as well.

Longer opening hours for NSPs and liberal exchange policies, political activism and public funding are associated with higher coverage of IDU populations and lower rates of risk behaviour (Templaski et al., 2008; Bluthenthal et al., 2007a; Bluthenthal et al., 2007b). Increased coverage was followed by substantial reductions in HIV prevalence and incidence among IDUs in the United States (Santibanez et al., 2006). Exchange Supplies in the United Kingdom offers syringes with coloured plungers and 'syringe-IDs' (a little colour- and pattern-marked clip for the back of the plunger), developed to allow stimulant injectors in particular to distinguish their personal syringe when injecting collectively (see illustration above).

In response to home-made stimulants, some NSPs in Eastern Europe offer syringes both for injecting and for preparing drugs (Grund and Merkinaite, 2009). Harm reduction networks in Georgia, Russia and Ukraine are developing interventions and information materials for home-made stimulant users. Distributing litmus paper to home-made stimulant users to allow production of less acidic drugs has been proposed but not yet implemented (Agafonova, 2008).

Traditional harm reduction programmes may fail to reach problem stimulant users due to opiate-centered services and social barriers to young or female users (see e.g. Grund and Merkinaite, 2009). Outreach, secondary exchange, or peer-driven strategies are needed to reach those not attending established service programmes (Needle et al., 2005; Coyle et al., 1998; Des Jarlais et al., 2009; Wood et al., 2003; Grund et al., 1992a; Broadhead et al., 1998). An unsanctioned peer-based and all-night NSP, located on the street in Vancouver's open drug scene, was able to reach and deliver harm reduction services to the city's most at risk cocaine injectors (Wood et al., 2003). Syringe dispensing machines (SDMs) and mobile NSPs provide confidential access to sterile equipment at times and places where coverage is poor (Islam and Conigrave, 2007), to younger users (Moatti et al., 2001; Obadia et al., 1999) with shorter injection histories than NSP or pharmacy users, less drug dependence, less access to established services (Stark et al., 1994; Leicht, 1993), less licit income, and lower socioeconomic status (Moatti et al., 2001). Patrons of mobile outlets are likely to be younger, indigenous and female, inject more frequently and do so more often on the street, be engaged in sex work and not be in drug treatment (Miller et al., 2002; Riley et al., 2000; Islam and Conigrave, 2007). SDMs are not advised as stand-alone interventions as there is little chance for health education, but they can serve as strategic adjuncts to conventional NSPs and pharmacy distribution (Islam and Conigrave, 2007; Agnoletto et al., 1993; Cox et al., 2000).

Despite shifts towards smoking drugs in many EU countries, public health efforts remain almost exclusively focused on IDU (Jauffret-Roustide, 2004; Jauffret-Roustide et al., 2008a; Haydon and Fischer, 2005; Cheung, 2000). Canada and several US programmes have implemented specific programmes for cocaine smokers (Boyd et al., 2008; Leonard et al., 2006; Leonard et al., 2007), such as the distribution of so-called 'crack kits', containing supplies to prevent oral or respiratory lesions from smoking (Porter and Bonilla, 1993; Malchy et al., 2008; Collins et al., 2005). Studies of the out-of-treatment cocaine and heroin users suggest that the principles and evidence base of needle exchange (Wodak and Cooney, 2005; Hunt et al., 2003; Hunt et al., 2005; WHO, 2005; WHO et al. and UNODC, 2004) may apply to crack kits or other drug use utensils as well (Grund, 1991a; Grund, 1993; Pizzey and Hunt, 2008).

Although many supervised drug consumption facilities prohibit injected or smoked cocaine due to the chaotic and frenetic nature of use, several supervised injection facilities (SIFs) in the EU now include rooms for smoking cocaine and other drugs (Hunt, 2006), a trend that may extend to Vancouver's SIF (Shannon et al., 2006). Managing a smoking room has proven similar to an injection room; SIFs that do allow cocaine use have not reported major problems (Poschadel et al., 2002; Verthein et al., 2001; Zurhold et al., 2001; Zurhold et al., 2003; Vogt and Zeissler, 2005; Broadhead et al., 2002; Poel, et al., 2003; Hedrich, 2004; IWGDCR, 2006). Programmes targeting smokers should emphasise women through gender-sensitive programmes that have been developed, although few of these have been evaluated (Boyd et al., 2008; Wechsberg et al., 2004; Butters and Erickson, 2003). Programming for women may work better when biological, behavioural, psychological and social characteristics of women are considered and individual and community support measures combined (Latka, 2003), supporting increased autonomy of women over their drug use and sexuality to minimise exposure to BBVs (Jauffret-Roustide et al., 2008b; Gollub, 2008).

Sexually transmitted diseases, bacterial infections and other complications

Ample supply of injection and sexual protection supplies may also contribute to reducing sexually transmitted diseases (STDs) and bacterial infections (Beek et al., 2001; Kerr et al., 2005). Proper injection techniques, antibacterial creams and ointments and rotation of injection sites may help reduce vein loss and effectively treat minor SSTIs (Stern, 1992). Basic hygiene (hand washing, short nails) and vein care as well as simple wound care and training in safer injection may prevent infections in cocaine injectors (Beek et al., 2001; Kerr et al., 2005; Rhodes et al., 2007). Wound and abscess services within NSPs may increase patient–clinician interactions, providing opportunities for referrals to services such as HIV counseling and testing, medical care, and drug treatment at an estimated cost of $5 per patient (Grau et al., 2002). There is no consensus on whether groin injection should be actively discouraged or safer techniques provided (as in the United Kingdom; Maliphant and Scott, 2005; Zador, 2007; Strang et al., 2008), although investigators agree that transitions to groin injection or crack injection should be discouraged (Rhodes et al., 2007).

Neurologic effects

Efforts to reduce the neurologic sequelae of stimulants are primarily related to the use of 'club drugs'. Reducing frequency of use is the most common strategy for reducing the delayed 'comedown' of stimulants, depression, and concerns about neurologic damage (Allott and Redman, 2006). 'Pre-loading' or 'post-loading' with a variety of substances is another approach, involving vitamins, foods, antidepressant medications, sleeping tablets, or amino acids. While there are no data evaluating the effect of these common methods (Kelly, 2009), a combination of amphetamines and most anti-depressant medications poses the risk of a life-threatening reaction known as serotonin syndrome (Copeland et al., 2006). A Dutch website (http://www.cocaineinfo.nl/) provides neurological explanations for the 'Coke Shuffle', advising temporary cessation of use, massage, a warm environment or a visit to the sauna, as this might help to reduce cramps. Sometimes benzodiazepines are prescribed to problem cocaine users, mostly for sleep, but these may also alleviate joint and muscle pains.

Cardiovascular effects

Routine cardiovascular care, involving diet and exercise, management of high blood pressure and cholesterol, as well as reducing other risk factors such as tobacco use, are likely to be the most powerful harm reduction strategies, as they are for the general population. Reducing dosage and frequency of all stimulant use may reduce cardiovascular toxicities, as may reducing concomitant alcohol consumption. Although no controlled studies or specific interventions have been conducted, patients maintained on amphetamines (Vitiello, 2008) and Andean users of low-potency coca products (Knuepfer, 2003) are believed to be at only mild to moderately increased risk of cardiovascular toxicities. As cocaine is directly toxic to heart muscle cells while amphetamines exert toxicity primarily through blood pressure elevation, reducing or discontinuing use with onset of the cardiovascular disease that comes with age is paramount to reducing the harm of these drugs.

Pulmonary and other health effects

While marijuana can be filtered for some reduction in exposure to particulate matter (McPartland and Pruitt, 1997), filtering stimulant drugs is less likely to reduce the impact of these drugs on pulmonary tissue. Nonetheless, providing filters may reduce oropharyngeal exposure to hot embers, thus reducing burns to the mouth and throat. Harm reduction providers in Canada, and the United States offer 'crack kits' that include Pyrex pipes or rubber mouthpieces (Leonard et al., 2006; Leonard et al., 2007; Aidslaw, 2007), which may reduce lacerations to the lips. Mainline in Amsterdam offered street cocaine smokers lung, blood and heart measurements, safer smoking advice and self-regulation training (Boekhout van Solinge, 2001), but roll-out of the methodology in mainstream drug services proved challenging (Bruin et al., 2008). Other strategies to reduce pulmonary damage could include vaporisation and other means to filter out talc and other particles. Sufficient hydration contributes to lip, skin and other organ health. The frequency of pneumonia might be mitigated by pneumococcal vaccination and tuberculosis prevention, diagnosis and treatment.

The American Dental Association has developed a patient folder on 'meth mouth,' that includes drug treatment locators, a guide for parents and 'a calculator to figure out how much it costs to support a drug habit' (American Dental Association, 2005), but provides no advice on oral hygiene. Drug users in Amsterdam can get dental care at a special clinic and referrals to regular dentists. In Frankfurt in the 1990s, the Integrative Drogenhilfe was reportedly successful in finding IDUs dentists in the community using case management and advocacy strategies, as part of a 'Vermittlung in die Normalität' philosophy towards all their clients' health, social and legal problems (personal communication Marion Nickolai, 15 August 2009).

Overdose

Cocaine overdose is frequently cardiovascular (i.e. heart attack, fatal arrhythmia, or stroke) and demands rapid and sophisticated medical management. Concomitant use of opioids, alcohol or other depressant drugs is closely associated with cocaine overdose (Kaye and Darke, 2004), suggesting that limiting other drug use while using cocaine may reduce the risk

of overdose. Cardiopulmonary resuscitation delivered by bystanders has been demonstrated to improve outcomes in opioid overdose (Dietze et al., 2002) and may translate to stimulant overdoses. Naloxone will not reverse a stimulant overdose, therefore ensuring rapid access to nonjudgmental medical care without police intervention is essential to reducing fatalities.

Mental health problems

Many mental health problems associated with stimulant use are dose, frequency and mode of administration related, and might be mitigated by specific harm reduction measures. Care providers should use a sensitive, respectful approach toward stimulant users, even when chaotic, and treat people with signs of drug toxicity, such as cocaine-induced psychosis (Beek et al., 2001). Brief interventions among recreational amphetamine users should include information about potential mental health problems arising from regular use (Baker et al., 2004) and more than weekly use or injection should be discouraged (Hall et al., 1996). A randomised-controlled trial of Assertive Community Treatment for chronic crack users in Rotterdam found good programme compliance and improvements in physical and mental health (Henskens, 2004).

Cessation of cocaine injecting or smoking may be necessary for recovery from cocaine-related mental health morbidity (Beek et al., 2001), but self-regulation to control use may also prove helpful (Prinzleve et al., 2002; Haasen et al., 2005; Cramer and Schippers, 1994/1996). Stimulant users often self-medicate with heroin or other downers to control side-effects of anxiety and irritability (Grund, 1993; Decorte, 2001). Acupuncture, while of little use as monotherapy, may reduce cocaine craving when provided as an adjunct treatment (Gates et al., 2006; Kim et al., 2005) and the service may retain users in care (NTA, 2002). In New York, the Lower East Side Harm Reduction Center offers acupuncture, Reiki and other alternative treatments to cocaine users (personal communication Raquel Algarin, 23 November 2009).

Other practical suggestions for dealing with the behavioural peculiarities include immediate and flexible walk-in services (Haasen et al., 2003, Beek et al., 2001) and offering a calming, tranquil environment (Stöver, 2002), similar to 'chill-out' rooms at dance parties. 'Tagesruheräume', or daytime rest rooms, for cocaine injectors and crack smokers have been established in Frankfurt am Main and integrated within a low-threshold drug help centre, which offers counselling, medical and psychiatric care, a consumption room and a shelter in Hamburg (Vogt et al., 2000; Stöver, 2001; Verthein et al., 2001). Organisations such as HIT in Liverpool, Lifeline in Manchester and Mainline in Amsterdam have developed several explicit flyers for cocaine users with tips for managing mental health risks and controlling use of cocaine. While a focus of many programmes, approaches developed for stimulant users are rarely published in the scientific literature.

Pregnancy and parenting

An ethnographic evaluation of drug-using pregnant women demonstrated numerous self-employed harm reduction strategies, such as use of less dangerous substances (e.g. marijuana), reduced dose and frequency, and improved diet and self-care, as well as less helpful strategies like avoiding medical care for fear of stigma or prosecution (Kearney et al.,

1995; Murphy and Rosenbaum, 1999). Long-term outcome data on early intervention programmes for cocaine-exposed children suggest that the impact of poverty far overshadows that of cocaine, and that early intervention can improve developmental outcomes (Kilbride et al., 2000). Furthermore, among cocaine-exposed children who do not receive early interventions, remaining with their birth mothers may result in improved social interactions (Kilbride et al., 2006). Substantial harm reduction efforts around stimulants and pregnancy in North America have been legal defense and policy reform to reduce the criminalisation of women's behaviour during pregnancy (Lester et al., 2004).

Discussion

Appraisal of the quality of evidence reviewed and limitations of the study

Research has established the rationale for many harm reduction interventions for stimulant users (Wodak and Cooney, 2005; Farrell et al., 2005; Hunt et al., 2003; Hunt et al., 2005; WHO et al., 2004). Nonetheless, scientific literature is overwhelmingly weighted toward the harms of stimulants, with minimal literature on harm reduction interventions. Investigations frequently consider stimulants users a subset, rather than the target population of a study. Several interventions for stimulant users, such as providing materials for safer crack smoking or safer groin injection training, remain controversial or illegal and thus systematic evaluations are lacking. Funding mechanisms for evaluating new interventions are also limited, partly due to the reliance of most investigators on HIV funding streams.

Potential harms addressed by harm reduction interventions

The effectiveness of pharmacological and psychosocial interventions for stimulant users is limited (De Lima et al., 2002; EMCDDA, 2007e; Pirona and Hedrich, 2009), thus interventions to stabilise and minimise the negative consequences of ongoing stimulant use are of paramount importance. The evidence suggests that there are no fundamental challenges in adjusting regular harm reduction interventions, such as NSPs and SIFs, towards BBV prevention among problem stimulant users. However, a wide range of health and social problems associated with stimulant use are largely unaddressed by current services (e.g. specific harm reduction approaches to SSTIs have been developed but are not widely implemented (Grau et al., 2002; Kerr et al., 2005)).

Prevention of SSTIs, overdose or pulmonary, neurologic, or cardiovascular damage is a relatively new focus in harm reduction and there is much ground to be gained in prevention and early treatment of these conditions. 'Crack kits' may prove useful in preventing certain infections. Widely available SSTI, and cardiac primary care services, may lessen the burden of disease. The rapidly expanding literature on overdose prevention programming (Sporer and Kral, 2007; Maxwell et al., 2006; Coffin et al., 2007; Coffin, 2008) suggests a need to extend the harm reduction philosophy even further. Innovative service development paired with critical evaluation is necessary in translating the successes of harm reduction towards heroin to stimulant use.

Community-based research, programme evaluations and best practice examples underscore the need for services that enhance the ability of stimulant users to manage their intake levels, chaotic behaviour and mental health problems. Several harm reduction programmes informally aid stimulant users in money management, at times even holding clients' benefit cheques until after a binge. At hundreds, if not thousands, of blogs and Internet discussion lists, users discuss stimulant and other drug use openly and in detail, including many of the harms discussed in this review, dietary advice and 'street pharmacology' approaches to self-regulation (e.g. 'Harm Reduction for Stimulants', http://www.drugs-forum.com/forum/archive/index.php/t-24802.html).

Rhodes and colleagues reported what could be termed an epidemic of groin injecting. When groin injection becomes an 'acceptable risk' (Rhodes et al., 2006), one wonders what other risks have pushed the normalisation of this hazardous behaviour down the injector's 'hierarchy of risk' (Connors, 1992). Rhodes and colleagues not only point towards increasing crack/speedball injection in their explanation, they also emphasise the changing 'risk environment' of drug injecting (Rhodes, 2002). Groin injection is reportedly viewed as 'reliable, speedy, and discreet'. As one of their respondents explained, 'you can do it under a camera' (Rhodes et al., 2006). The omnipresence of camera and human surveillance, zero tolerance towards deviance in the public space and the resulting lack of spaces where homeless IDUs could withdraw to inject in British (and other) cities can thus be seen to engender a risk environment in which 'macro risk factors' synergise the risks of crack injection towards aggravating injecting-related harm (Rhodes, 2002; Rhodes et al., 2006; Rhodes, 2009). Such environmental factors are mostly beyond the scope of harm reduction interventions, which focus primarily on the substance and its users. Nonetheless, in the early 1980s, when cocaine landed in the urban heroin scenes of the Netherlands and injecting was still the dominant mode of drug administration, IDUs did not turn 'en masse' towards groin injecting (Grund et al., 1991b). Instead, smoking cocaine at 'house addresses' became the norm (Grund et al., 1991a; Grund and Blanken, 1993; Blanken et al., 1997).

The harms associated with problem stimulant use interact at multiple levels in the risk environment (Rhodes, 2002; Zinberg, 1984). Not only can specific harms influence one another, but they are also aggravated by external factors, such as international drug legislation, policing and other public policies in a process of 'contingent causality' (Rhodes, 2009). Developing proper and timely responses to such policy-related harms is a crucial challenge to harm reduction. Not because the proper harm reduction tools are absent or cannot be imagined, but because the larger risk environment might make such efforts null and void (Grund et al., 1992b; Rhodes et al., 2006; Gostin, 1998). Policymakers should therefore find ways to reduce the harms from counter-effective drug policies, harsh social policies and policies affecting our public space and private behaviours, and strengthen the ability of drug consumers and society to learn from past experience.

History is full of examples of the acculturation of 'new' psychoactive drugs across various cultures. As part of the mainstream social fabric, most drinking is restrained by explicit and implicit social rules passed from generation to generation. Unfortunately, the collective knowledge on cocaine and amphetamines is accumulated through peer-based learning and

not necessarily passed on automatically to new generations of users. The potential to respond in a rational and healthy fashion to 'new' illicit drugs is — among users and policymakers alike — hampered by what Lloyd Johnston termed 'generational forgetting' (Johnston et al., 2004). Yet, this learning is crucial to peacefully controlling problem drug use, a role recently adopted by harm reduction providers in many countries.

Implications for future intervention development, research and policy

There is a strong base of needle exchange programming in many, but not all, EU Member States, but their coverage of the IDU population may vary and stimulant users are poorly reached. Developing sufficient coverage for NSP and other interventions is a clear but complex issue (Des Jarlais et al., 2009) (see Kimber et al., 2010). Therefore, internal and external regulatory barriers, such as one-for-one exchange policies and laws that impede harm reduction programmes from distributing other safer use supplies (e.g. crack pipes and smoking foil) should be reconsidered. While returning used injecting equipment should be encouraged, the strict combination of distribution and collection is an unsavoury choice as it hinders access to ample quantities of injecting equipment at places and times when these are most needed. Therefore, independent distribution and collection schemes should be developed (Des Jarlais et al., 2009; Wood et al., 2003; Grund et al., 1992a).

The volume of injection equipment or condoms provided to clients should be determined based on a thorough assessment of clients' needs and network characteristics (Braine et al., 2008; Friedman et al., 2007; Rothenberg, 2007). All this requires a paradigm shift in service provision — from institutional provider–client relationships to facilitation of peer prevention in user networks (Broadhead et al., 1998) through peer-based outreach and secondary exchange. Syringe vending machines and mobile programmes can be useful adjuncts to 'reaching the unreached' but should be firmly based in flexible, attractive and human-delivered services.

Safer injecting and smoking education and interventions supporting transition to less harmful routes of drug administration, as well as overdose prevention and medical care of vein, skin and other infections should become standard features of SIFs and NSPs, and moved into the mainstream of harm reduction. NSPs and SIFs should not only create a healthy atmosphere, but also a setting that allows for the pleasurable effects of stimulants while minimising negative experiences, possibly by emphasising more controlled and less frenetic use. Relaxation techniques and alternative therapies may help stimulant users to ameliorate some of the mental health effects of heavy or frequent stimulant use, as well as physical complaints such as musculoskeletal pain. Offering sleep and day rest facilities may help to reduce sleep deprivation, which may alleviate the mental health strain of stimulant use. Involving participants in service provision and other activities may further help reduce the frequency and amounts of stimulant use, potentially leading to improvements in mental health and social functioning. Collaborations between various medical specialties, drug users, service providers and researchers in designing harm reduction strategies towards the pulmonary, cardiovascular and neurologic effects of stimulant use are equally important.

The reviewed studies suggest that problem stimulant use requires innovative, integrated and multidisciplinary medical and social services, but also drug and social policies that do not exacerbate the already considerable potential for harm of stimulants. The recent attention being paid to the unintended consequences of drug policy at UNODC is encouraging, but needs to be translated into effective action. At present, international drug and other public policies emphasise maximising harm to reduce casual drug use. Stimulant and other drug users must enjoy the fundamental human right to health protection, as stipulated by Article 25 of the Universal Declaration of Human Rights (General Assembly of the United Nations, 1948). In 1945, at the brink of war and peace, Sir Karl Popper published his influential *The open society and its enemies*, in which he wrote 'The role of the state is not to make people happy but to relieve avoidable suffering.' For the state and its agents to live up to these calls is amongst the principal challenges of harm reduction.

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