Substance abuse in HIV-infected patients: what the clinicians should know

Marta Boffito, MD, PhD
Head of Clinical Trials, St. Stephen's Centre (SSAT)
Consultant Physician, Chelsea and Westminster Foundation Trust
Reader, Imperial College
LONDON, UK

Mr P

- 63 years old
- British White Male
- MSM
- Specialist Nurse (TB)

Past medical history

• 1985	Acute hepatitis B
• 2002	HIV diagnosis, CD4 324 cells/mm3, VL 43282 c/mL, baseline resistance test: WT
• 2007	Criptosporidiosis
• 2013	Hiatus hernia with acid reflux

Mr P

Antiretroviral drug history

- Apr 2008 Atripla
- JUL 2008 VL < 40 c/mL
- Vivid dreams + restless sleep

- Aug 2014 Symptoms exacerbated, nightmares, disturbed sleep, fatigue, difficulty in concentrating, forgetfulness

Mr P

- Mar 2015 — Switched to TDF/FTC + DTG within a clinical trial (SSAT056), VL < 40 c/mL, CD4 711 (33.9%)
- Apr 2015 — Discloses recent (3-4 months) use of *Chems* (GHB, crystal meth, mephedrone) – injecting… no hx of recreational drugs use

Mr P

- May 2015 — On TDF/FTC+DTG, no more vivid dreams/nightmares, happier, still tired
- Aug 2015 — End of Study
  Switched from TDF/FTC + DTG to Triumeq (HLAB*5701 negative)
  Reports occasional use of mephedrone (injecting)

Mr P

- Sep 2015 Agitated, nervous, extremely anxious, paranoid; wants to come off Triumeq due to side effects

- Explains that the week before :

- Resigned at work after feeling very confused, with episodes of difficulty speaking, agitation and confusion

- Attended A&E department for onset of confusion, paresthesia in both arms, dry mouth, anxiety ++ and “near to death” feeling, discharged with flucloxacillin for thromboflebitis

Mr P

No signs of cerebral vascular accidents/TIAs

No previous hx of mental health disease

No typical ABC/Triumeq AEs

Anorexia, nausea, vomiting, diarrhea
Headache
Rash (without systemic symptoms
Fever, lethargy, fatigue
Hypersensitivity reactions

When asked about Chems:

- Injected crystal meth and mephedrone at least 5 times in previous week and in other occasions in previous month
- Long discussion about Chems AEs, come-down post use, unlikelihood of symptoms to be Triumeq but refused to continue and switched to TDF/FTC + RAL
- Diazepam 2.5 mg for 2-3 days
- Referral to Chemsex support

Epidemiology of CHEMSEX

… of what?

Chemsex

- Recreational drug use linked with HIV/AIDS, commonest substances (early days) being ‘street drugs’: opiates, crack and cocaine
- Other recreational drugs are today used by MSM and BM
- Called ‘party drugs’ or ‘club drugs’, consumed in club or house parties, often during sex, which can last for several days

- Mix of substances used in a sexualized context such as:
  - methylenedioxymethamphetamine (MDMA)
  - ketamine
  - benzodiazepines (e.g. diazepam)
  - methamphetamine
  - gamma-hydroxybutyrate (GHB)
  - mephedrone
  - poppers
  - erectile dysfunction agents (EDA)

London, UK

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  - methamphetamine
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  - mephedrone
  - poppers
  - erectile dysfunction agents (EDA)

Chems

Chemsex 'prevalence' (Europe)

- The European MSM Internet Sex (EMIS) survey

- **Survey of 174,000 MSM across 38 countries**
- **Type and recency of drug use**
- **Prevalence of injection drug use**

Bourne et al 1st Chemsex Forum 2016

Chemsex 'prevalence' (Europe)

COUNTRY: France

DESIGN: Qualitative study

FOCUS: Slamming among MSM in Paris

KEY CONTEXTUAL FINDINGS:

- Injection drug use has emerged as new behaviour among MSM in Paris
- Acute need for safe injection advice
- Potential role of chemsex party organisers

STATUS: Published (Fourer et al, 2014)

Bourne et al 1st Chemsex Forum 2016

Chemsex 'prevalence' (Europe)

COUNTRY: Spain

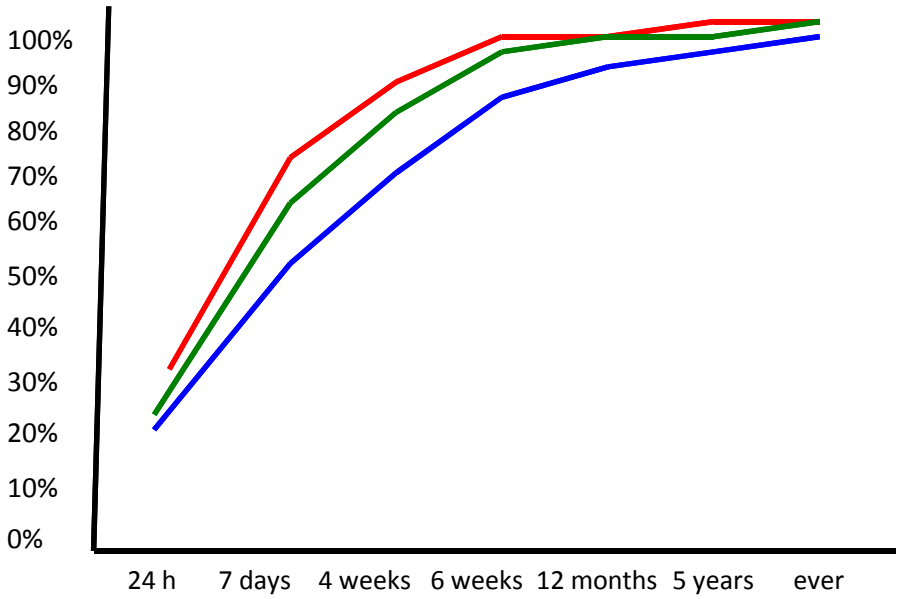
DESIGN: Ethnography

FOCUS: Chemsex among MSM visiting saunas in Barcelona

STATUS: Poster presentation at 1st Chemsex forum 2016

Bourne et al 1st Chemsex Forum 2016

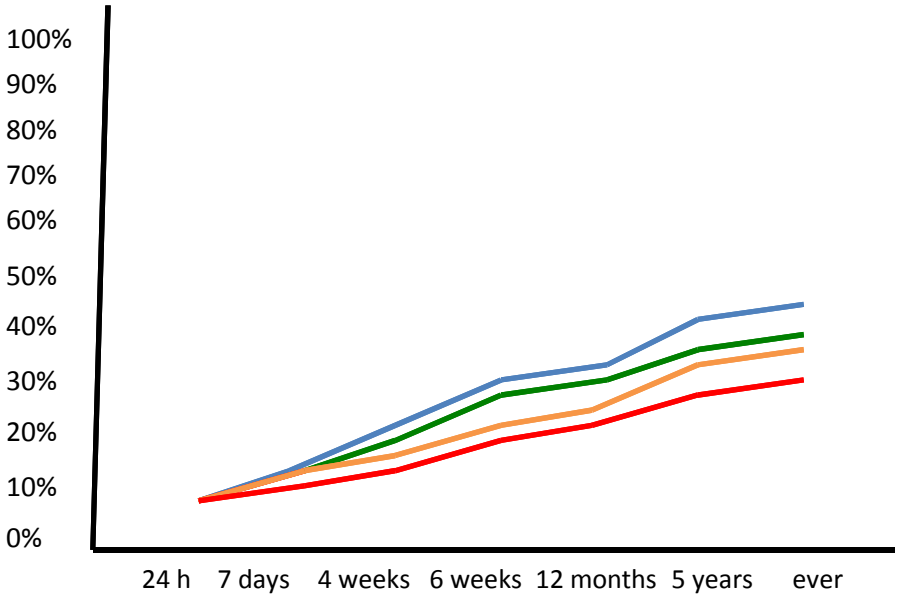
Recency of any sex with a man



Barcelona
Turin
Amsterdam
Paris
Milan
Bologna
Madrid
Zurich
Brussels
Copenhagen
London
Rome
Sofia

Schmidt et al 1st Chemsex Forum 2016

Recency of chemsex drug use



Brighton
London
Amsterdam
Barcelona

Schmidt et al 1st Chemsex Forum 2016

Chemsex 'prevalence' (Europe)

COUNTRY: Germany

DESIGN: Qualitative study

FOCUS: Drug use among MSM in Berlin, Frankfurt and Cologne

KEY CONTEXTUAL FINDINGS:

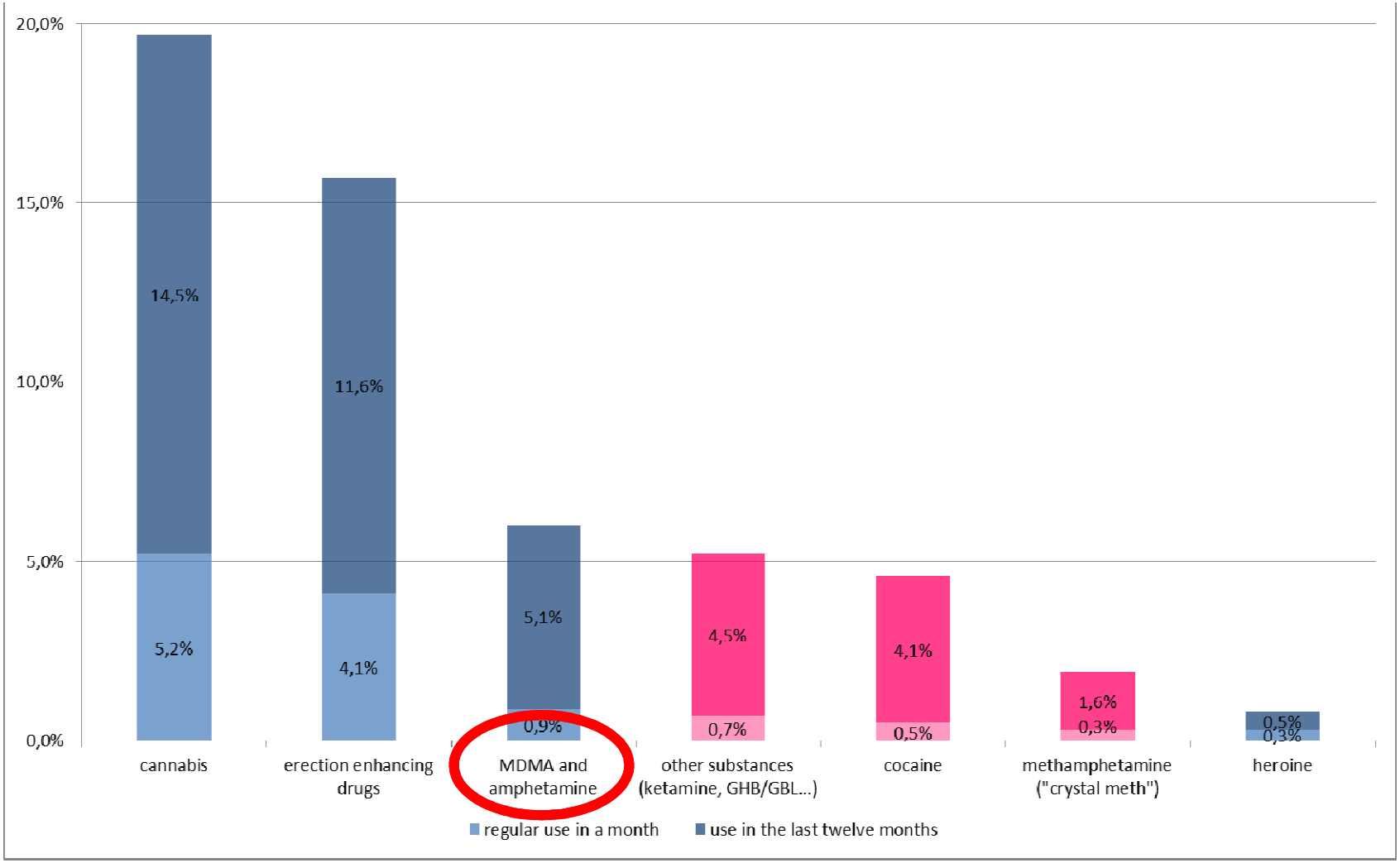
- Addiction issues that are hard to address in generic drug services
- Demands placed on HIV organisations for drug support

STATUS: Conference proceeding (Deimel & Stover, 2015)

Bourne et al 1st Chemsex Forum 2016

Chemsex among MSM in Germany

Prevalences of (sexualised) drug use



Dichtl & Graf, Chemsex Forum, London, 2016

Impact of sexualised drug use on well-being

Physical, psychological & social well-being

physical harms	psychological harms	social harms
overdosing	increased aggression	problems in work environment
vulnerability to diseases	listlessness	problems in private settings
changing of one´s appearance	hallucinations/loss of touch with reality	social withdrawal
interactions with ART	psychoses, anxiety, depressions	legal consequences

MDMA

Metabolized by CYP2D6 and CYP3A4 (30%)

Fatal interaction between ritonavir and MDMA

J A Henry, I R Hill

Information on drug interactions between prescribed drugs is generally available, but interactions between prescribed medication and illicit drugs are more anecdotal and seldom reported. We report on a fatal interaction between ritonavir and 3,4-methylenedioxymethamphetamine (MDMA, "Ecstasy").

A man born in June, 1964, tested HIV-1 positive in 1991, and developed AIDS in 1995. He had been a heavy alcohol drinker with strikingly abnormal liver function, and a fatty liver was seen on ultrasonography. He had decreased his alcohol intake to a few units per week from March, 1996, onwards, which led to improved liver function, but his aspartate transaminase remained raised at 173 IU/L (normal 11–55 IU/L). His treatment for AIDS was altered to add ritonavir 600 mg twice daily on Sept 20, 1996, to his regular medication of zidovudine 200 mg three times daily and lamivudine 150 mg twice daily. He had taken MDMA on several occasions without untoward effects, and had kept three tablets from his last supply of the drug. He went to a club on Oct 6, 1996, and took the tablets with him and was seen drinking beer. 4 h after arrival he was obviously unwell. When assessed by a nurse who was attending the club, he was hypertonic, sweating profusely, tachypnoeic

Fatal MDMA intoxication

Sir—J A Henry and I R Hill (Nov 28, p 1751)[1] report a fatal interaction between ritonavir and 3,4-methylenedioxymethamphetamine (MDMA, "Ecstasy"). MDMA plasma concentrations measured in their patient largely exceeded those expected after ingestion of 180 mg MDMA. They argue that concomitant treatment with ritonavir could be responsible for a metabolic interaction between both drugs, leading to toxic concentrations of MDMA, and that CYP2D6 (a polymorphic isoenzyme of cytochrome P450) would be involved in such interaction.[2] Ritonavir is mainly a CYP3A substrate and secondarily a CYP2D6 and CYP2C9 substrate. Clinical interactions reported until now with CYP2D6 substrates seem less relevant than those associated with CYP3A.[3]

As the investigators mention, three factors should be taken into account: the patient had an impaired liver function because of alcoholism; treatment with ritonavir was started 2

mg), $AUC_{0\text{-}24h}$ and C_{max} increased by a factor of 10 and 6, respectively:

MDMA dose (mg)	AUC $_{0\text{-}24\,h}$ (ng mL^{-1} h^{-1})	C_{max} (ng/mL)
50	457 (505)	51 (45)
75	1332 (646)	126 (38)
100	2057 (283)	190 (20)
125	2624 (573)	229 (46)
150	5439 (411)	465 (122)

Data are mean (SD).

The lack of linearity of MDMA pharmacokinetics implies that fairly small increases in the dose of MDMA ingested could lead to disproportionate increases in MDMA plasma concentrations and, consequently, with an increased risk for MDMA acute intoxication. In addition to drug to drug interactions and the individual's metabolic status, which Henry and Hill mention, a possible phenomenon of non-linear pharmacokinetics could be another factor that may explain the high plasma concentrations of MDMA.

This study was supported by grants FIS 97/1198, CIRIT (1997SGR00077), ISCIII 97/4344 and Plan Nacional sobre Drogas, Madrid

*Rafael de la Torre, Jordi Ortuño, Marta Mas, *Magí Farré, Jordi Segura*

The Lancet, Volume 353, February 1999

Fatal MDMA intoxication

Dr Matthias Schwab, Eva Seyringer, Robert B Brauer, Achim Hellinger, Ernst-Ulrich Griese

Sir

Entactogens represents a class of psychoactive synthetic compounds abused as recreational designer drugs, for example MDMA, methylene-dioxyethylamphetamine (MDE), or 3,4-methylenedioxyamphetamine (MDA). Originally these drugs were regarded as being "safe", but an increasing number of severe adverse effects and even deaths have been reported, such as the report by J A Henry and I R Hill.1 Additionally, several cases of MDMA-induced hepatic damage requiring subsequent liver transplantation have been described.2, 3

The responsible underlying mechanism is still unclear. One possible explanation is that deficiency in cytochrome P4502D6 (CYP2D6) expression could be a genetic factor that predisposes to an increased risk of MDMA-related toxic effects due to an accumulation of MDMA or MDMA-related drugs. In-vitro studies have shown that demethylenation of MDMA, MDA, and MDE is a major metabolic pathway catalysed by the CYP2D6 enzyme.4 This enzyme exhibits a genetic polymorphism with 7—10% of white people expressing no functional enzyme (poor metaboliser).5

The Lancet, Volume 353, February 1999

Chemsex 'prevalence' (Europe)

COUNTRY: UK

DESIGN: Numerous studies

FOCUS: Drug use among MSM in London

Different publications from different areas in London and UK (England and Wales)

Bourne et al 1st Chemsex Forum 2016

Recreational drug use, polydrug use, and sexual behaviour in HIV-diagnosed men who have sex with men in the UK: results from the cross-sectional ASTRA study

Marina Daskalopoulou, Alison Rodger, Andrew N Phillips, Lorraine Sherr, Andrew Speakman, Simon Collins, Jonathan Elford, Margaret A Johnson, Richard Gilson, Martin Fisher, Ed Wilkins, Jane Anderson, Jeffrey McDonnell, Simon Edwards, Nicky Perry, Rebecca O'Connell, Monica Lascar, Martin Jones, Anne M Johnson, Graham Hart, Alec Miners, Anna-Maria Geretti, William J Burman, Fiona C Lampe

Lancet HIV 2014; 1: e22–31

Published Online
September 8, 2014
http://dx.doi.org/10.1016/S2352-3018(14)70001-3

Summary

Background Recreational drug use in men who have sex with men (MSM) is of concern because it might be linked to the transmission of HIV and other sexually transmitted infections. Evidence about drug use in HIV-diagnosed MSM in the UK is limited by representativeness of the study populations. We describe patterns of drug use and associations with sexual behaviours in HIV-diagnosed MSM in the UK.

Methods We used data from the cross-sectional ASTRA study, which recruited participants aged 18 years or older with HIV from eight HIV outpatient clinics in the UK between Feb 1, 2011, and Dec 31, 2012. We examined data for MSM, assessing the prevalence of recreational drug use and polydrug use in the previous 3 months and associations with sociodemographic and HIV-related factors. We examined the association of polydrug use with measures of condomless sex in the previous 3 months and with other sexual behaviours.

Findings Our analysis included data for 2248 MSM: 2136 (95%) were gay, 1973 (89%) were white, 1904 (85%) were on antiretroviral treatment (ART), and 1682 (76%) had a viral load of 50 copies per mL or lower. 1138 (51%) used recreational drugs in the previous 3 months; 608 (27%) used nitrites, 477 (21%) used cannabis, 460 (21%) used erectile dysfunction drugs, 453 (20%) used cocaine, 280 (13%) used ketamine, 258 (12%) used 3,4-methylenedioxy-N-methylamphetamine (MDMA), 221 (10%) used gamma-hydroxybutyrate or gamma-butyrolactone, 175 (8%) used methamphetamine, and 162 (7%) used mephedrone. In the 1138 individuals who used drugs, 529 (47%) used three or more drugs and 241 (21%) used five or more. Prevalence of injection drug use was 3% (n=68). Drug use was independently associated with younger age ($p<0·0001$), not being religious ($p=0·001$), having an HIV-positive stable partner ($p=0·0008$), HIV-serostatus disclosure ($p=0·009$), smoking ($p<0·0001$), evidence of harmful alcohol drinking ($p=0·0001$), and ART non-adherence ($p<0·0001$). Increasing polydrug use was associated with increasing prevalence of condomless sex (prevalence range from no drug use to use of five or more drugs was 24% to 78%), condomless sex with HIV-seroconcordant partners (17% to 69%), condomless sex with HIV-serodiscordant partners (10% to 25%), and higher-HIV-risk condomless sex after taking viral load into account (4% to 16%; $p\leq0·005$ for all). Associations were similar after adjustment for sociodemographic and HIV-related factors. Methamphetamine was more strongly associated with higher-HIV-risk condomless sex than were other commonly used drugs.

Interpretation Polydrug use is prevalent in HIV-diagnosed MSM and is strongly associated with condomless sex. Specialist support services for MSM with HIV who use recreational drugs might be beneficial in the reduction of harm and prevention of ongoing transmission of HIV and other sexually transmitted infections.

Funding National Institute for Health Research.

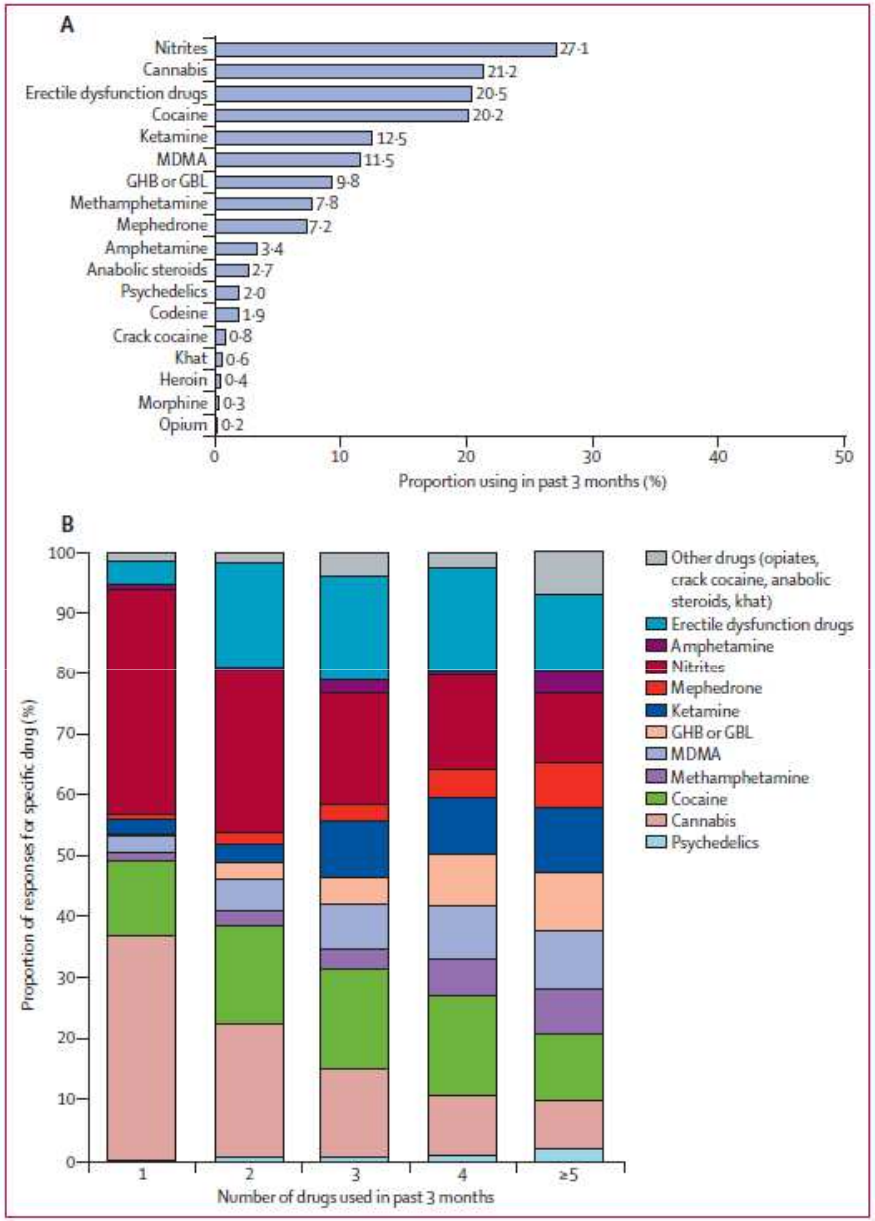
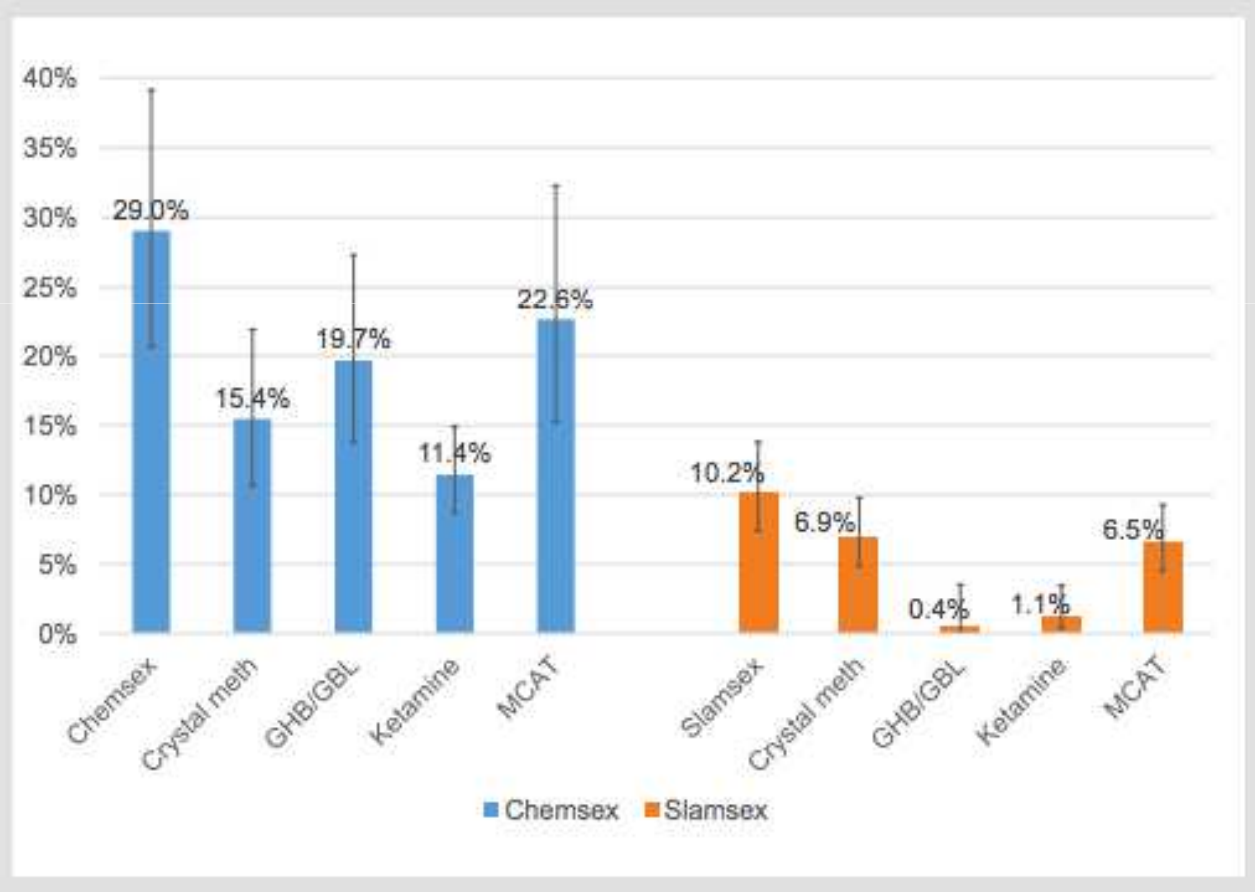


Figure 1: **Recreational drug use in the past 3 months in HIV-diagnosed men who have sex with men**
(A) Prevalence of recreational drug use in 2248 individuals. (B) Type of drug according to number of drugs used in 1138 individuals who used at least one drug. GHB=gamma-hydroxybutyrate. GBL=gamma-butyrolactone. MDMA=3,4-methylenedioxy-N-methylamphetamine.

Chemsex at CROI 2016

Positive voices: online survey of 777 PLWH (MSM=532)
30 HIV clinic in England and Wales May-Nov 2014

Adjusted percentage of sexually active HIV-positive MSM engaging in chemsex and slamsex and drug used (n=387)



Pufall et al. CROI, Boston, abstract 913, 2016

Is there an association between chemsex and STI diagnoses?

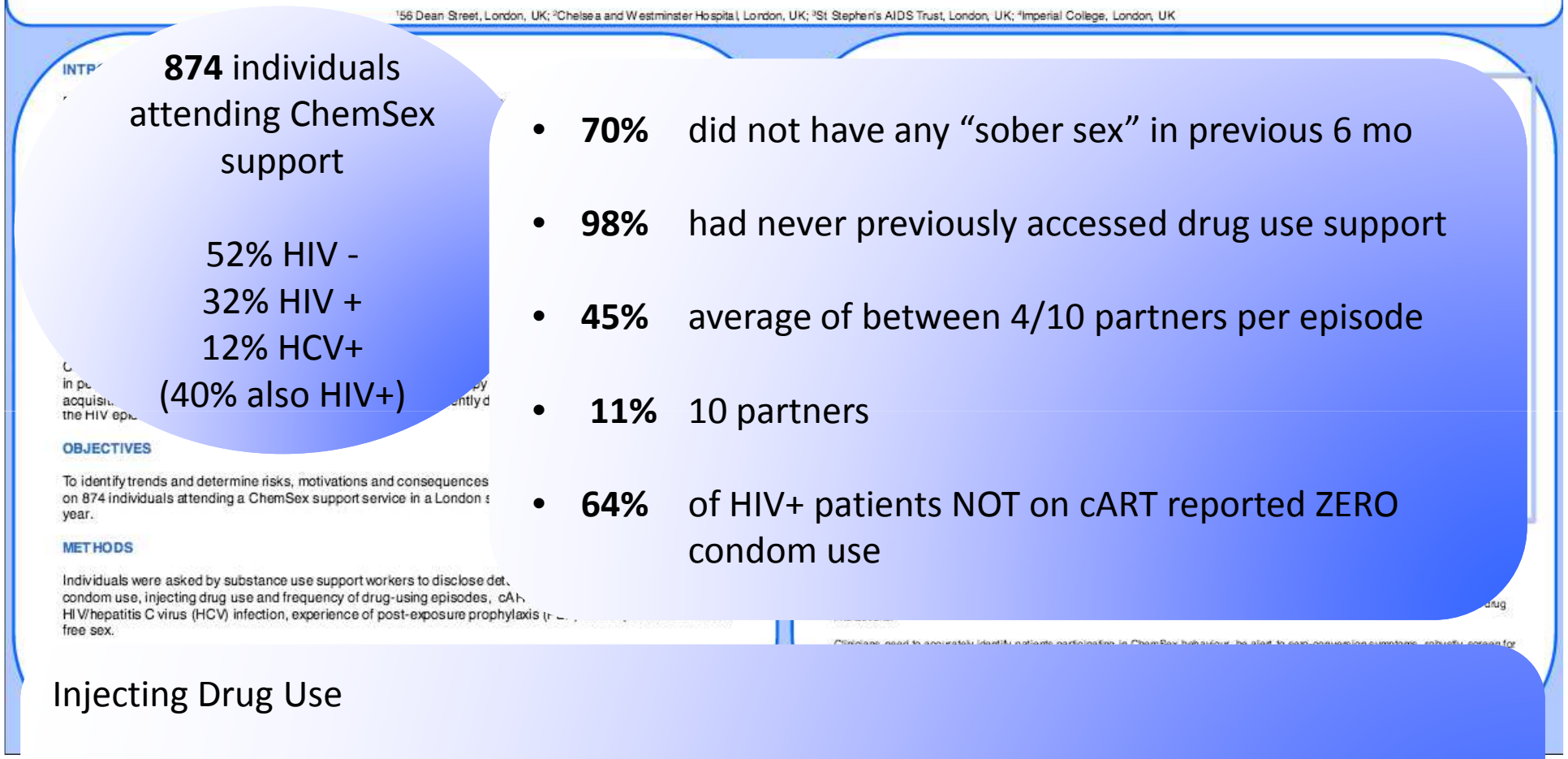
- 50% of men reported a bacterial STI diagnosis in the previous year, and 9.4% had ever been diagnosed with hepatitis C
- **Chemsex** was associated with an increased risk of being diagnosed with:
  - any STI (AOR: 3.42, 95% CI: 1.71-6.83)
  - gonorrhea (AOR: 2.76, 95% CI: 1.31-5.82)
  - hepatitis C (AOR: 6.26, 95% CI: 2.05-19.1)
- **Slamsex** was associated with increased odds of being diagnosed with:
  - any STI (AOR: 3.85, 95% CI: 1.26-11.8)
  - multiple STIs (AOR: 1.82, 95% CI: 1.18-2.79)
  - chlamydia (AOR: 3.09, 95% CI: 1.11-8.62)
  - hepatitis C (AOR: 9.12, 95% CI: 2.40-34.6)

Pufall et al. CROI, Boston, abstract 913, 2016

ChemSex: Data on Recreational Drug Use and Sexual Behaviour in Men Who Have Sex with Men (MSM) from a Busy Sexual Health Clinic in London, UK

David Stuart[1,2], Nneka Nwokolo[1,2,3], Alan McOwan[1,2], Margherita Bracchi[2,3], Marta Boffito[1,2,3,4]

[1]56 Dean Street, London, UK; [2]Chelsea and Westminster Hospital, London, UK; [3]St Stephen's AIDS Trust, London, UK; [4]Imperial College, London, UK



874 individuals attending ChemSex support

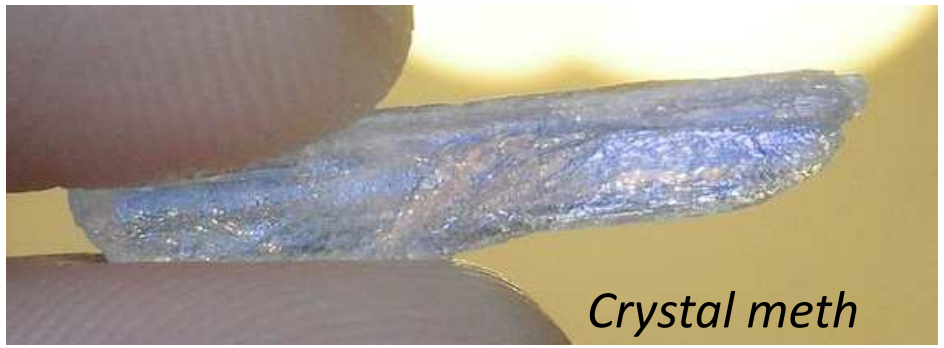
52% HIV -
32% HIV +
12% HCV+
(40% also HIV+)

- **70%** did not have any "sober sex" in previous 6 mo
- **98%** had never previously accessed drug use support
- **45%** average of between 4/10 partners per episode
- **11%** 10 partners
- **64%** of HIV+ patients NOT on cART reported ZERO condom use

Injecting Drug Use

29% were injecting drug users:

- 23% shared needles
- 27% never injected themselves (allowing others to inject them)
- 30% had been injected by both themselves and others



Crystal meth

2005: 3% of all presentations among MSM and bisexual men

2012: 85% of presentations

antidote @friend
LGBT drug and alcohol support

GHB/GBL

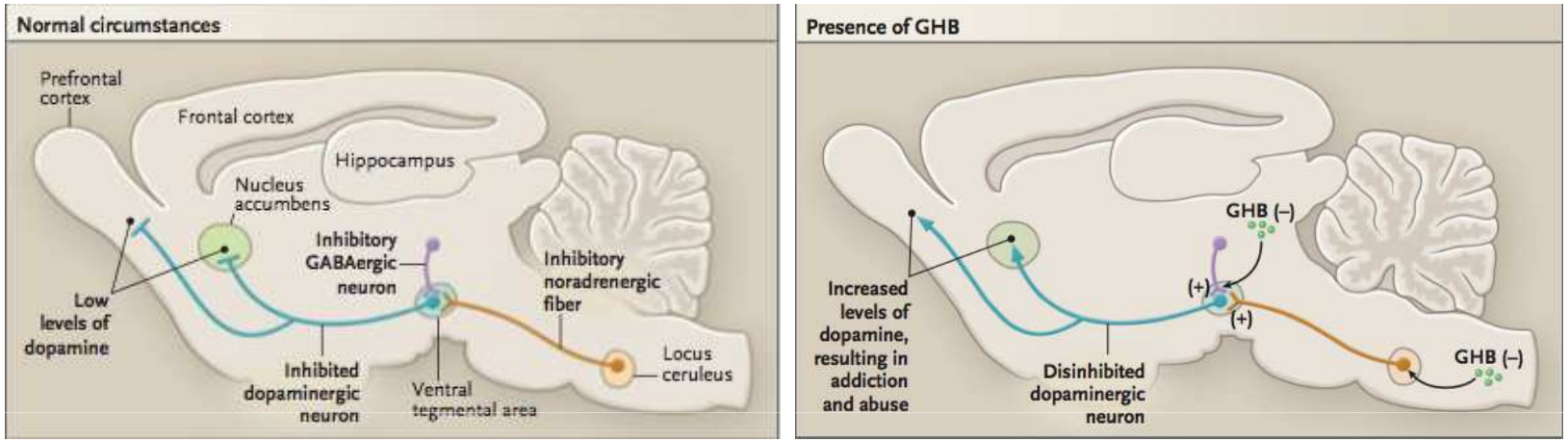
Gamma-hydroxybutyrate (GHB) and its precursors, GBL and 1,4-butanediol (1,4-BD) are **central nervous system depressants**

- GBH exists naturally in the brain as a metabolite and precursor of GABA
- Had been used in medicine since the 1960s for various purposes (as anaesthetic, alcohol and opiates withdrawal...)
- GBL is:
  - a solvent and reagent in chemistry
  - used as a flavouring
  - a cleaning solvent
  - a superglue remover

Cheap and easily accessible online (10 pence per dose)

Snead OC 3rd, Gibson KM. Gamma-hydroxybutyric acid. N Engl J Med 2005; 352:2721–2732

GHB/GBL



Neuromodulates the GABA system, acting on dopamine release

Effects: induces euphoria and relaxation, enhances libido → facilitating sexual intercourses

Physically addictive

Snead et al. N Engl J Med 2005; 352:2721–2732

GHB/GBL

Consumed as a liquid (colourless, odourless, and tasteless)

Pharmacokinetic/dynamic data:

- Short half-life (20-60 minutes), multiple doses
- **Narrow therapeutic index** → ANY DOSE CAN BE DANGEROUS
- Metabolised by plasma enzymes (GHB dehydrogenase), enters the citric acid cycle and is excreted mainly through breath as CO_2

High doses = 3 mL can be life threatening (normal doses 0.5 – 1.5 mL)

Data extrapolated from animal studies show **high first pass metabolism**: Possible role of CYP 450 family in the metabolism of GHB?

Andresen et al. Drug Test Anal 2011; 3:560–568

GHB/GBL

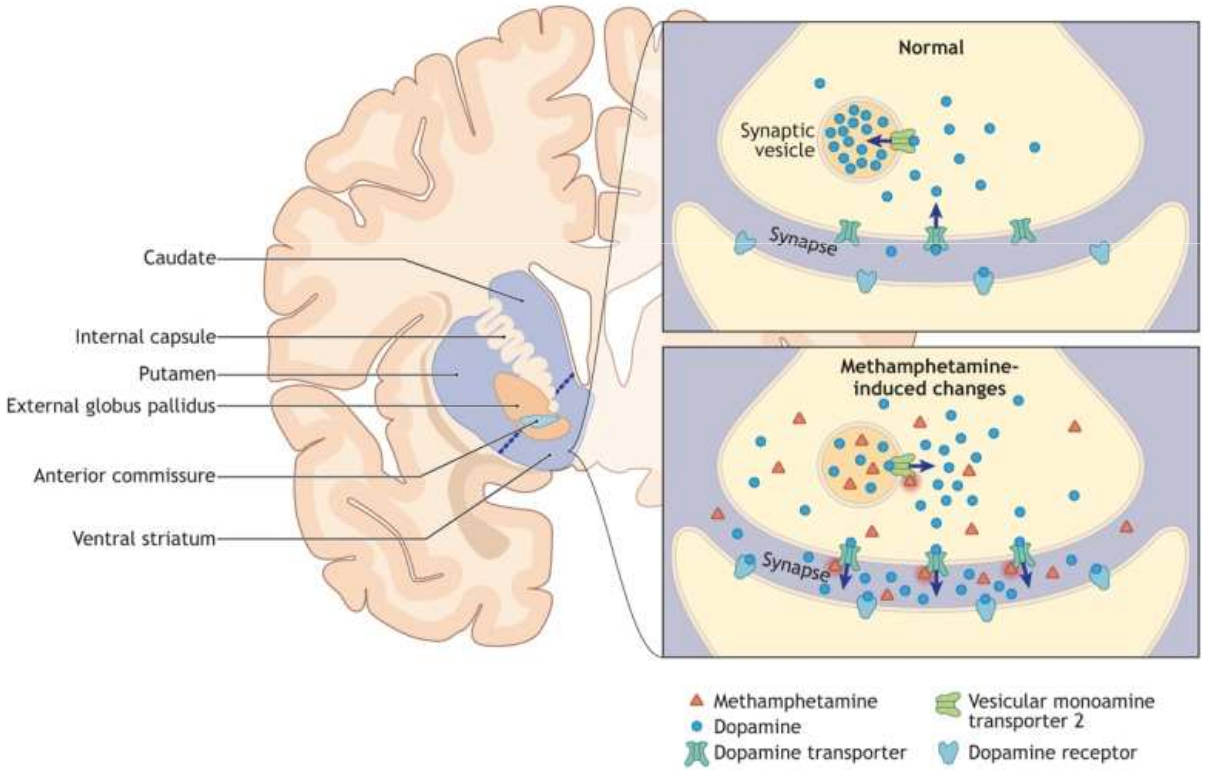
ADVERSE EFFECTS

- Respiratory depression
- Tonic-clonic seizures
- CNS depression and coma
- Death
- **Withdrawal syndrome:** auditory and visual hallucinations, tremors, tachycardia and hypertension - can last for several days, potentially life-threatening

Schep et al Clinical toxicology. 2012;50(6):458-70

Crystal Methamphetamine

Potent **psychostimulant** (*phenethylamine* and *amphetamine* classes), acts through release of noradrenaline, dopamine and serotonin



EFFECTS:

- Increases energy
- Induces confidence
- Enhances libido
- Allows for long-lasting sexual intercourses

Kish, *CMAJ* 2008,178:1679-1682

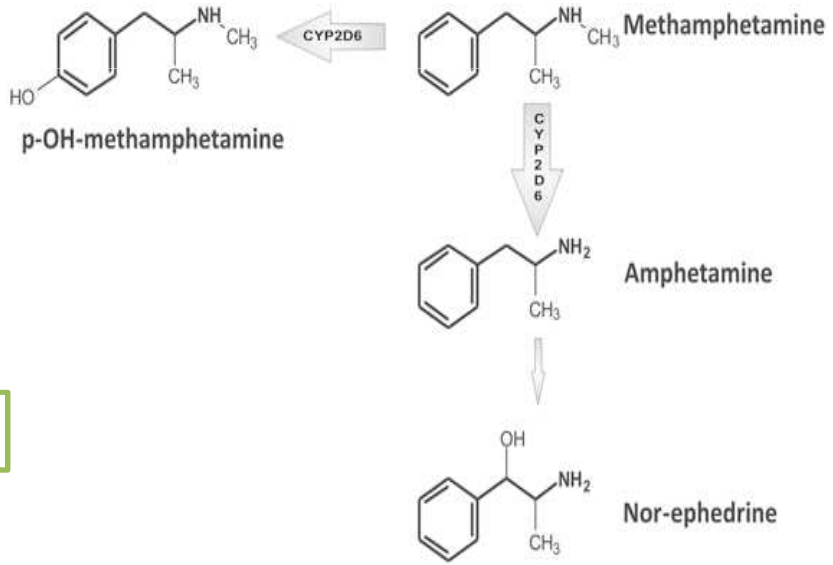
Crystal Methamphetamine

- Costly: £100 per gram- usually unadulterated & in crystalline form

- Consumed in different ways (snorted, injected, smoked in a pipe)

Pharmacokinetic/dynamic data:

- Long half-life (up to 12 hours)
- High bioavailability
- Lipophilic, easily passes the BBB and reaches high concentrations in the CNS



Metabolised by enzyme CYP2D6 (CYP450 family)

Lin *Drug Metab Dispos* 1997,**25**:1059-1064

Crystal Methamphetamine

ADVERSE EFFECTS

- Anxiety
- Psychosis with persecutory delusions
- Hallucinations & paranoia
- "Comedown" post use: sleeplessness followed by increased somnolence, low mood, malaise

Chronic use:

- neurocognitive impairment
- pulmonary hypertension
- dilated cardiomyopathy

Grant et al. Journal of the Society on NeuroImmune Pharmacology. 2012;7(1):113-39

Mephedrone

“Amphetamine-like” substance: it promotes the release of monoamine neurotransmitters and inhibits their reuptake

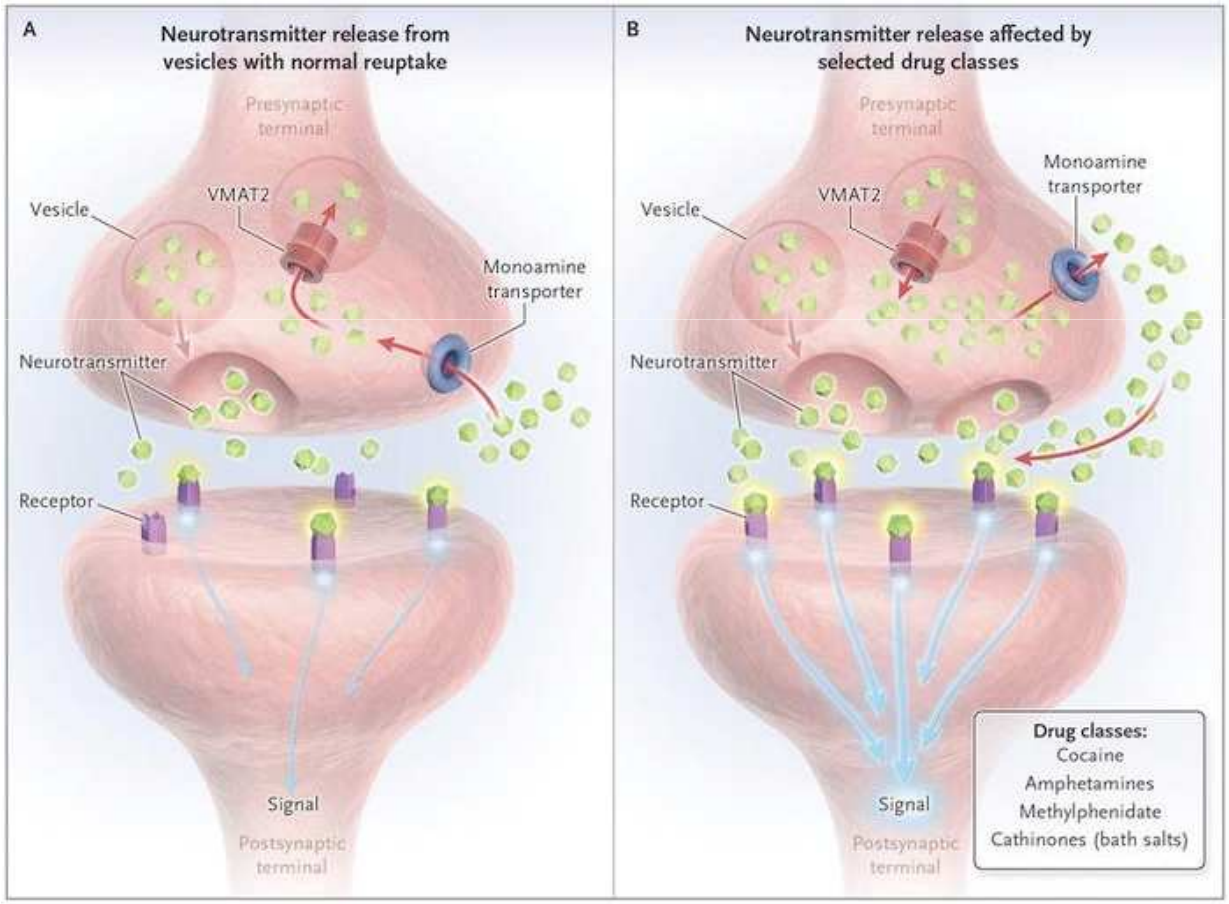


Image by https://infogr.am/synthetic-stimulants

Mephedrone

- Semi-synthetic substance, belonging to the class of **CATHINONE** derivatives

  → Synthetic cathinones (mephedrone, methcathinone and methylone) used to be sold as "*plant food*" or "*salt baths*" – (legal highs)

- Available as a white/yellowish powder, soluble in water

- Snorted (common), ingested (bombed), inserted in rectum, injected

- Generally it's highly adulterated and quite cheap (£10 to £15 per gram)

Gregg et al. Life Sci 2014; 97:27–30

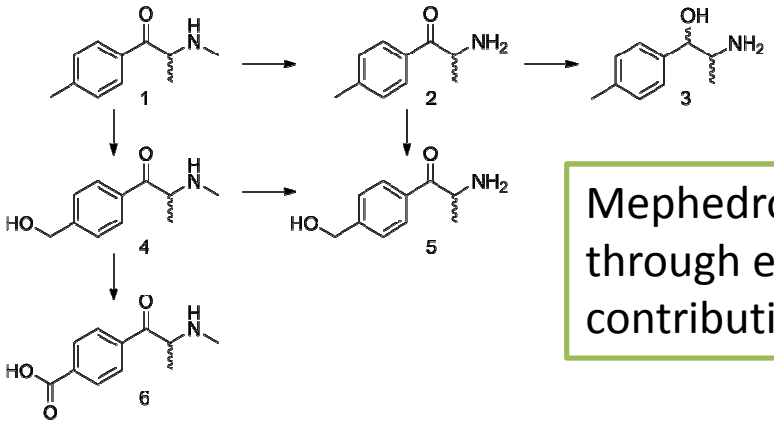
Mephedrone

Pharmacokinetic/dynamic data:

- Short half-life (0.5-1.5 h):
  following oral ingestion/nasal insufflation the effects last up to 2 – 3 hours
  following intravenous injection, about 15 – 30 minutes

- Tolerance mechanism

- Multiple doses to maintain the desired effects (1-4 g of mephedrone per session)



Mephedrone metabolism occurs mainly through enzyme CYP2D6, with minor contribution of other enzymes

Pedersen et al. Drug testing and analysis. 2013;5(6):430-8

Mephedrone

ADVERSE EFFECTS

- Tremors
- Anxiety
- Hallucinations
- Tachycardia
- High blood pressure
- Respiratory and urinary difficulties
- Nasal irritation and bleeds

Schifano et al. Psychopharmacology. 2011;214(3):593-602

12 *Current Neuropharmacology*, 2015, *13*, 12-20

Synthetic Cathinones: A New Public Health Problem

Laurent Karila[1,*], Bruno Megarbane[2-5], Olivier Cottencin[6] and Michel Lejoyeux[7]

[1]Addiction Research and Treatment Center, Paul Brousse Hospital, Paris-Sud University, Villejuif 94800, France; CEA-INSERM, Orsay, France; [2]Inserm, U1144, Paris, F-75006, France; [3]Paris-Descartes University, UMR-S 1144, Paris, F-75006, France; [4]Paris-Diderot University, UMR-S 1144, Paris, F-75013, France; [5]Department of Medical and Toxicological Critical Care, Lariboisière Hospital, Paris-Diderot University, 75010 Paris, France; [6]Department of Psychiatry and Addictology, CHRU Lille, France; [7]Department of Psychiatry and Addictology, Bichat Hospital, Paris-Diderot University, Paris, France

… new psychoactive substances completely modified the drug scene … synthetic cathinones ("legal highs") produced/used **to mimic effects of cocaine, MDMA, and methamphetamine** … produced in China and South East Asia … **internet** new … intentionally mislabelled and sold on-line under slang terms such as bath salts, plant food, plant feeders and research chemicals … **reasonable costs** … not only health actors but also the general public need to be clearly informed and **aware of dangers** … somatic, mental, and addictive consequences … with persistent unknowns for the future …

ChemSex: concerns

1

Expansion of the HIV and HCV epidemic…
…and all other STDs

Subjects with acute HIV infection – Chems may mask seroconvertion symptoms

Ostro et al, J Acquir Immune Defic Syndr 2009; Daskalopoulou et al. LANCET HIV 2014

ChemSex: concerns

AIDS. 2015 Aug 7. [Epub ahead of print]

Incidence of sexually transmitted hepatitis C virus infection in HIV-positive MSM: a systematic review and meta-analysis.

Hagan H[1], Jordan AE, Neurer J, Cleland CM.

HCV seroconversion increased from an estimated rate of:

0.42/100 person-years in 1991

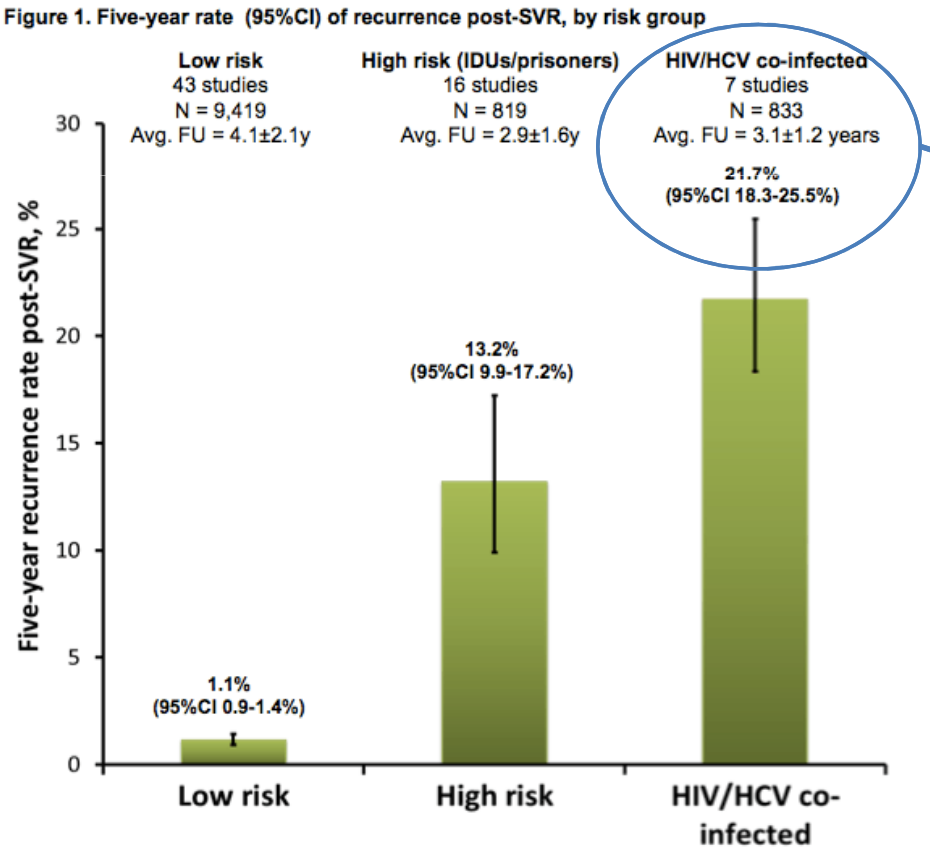
to

1.34/100 person-years in 2012

"Among the seroconverters, a large proportion of infections were attributable to high-risk behaviors including mucosally traumatic sex and sex while high on methamphetamine"

ChemSex: concerns

Risk of late relapse or re-infection with Hepatitis C after Sustained Virological Response: meta-analysis of 66 studies in 11,071 patients



>21% of reinfections with Hep C in 5 years

Hill et al. CROI 2015 Feb 23-26, Seattle WA

ChemSex: concerns

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Negative experiences and harms

- Paranoia/anxiety/panic attacks
- Hallucinations
- Severe respiratory depression
- **Overdose/death**
- Lungs/ heart toxicity
- Withdrawal symptoms (sleeplessness/anxiety/paranoia/muscle waste/weight loss)

SOCIAL CONSEQUENCES

ChemSex: concerns

3 Poor adherence to cART and possible emergence of resistant viruses

?

ChemSex: concerns

4

Risk for drug-drug interactions:

Increased exposure of Chems secondary to concomitant ARVs intake ?

- No DDI PK/dose-effect relationships data between Chems and ARVs
- Information regarding potentially toxic DDIs can be theorized from case reports or cohort studies

Letter

Possible fatal interaction between protease inhibitors and methamphetamine

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On ritonavir (400 mg twice daily), soft gel saquinavir (400 mg twice daily) and stavudine (40 mg twice daily)

TABLE 1. Party drugs' pharmacological characteristics.

Drug name (alternative/ street names)	Route of administration	Bioavailability when orally administered	Metabolism	Half-life	Interaction potential
Crystal methamphetamine (Crystal, Tina, Meth)	Oral ingestion, smoke, insufflation, rectal insertion, IV	67–80%	CYP2D6; Other non-CYP pathways (minor)	~12 h	Moderate (COBI/RTV inhibition of CYP2D6)
MDMA (Ecstasy, X, Mandy)	Oral ingestion insufflation (capsules/ tablets/powder)	40–60%	CYP2D6; CYP1A2, CYP2B6 and CYP3A4 (minor)	~7 h	Moderate (COBI /RTV inhibition of CYP2D6)
Mephedrone (Miaw Miaw, plant food, bath salts)	Oral ingestion, insufflation (most common), rectal insertion (dissolved or as gel forms), IV	10%	CYP2D6; NAPDH-dependent enzymes (minor)	30 min–1.5 h	Moderate (COBI /RTV inhibition of CYP2D6)
Cocaine (Charlie, C, Coke)	Oral ingestion Insufflation (most common), smoke, IV	30–60%	Plasma/liver cholinesterases	0.5–2 h	Low to moderate
Ketamine (K, vitamin K, special K)	Oral ingestion, insufflation, IV or IM	20–45%	CYP3A4; CYPB6 and CYP2C9 (minor)	1.8–2.8 h	High (COBI /RTV inhibition of CYP3A4)
GHB/GBL/1,4 GD (G, Gina, liquid E)	Oral ingestion (liquid), (rarely IV)	GHB: 59–65% GBL: 85%	GHB: GHB-DH and SSA-DH GBL: Lactonase 1,4 BD: alcohol DH and aldehyde DH	GHB: 20–60 min (GLB and 1,4 BD are rapidly converted to GHB)	Unknown
Benzodiazepines (alprazolam, diazepam)	Oral ingestion (tablets) rectal (gel forms) IV (crushed tablets)	Diazepam: 100% Alprazolam: 90%	Diazepam: CYP3A4; CYP2C19 (minor) Alprazolam: CYP3A4	Alprazolam: 12–15 h Diazepam: 43–56 h	High (COBI /RTV inhibition of CYP3A4)
EDAs (sildenafil, tadalafil, vardenafil)	Oral ingestion (tablets)	Sildenafil: 41% Tadalafil: 80% Vardenafil: 15%	CYP3A4	Sildenafil: 4 h Tadalafil: 17.5 h Vardenafil: 4.5 h	High (COBI /RTV inhibition of CYP3A4)

1,4 BD, 1,4 butanediol; COBI, cobicistat; DH, dehydrogenase; EDA, erectile dysfunction agents; GBL, gamma-butyrolactone; GHB-DH, gamma-hydroxybutyrate dehydrogenase; IM, intramuscular; IV, intravenous; RTV, ritonavir; SSA-DH, succinic semialdehyde dehydrogenase.

Increasing use of 'party drugs' in people living with HIV on antiretrovirals: a concern for patient safety

Margherita Bracchi[a], David Stuart[b], Richard Castles[c], Saye Khoo[d], David Back[d] and Marta Boffito[a,b,e]

ChemSex: concerns

Other substances:

Poppers

Ketamine (CYP3A4)

Cocaine (CYP2D6)

EDA (erectile dysfunction agents) (CYP3A4)

Benzodiazepines (CYP3A4/2D6)

ChemSex: concerns

Not all recreational drugs and antiretrovirals are characterized by a high potential for drug–drug interactions:

Efavirenz, etravirine and nevirapine can induce drug metabolism and decrease desired effect (e.g EDA, BDZ)

NRTIs, rilpivirine, raltegravir, dolutegravir, and maraviroc are characterized by a low potential for drug–drug interactions

www.hiv-druginteractions.org

UNIVERSITY OF LIVERPOOL

Antiretrovirals and Recreational Drugs

Charts produced October 2014. Full information available at www.hiv-druginteractions.org and www.hiv-druginteractionslite.org

		ATV/r	DRV/r	FPV/r	IDV/r	LPV/r	SQV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL	ABC	FTC	3TC	TDF	ZDV
Stimulants	Amyl nitrate (Poppers)	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Cocaine	↑[ab]	↑[a]	↑[a]	↑[a]	↑[ab]	↑[ab]	↑[c]	↑[c]	↑[c]	↔[b]	↔	↔	↑[a]	↔	↔	↔	↔	↔	↔
	Ecstasy (MDMA)	↑[d]	↑[d]	↑[d]	↑[d]	↑[d]	↑[d]	↔	↔	↔	↔	↔	↔	↑[d]	↔	↔	↔	↔	↔	↔
	Mephedrone	↑[e]	↑[e]	↑[e]	↑[e]	↑[e]	↑[e]	↔	↔	↔	↔	↔	↔	↑[e]	↔	↔	↔	↔	↔	↔
	Methamphetamine	↑	↑	↑	↑	↑	↑	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔
Depressants	Alcohol	↔	↔	↔[f]	↔	↔[f]	↔	↔	↔	↔	↔	↔	↔	↔	↔	↑	↔	↔	↔	↔
	Alprazolam	↑[g]	↑[g]	↑[g]	↑[h]	↑[g]	↑[g]	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔
	Codeine	↑[i]	↑[i]	↑[i]	↑[i]	↑[i]	↑[i]	↓[i]	↓[i]	↓[i]	↔	↔	↔	↑[i]	↔	↔	↔	↔	↔	↔
	Diazepam	↑	↑	↑	↑[h]	↑	↑	↓	↑	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔
	GHB (gamma hydroxybutyrate)	↑[j]	↑[j]	↑[j]	↑[j]	↑[j]	↑[j]	↔	↔	↔	↔	↔	↔	↑[j]	↔	↔	↔	↔	↔	↔
	Heroin (Diamorphine)	↔[k]	↔[k]	↔[k]	↔[k]	↔[k]	↔[k]	↔[k]	↔	↔	↔	↔	↔	↔[k]	↔	↔	↔	↔	↔	↔
	Hydrocodone	↑	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔
	Hydromorphone	↓	↓	↓	↓	↓	↓	↑	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Ketamine	↑	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔
	Pethidine (Meperidine)	↓[l]	↓[l]	↓[l]	↓[hl]	↓[l]	↓[l]	↓[l]	↓[l]	↓[l]	↔	↔	↔	↑?	↔	↔	↔	↔	↔	↔
	Methadone	↓[b]	↓16%	↓18%	↓	↓53%[b]	↓19%[bm]	↓52%	↑6%	↓~50%	↓16%[b]	↔	↔	↑7%	↔	↓	↔	↔	↔	⇑
	Midazolam (oral)	↑[n]	↑[n]	↑[n]	↑[n]	↑[n]	↑[n]	↓[n]	↓	↓	↔	↔	↔	↑[n]	↔	↔	↔	↔	↔	↔
	Morphine	↓[o]	↓[o]	↓[o]	↓[o]	↓[o]	↓[o]	↑	↔[o]	↔	↔	↔	↔	↔[o]	↔	↔	↔	↔	↔	↔
	Oxycodone	↑	↑	↑	↑	↑	↑	↓	↓	↓	↔	↔	↔	↑	↔	↔	↔	↔	↔	↔
	Temazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Triazolam	↑[n]	↑[n]	↑[n]	↑[n]	↑[n]	↑[n]	↓[n]	↓	↓	↔	↔	↔	↑[n]	↔	↔	↔	↔	↔	↔
Hallucinogens	Cannabis	⇓	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔	↔
	Lysergic acid diethylamide (LSD)	↑[p]	↑[p]	↑[p]	↑[p]	↑[p]	↑[p]	↓	↓	↓	↔	↔	↔	↑[p]	↔	↔	↔	↔	↔	↔
	Phencyclidine (PCP, angel dust)	↑[q]	↑[q]	↑[q]	↑[q]	↑[q]	↑[q]	↓	↓	↓	↔	↔	↔	↑[q]	↔	↔	↔	↔	↔	↔

Management

Crystal Meth/mephedrone

If patients present with what appears to be drug-induced psychosis:

- Re-assure that they are safe
- Assess if patient is a risk to themselves or to others, and refer to A&E if you feel it appropriate
- Diazepam 5 mg twice daily for 2 days maybe useful

Management

GHB/GBL detox

If patients are using GHB/GBL:

- Check if they are **using every day (for 4 consecutive days or more**) → in this case, they should be advised ***not*** to stop using without medical advice

- If they have no more supply of GBL, they ought to go immediately to A&E. Call ahead to ensure the A&E duty staff are aware of the GBL withdrawal dangers

- Detox involves high levels of benzodiazepines, and baclofen over 5 days

Guy's and St Thomas' Poisons Unit

Guy's and St Thomas' NHS
NHS Foundation Trust

Guidelines on when to call an ambulance to take recreational drug users to A&E

Call an ambulance if ANY of the following are present:

1. AVPU assessment graded as either P or U
   - A=Alert
   - V=Responds to voice i.e. talking to
   - P= Responds to painful stimuli only
     (e.g. pressure across a finger nail)
   - U=Unconscious

2. Chest pain similar to a 'heart attack' (i.e. like a pressure on the chest, like a band around the chest).

3. Any history of seizures (i.e. a convulsion similar to an epileptic fit) during this episode

4. More than 2 'poisoned clubbers' per 'club medic'

5. Temperature >38°C not settling after 15 minutes of rest
   OR a temperature >40°C at any time

6. Heart rate >140 beats per minute not settling within 15 minutes

7. Blood pressure Systolic <90 or >180, Diastolic >110 on 2 readings 5 minutes apart

8. Confusion, significant agitation (e.g. pacing around the room) or significant aggression not settling within 15 minutes

9. Any concerns on behalf of the medical personnel involved

10. IF IN DOUBT CALL AN AMBULANCE

Guidance for paramedics in Clubs…

What does the clinician need to know?

- Importance of asking about Chems use
- Increased STI / HIV / HCV transmission risk
- Adherence to cART
- Drug interactions with cART?
- Management
- Management of come-down post use
- Referral pathways for support

Acknowledgements

- David Stuart
- Paul, Steve, Lukas, Marc and many more
- Nneka Nwokolo
- Tristan Barber
- Saye Khoo
- David Back
- Margherita Bracchi
- Owen Bowden Jones
- Dima Abdulrahim