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Improving the health of people who use **Stimulants**: Where to next?

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Acknowledgements

Responding to global stimulant use: challenges and opportunities
Lancet, 2019

Professor Michael Farrell[1], MB, Natasha K. Martin[2,3], DPhil, Emily Stockings[1], PhD, Annick Bórquez[2,4], PhD, Javier A. Cepeda[2], PhD, Professor Louisa Degenhardt[1], PhD, Robert Ali[5], MD, Lucy Thi Tran[1], BPsySc(Hons), Professor Jürgen Rehm[6,7,8,9,10], PhD, Professor Marta Torrens[11,12,13], PhD, Professor Steve Shoptaw[14,15, 16,17], PhD, Rebecca McKetin[1], PhD

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Types of stimulants that may be used extra-medically

Cocaine

Amphetamine

Methamphetamine

MDMA ("ecstasy")

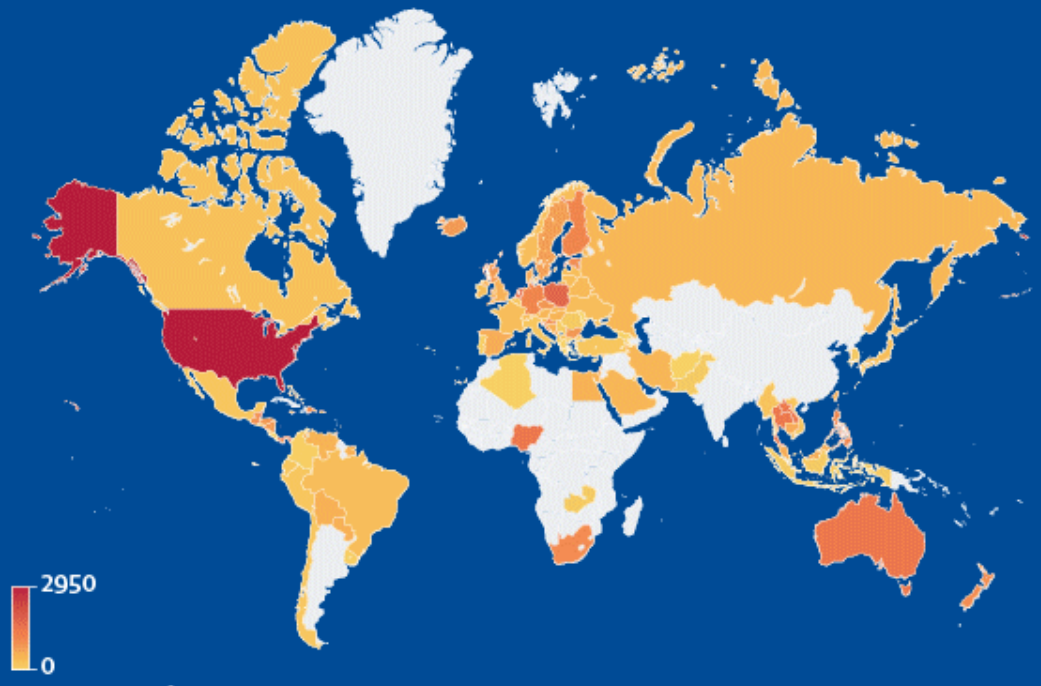
Ephedrine

Adrenalin

BZP and other piperazine derivatives

Khat

Cathinone derivatives (e.g. flephedrone, mephredrone)



Prevalence of amphetamine use per 100 000 population

Globally in 2017

7 in 1000

people used **amphetamines**

11%

became dependent

Series: Drug use

THE LANCET

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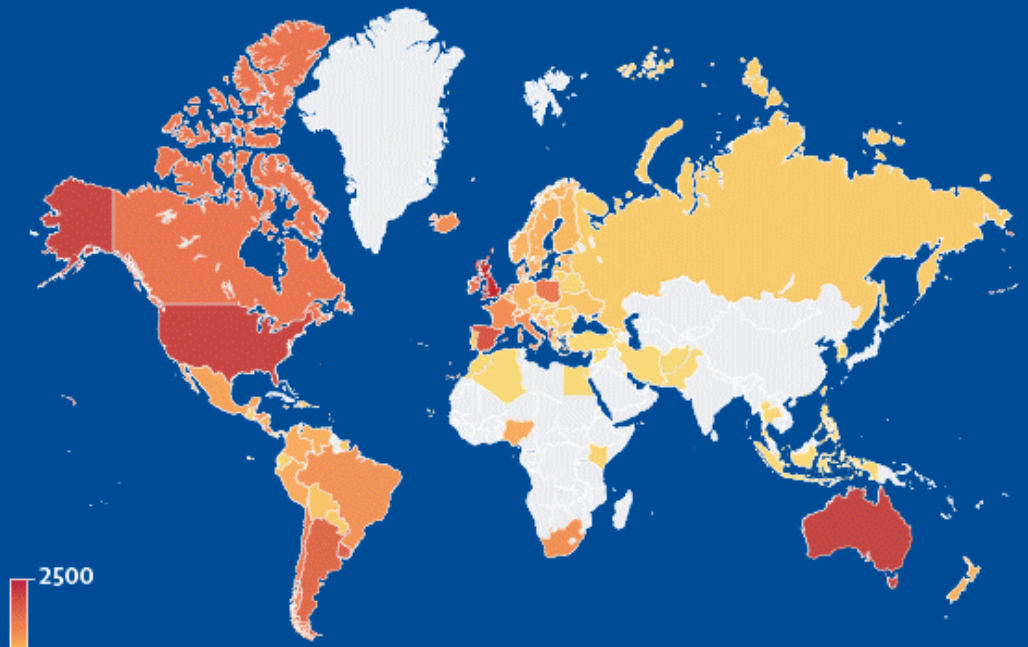

Prevalence of cocaine use per 100 000 population

Globally in 2017

4 in 1000

people used **cocaine**

16%

became dependent

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Cannabis

Alcohol

Opioids

etc

Polysubstance use and co-intoxication (e.g., goofballs)

Polydrug use

Fatal harms

Evidence on the potential effects of stimulants on a range of health harms

	Amphetamines[16]		Cocaine*	
	Crude mortality per 100 patient-years	Standardised mortality ratio	Crude mortality per 100 patient-years	Standardised mortality ratio
Suicide	0·20 (0·07–0·55)	12·20 (4·89–30·47)	0·07 (0·04–0·10)	6·26 (2·84–13·80)
Drug poisoning	0·14 (0·06–0·34)	24·70 (16·67–36·58)	0·34 (0·10–1·15)	NA
Accidental injury	0·20 (0·08–0·47)	5·12 (2·88–9·08)	0·09 (0·04–0·22)	6·36 (4·18–9·68)
Cardiovascular	0·13 (0·06–0·29)	5·12 (3·74–7·00)	0·13 (0·07–0·24)	1·83 (0·39–8·57)
Homicide	0·03 (0·02–0·06)	11·90 (7·82–18·12)	0·09 (0·01–0·54)	9·38 (3·45–25·48)
All-cause	1·14 (0·92–1·42)	6·83 (5·27–8·84)	1·24 (0·86–1·78)	6·13 (4·15–9·05)

NA=not applicable.*Peacock A, University of New South Wales Sydney, personal communication. For details of the search strategies used see appendix p 15.

Table 1: **Summary of causes of mortality summarised across cohorts of people with regular or problematic amphetamine or cocaine use**

Mortality

6 x higher

	Amphetamines[16]		Cocaine*	
	Crude mortality per 100 patient-years	Standardised mortality ratio	Crude mortality per 100 patient-years	Standardised mortality ratio
Suicide	[illegible]	[illegible]	[illegible]	6·26 (2·84–13·80)
Drug poisoning	[illegible]	[illegible]	[illegible]	NA
Accidental injury	0·20 (0·08–0·47)	5·12 (2·88–9·08)	0·09 (0·04–0·22)	6·36 (4·18–9·68)
Cardiovascular	[illegible]	[illegible]	0·13 (0·07–0·24)	1·83 (0·39–8·57)
Homicide	[illegible]	[illegible]	[illegible]	9·38 (3·45–25·48)
All-cause	1·14 (0·92–1·42)	[illegible]	1·24 (0·86–1·78)	6·13 (4·15–9·05)

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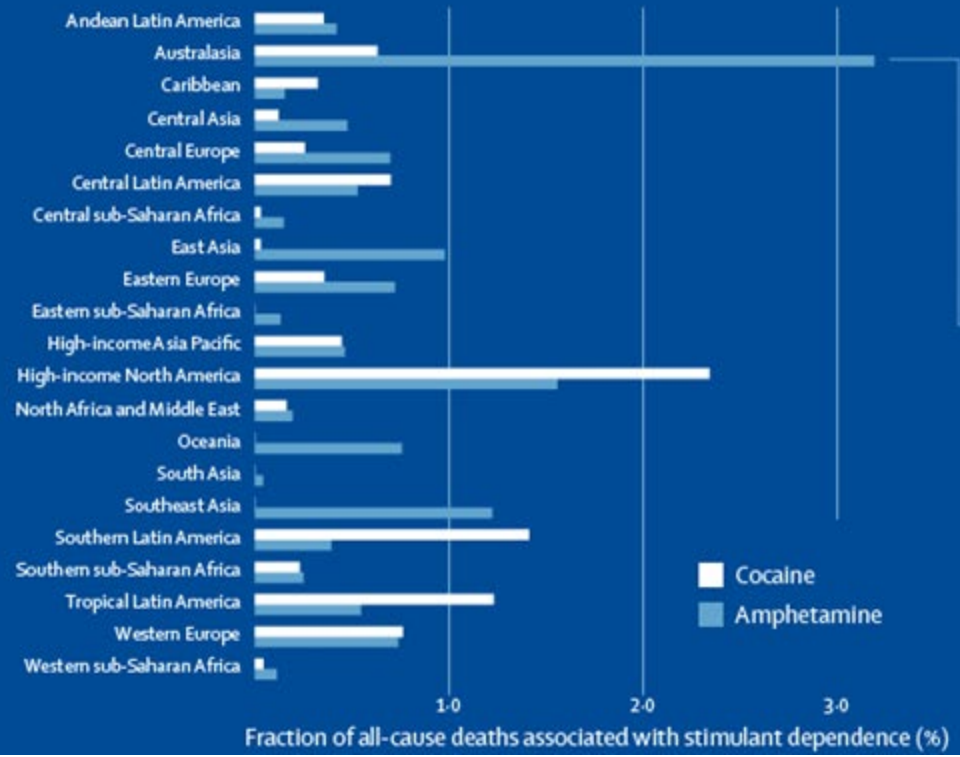
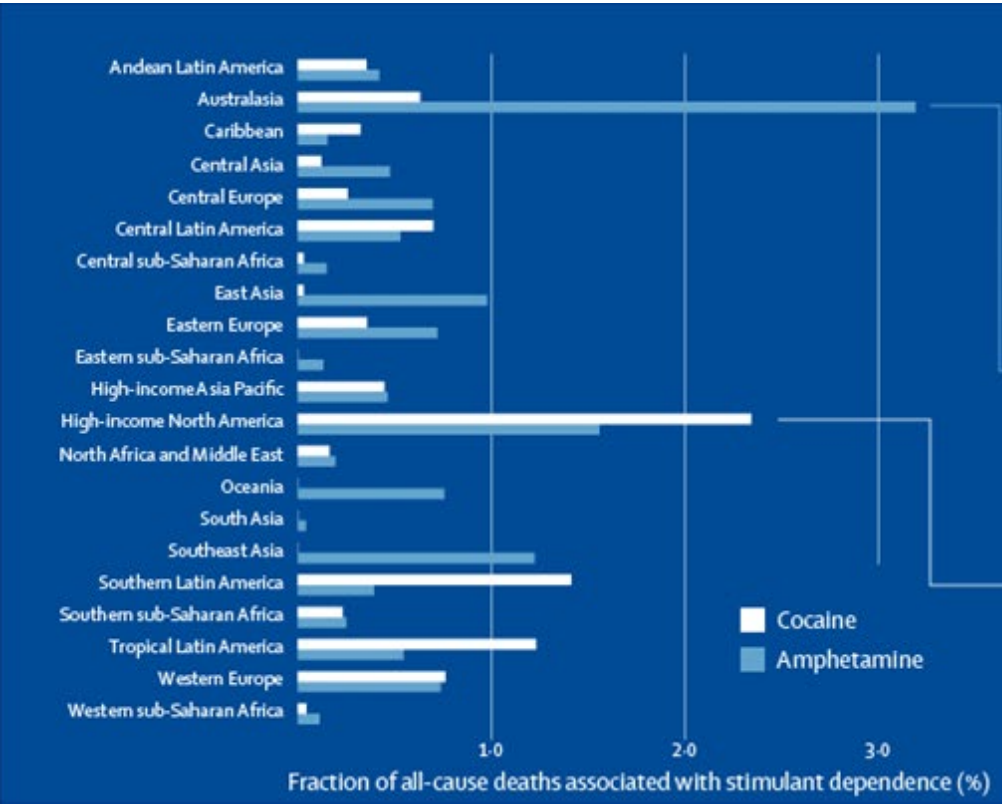
STIMULANTS



The highest fraction of death associated with **amphetamine** dependence is reported from **Australasia**

Series: Drug use

STIMULANTS



The highest fraction of death associated with **amphetamine** dependence is reported from **Australasia**

and for **cocaine** from **North America**

Series: Drug use

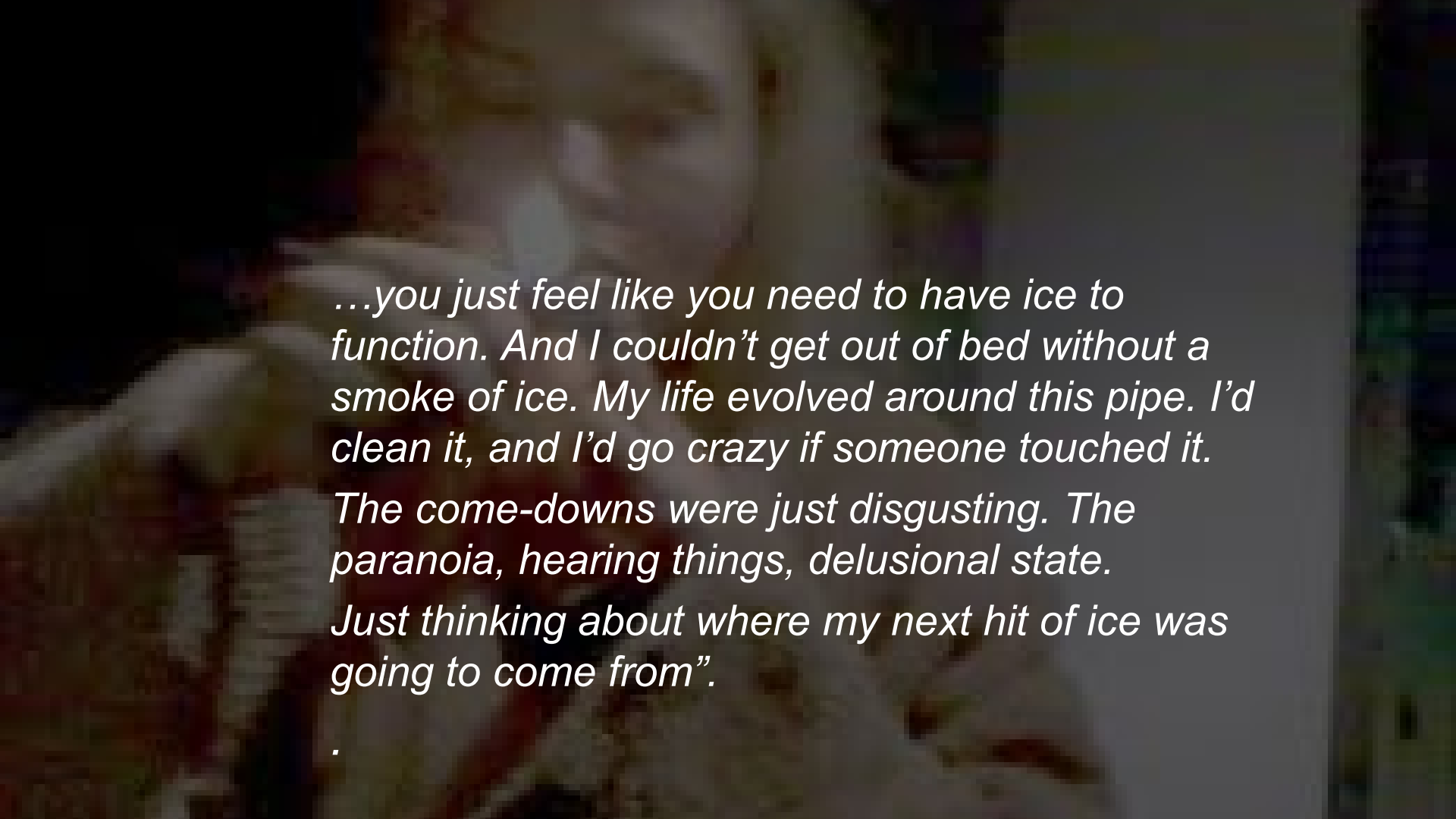
Non-fatal harms

Evidence on the potential effects of stimulants on a range of health harms

Level of evidence: B=findings across cohorts, representative, population-based. C=findings across cohorts of people who use drugs. D=findings across cross-sectional studies, representative population-based, or case-control studies. E=cross-sectional associations among non-representative samples of people who use drugs, case series suggesting outcomes. *Any use versus no use of amphetamine or methamphetamine. †Increased for injecting cocaine use; results for other cocaine use not consistent. ‡Effect in female sex workers and people who inject drugs. §Effect in people who inject drugs.

Table 2: **Evidence for potential causal impacts of amphetamine and cocaine use on a range of non-fatal health harms**

	Amphetamines		Cocaine	
	Effect	Level of evidence	Effect	Level of evidence
Substance use				
Dependence	Increase	B[25]	Increase	B[26]
Non-fatal overdose and poisoning	Increase	C[17]	Increase	C[27]



…you just feel like you need to have ice to function. And I couldn't get out of bed without a smoke of ice. My life evolved around this pipe. I'd clean it, and I'd go crazy if someone touched it.

The come-downs were just disgusting. The paranoia, hearing things, delusional state.

Just thinking about where my next hit of ice was going to come from".

.

Level of evidence: B=findings across cohorts, representative, population-based. C=findings across cohorts of people who use drugs. D=findings across cross-sectional studies, representative population-based, or case-control studies. E=cross-sectional associations among non-representative samples of people who use drugs, case series suggesting outcomes. *Any use versus no use of amphetamine or methamphetamine. †Increased for injecting cocaine use; results for other cocaine use not consistent. ‡Effect in female sex workers and people who inject drugs. §Effect in people who inject drugs.

Table 2: **Evidence for potential causal impacts of amphetamine and cocaine use on a range of non-fatal health harms**

	Amphetamines		Cocaine	
	Effect	Level of evidence	Effect	Level of evidence
Mental health				
Depression*	Increase	D[28]	Increase	B[18]
Anxiety	Unclear	D[28]	No effect	B[18]
Psychosis	Increase	E[28]	Increase	C[29]
Violence*	Increase	D[28]	Potential increase†	E[18]

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ORIGINAL ARTICLE

Dose-Related Psychotic Symptoms in Chronic Methamphetamine Users

Evidence From a Prospective Longitudinal Study

Rebecca McKetin, PhD; Dan I. Lubman, PhD, FRANZCP, FAChAM; Amanda L. Baker, PhD; Sharon Dawe, PhD; Robert L. Ali, FAChAM, FFPHM

Results: There was a 5-fold increase in the likelihood of psychotic symptoms during periods of methamphetamine use relative to periods of no use (odds ratio [OR], 5.3 [95% CI, 3.4-8.3]; $P<.001$), this increase being strongly dose-dependent (1-15 days of methamphetamine use vs abstinence in the past month: OR, 4.0 [95% CI, 2.5-6.5]; ≥16 days of methamphetamine use vs abstinence in the past month: OR, 11.2 [95% CI, 5.9-21.1]). Frequent cannabis and/or alcohol use (≥16 days of use in the past month) further increased the odds of psychotic symptoms (cannabis: OR, 2.0 [95% CI, 1.1-3.5]; alcohol: OR, 2.1 [95% CI, 1.1-4.2]).

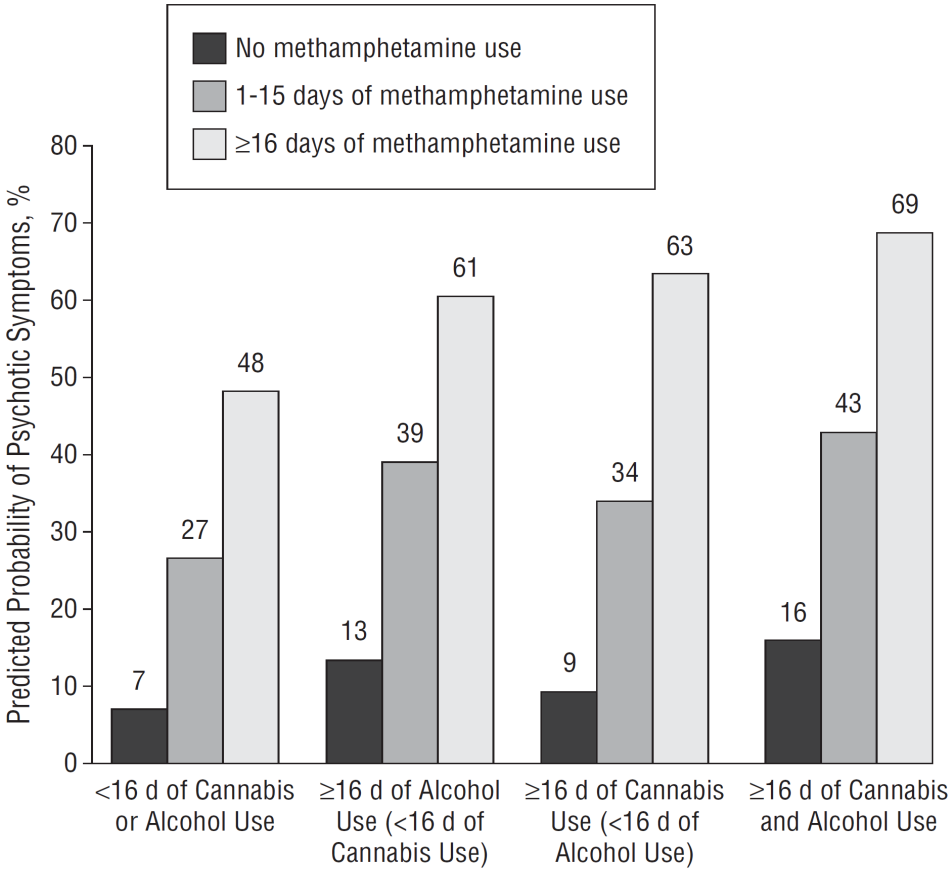


Figure. Predicted probability of psychotic symptoms by level of methamphetamine, alcohol, and cannabis use.

Methamphetamine Use and Schizophrenia: A Population-Based Cohort Study in California

Russell C. Callaghan, Ph.D.

James K. Cunningham, Ph.D.

Peter Allebeck, M.D., Ph.D.

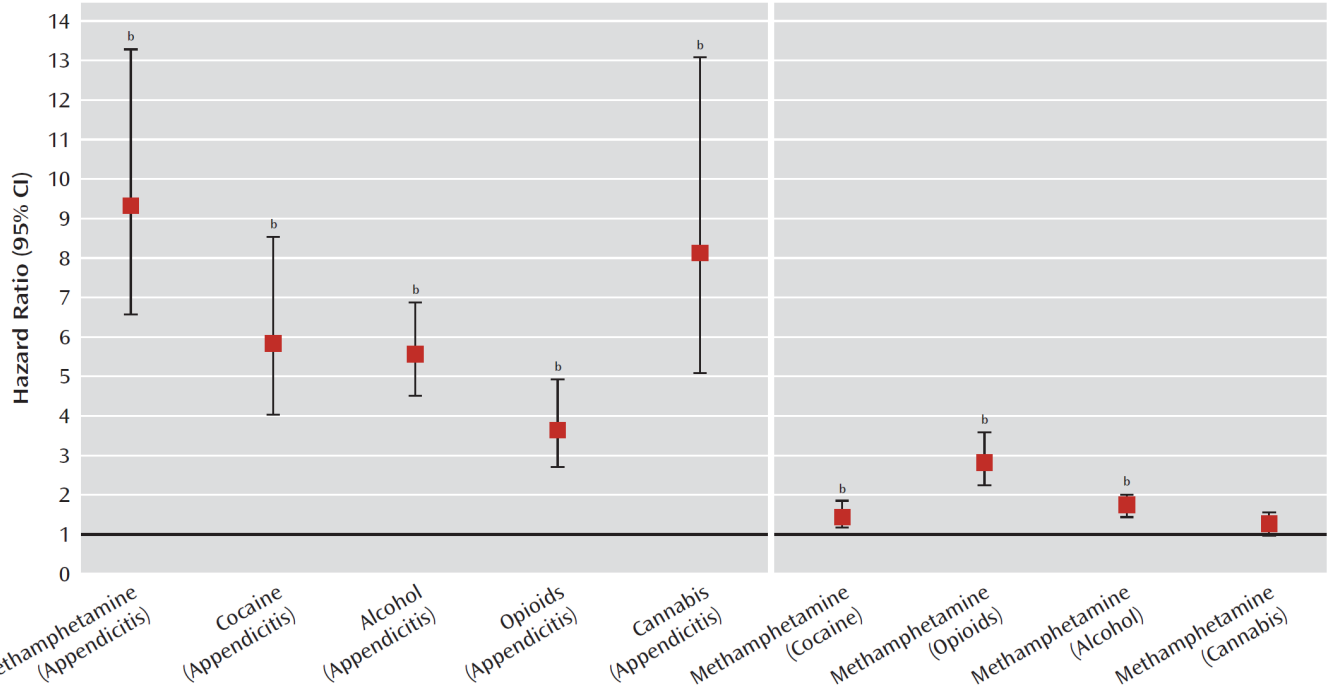
Tamara Arenovich, M.Sc.

Gautam Sajeev, M.Sc.

Gary Remington, M.D., Ph.D.

Isabelle Boileau, Ph.D.

Stephen J. Kish, Ph.D.



[a] Reference group in parentheses.
[b] Statistically significant difference, $p<0.005$.

(Am J Psychiatry 2012; 169:389–396)

Level of evidence: B=findings across cohorts, representative, population-based. C=findings across cohorts of people who use drugs. D=findings across cross-sectional studies, representative population-based, or case-control studies. E=cross-sectional associations among non-representative samples of people who use drugs, case series suggesting outcomes. *Any use versus no use of amphetamine or methamphetamine. †Increased for injecting cocaine use; results for other cocaine use not consistent. ‡Effect in female sex workers and people who inject drugs. §Effect in people who inject drugs.

Table 2: **Evidence for potential causal impacts of amphetamine and cocaine use on a range of non-fatal health harms**

	Amphetamines		Cocaine	
	Effect	Level of evidence	Effect	Level of evidence
Stroke and myocardial infarction	Increase	C[30]	Increase	C[31]
Respiratory and lung disease	Increase	C[32]	Increase	C[18]
Skin and soft tissue infection	Increase	B[33]	Increase	B[33]

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Table 2: **Evidence for potential causal impacts of amphetamine and cocaine use on a range of non-fatal health harms**

	Amphetamines		Cocaine	
	Effect	Level of evidence	Effect	Level of evidence
Other harms				
Non-fatal Injury	Increase	B[21]	Potential increase	B[21]
Neonatal outcomes	Increase	B[41]	Increase	B[18]
Parkinson's disease	Increase	C[42]	Unknown	..

Level of evidence: B=findings across cohorts, representative, population-based. C=findings across cohorts of people who use drugs. D=findings across cross-sectional studies, representative population-based, or case-control studies. E=cross-sectional associations among non-representative samples of people who use drugs, case series suggesting outcomes. *Any use versus no use of amphetamine or methamphetamine. †Increased for injecting cocaine use; results for other cocaine use not consistent. ‡Effect in female sex workers and people who inject drugs. §Effect in people who inject drugs.

Table 2: **Evidence for potential causal impacts of amphetamine and cocaine use on a range of non-fatal health harms**

	Amphetamines		Cocaine	
	Effect	Level of evidence	Effect	Level of evidence
Bloodborne viruses and sexually transmitted infections				
HIV	Increase	B[17,34,35]	Increase‡	B[18,35]
Hepatitis C virus	Increase§	C[36,37]	Increase	B[18]
Sexually transmitted infections	Unclear	C[8,38–40]	Increase	B[18]

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Interventions to address stimulant use and related harms

Table 3: Summary of the evidence of interventions to reduce stimulant use

Pharmacotherapies	Effect	Size of effect	Level
Psychostimulant drugs	↓	1.36 (1.05 – 1.77)	A
Dopamine agonists	✕	1.12 (0.85-1.47)[COC]	A
Antidepressants	✕	1.22 (0.99-1.51) [COC]	A
Antipsychotics	✕	1.30 (0.72-2.33) [COC]	A

A = consistent conclusions across meta-analyses, high-quality systematic reviews, or multiple RCTs
B = evidence from 1-2 RCTs only
C = systematic reviews with some inconsistent conclusions, multiple consistent ecological studies or cohort studies
D = cross-sectional association, case series, single cohort study

Psychostimulant drugs: only for cocaine and very low quality evidence

Naltrexone: 3 trials with mixed outcomes

Ongoing trials: Mirtazapine, N-Acetyl Cysteine, Ibulidast, Lisdexamphetamine, combination approaches

Table 3: Summary of the evidence of interventions to reduce stimulant use

Psychosocial Intervention	Effect	Size of effect	Level
Contingency management	↓	**2.22 (1.59-3.10)**	**A**
Peer-based support groups (12 step programs, NA)	↓?	Insufficient evidence[SUB]	B
Family interventions, multi-systemic therapy	↓?	No pooled estimate available	B
Other law enforcement interventions	?	Drug courts 1.49 (0.88 – 2.53)[AMPH]	D
Screening and brief intervention	✕	0.97 (0.77-1.22)	B
Motivational enhancement therapy[#]	✕	1.16 (0.95 – 1.42)	B
Self-help interventions	✕	0.13 (-0.05-0.31)	A
Self-help interventions involving peers	✕	0.75 (0.30-1.86)	A
Cognitive behaviour therapy	✕	1.17 (0.79-1.74)	A
Community reinforcement approach	✕	2.10 (0.67-6.59)	A
Acceptance and commitment therapy	✕	0.73 (0.26–2.07) compared to CBT	B
Meditation-based therapies	✕	1.37 (0.48-3.93)	A
Therapeutic communities	✕	1.05 (0.87-1.27)[COC]	C

A = consistent conclusions across meta-analyses, high-quality systematic reviews, or multiple RCTs
B = evidence from 1-2 RCTs only
C = systematic reviews with some inconsistent conclusions, multiple consistent ecological studies or cohort studies
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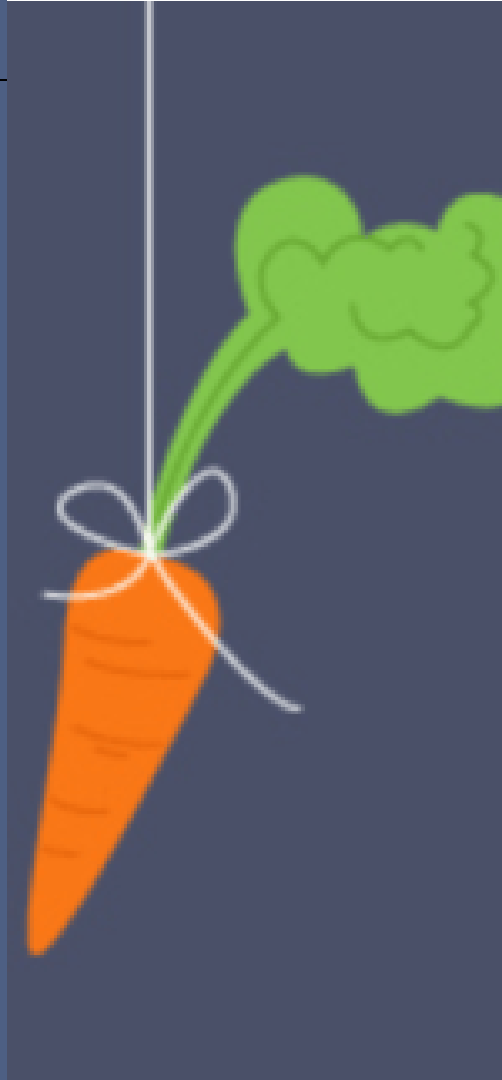
Contingency Management (CM)

No drug = $$ reward

	Drug tests	Reward		Cumulative total
Day 1	☑	$3		$3
Day 3	☑	$5		$8
Day 6	☑	$7	$10 bonus	$25
Day 9	☑	$10		$35
Day 12	☒	$0		
Day 15	☑	$3		$38
Day 18	☑	$5		$43
Day 21	☒	$0		$43
Day 24	☑	$3		$46
Day 27	☑	$5		$51
Day 30	☑	$7	$10 bonus	$68



Implement Contingency Management as standout treatment?

- US-based intervention with limited implementation
- Issues around acceptability and feasibility
- Growing literature on modification – internet/phone based

→ Adapt and evaluate in-situ

Mental health

No treatments for meth psychosis – major drug specific harm

Antidepressants work with cocaine dependence
(but some contraindicated with methamphetamine)

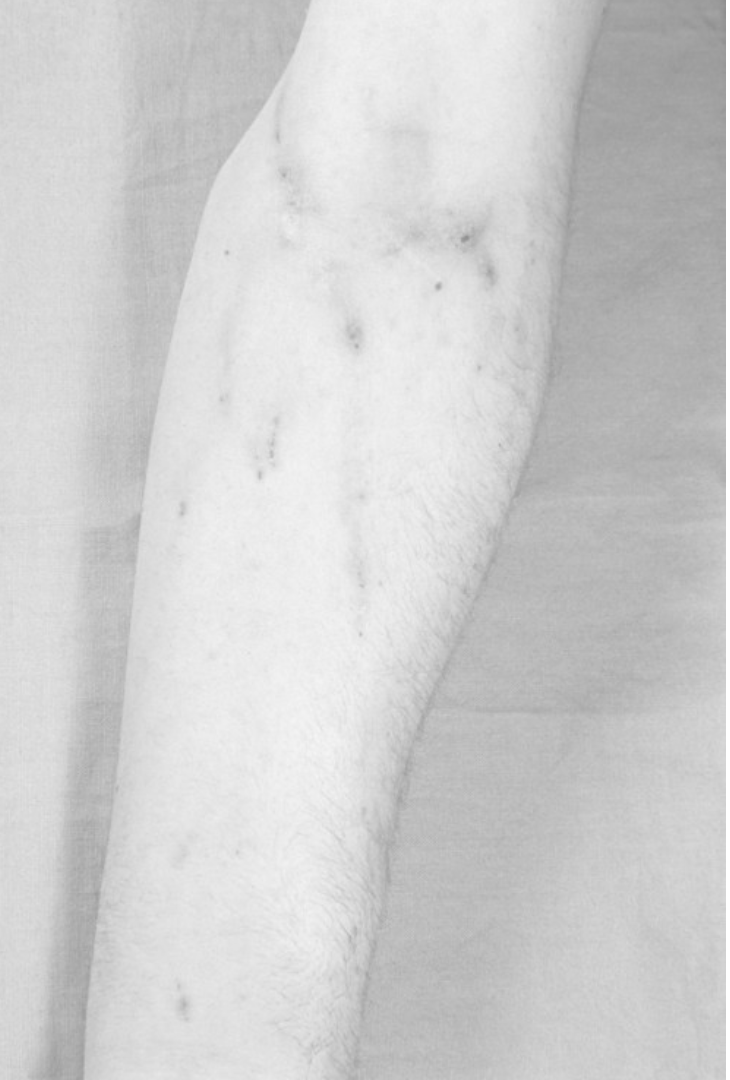
Psychological treatments work for depression
(but no evidence they work for people with substance use)

Suicide risk: Brief interventions and CBT should work…

→ Brief interventions in NSPs or other primary health care venues?

Interventions to reduce HIV/HCV for people who inject drugs

- ☑ Condoms
- ☑ Providing sterile injecting equipment
- ☑ HCV treatment
- ☑ HIV Treatment
- ☑ PreP



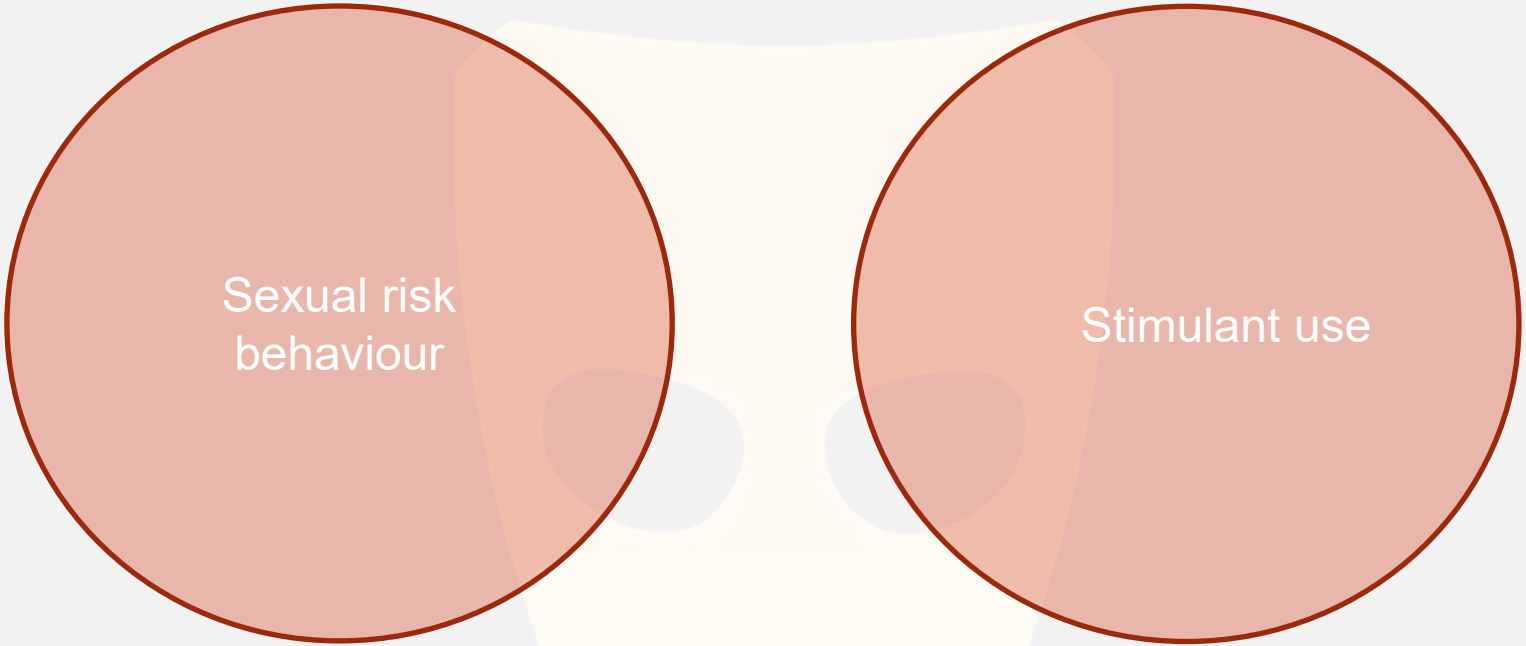
Modelling indicates an additional 3–10% of new HIV and Hepatitis C virus infections in people who inject drugs in the next year could be attributable to each 10% increase in the prevalence of stimulant injection.

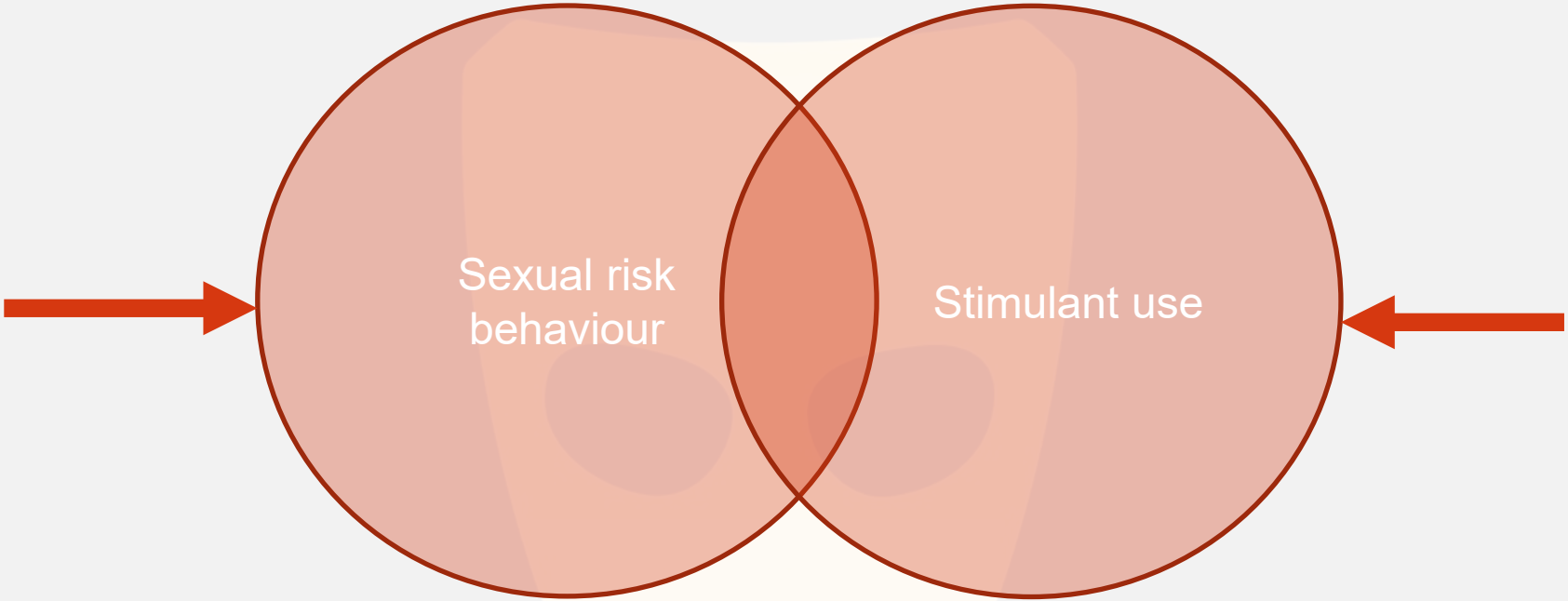
→ **Comprehensive harm reduction approaches are needed to reduce these risks**

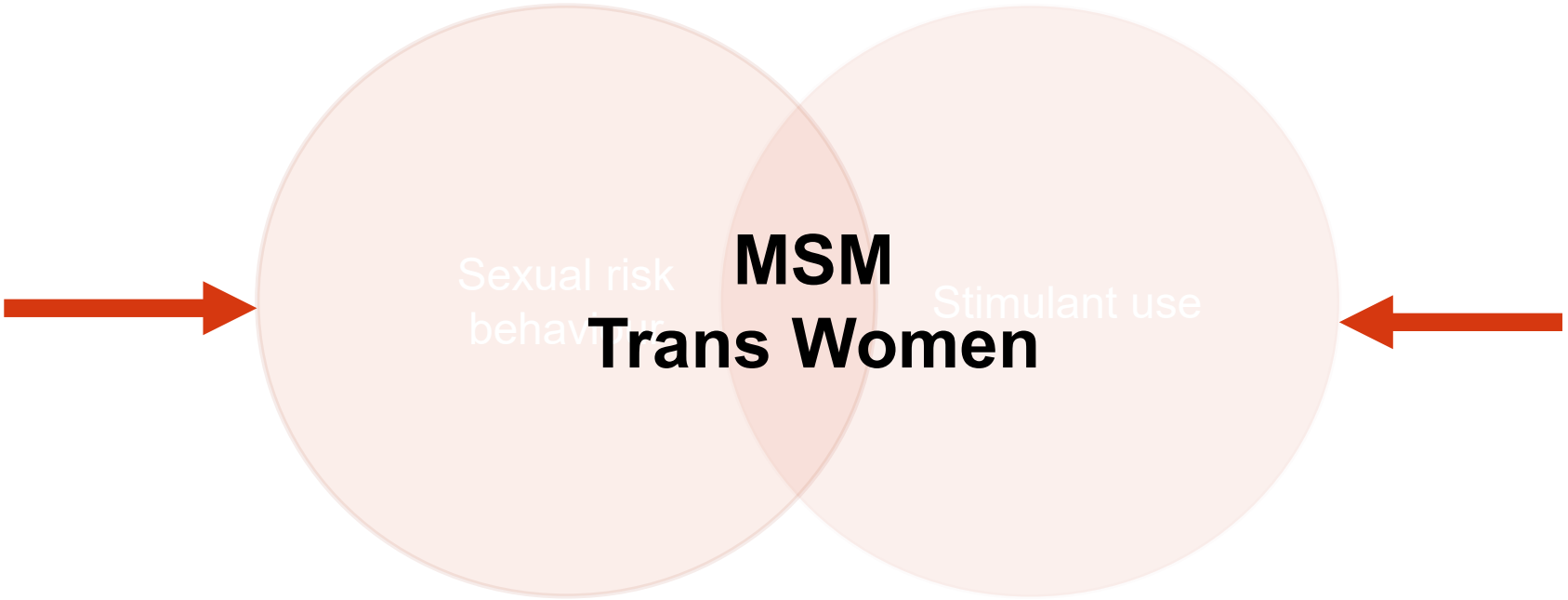
Interventions to reduce HIV/HCV for people who inject drugs

- ☑ Condoms
- ☑ Providing sterile injecting equipment
- ☑ HCV treatment
- ☑ HIV Treatment
- ☑ PreP

What about people who don't inject?


Sexual risk behaviour
Stimulant use


Sexual risk behaviour
Stimulant use



High risk for HIV and STI

Modelling suggests scaling up PreP (100%) in MSM and trans women who use stimulants should prevent an 19% more HIV infections.

→ **Prioritise PreP in MSM and trans women who use stimulants**

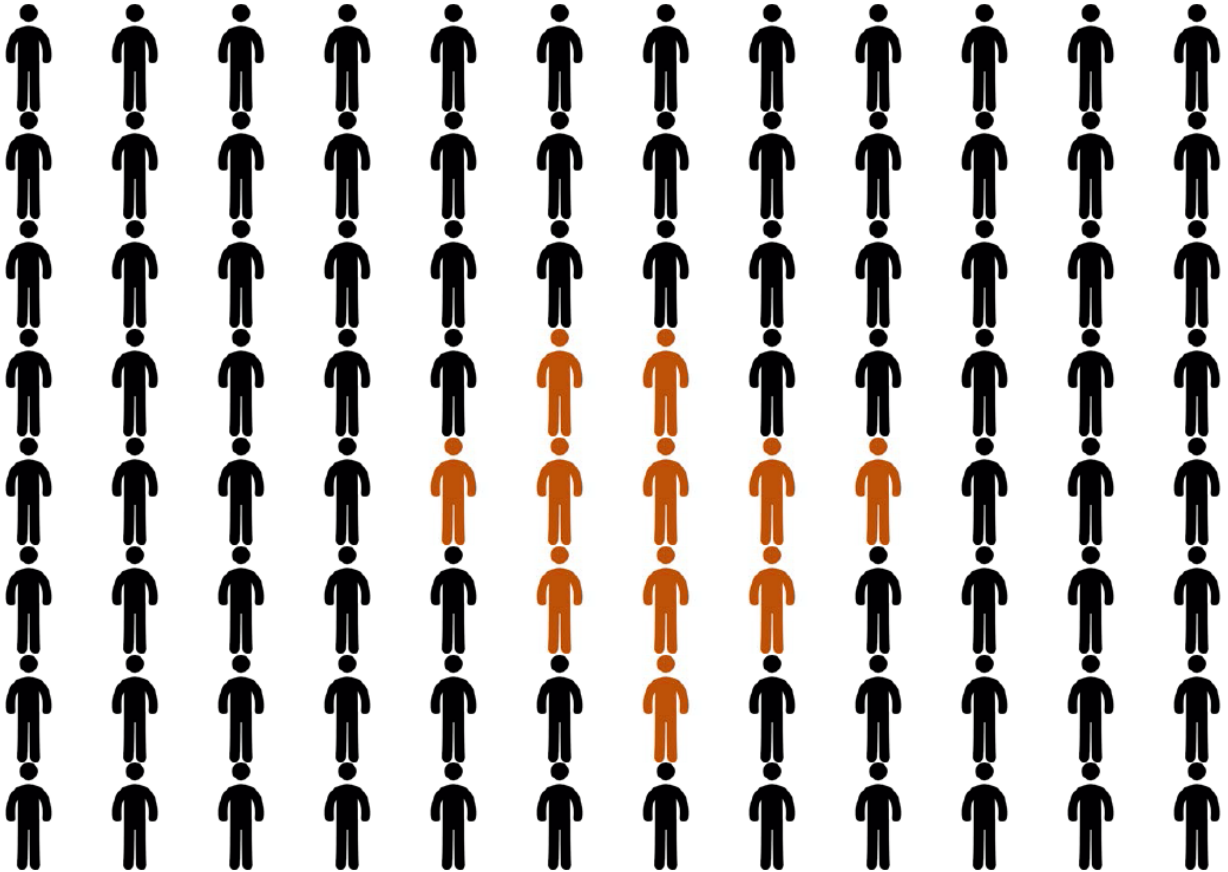
What about heterosexuals who don't inject?

Growing number of people seeking help for smoking crystal meth

- Most straight – males, employed, 20s
- Regional areas
- No history of opioid use
- Many are treatment naïve
- Don't access NSPs

→ **How do we provide harm reduction services to these people?**

Treatment coverage in regional Australian sample of people dependent on meth



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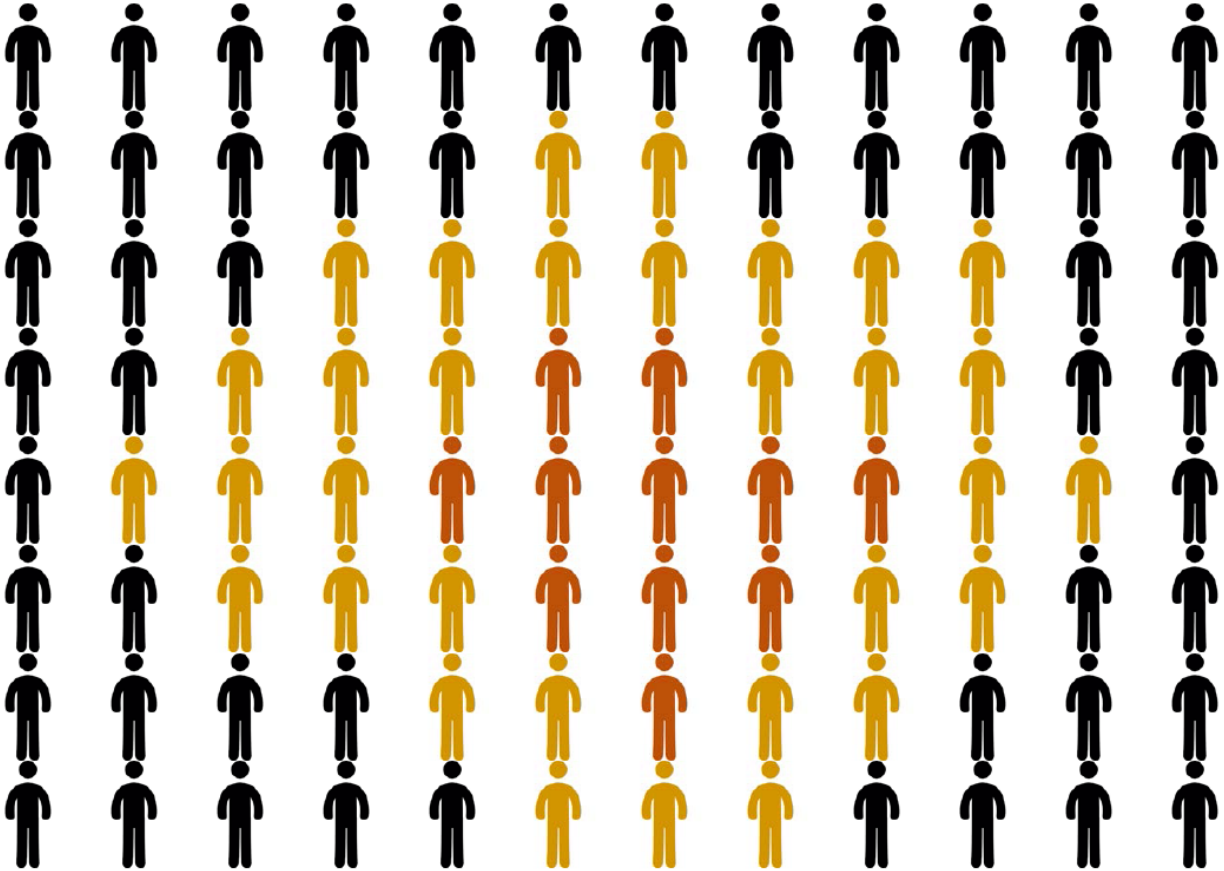

What next?

1. Better evidence
2. Better implementation
3. Target high risk groups with harm reduction
4. Improve access/service coverage of broader population

This growing problem presents a challenge to health and justice services worldwide

Investment is needed in this underserved area with limited effective treatments

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