3rd International Conference on
NOVEL PSYCHOACTIVE SUBSTANCES
15TH - 16TH MAY, 2014. ROME, ITALY

Establishing the patterns of acute toxicity associated with NPS

Problems, solutions & the Euro-DEN Project

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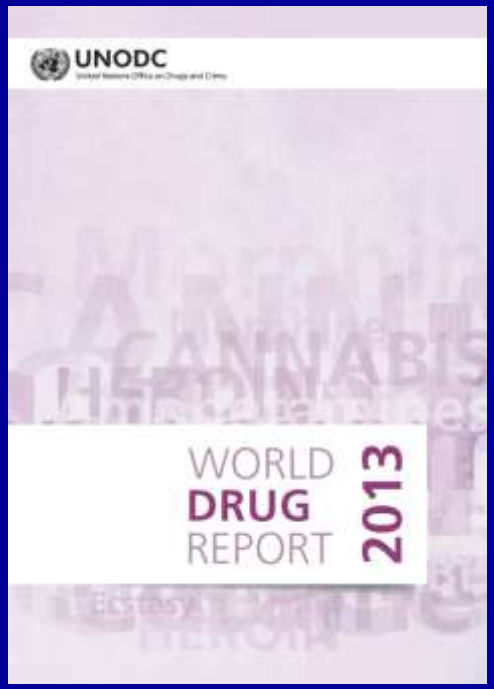
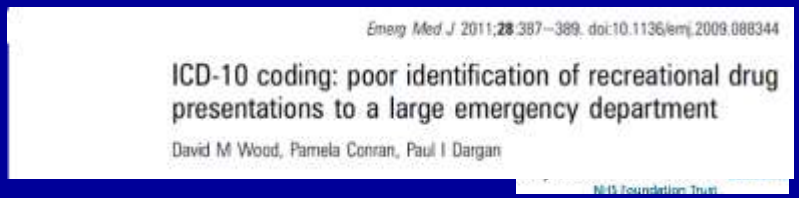
Acute Drug Toxicity Data

- Recreational drug use is common
- Systematic data is available on:
  - Prevalence of drug use
  - Drug seizures
  - Use of treatment agencies for problem drug use
  - Drug-related fatalities
- There is no *systematic* data on acute recreational drug toxicity
  - Despite this being a key public health indicator



Currently Available National Data on Recreational Drug Toxicity

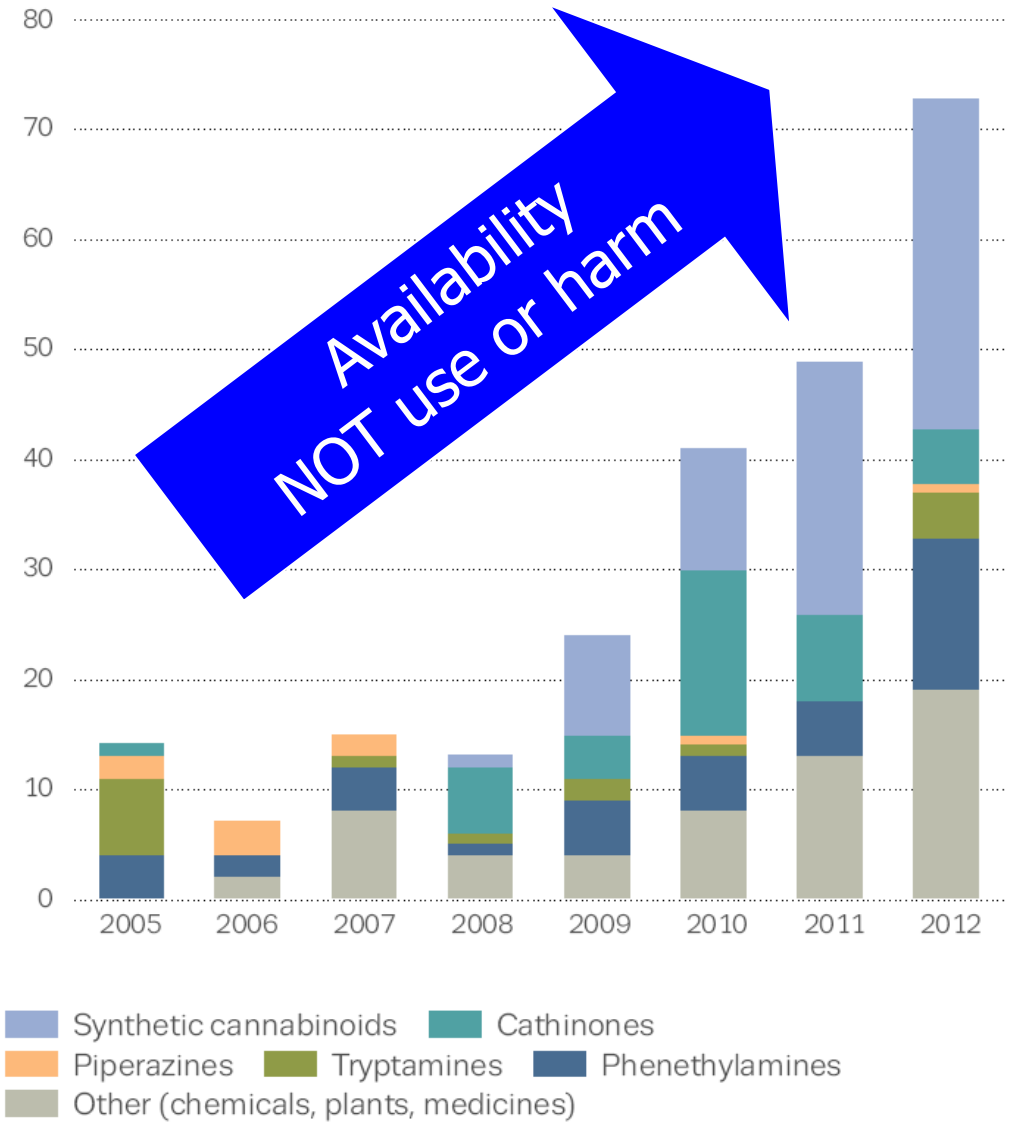
- Some sub-population hospital/pre-hospital data collected e.g. Spain, UK and Netherlands
  - Recent EMCDDA study: cocaine
- Hospital coding of admissions (discharges)
  - Only captures admitted patients (50%)
  - Based on ICD-10: very poor coding capture
    - Many drugs not included
    - Many cases coded by the presenting feature


Emerg Med J 2011;28:387–389. doi:10.1136/emj.2009.088344

ICD-10 coding: poor identification of recreational drug presentations to a large emergency department

David M Wood, Pamela Conran, Paul I Dargan

Number and main groups of new psychoactive substances notified to the EU Early warning system, 2005–2012



European Monitoring Centre for Drugs and Drug Addiction

Risk assessment of new psychoactive substances

Operating guidelines

A. Physical, chemical, pharmaceutical and pharmacological information
B. Dependence and abuse potential
C. Prevalence of use
D. Health risks
E. Social risks
F. Involvement of organised crime

Data triangulation of information on new psychoactive substance toxicity

- Numerous sources of information on the acute toxicity of new psychoactive substances
  - No single one provides the complete picture
  - Each has its own limitations
- Traingulation combines the various sources to minimise the limitations and increase the strength of the combination
  - Requires an understanding of the data sources

Understanding How Data Triangulation Identifies Acute Toxicity of Novel Psychoactive Drugs

D. M. Wood · P. I. Dargan

J. Med. Toxicol. (2012) 8:300–303
DOI 10.1007/s13181-012-0241-3

THE Sun
Friday, 12 February 2010

NEWS

Legal drug teen ripped his scrotum off

Data triangulation examples

J. Med. Toxicol.
DOI 10.1007/s13181-012-0241-3

REVIEW ARTICLE

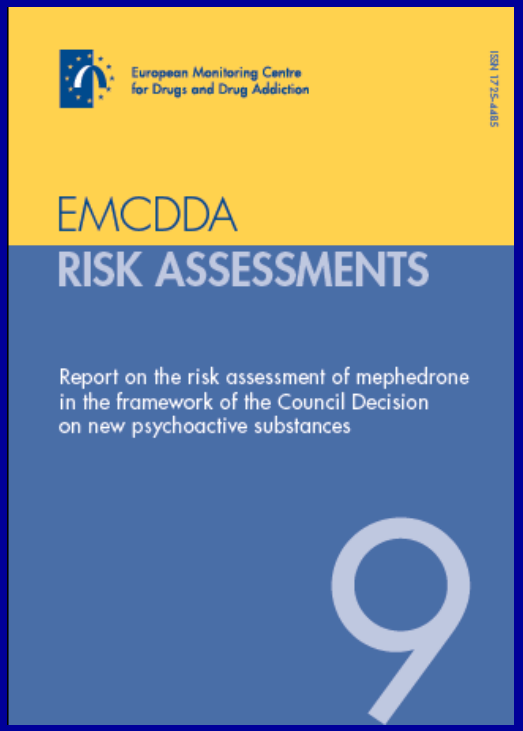
Understanding How Data Triangulation Identifies Acute Toxicity of Novel Psychoactive Drugs

D. M. Wood · P. I. Dargan

The clinical toxicology of the designer "party pills" benzylpiperazine and trifluoromethylphenylpiperazine

Clinical Toxicology (2011) **49**, 131–141

LEO J. SCHEP[1], ROBIN J. SLAUGHTER[1], J. ALLISTER VALE[2], D. MICHAEL G. BEASLEY[1], and PAUL GEE[3]



Review
Drug Testing and Analysis
Received: 18 January 2011 Revised: 24 March 2011 Accepted: 24 March 2011 Published online in Wiley Online Library
(www.drugtestinganalysis.com) DOI 10.1002/dta.312

The pharmacology and toxicology of the synthetic cathinone mephedrone (4-methylmethcathinone)

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Potential sources of information on novel drug use and toxicity

- *In vitro* pharmacological studies
- Animal studies
- User reports and sub-population surveys
- Poisons Information Services
- Pre-hospital emergency services data
- Clinical reports
  - Case reports / series
  - ED presentations, linked sentinel centres

In vitro pharmacological studies?

- Often very little known about their pharmacology or potential for toxicity
  - Except some NPS which have been used previously in pharmaceutical industry
- More recent studies allow characterisation of likely pharmacological mechanisms of action
  - 'Prediction' of pharmacological activity and *potential* toxicity
  - Need to interpret with caution

Contents lists available at SciVerse ScienceDirect

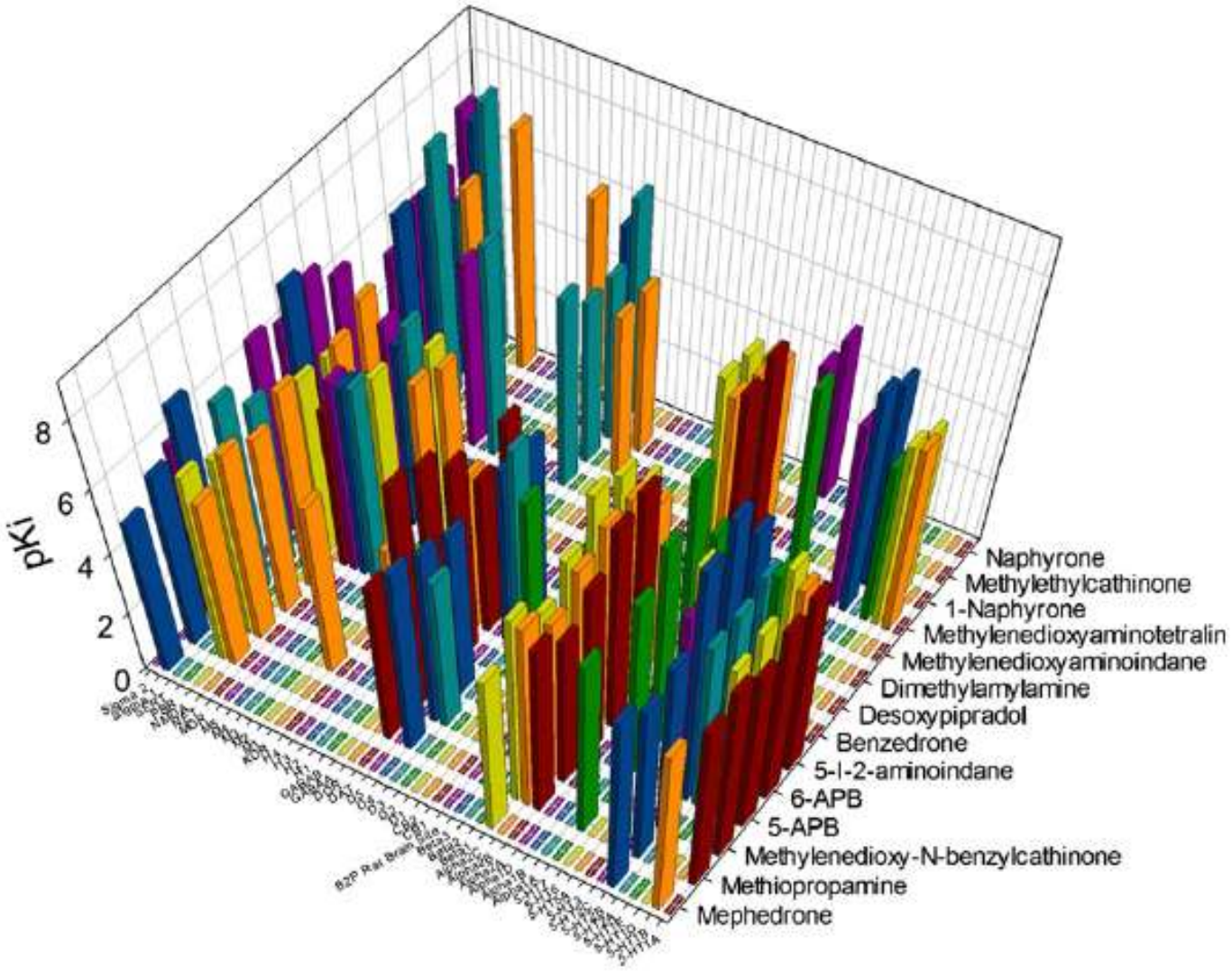
European Journal of Pharmacology

journal homepage: www.elsevier.com/locate/ejphar

Neuropharmacology and analgesia

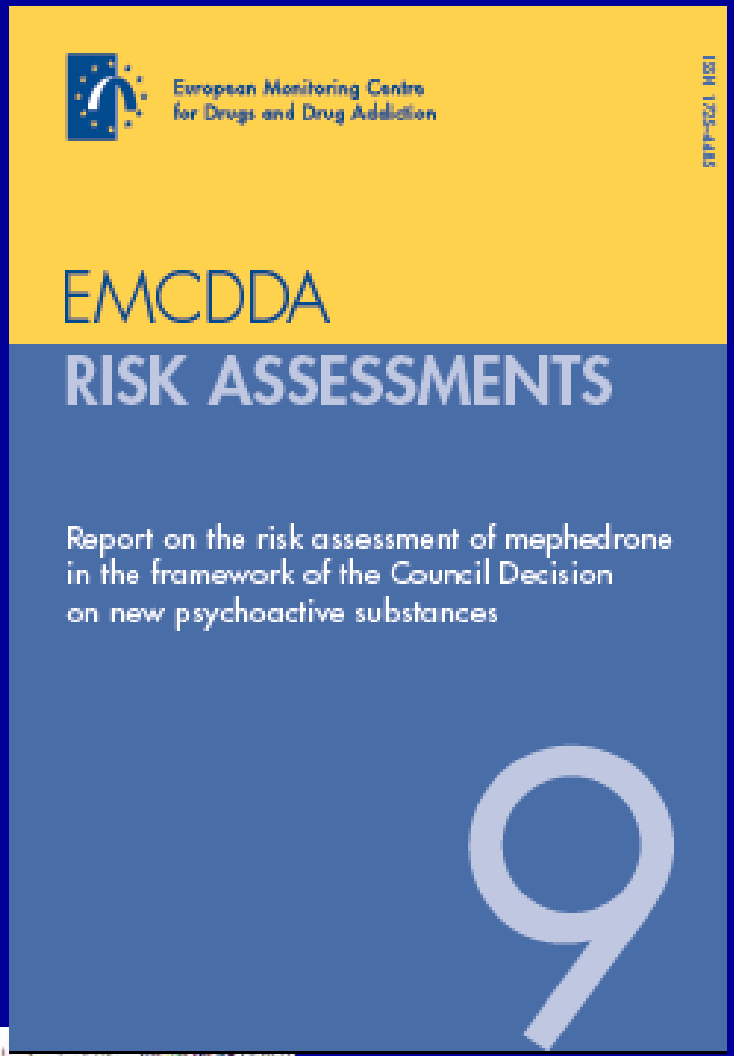
Neurochemical profiles of some novel psychoactive substances

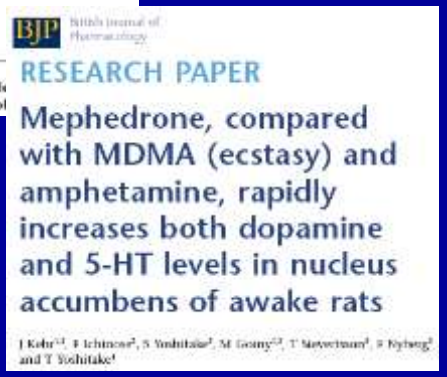
Les Iversen[a,*], Simon Gibbons[b], Ric Treble[c], Vincent Setola[d], Xi-Ping Huang[d,1], Bryan L. Roth[d,1]



What about animal studies?

- Generally lag significantly behind other data sources





Internet based discussion forums

- Need to interpret with caution
  - Self-reported by users, no corroboration
  - BUT, can be useful source of initial information

Sub-population user surveys

- Examples: MixMag/GDS, *in situ* nightclub surveys, focus group surveys, internet surveys
- 454 (18%) "medical help" due to drugs
  - 20% cathinones, 8% other NPS
- Data from most recent episode
  - Collapse 32%
  - Palpitations 30%
  - Chest pain 29%
  - Panic / paranoia 25%
  - Hallucinations 22%

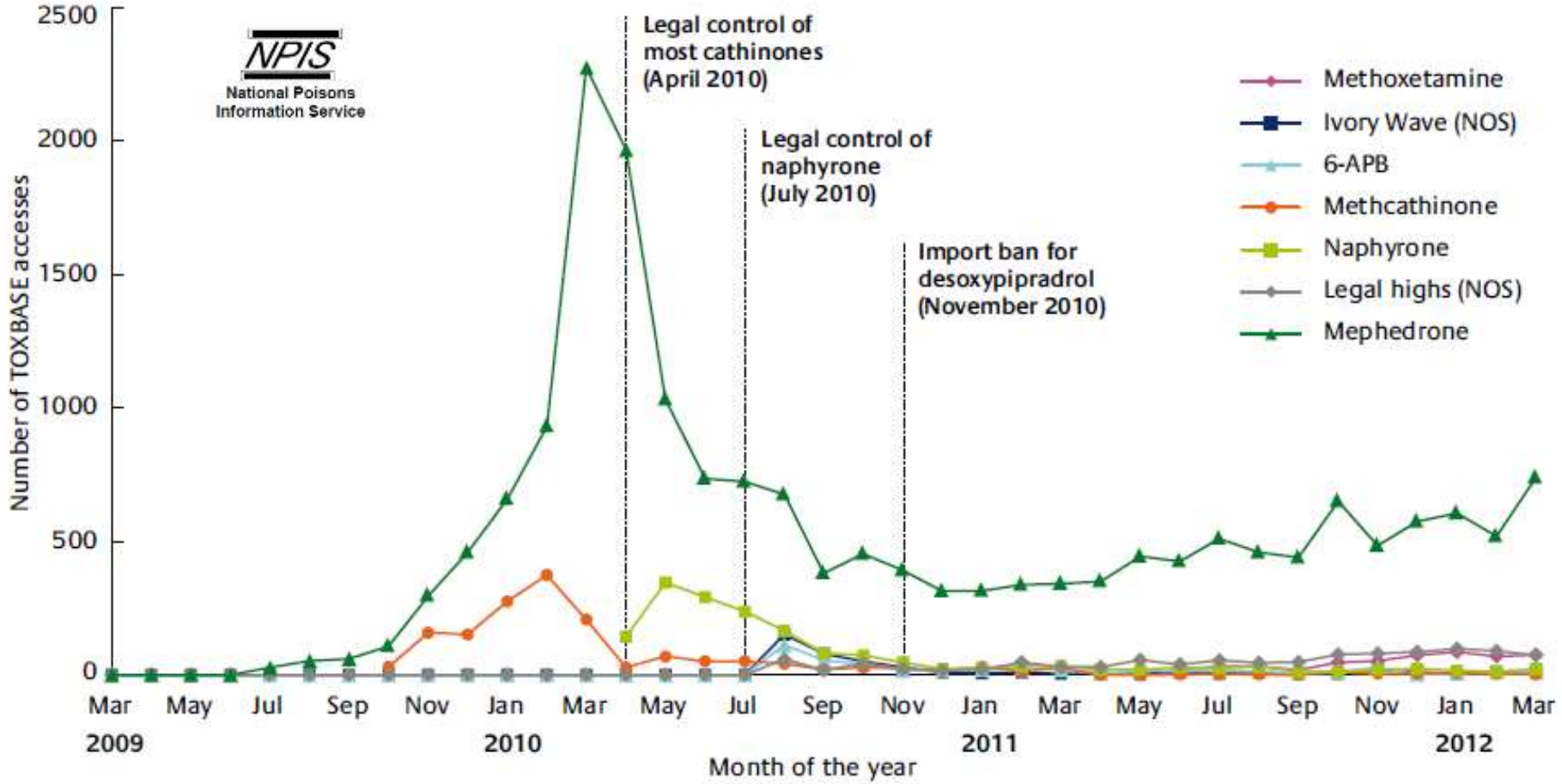
Hospital and prehospital emergency service utilisation as an impact of acute recreational drug and ethanol toxicity

Journal of Substance Use, 2013; 18(2): 129–137

J. R. H. ARCHER[1], P. I. DARGAN[1,2], D. M. WOOD[1,2], & A. R. WINSTOCK[3]

Poisons Information Services

- Provide information to clinicians on management of drug toxicity AND collect data on these cases
- Can collate data on
  - Geographical and time patterns
  - Clinical patters of toxicity



TOXBASE accesses

Table 2 Clinical features reported with exposure to mephedrone alone or in combination with alcohol as reported in telephone enquiries (n=131) or uploaded to TOXBASE (n=18)

	Telephone enquiries		TOXBASE reports	
	n	% (95% CI)	n	% (95% CI)
Clinical features				
Agitation, aggression	32	24 (18 to 33)	9	50 (26 to 73)
Tachycardia	29	22 (16 to 30)	7	39 (18 to 64)
Anxiety	19	15 (9 to 22)	3	17 (4 to 42)
Confusion, psychosis	18	14 (9 to 21)	3	17 (4 to 42)
Chest pain	17	13 (8 to 20)	5	28 (11 to 54)
No features	17	13 (8 to 20)	3	17 (4 to 42)
Nausea	15	11 (7 to 18)	4	22 (7 to 48)
Palpitations	14	11 (6 to 18)	5	28 (11 to 54)
Fever, sweating	12	9 (5 to 16)	2	11 (2 to 36)
Breathlessness	11	8 (4 to 15)	2	11 (2 to 36)
Dizziness	10	8 (4 to 14)	2	11 (2 to 36)
Peripheral vasoconstriction	10	8 (4 to 14)	1	6 (3 to 29)
Mydriasis	9	7 (3 to 13)	2	11 (2 to 36)
Skin changes, rash	9	7 (3 to 13)	1	6 (3 to 29)
Headache	7	5 (2 to 11)	3	17 (4 to 42)
Reduced level of consciousness	7	5 (2 to 11)	4	22 (7 to 48)
Abdominal pain	6	5 (2 to 10)	2	11 (2 to 36)
Hypertension	5	4 (1 to 9)	0	0 (0 to 22)
Parasthesiae	5	4 (1 to 9)	0	0 (0 to 22)
Insomnia	5	4 (1 to 9)	0	0 (0 to 22)
Convulsions	4	3 (1 to 8)	2	11 (2 to 36)
Loin pain	4	3 (1 to 8)	1	6 (3 to 29)
Tongue disorder	4	3 (1 to 8)	0	0 (0 to 22)
Myoclonus/abnormal movements	3	2 (1 to 7)	2	11 (2 to 36)
Tremor	3	2 (1 to 7)	2	11 (2 to 36)
ECG abnormal	3	2 (1 to 7)	0	0 (0 to 22)
Local effects (mouth/pharynx)	3	2 (1 to 7)	0	0 (0 to 22)
Dystonic reaction	2	2 (1 to 7)	0	0 (0 to 22)
Abnormal vision	2	2 (1 to 7)	1	6 (3 to 29)
Liver function tests abnormal	2	2 (1 to 7)	0	0 (0 to 22)
Raised creatine kinase	1	1 (0 to 4)	3	17 (4 to 42)
Acidosis	1	1 (0 to 4)	1	6 (3 to 29)
Epistaxis	1	1 (0 to 4)	1	6 (3 to 29)

Clinical characteristics of mephedrone toxicity reported to the UK National Poisons Information Service

Emerg Med J 2011;28:686–689.

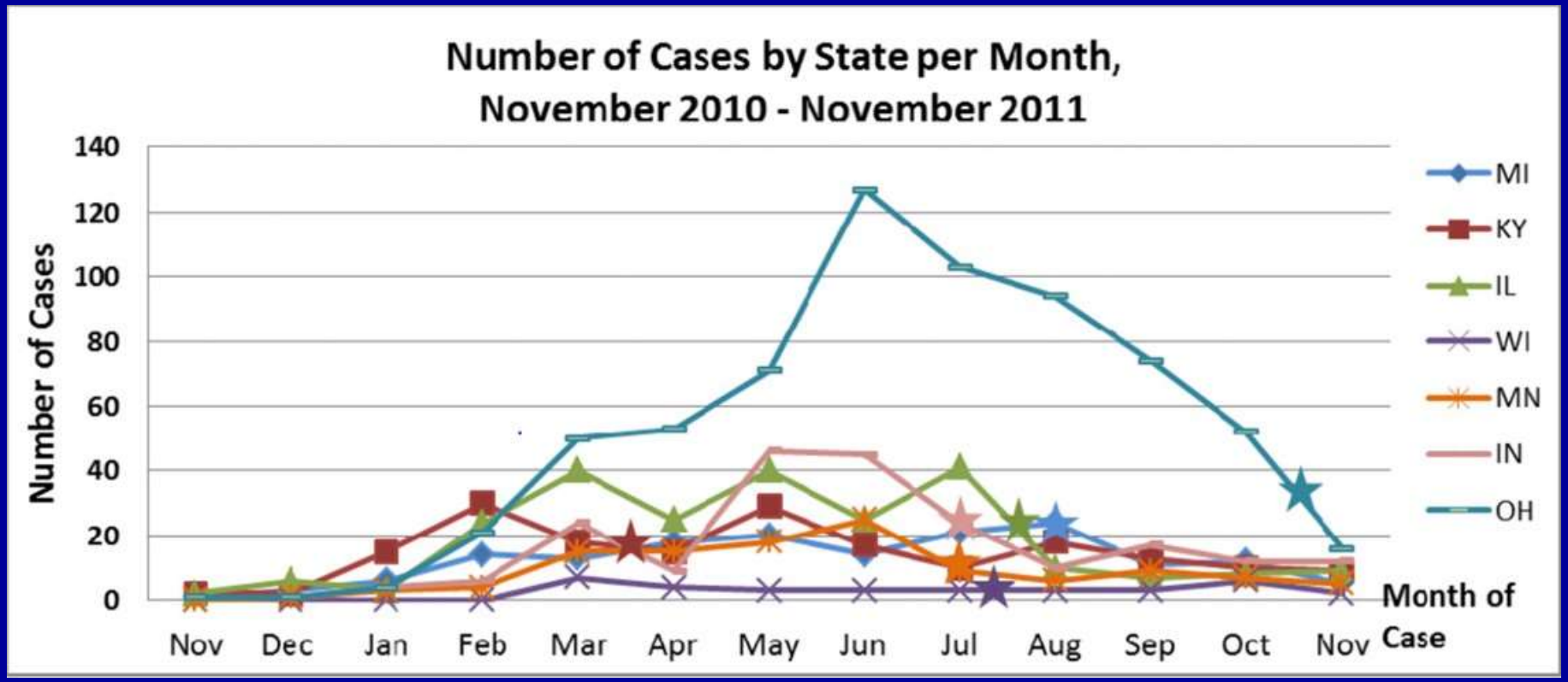
D James,[1] R D Adams,[2] R Spears,[3] G Cooper,[3] D J Lupton,[2] J P Thompson,[3] S H L Thomas,[1] on behalf of the National Poisons Information Service

TOXICOLOGY/ORIGINAL RESEARCH

A 9-State Analysis of Designer Stimulant, "Bath Salt," Hospital Visits Reported to Poison Control Centers

Brandon J. Warrick, MD; Meredith Hill, DO; Kimberly Hekman, MPH; Rachelle Christensen, PharmD; Robert Goetz, PharmD; Marcel J. Casavant, MD; Michael Wahl, MD; James B. Mowry, PharmD; Henry Spiller, MS; Deborah Anderson, PharmD; Alfred Aleguas, PharmD; David Gummin, MD; Ronald Thomas, PhD; Christopher Nezlek, DO; Susan Smolinske, PharmD

http://dx.doi.org/10.1016/j.annemergmed.2012.12.017



Cases per one million population	
OH	57.7
KY	43.0
IN	32.4
MN	21.9
IL	18.6
SD	16.9
MI	16.4
WI	5.9

Cases Per 3 Digit Zip Code

- 1-5
- 6-15
- 16-25
- 26-35
- >36

Poisons Information Service Data

- Potential useful source of data
- Can be useful in following trends in 'established' NPS
- Need to interpret with caution
  - May get multiple calls about one case
  - Requires clinicians to contact poisons services AND to report all used drugs
  - Needs awareness of the NPS by the poisons centre
- Early information often lags behind availability of NPS on the recreational drug market

Ambulance and pre-hospital data

- Ambulance data sets
  - UK: >90% cases brought to hospital by ambulance
  - Ambulance datasets not widely available/published
    - No standard EU / International coding system
  - Data linkage occurs in some areas (e.g. Holland)
- Other pre-hospital facilities
  - Data not routinely available but can be useful
    - e.g. ↑ketamine pre- vs in-hospital

Epidemiology of Recreational Drug Toxicity in a Nightclub Environment

DAVID M. WOOD,[1] MICHELLE NICOLAOU,[2] AND PAUL I. DARGAN[1]

Substance Use & Misuse, 44:1495–1502

Case reports and case series

- Requires clinicians to be aware of NPS
- Initial reports tend to be based on user self-report
- Analytically confirmed cases are the 'gold standard'
  - Needs access and funding for specialist analytical facilities to confirm that cases are related to potential novel drug
  - Analytical confirmation can be challenging and is costly

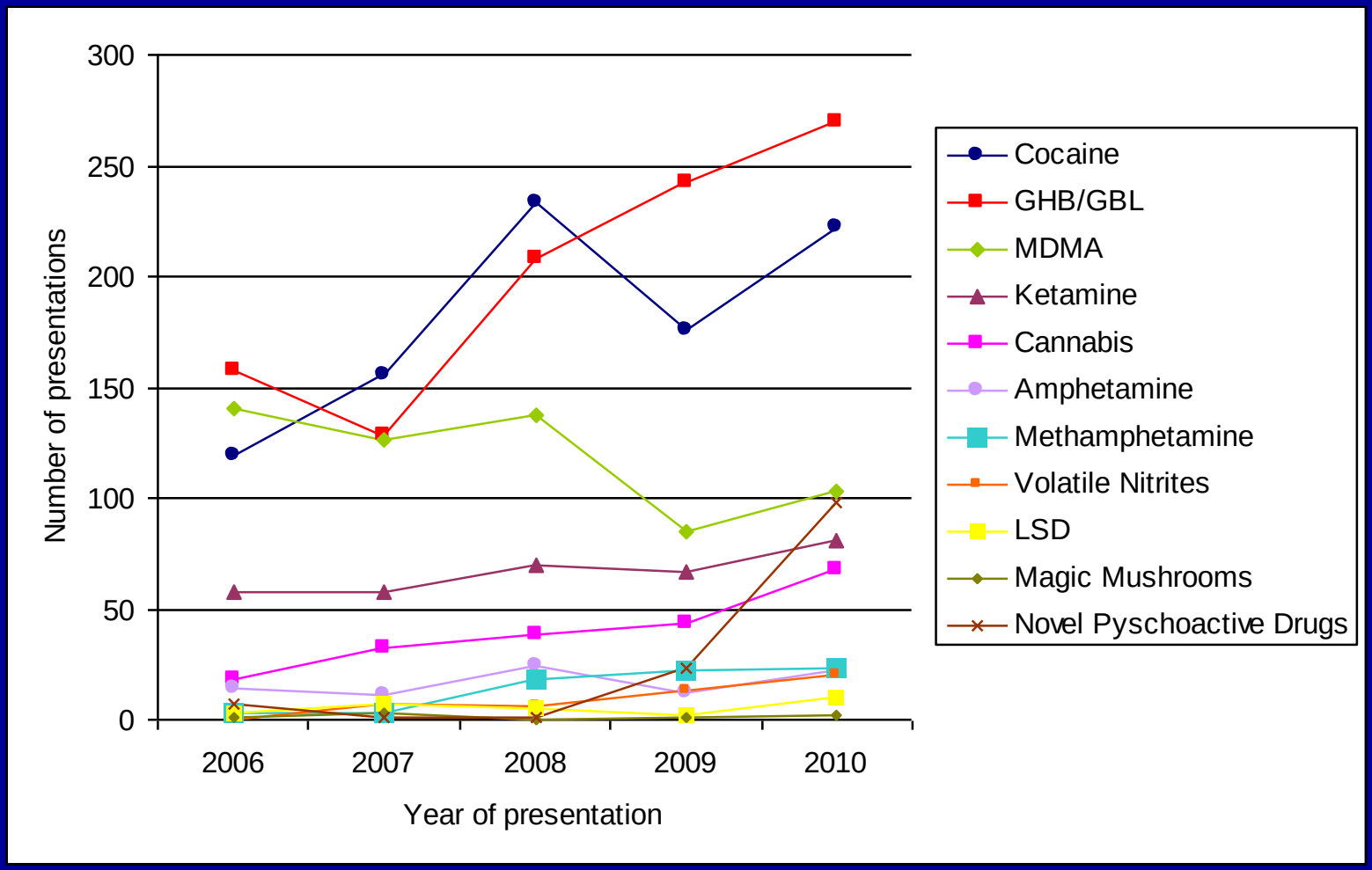
Specialist / Sentinel Centres

- Single centre datasets can collect detailed clinical data on prevalence of novel drug use
  - May include links with specialist analytical facilities
  - Requires interest (and finance)
  - Particularly to monitor trends in areas with high volume drug use
- Single centres can be "linked" to allow comparison between different geographical regions

Five-year trends in self-reported recreational drugs associated with presentation to a UK emergency department with suspected drug-related toxicity

David M. Wood[a,b], Shaun L. Greene[a] and Paul I. Dargan[a,b]

European Journal of Emergency Medicine 2012,



Clinical Toxicology (2014), **52**, 239–241

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DOI: 10.3109/15563650.2014.898771

informa
healthcare

COMMENTARY

The European Drug Emergencies Network (Euro-DEN)

D. M. WOOD,[1,2] F. HEYERDAHL,[3] C. B. YATES,[4] A. M. DINES,[1] I. GIRAUDON,[5] K. E. HOVDA,[3] and P. I. DARGAN[1,2]

European Commission

Guy's and St Thomas' NHS

Euro-DEN Project
European-Drug Emergencies Network

- Full scoping exercise on current European data collection
- Network of 16 specialist ED centres
  - Clinical interest in drug toxicity
  - Data collection over 1 year using minimum dataset
  - Establish seasonal trends
  - Compare drugs responsible for toxicity across Europe
  - Document patterns of NPS toxicity
- Also night-time economy training in drug toxicity

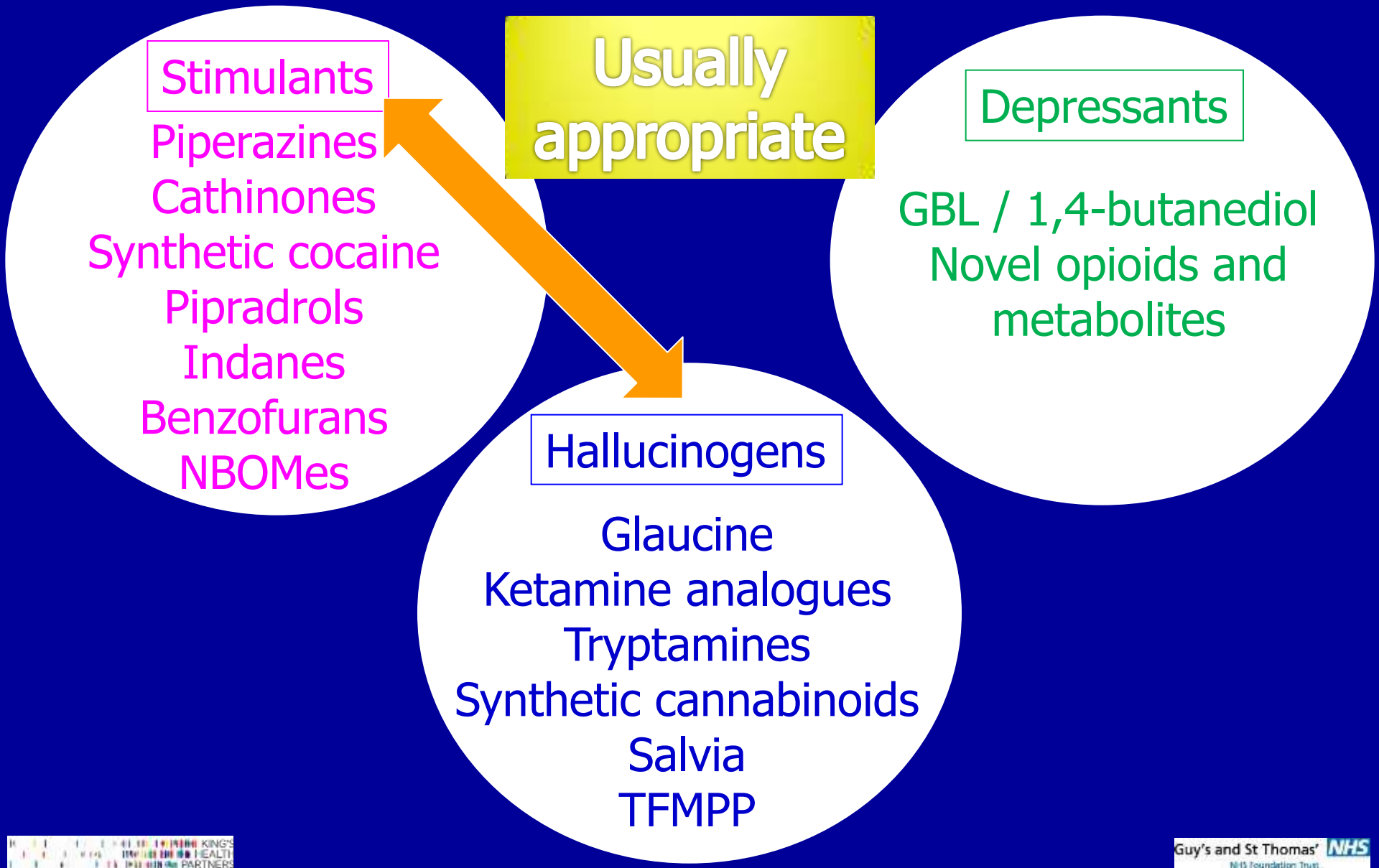
Euro-DEN Project
European-Drug Emergencies Network

- First 4 months of data from 13 (81%) centres
- 1290 cases
- Top 8 drugs:
  - Heroin, cocaine, GHB/GBL, cannabis, amphetamine, MDMA, clonazepam, mephedrone
- NPS
  - 126 (9.8%) cases in 6 (46%) countries
  - UK, Poland, Germany, Spain, Norway, Switzerland

Classifying acute toxicity of new psychoactive substances

- Established recreational drugs are clinically grouped together on the on basis of their unwanted effects
  - Stimulants
  - Hallucinogens
  - Depressants
- Management then guided by clinical pattern of toxicity rather than being drug/substance specific
- Is this also appropriate for NPS?

"Novel Drugs" Clinical Classification



Some NPS have additional toxicity

- Methoxetamine
  - Stimulant features
  - Cerebellar toxicity
- Synthetic cannabionoid receptor agonists
  - Stimulant features
- Pipradrols
  - Prolonged neuropsychiatric features
- Increasing chemical & structural diversity of NPS

  ⇒ Increases risk of additional, unexpected toxicity
- Potency is another concern (e.g. NBOMes)

Wood DM *Eur J Clin Pharmacol* 2011 & 2012, Ward J *Clin* Tox 2012, Murray D *Clin Tox* 2012, Dargan PI *Clin Tox* 2012, Hofer KE *Ann Emerg Med* 2012, Hills S *Clin Tox 2013*

Conclusions

- Significant potential for acute harm associated with NPS
- No pan-European data collection systems on the acute harms related to novel substances
- Data triangulation from multiple sources allows patterns of acute toxicity to be determined
- Poisons information services can provide useful information: need to be co-ordinated
- Euro-DEN project is novel pan-European co-ordinated approach to collecting Emergency Department data

The ideal would be an acute harm indicator for reporting to ECMDDA: hospital and poisons centre data