

Prescription medicine misuse and related acute toxicity

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I have no conflict of interest to declare

Prescription medicines in Euro-DEN Plus definitions and inclusion criteria

- 'Prescription medicines' included in Euro-DEN Plus are registered medicines that are available:
 - As *prescription only medicines*
 - Or *over the counter medicines* at a pharmacy or on general sale (supermarkets, grocery stores, newsagents, etc.)
- These 'prescription medicines' are included in Euro-DEN Plus if they are *misused* as part of the index presentation
 - This may be lone misuse of prescription medicines, or together with conventional recreational drug(s)/NPS

Interest in prescription medicines

- Growing concern in Europe about misuse of medicines, especially with prescription opioid misuse in USA
- Certain groups of medicines likely to be misused such as sedatives and hypnotics; opioids and stimulants for attention deficit and hyperactivity disorder
- Concern identified in certain groups of general population; elderly, women and high-risk opioid users



PERSPECTIVES ON DRUGS

**The misuse of benzodiazepines
among high-risk opioid users
in Europe**



**Concurrent Use of Benzodiazepine by Heroin Users—What Are
the Prevalence and the Risks Associated with This Pattern of Use?**

T. Yamamoto¹ • P. I. Dargan^{1,2} • A. Dines¹ • C. Yates³ • F. Heyerdahl⁴ • K. E. Hovda⁴ • I. Giraudon⁵ • R. Sedefov⁵ •
D. M. Wood^{1,2}  • On behalf of the Euro-DEN Research Group

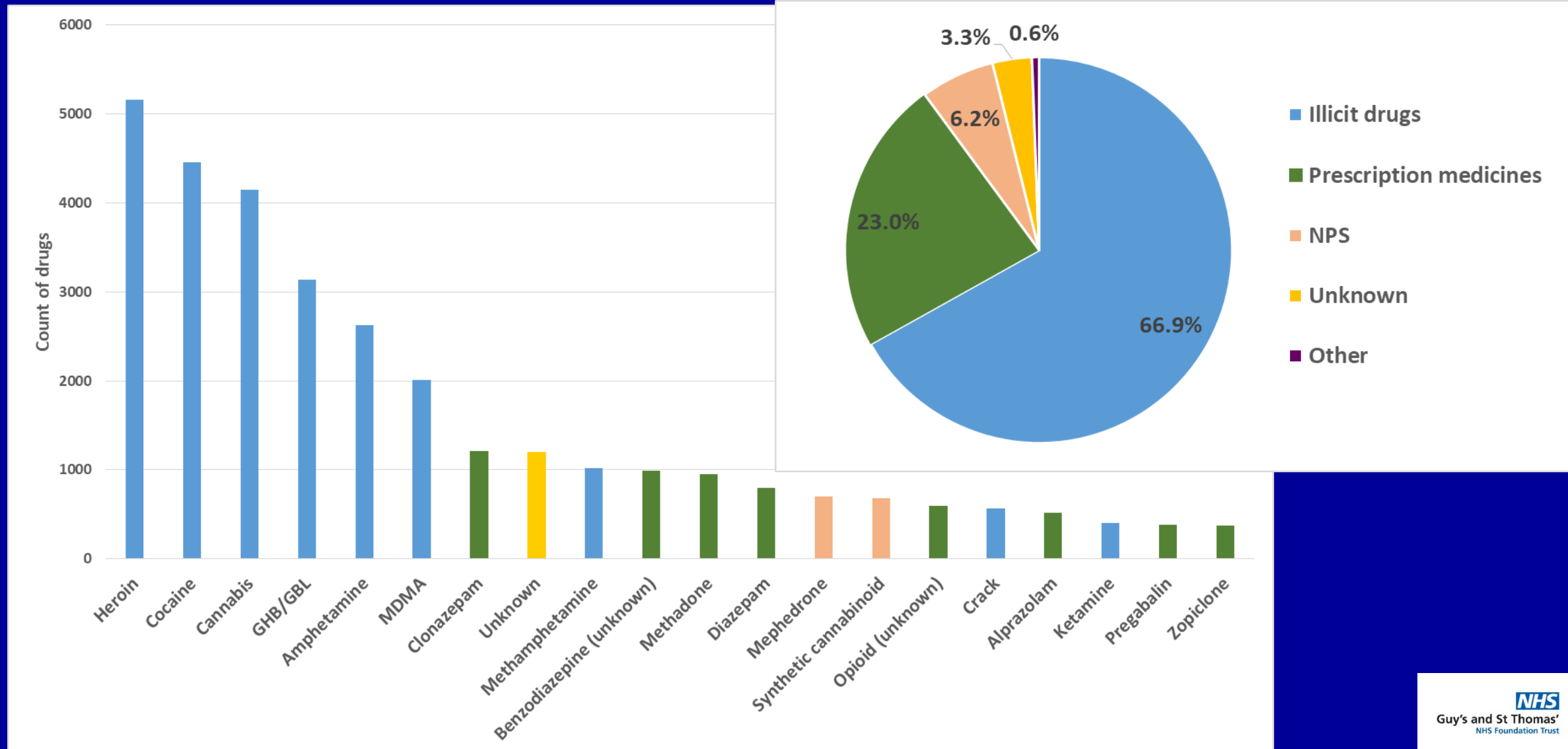
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- 5529 presentations October 2013 – September 2014
- 662 lone heroin users & 191 co-used heroin with ≥ 1 benzodiazepine
- Co-users more likely than lone heroin users:
 - reduced respiratory rate at presentation 12.7 ± 4.9 vs 13.6 ± 4.4 per minute ($p=0.02$)
 - require admission to hospital 18.3% vs 9.8% ($p<0.01$)
- No differences in critical care admission rates or length of stay in hospital

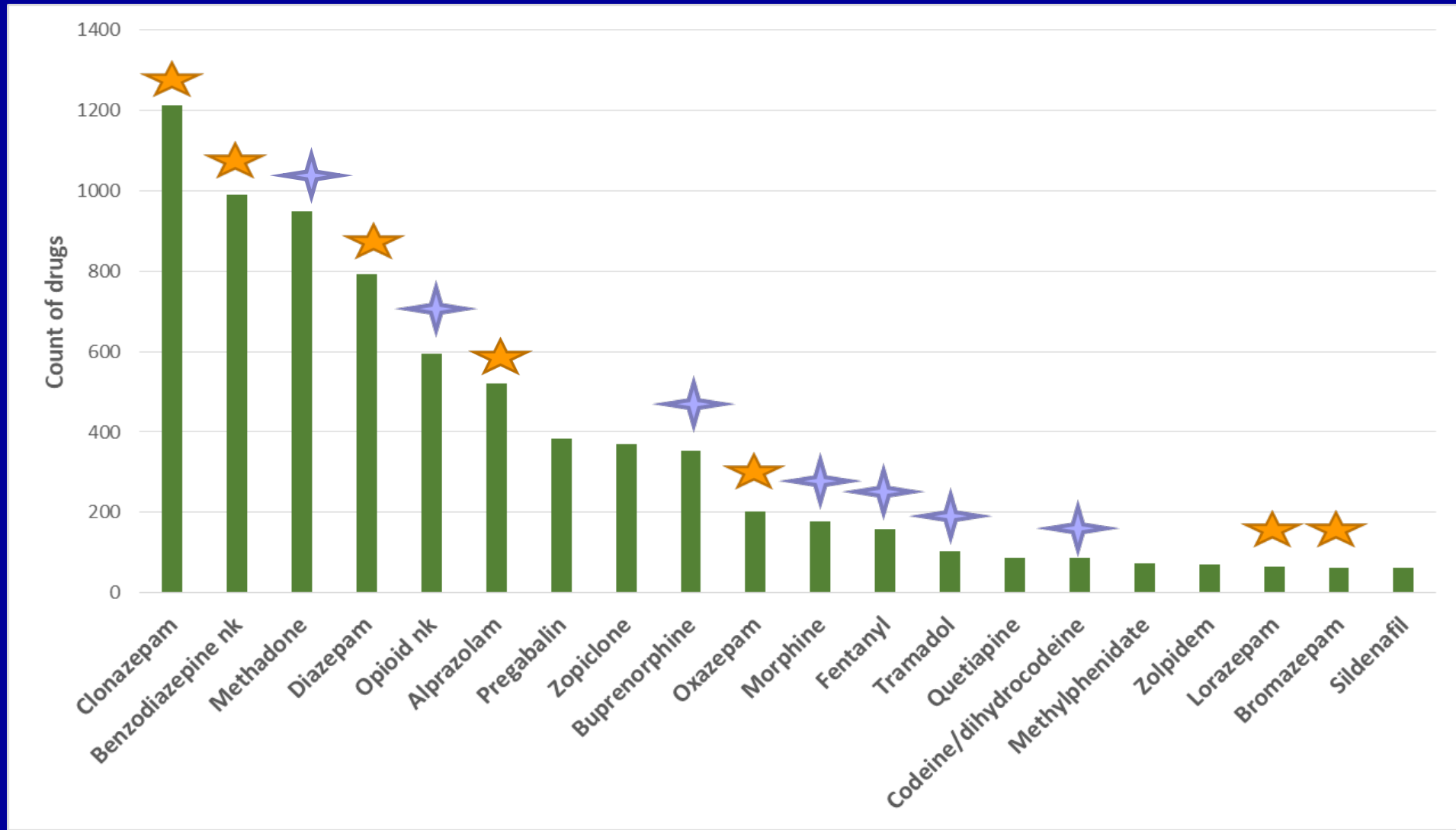
Prescription medicines in Euro-DEN Plus January 2014 – December 2017

- 23,947 presentations reported to the Euro-DEN project
- 6,207 (25.9%) included at least one prescription medicine
 - of these 2,876 involved ONLY prescription medicines
 - 12.0% of all presentations
 - 46.3% of the presentations including a prescription medicine
- Ethanol in prescription medicines presentations:
 - Yes 2,352 (37.8%); No 2,100 (33.8%); Not recorded in 1,755 (28.3%)

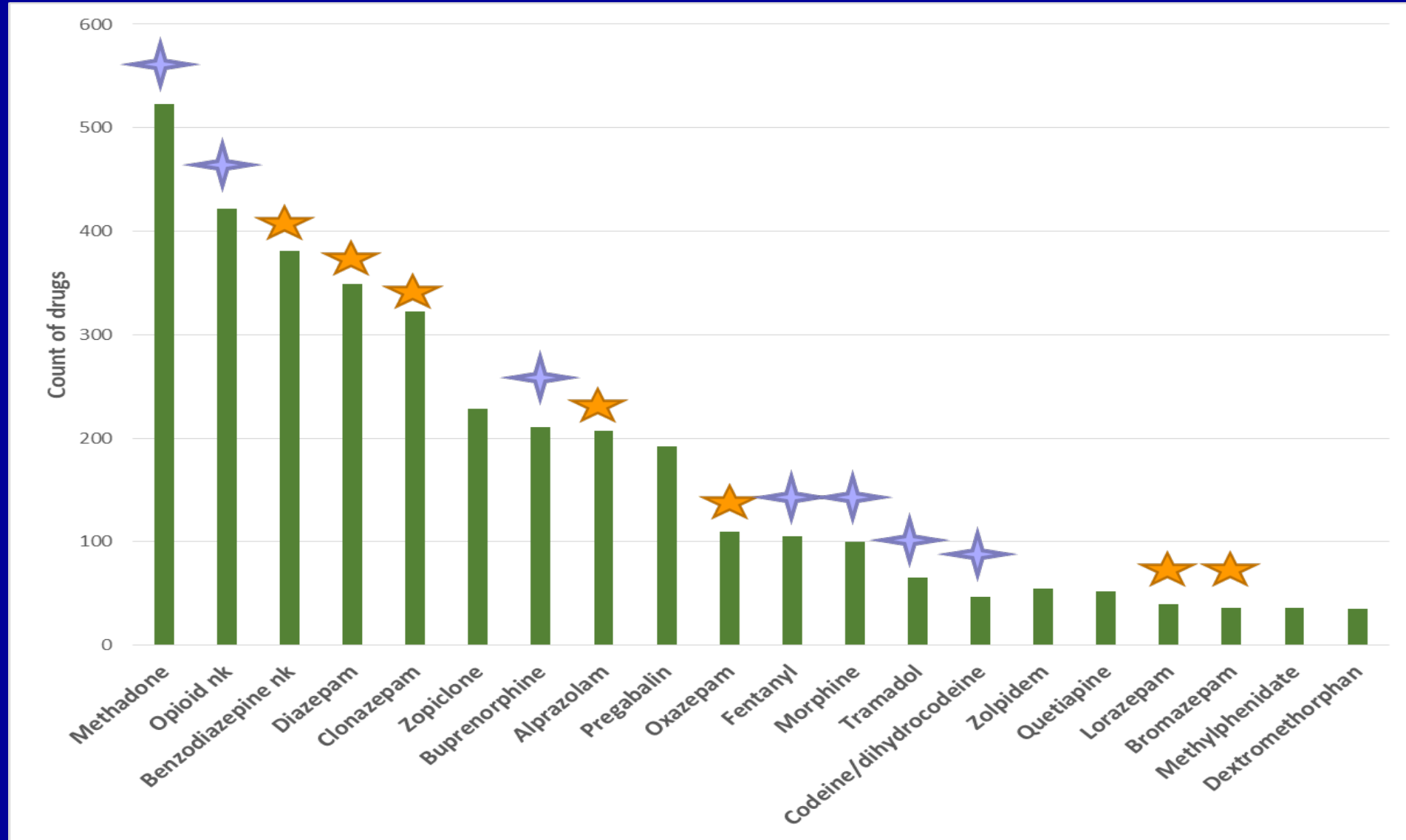
4 year Euro-DEN Plus dataset most frequently reported drugs (N=36,232)



'Top 20' reported prescription medicines in ALL presentations involving prescription medicines (n=8,339)



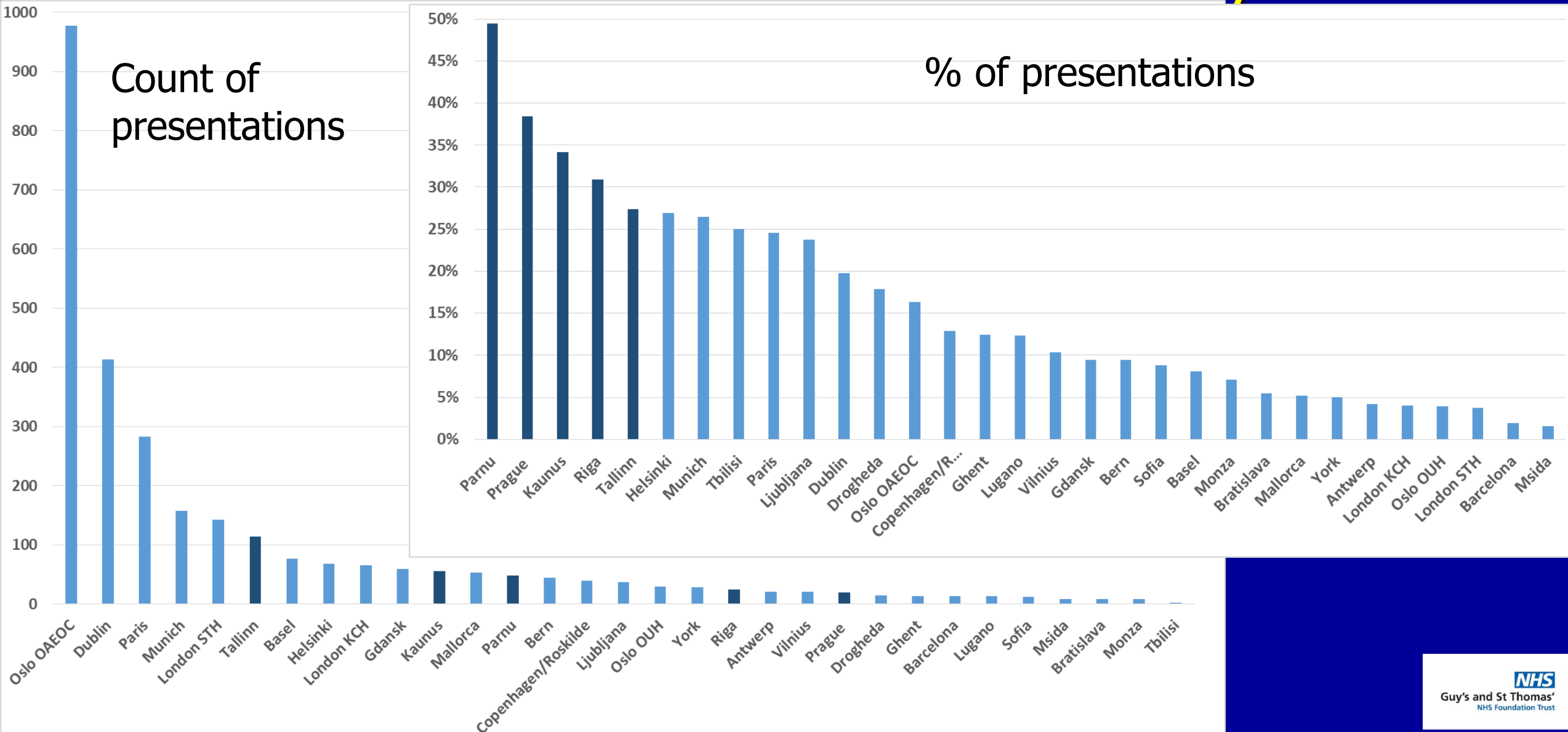
'Top 20' reported prescription medicines in prescription medicine ONLY presentations (n=4,063)



Prescription medicine only presentations


- Of the 2,876 prescription medicine only presentations (ethanol excluded):
 - 2,014 (70.0%) involved 1 prescription medicine
 - 620 (21.6%) involved 2 prescription medicines
 - 242 (8.4%) involved 3 – 6 prescription medicines
- Most common groups: opioids, benzodiazepines, z-drugs and pregabalin
- Few presentations with oxycodone and none with hydrocodone

Number of presentations/proportion per centre with prescription medicines only



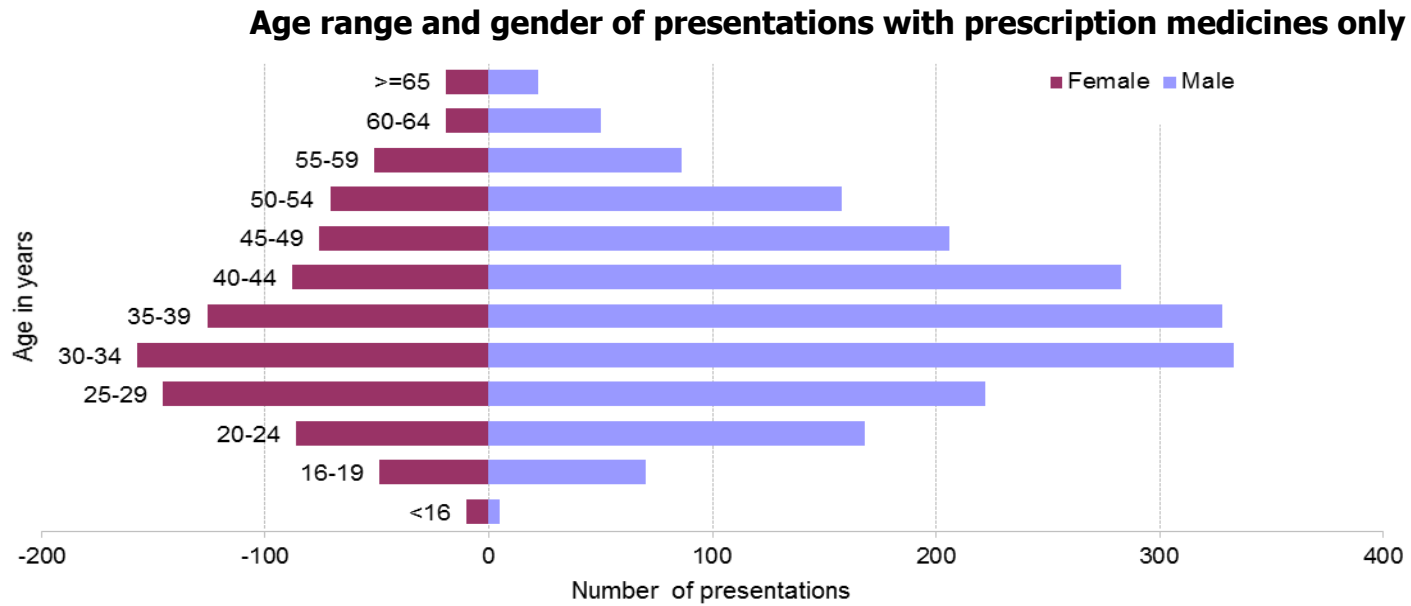


Presentations to the emergency department with non-medical use of benzodiazepines and Z-drugs: profiling and relation to sales data

C. Lyphout^{1,2}  · C. Yates³ · Z. R. Margolin⁴ · P. I. Dargan^{1,5} · A. M. Dines¹ · F. Heyerdahl⁶ · K. E. Hovda⁶ · I. Giraudon⁷ · B. Bucher-Bartelson⁴ · J. L. Green^{4,8} · Euro-DEN Research Group · D. M. Wood^{1,5}

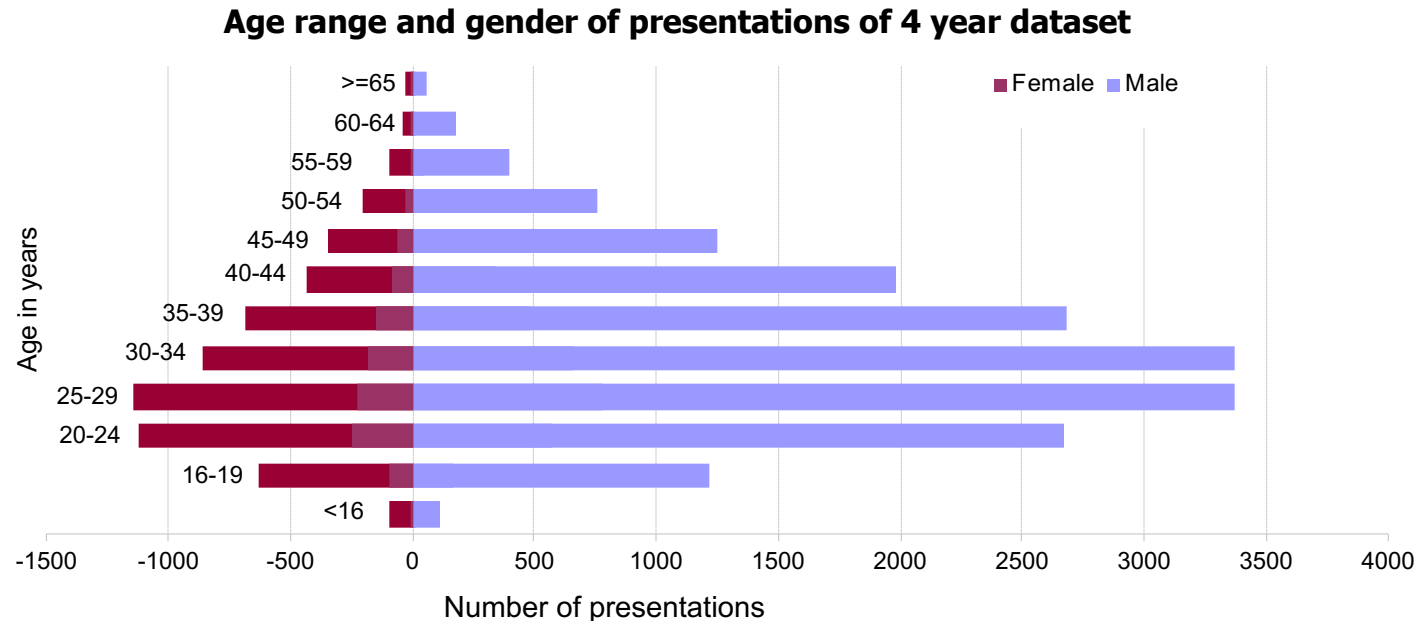
- Benzodiazepine and 'Z-drug' presentations reported by Euro-DEN centres from October 2013 – September 2015
- Sales data for the drugs obtained where possible
- Moderate (in Spain, UK, Switzerland) to high (in France, Ireland and Norway) positive correlation between ED presentation and sales data

Demographics



Median age: 34 (28-43) years

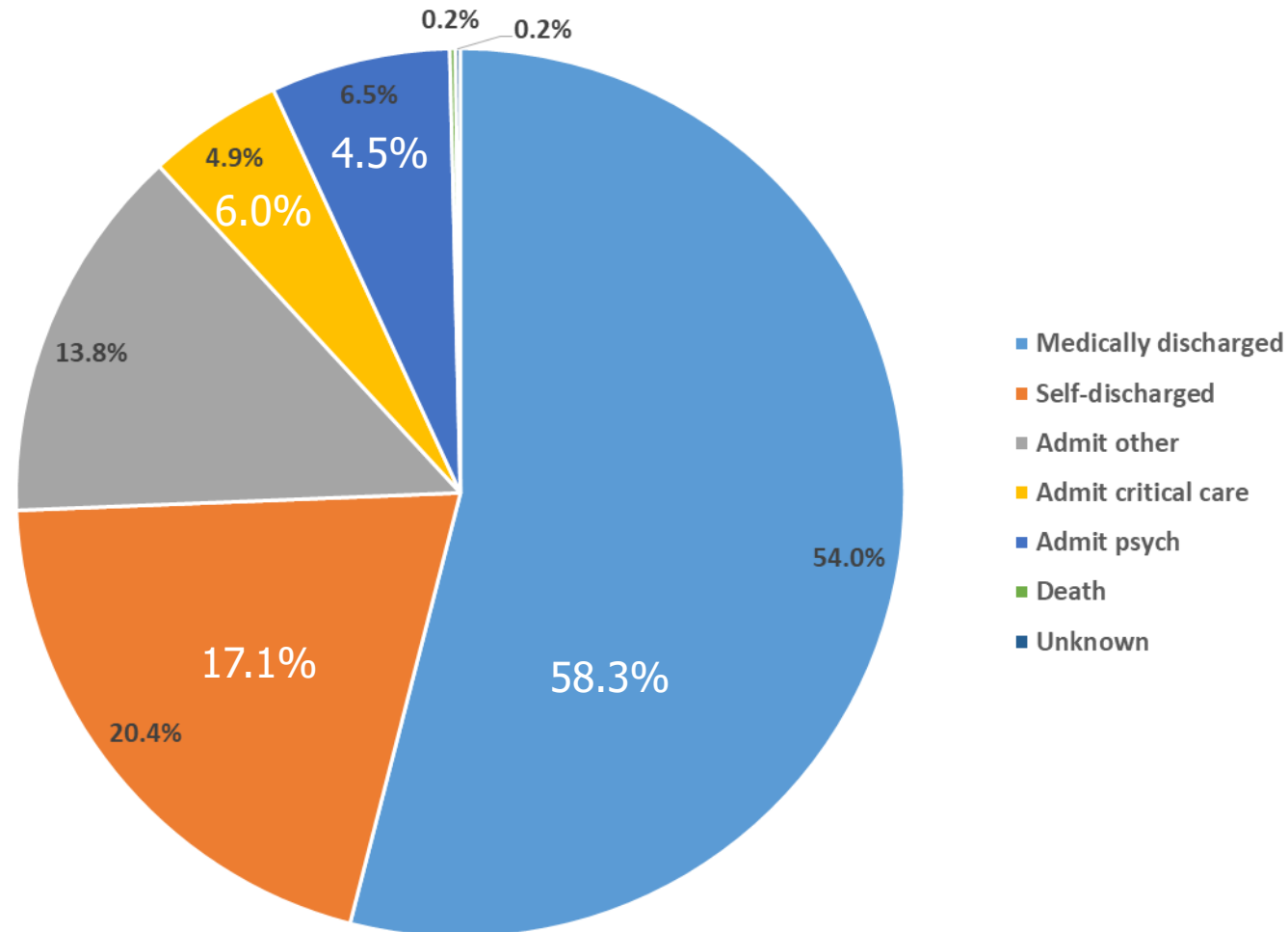
% male: 68.4%



Median age: 31 (25-39) years

% male: 76.2%

Disposition from the Emergency Department

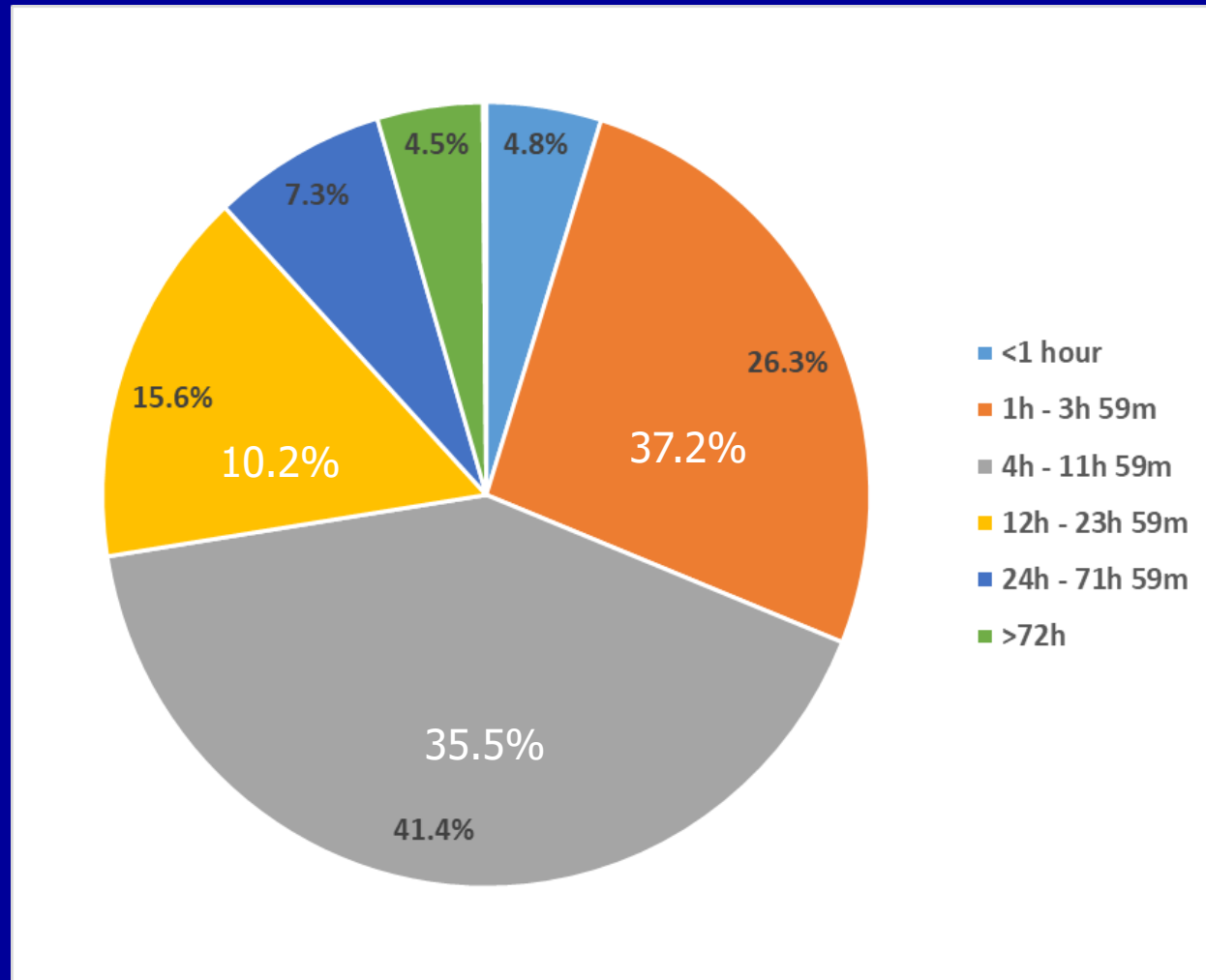


74.4%
discharged
from ED

VS

75.4% in the
overall 4 year
dataset

Length of stay in hospital



Prescription medicines only:
Median (IQR) length of stay
6 hr 07m (3 hr 20m – 13 hr 08m)

Total Euro-DEN population:
Median (IQR) length of stay
4 hr 45m (2 hr 34m – 9 hr 59m)

88.1% discharged within 24 hrs vs 88.9% total population

19 (0.7%) fatal presentations

12 presented in cardiac arrest

Case	Centre	Prescription medicines
62F	Antwerp	Codeine, unknown benzodiazepine
39F	Bern	Methadone
50F	Drogheda	Morphine, unknown benzodiazepine
44F	Dublin	Methadone, unknown benzodiazepine, pregabalin
44M	Dublin	Methadone, unknown benzodiazepine, unknown tricyclic
33M	London STH	Unknown opioid
38M	London STH	Methadone
38M	Munich	Buprenorphine, fentanyl, unknown opioid, unknown benzodiazepine
54F	Oslo OUH	Unknown opioid

Case	Centre	Prescription medicines
29M	Paris	Oxazepam, zolpidem, baclofen
27M	Parnu	Methadone
22F	Riga	Methadone, tramadol, diazepam
39M	Sofia	Methadone
23F	Tallinn	Fentanyl
34M	Tallinn	Fentanyl
39M	Tallinn	Fentanyl
47M	Tallinn	Fentanyl
20F	Tallinn	Fentanyl, methadone, unknown benzodiazepine
30M	Tallinn	Methadone

GABA-ergic drugs and tramadol

- Significant international interest in GABA-ergic drugs and tramadol misuse
- Recent changes in scheduling in some countries

ADDICTION **SSA** SOCIETY FOR THE STUDY OF ADDICTION
RESEARCH REPORT doi:10.1111/add.13843

Risk to heroin users of polydrug use of pregabalin or gabapentin

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Centre diction

European joint DRD expert meeting
Lisbon, 29-30 September 2016

Medicines in the context of the Early warning system

Tramadol related deaths

From 2004-2015 rise in pregabalin & gabapentin prescriptions & rise in deaths involving pregabalin & gabapentin correlated with this

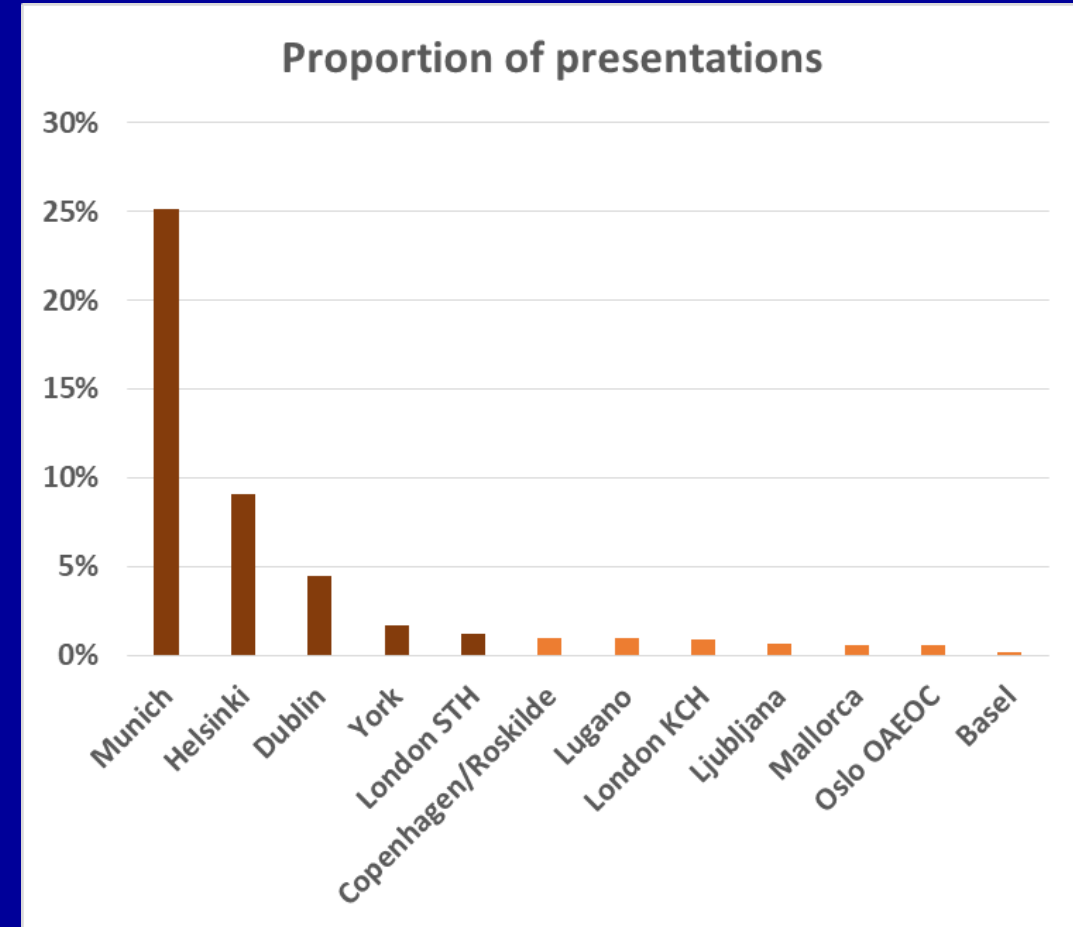
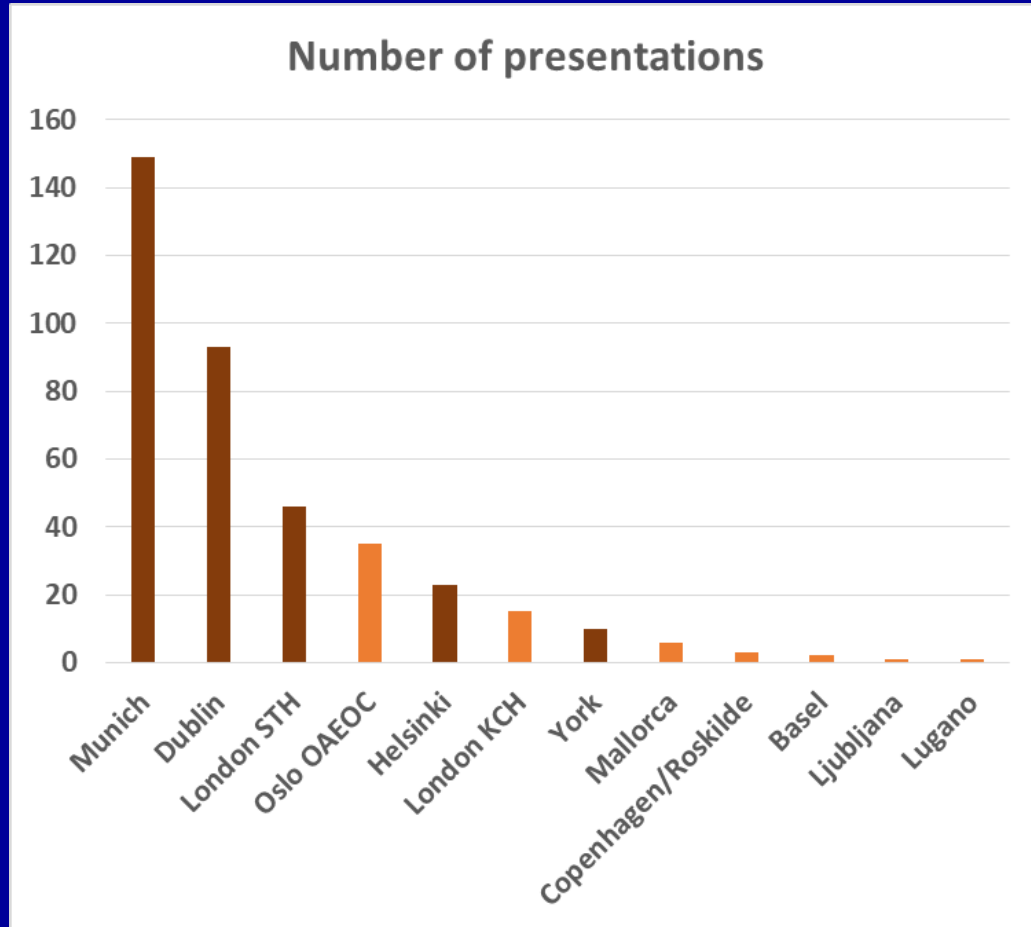
Euro-DEN Plus GABA-ergic drug presentations

In 23,947 Euro-DEN Plus presentations (January 2014 – December 2017)

- Pregabalin – 384 (1.6%)
 - geographical variation (next slide)
- Gabapentin – 21 (0.1%)
 - UK (8), Oslo (3), Paris (2), Helsinki (2)
- Baclofen – 10 (0.04%)
 - Paris (4), Tibilisi (2)
- Tramadol – 105 (0.4%)

Pregabalin – geographical variation (n=384)

No pregabalin in 20 of the 31 centres



Pregabalin and heroin vs heroin alone

- 384 presentations involved pregabalin alone (43, 11.2%) or with other drugs
- 244 (63.5%) used an opioid
- 89 (36.1%) used heroin
- 24 used pregabalin and heroin only
- 2517 presentations heroin taken alone (10.5% of all presentations)

Pregabalin and heroin vs heroin alone

- Use of heroin with pregabalin to heroin alone compared for admission, length of stay and significant clinical effects
- Increased medical admission (admit other) 33.3% vs 16.8% ($p=0.03$)
- Increased reports of seizures 17.4% vs 2.3% ($p<0.001$)
- No significant difference in level of consciousness (GCS), respiration rate on presentation, ICU admission or death
- 93.4% heroin and pregabalin group discharged within 24 hours

Summary

- Prescription medicines involved in 6,207 (25.9%) of all Euro-DEN Plus presentations
- 2,876 of these involved ONLY prescription medicines
 - 12.0% of all presentations
 - 46.3% of the presentations including a prescription medicine
- Opioids and benzodiazepines are most commonly reported
- Marked geographical variation in proportion of presentations reported
- Pregabalin misuse occurred in 1.6% of all presentations and commonly involved other drugs