# RADARS® SYSTEM 10th ANNUAL SCIENTIFIC MEETING


RADARS®
SYSTEM

**RADARS® System**
**International Pre-Symposium**
**05 May 2016**

# *Prescription Drug Misuse – A Global Crisis?*

# WELCOME

- **RADARS® System International Data Updates by Region**
  - Jody L. Green, PhD, CCRP
  - *Director of Research Administration, RMPDC – Denver Health and Hospital Authority*
- **Non-Prescription Fentanyl:  Canadian Fentanyl Trends Moving to the U.S.**
  - Steven P. Kurtz, PhD
  - *Professor and Director of the Center for Applied Research on Substance Use and Health Disparities, Nova Southeastern University*

# WELCOME

- **Misuse of Medications in the UK and Related Advisory Council on Misuse of Drugs (ACMD) Activities**
  - Professor Raymond G. Hill, B.Pharm., Ph.D, DSc (Hon), FMedSci
  - *Visiting Professor of Pharmacology Imperial College, London; Chair, Technical Committee UK Advisory Council on Misuse of Drugs*
- **Trends of Prescription Drug Misuse in the UK and Singapore**
  - David Wood, MD, FRCP, FEAPCCT, FACMT, FBPhS
  - *Consultant Physician and Clinical Toxicologist, Guy's and St Thomas' NHS Foundation Trust and King's Health Partners; Senior Lecturer, King's College London*
- **Panel Discussion**

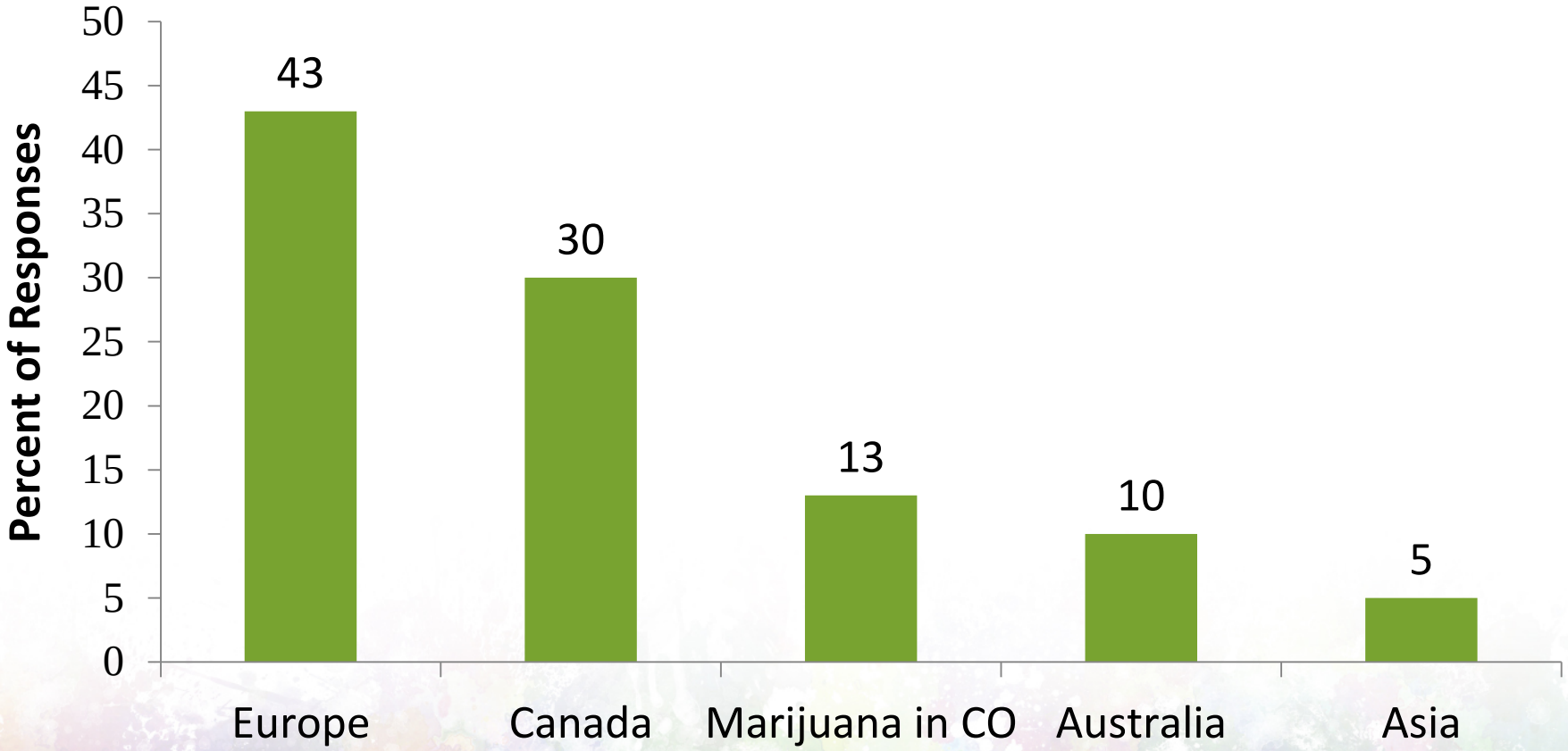
# 2015 International Pre-Symposium

Which region's prescription drug abuse trends are you most interested in hearing about?

- Australia
- Canada
- Europe
- Asia
- I thought we were here to talk about Marijuana in Colorado

# 2015 International Pre-Symposium

Which region's prescription drug abuse trends are you most interested in hearing about?



# Question:

There is a global crisis of prescription drug misuse.

A. True
B. False
C. Not sure yet

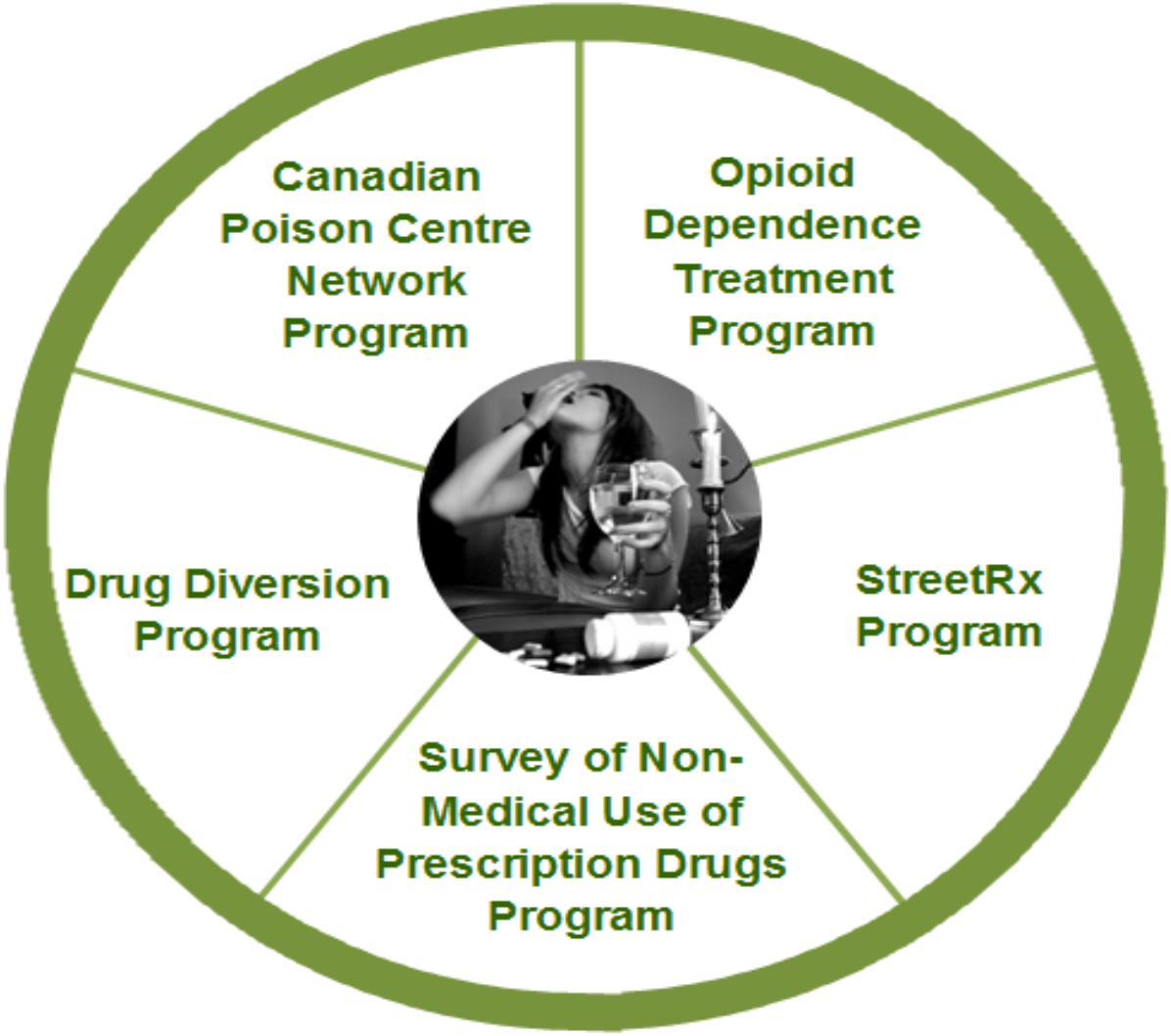
# RADARS® System International Updates by Region

**Jody L. Green, PhD, CCRP**

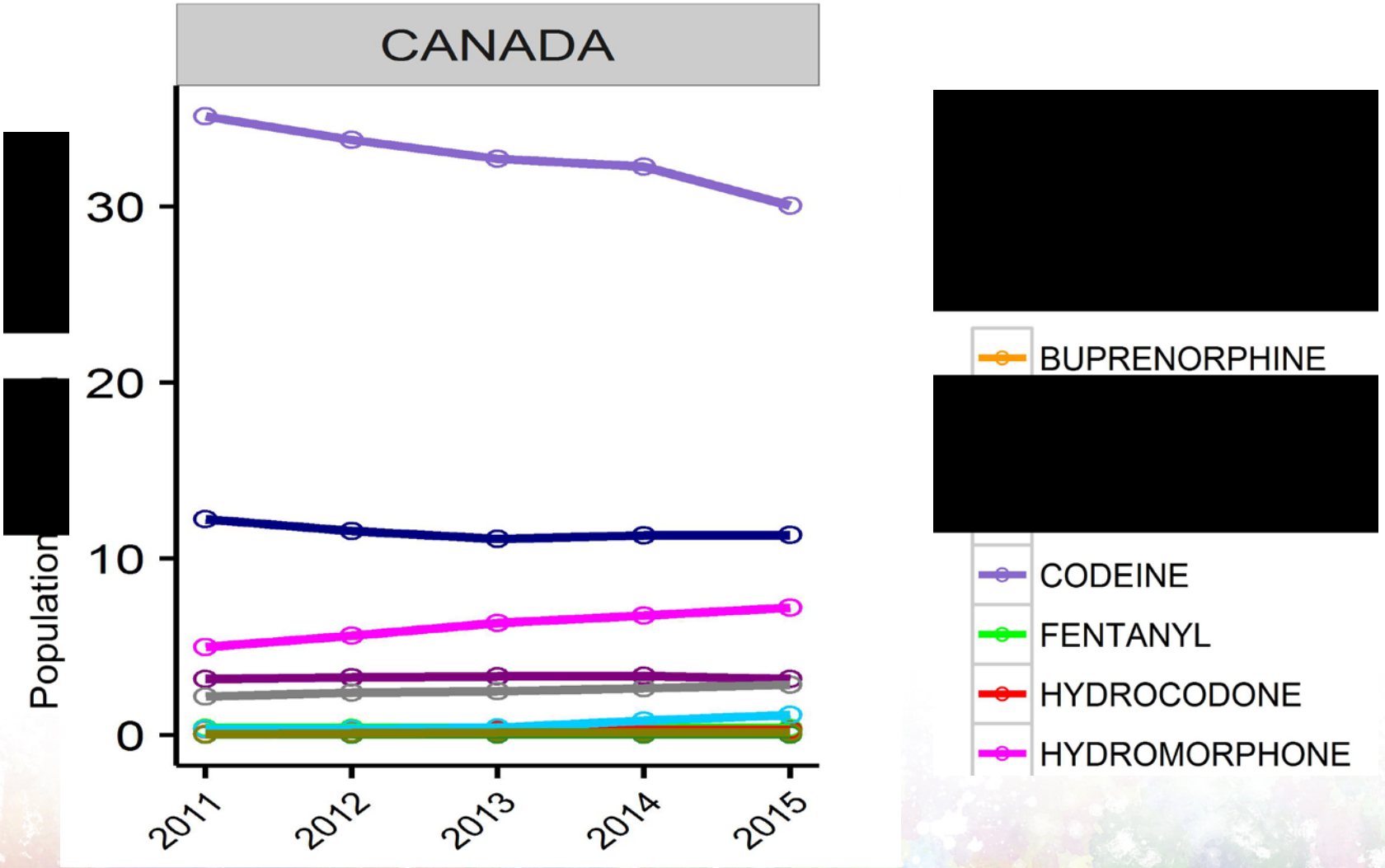
**RADARS System**

**Denver Health Rocky Mountain Poison & Drug Center**

# Mosaic Surveillance of Prescription Drug Abuse in Canada 2015



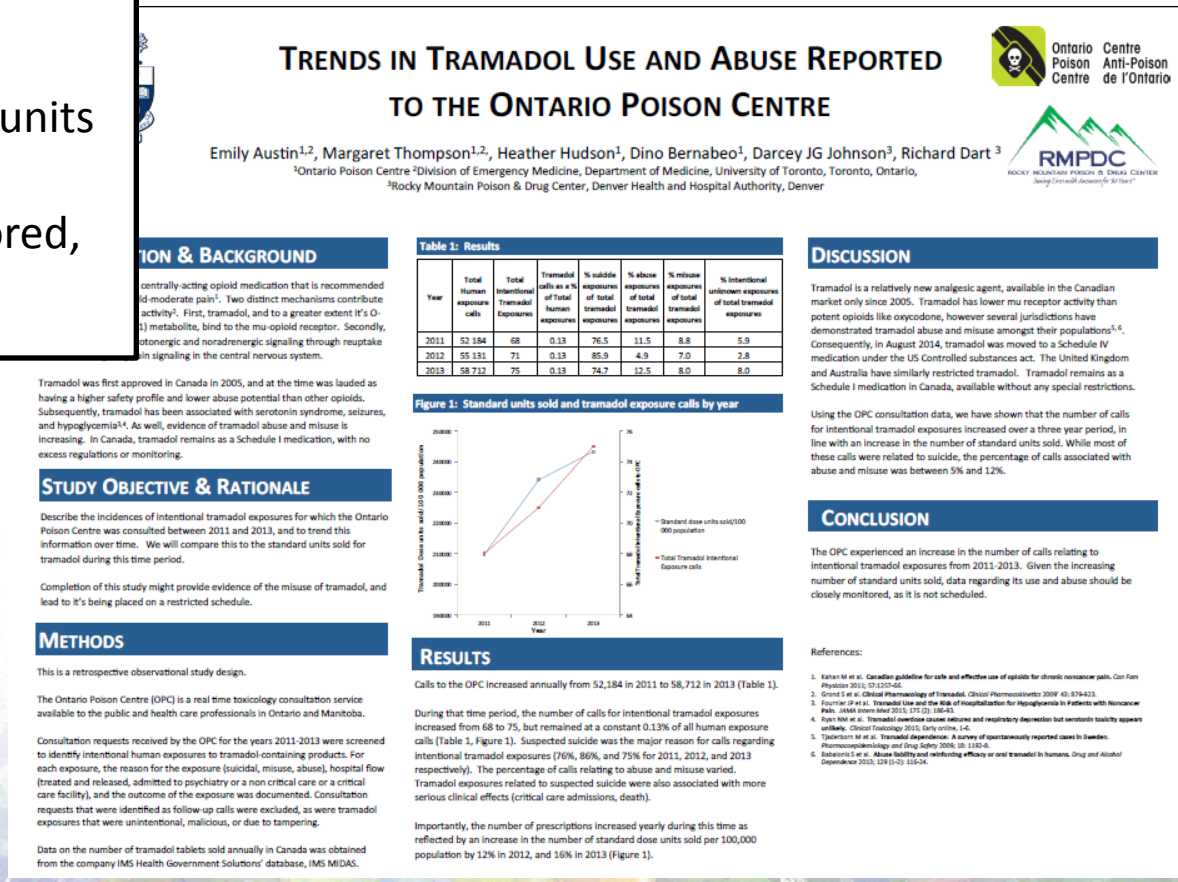
# IMS Canada – Standard Units per Population



# Canadian Poison Centre Network

## CONCLUSION

- The OPC experienced an increase in the number of calls relating to intentional tramadol exposures from 2011---2013. Given the increasing number of standard units sold, data regarding its use and abuse should be closely monitored, as it is not scheduled.



### TRENDS IN TRAMADOL USE AND ABUSE REPORTED TO THE ONTARIO POISON CENTRE

Emily Austin[1,2], Margaret Thompson[1,2], Heather Hudson[1], Dino Bernabeo[1], Darcey JG Johnson[3], Richard Dart [3]
[1]Ontario Poison Centre [2]Division of Emergency Medicine, Department of Medicine, University of Toronto, Toronto, Ontario,
[3]Rocky Mountain Poison & Drug Center, Denver Health and Hospital Authority, Denver

Ontario Poison Centre / Centre Anti-Poison de l'Ontario

RMPDC Rocky Mountain Poison & Drug Center

#### ION & BACKGROUND

centrally-acting opioid medication that is recommended d-moderate pain[1]. Two distinct mechanisms contribute activity[2]. First, tramadol, and to a greater extent it's O- 1) metabolite, bind to the mu-opioid receptor. Secondly, otonergic and noradrenergic signaling through reuptake in signaling in the central nervous system.

Tramadol was first approved in Canada in 2005, and at the time was lauded as having a higher safety profile and lower abuse potential than other opioids. Subsequently, tramadol has been associated with serotonin syndrome, seizures, and hypoglycemia[3,4]. As well, evidence of tramadol abuse and misuse is increasing. In Canada, tramadol remains as a Schedule I medication, with no excess regulations or monitoring.

#### STUDY OBJECTIVE & RATIONALE

Describe the incidences of intentional tramadol exposures for which the Ontario Poison Centre was consulted between 2011 and 2013, and to trend this information over time. We will compare this to the standard units sold for tramadol during this time period.

Completion of this study might provide evidence of the misuse of tramadol, and lead to it's being placed on a restricted schedule.

#### METHODS

This is a retrospective observational study design.

The Ontario Poison Centre (OPC) is a real time toxicology consultation service available to the public and health care professionals in Ontario and Manitoba.

Consultation requests received by the OPC for the years 2011-2013 were screened to identify intentional human exposures to tramadol-containing products. For each exposure, the reason for the exposure (suicidal, misuse, abuse), hospital flow (treated and released, admitted to psychiatry or a non critical care or a critical care facility), and the outcome of the exposure was documented. Consultation requests that were identified as follow-up calls were excluded, as were tramadol exposures that were unintentional, malicious, or due to tampering.

Data on the number of tramadol tablets sold annually in Canada was obtained from the company IMS Health Government Solutions' database, IMS MIDAS.

**Table 1: Results**

| Year | Total Human exposure calls | Total Intentional Tramadol Exposures | Tramadol calls as a % of Total human exposures | % suicide exposures of total tramadol exposures | % abuse exposures of total tramadol exposures | % misuse exposures of total tramadol exposures | % intentional unknown exposures of total tramadol exposures |
|---|---|---|---|---|---|---|---|
| 2011 | 52 184 | 68 | 0.13 | 76.5 | 11.5 | 8.8 | 5.9 |
| 2012 | 55 131 | 71 | 0.13 | 85.9 | 4.9 | 7.0 | 2.8 |
| 2013 | 58 712 | 75 | 0.13 | 74.7 | 12.5 | 8.0 | 8.0 |

**Figure 1: Standard units sold and tramadol exposure calls by year**




#### RESULTS

Calls to the OPC increased annually from 52,184 in 2011 to 58,712 in 2013 (Table 1).

During that time period, the number of calls for intentional tramadol exposures increased from 68 to 75, but remained at a constant 0.13% of all human exposure calls (Table 1, Figure 1). Suspected suicide was the major reason for calls regarding intentional tramadol exposures (76%, 86%, and 75% for 2011, 2012, and 2013 respectively). The percentage of calls relating to abuse and misuse varied. Tramadol exposures related to suspected suicide were also associated with more serious clinical effects (critical care admissions, death).

Importantly, the number of prescriptions increased yearly during this time as reflected by an increase in the number of standard dose units sold per 100,000 population by 12% in 2012, and 16% in 2013 (Figure 1).

#### DISCUSSION

Tramadol is a relatively new analgesic agent, available in the Canadian market only since 2005. Tramadol has lower mu receptor activity than potent opioids like oxycodone, however several jurisdictions have demonstrated tramadol abuse and misuse amongst their populations[5,6]. Consequently, in August 2014, tramadol was moved to a Schedule IV medication under the US Controlled substances act. The United Kingdom and Australia have similarly restricted tramadol. Tramadol remains as a Schedule I medication in Canada, available without any special restrictions.

Using the OPC consultation data, we have shown that the number of calls for intentional tramadol exposures increased over a three year period, in line with an increase in the number of standard units sold. While most of these calls were related to suicide, the percentage of calls associated with abuse and misuse was between 5% and 12%.

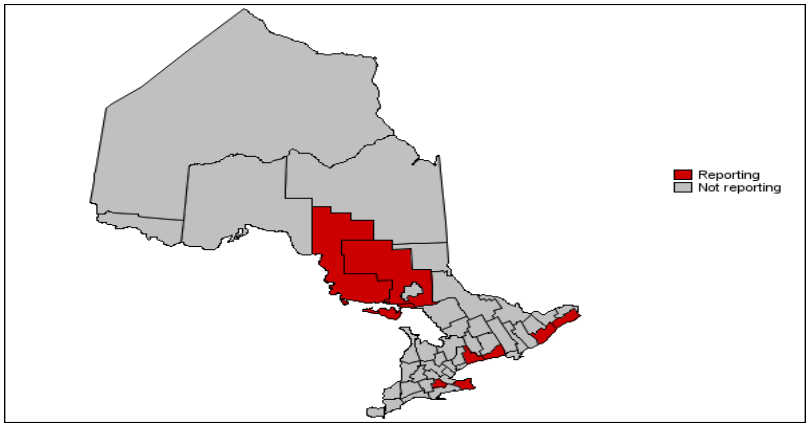
#### CONCLUSION

The OPC experienced an increase in the number of calls relating to intentional tramadol exposures from 2011-2013. Given the increasing number of standard units sold, data regarding its use and abuse should be closely monitored, as it is not scheduled.

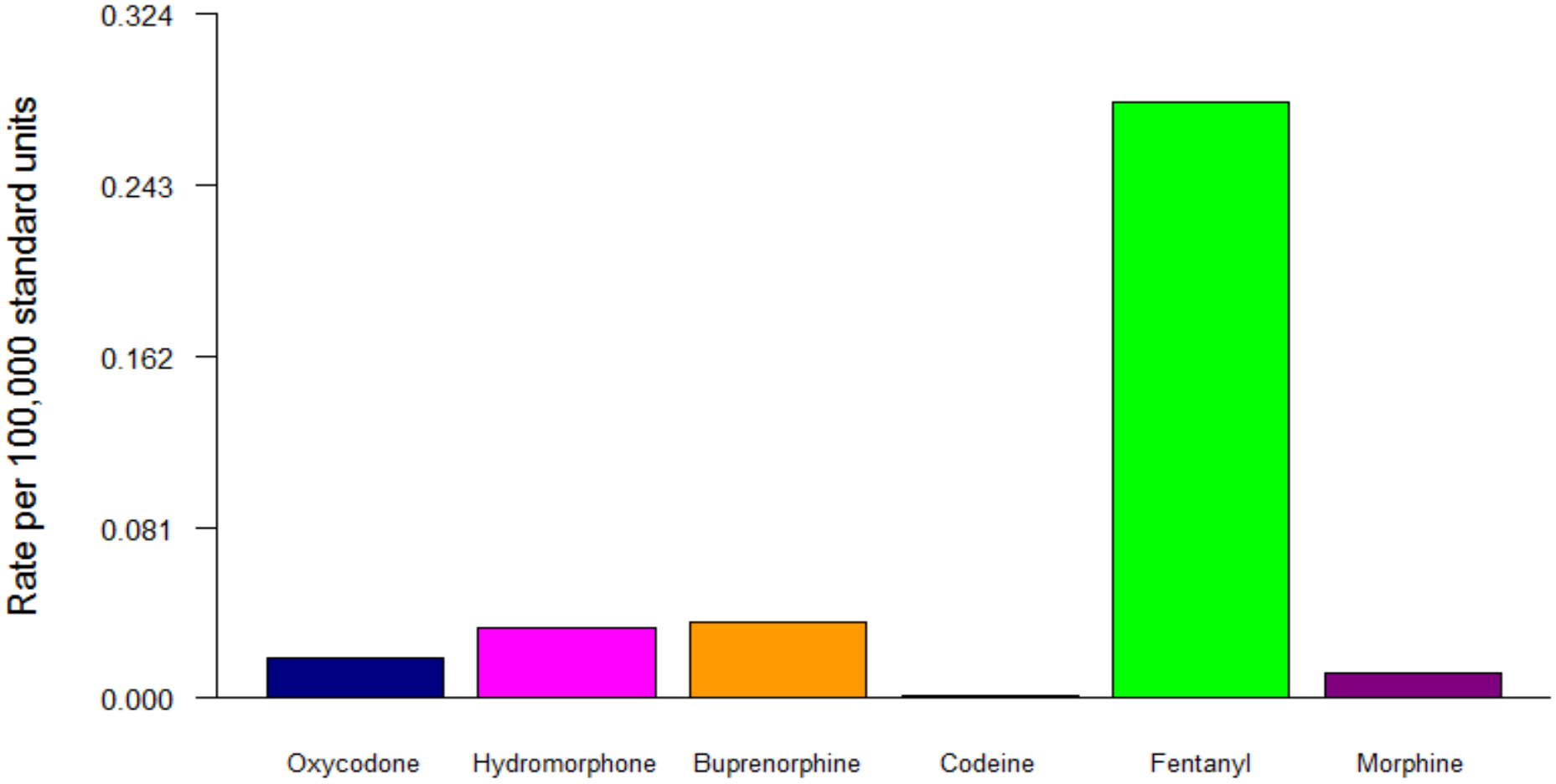
References:

1. Kahan M et al. **Canadian guideline for safe and effective use of opioids for chronic noncancer pain.** *Can Fam Physician* 2011; 57:1257-66.
2. Grond S et al. *Clinical Pharmacology of Tramadol. Clinical Pharmacokinetics* 2009' 43: 879-923.
3. Fournier JP et al. **Tramadol Use and the Risk of Hospitalization for Hypoglycemia in Patients with Noncancer Pain.** *JAMA Intern Med* 2015; 175 (2): 186-93.
4. Ryan NM et al. **Tramadol overdose causes seizures and respiratory depression but serotonin toxicity appears unlikely.** *Clinical Toxicology* 2015; Early online, 1-6.
5. Tjäderborn M et al. **Tramadol dependence. A survey of spontaneously reported cases in Sweden.** *Pharmacoepidemiology and Drug Safety* 2008; 18: 1180-6.
6. Babalonis S et al. **Abuse liability and reinforcing efficacy or oral tramadol in humans.** *Drug and Alcohol Dependence* 2010; 109 (1-2): 116-24.

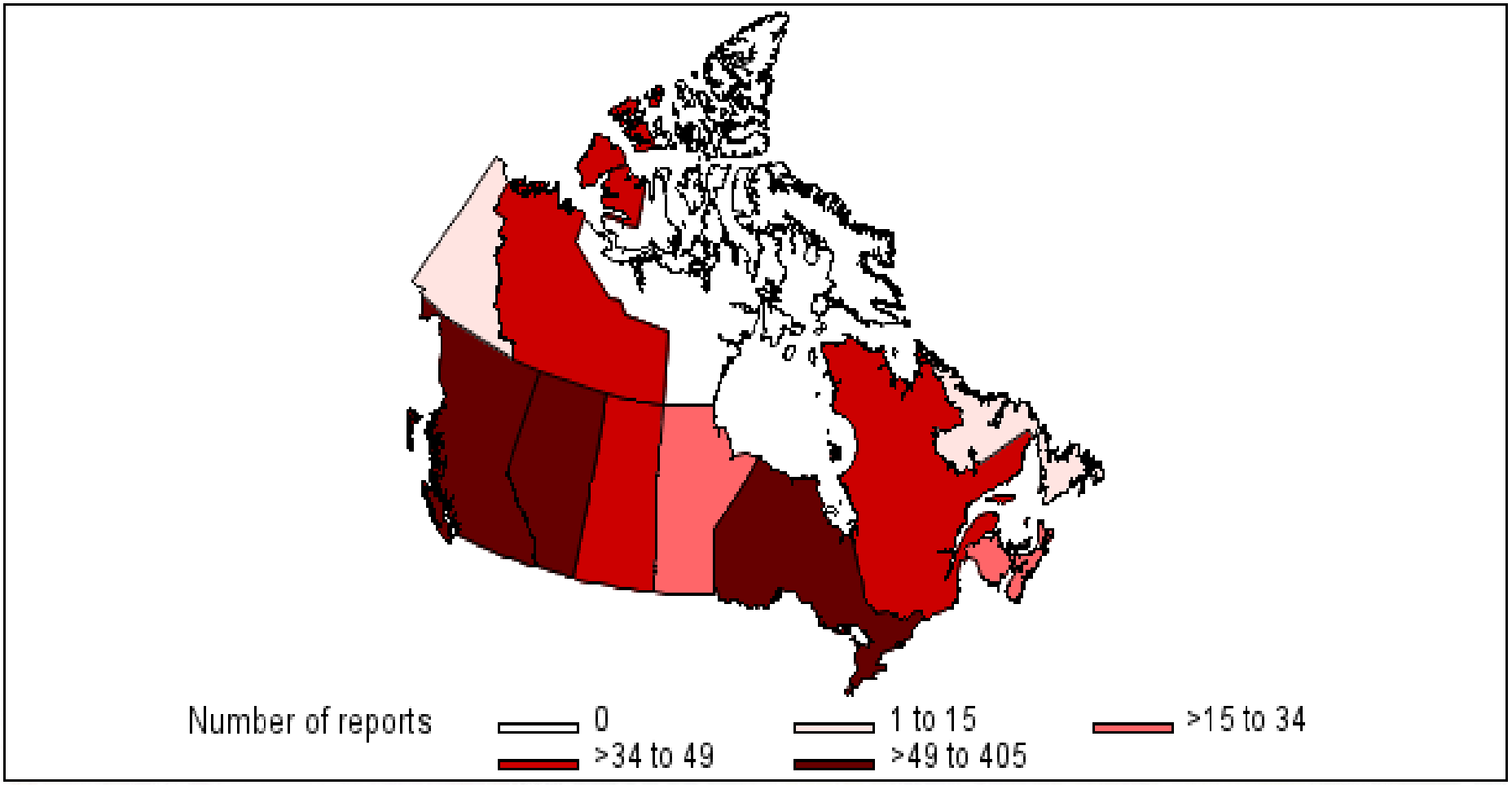
# Drug Diversion Program Cumulative Rates (per 100,000 Population) in Canada



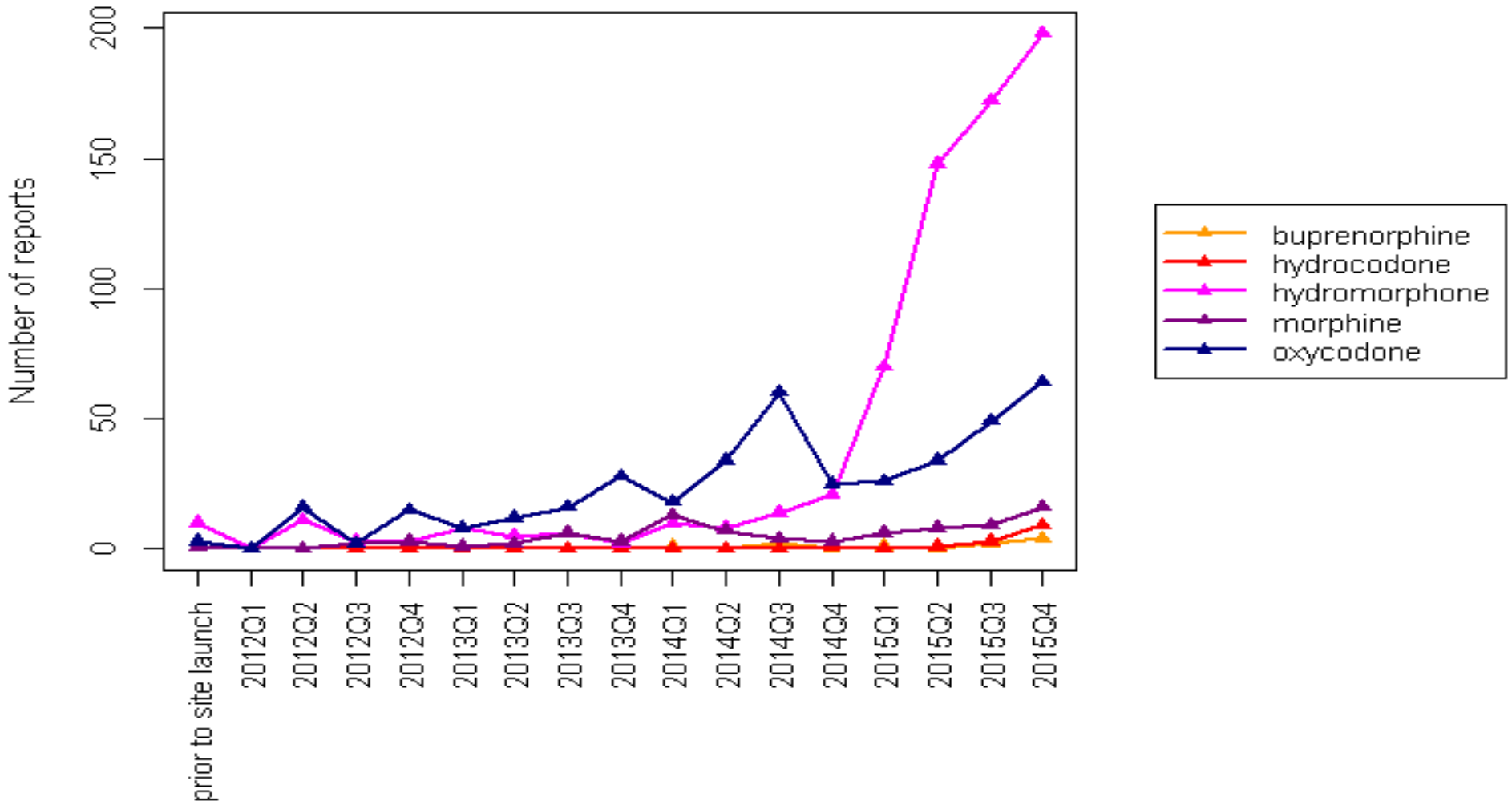
# Drug Diversion Program Cumulative Rates (per 100,000 Standard Units) in Canada



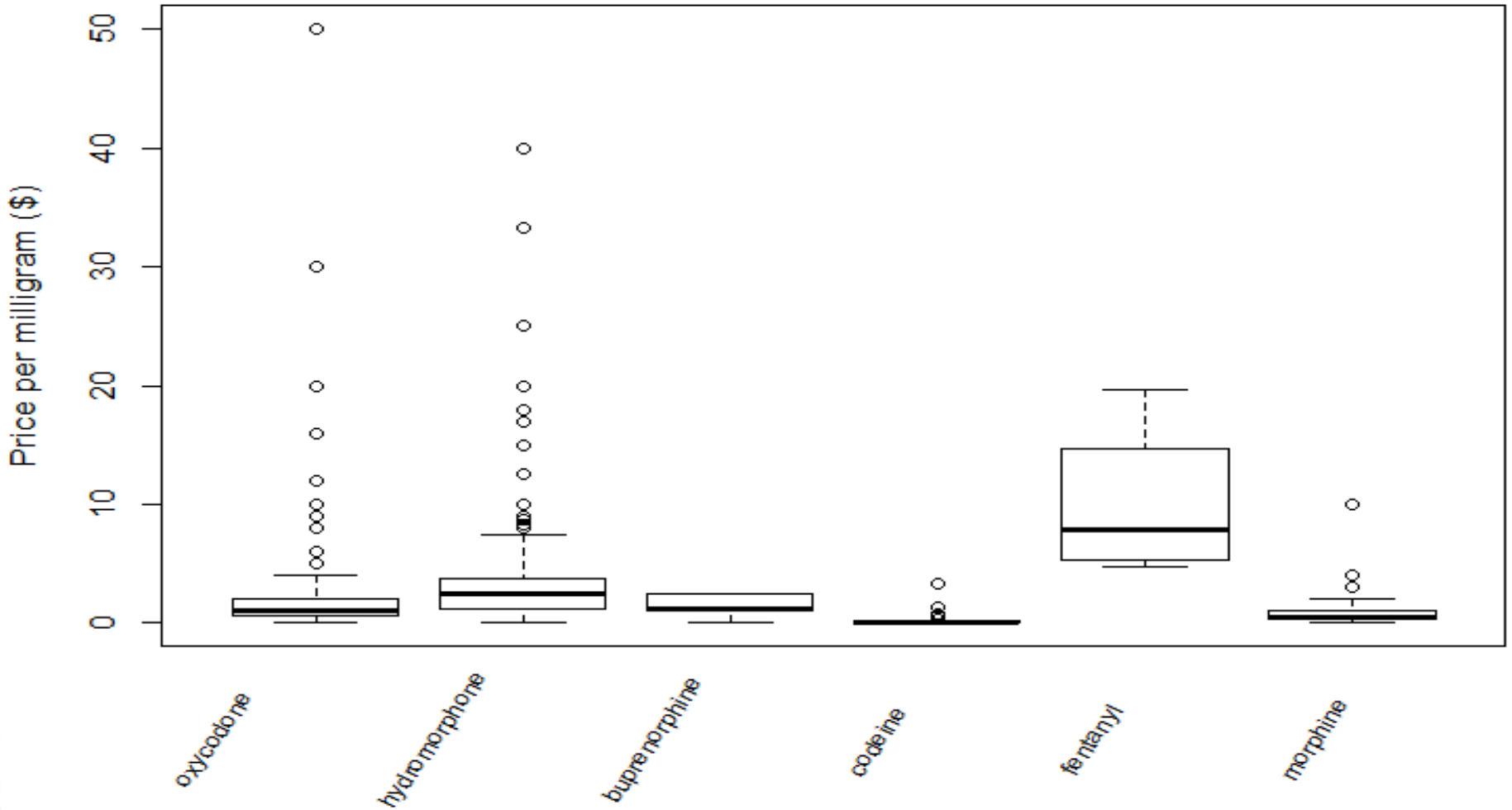
# StreetRx Program Combined Number of Submissions in Canada (1q2012-3q2015)



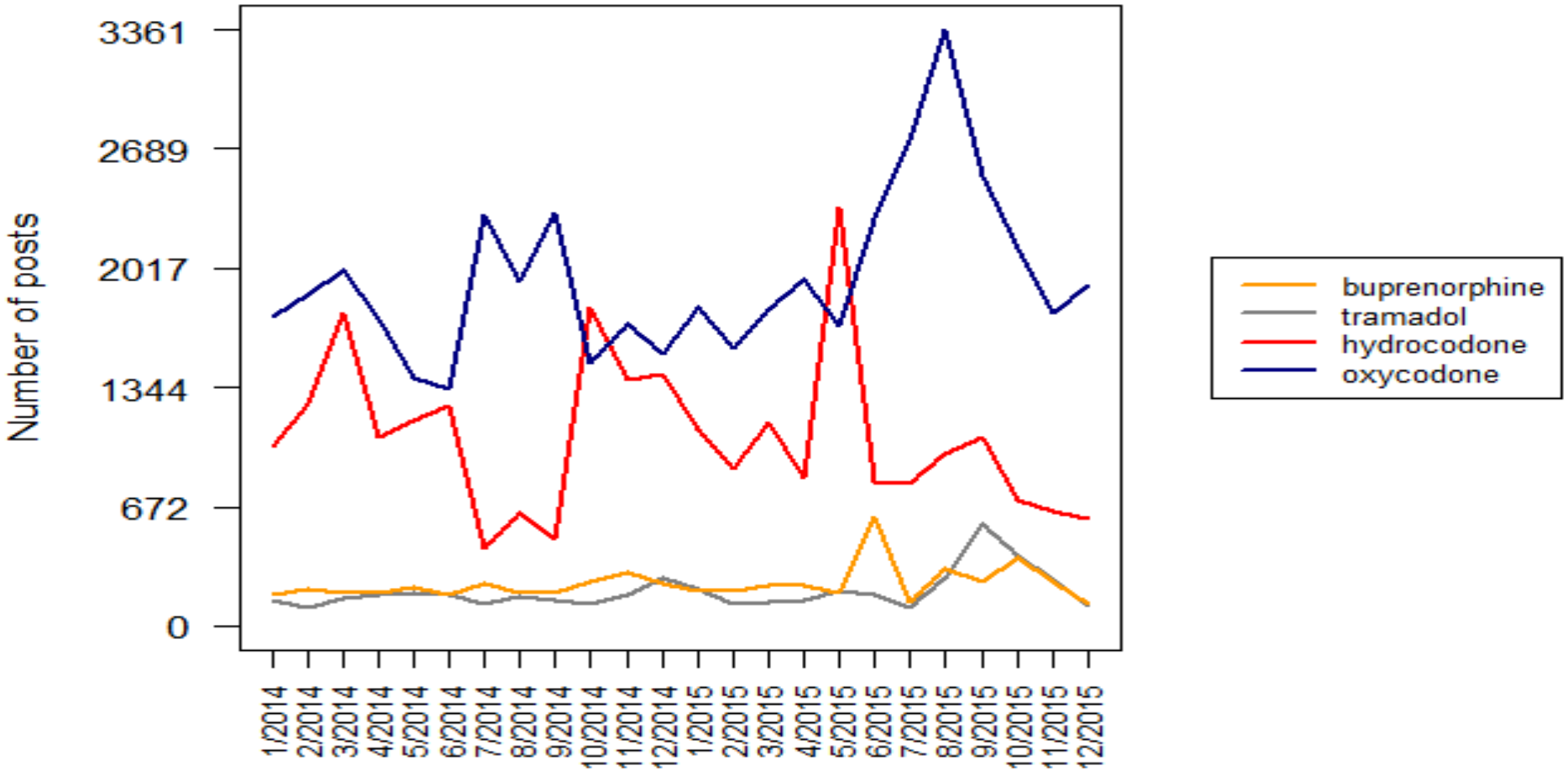
# StreetRx Program Number of Reports Over Time by Drug Substance in Canada



# StreetRx Program Price per Milligram in Canada (1q2012 – 3q2015)

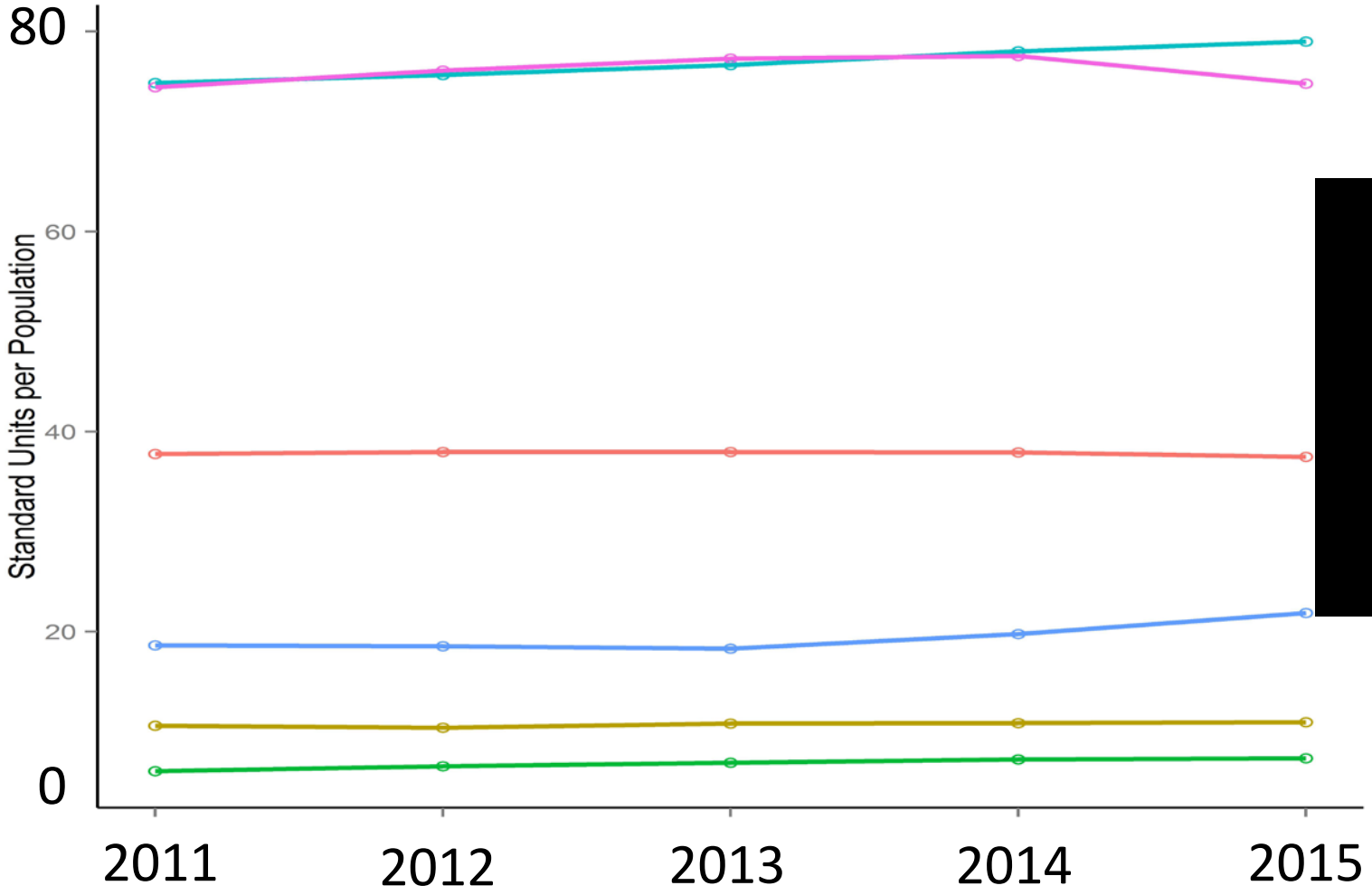


# Web Monitoring Program Monthly Posts Over Time by Drug Substance in Canada



# European Mosaic

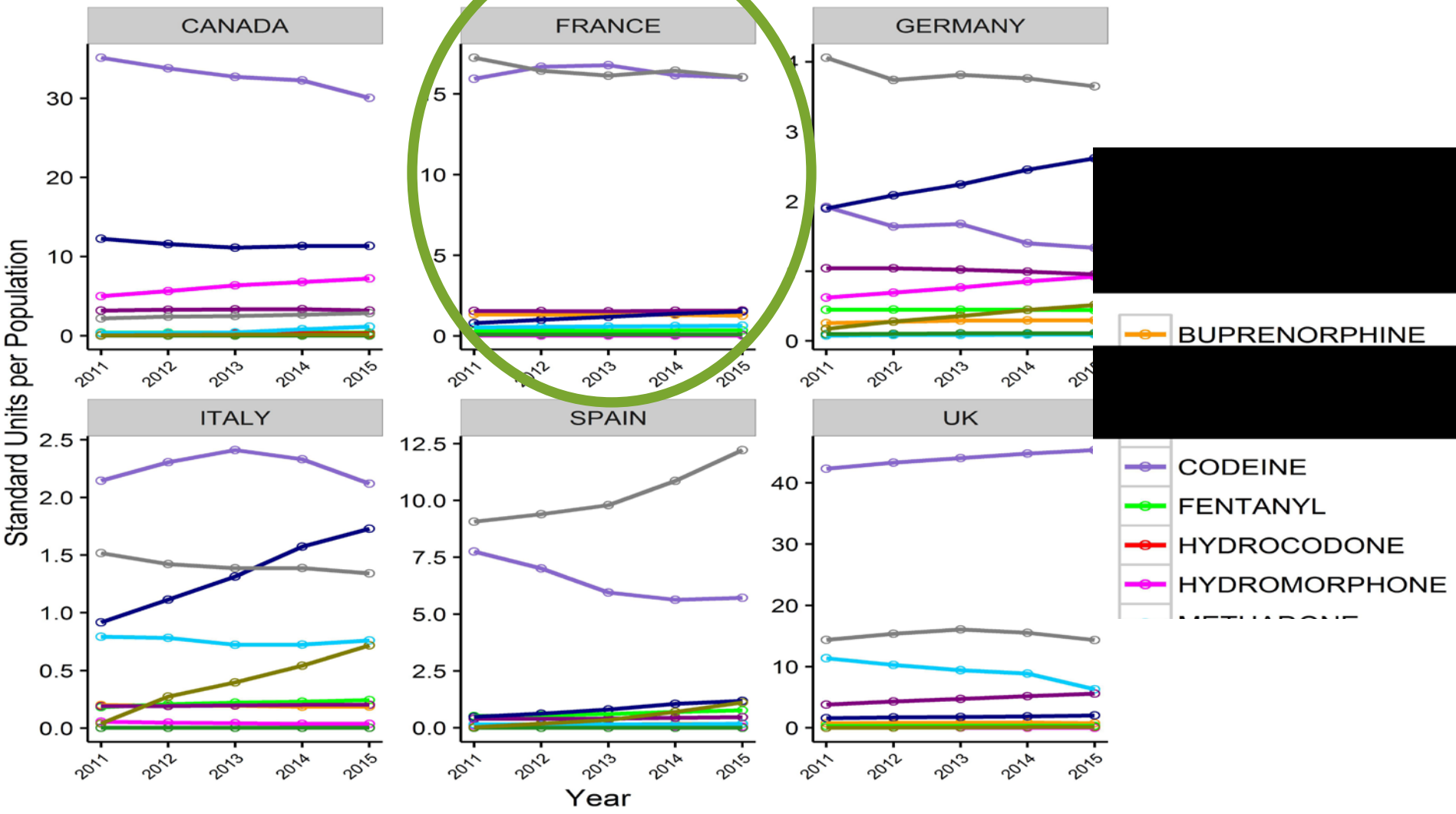
# Europe – Opioid Dosage Units per Population




[redacted]

**Includes: buprenorphine, codeine, fentanyl, hydrocodone, hydromorphone, methadone, oxycodone, sufentanil, tapentadol, tramadol**

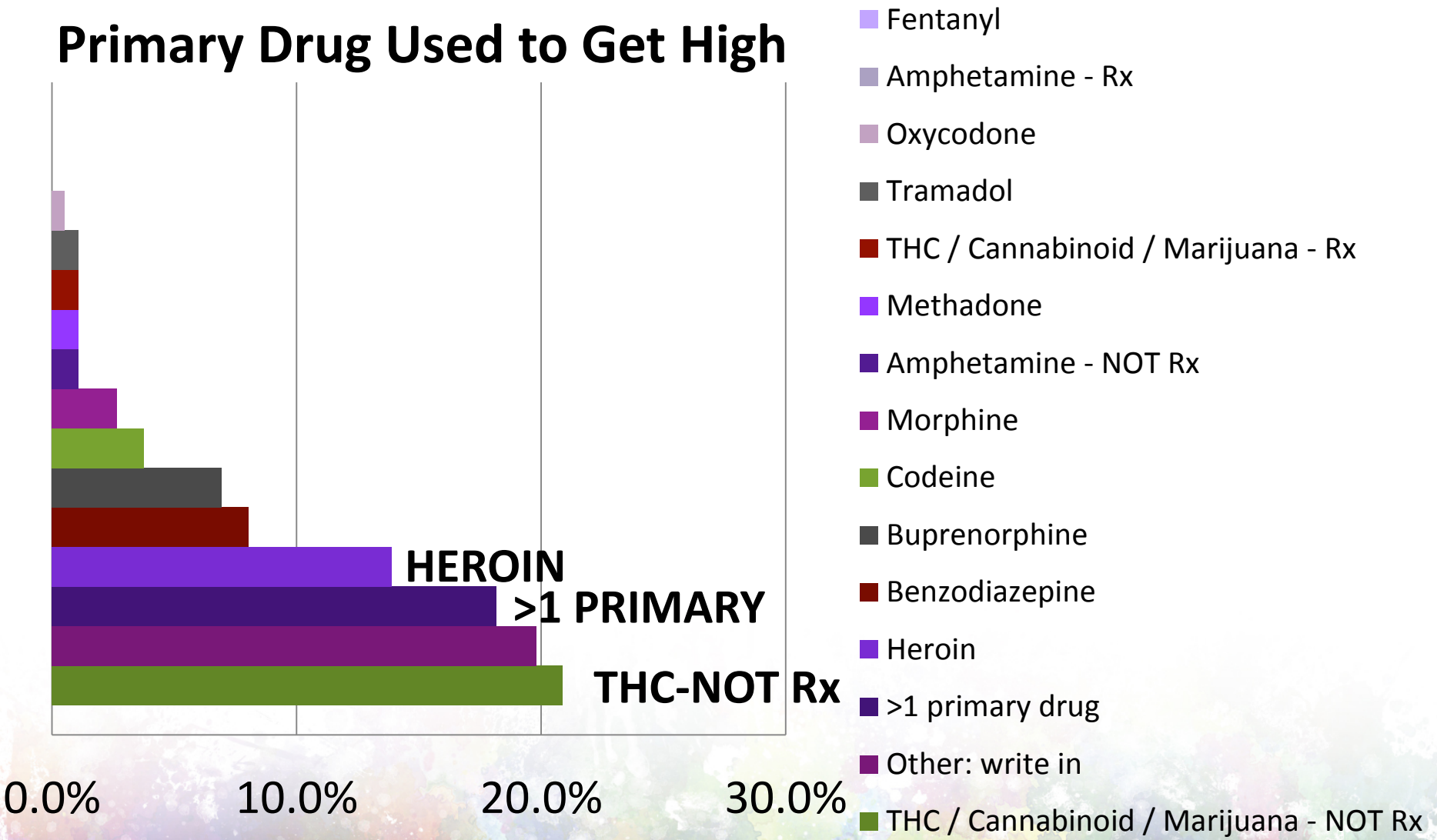
# Europe –Dosage Units per Population



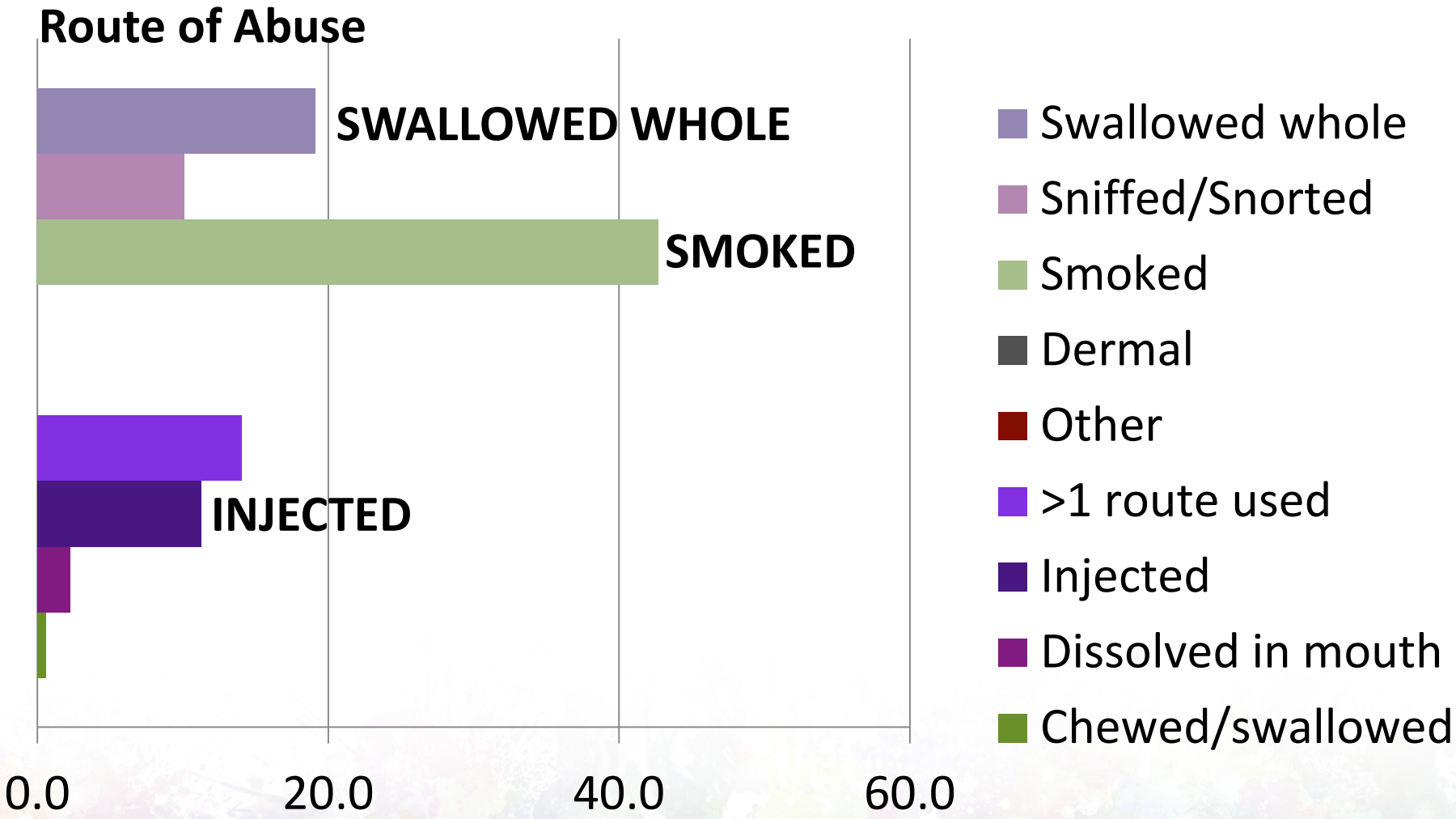
# France- EUROPAD

| | | France n=187 |
|---|---|---|
| **Age** | N | 187 |
| | Mean | 35.88 |
| | Median | 35 |
| **Gender** | Female | 46 (24.6) |
| | Male | 141 (75.4) |
| **Pregnant** | Yes | 3 (1.60) |

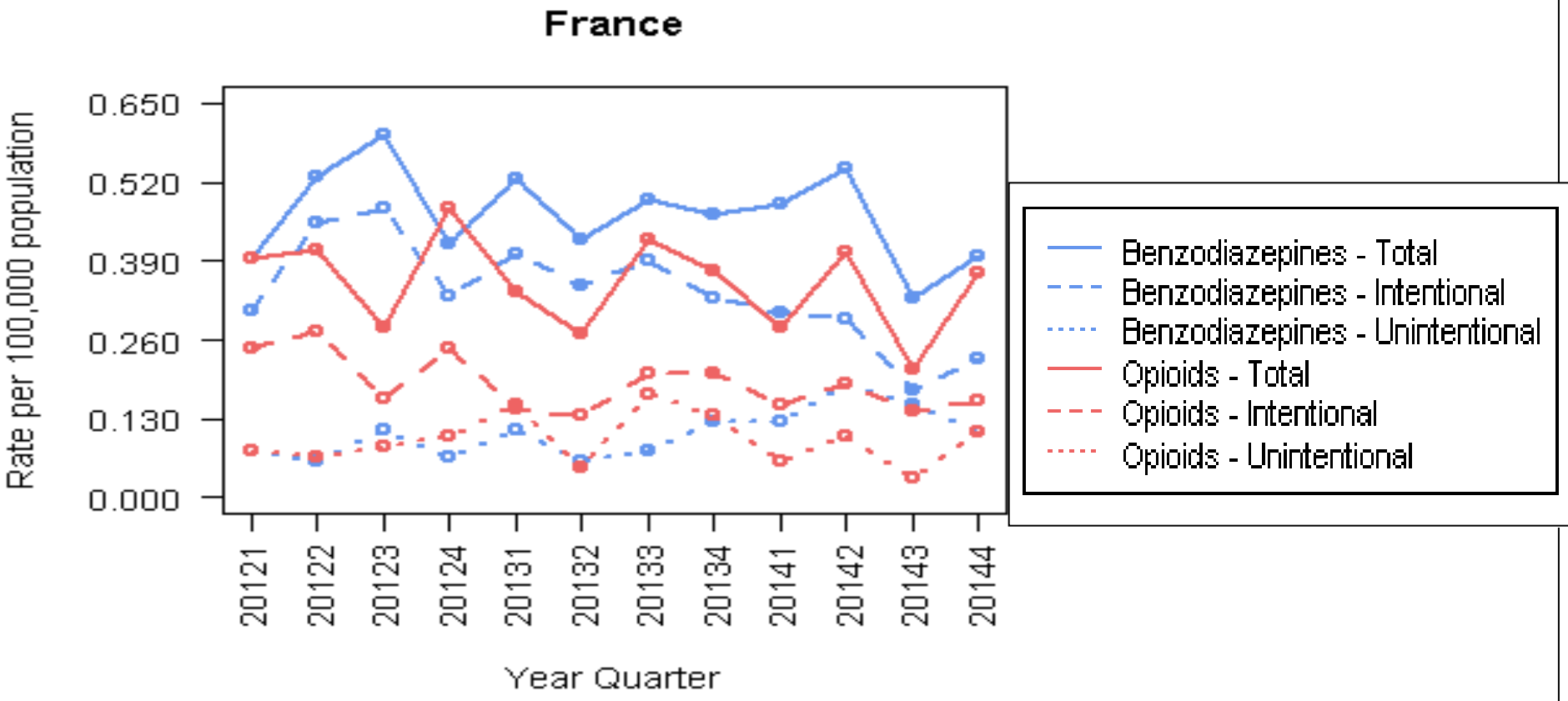
# France- EUROPAD



# France- EUROPAD



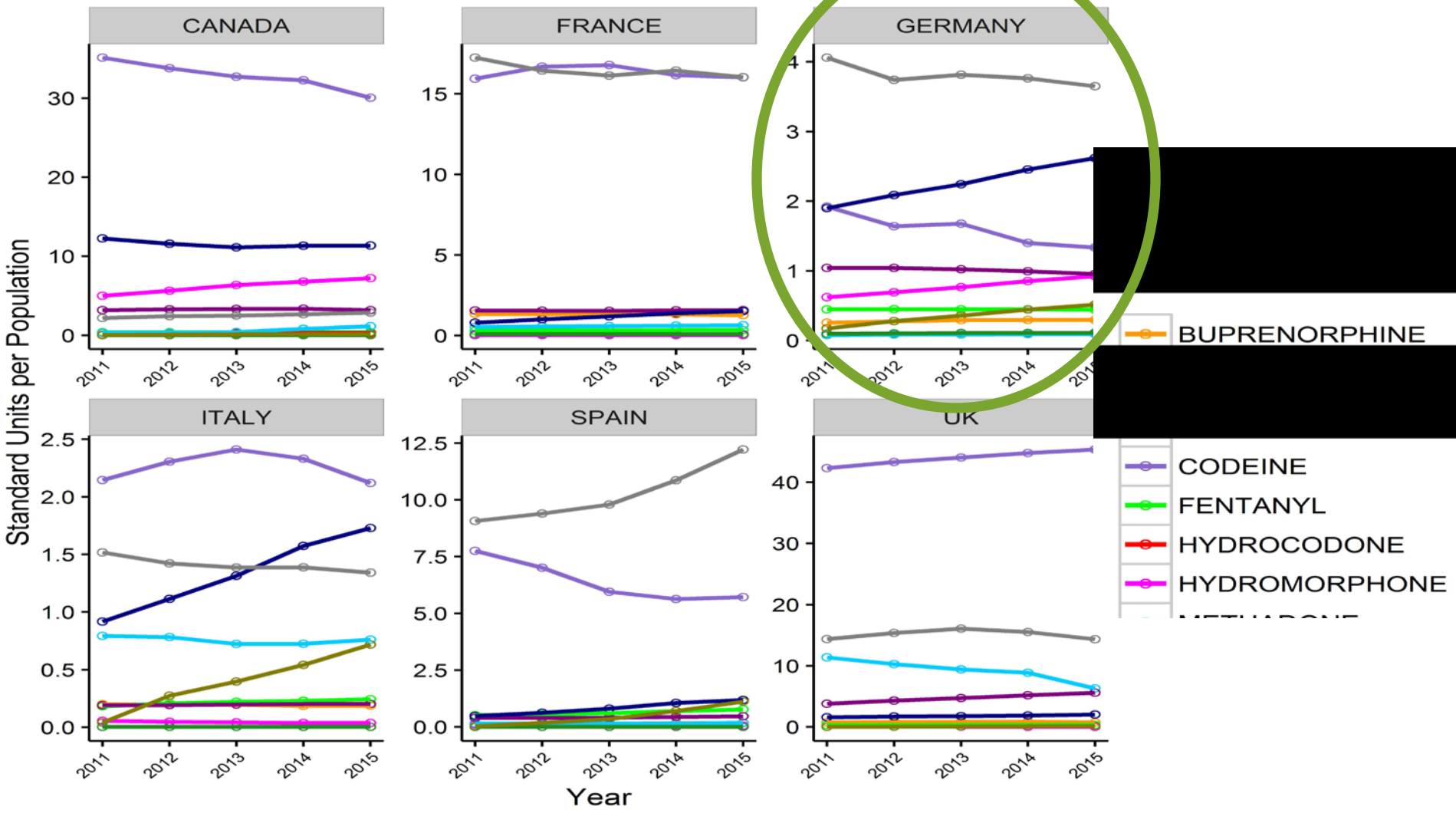
# France GTNet–Adult Human Exposures to Opioids and Benzodiazepines



# France Summary

- Codeine and tramadol by far the most utilized, oxycodone utilization increasing
- Patients entering substance abuse treatment most often report THC (not Rx), “other”, and heroin as their primary drug of abuse
  - Smoking reported by 43%
- Exposures of benzodiazepines and opioids have similar trends as reported to poison centres

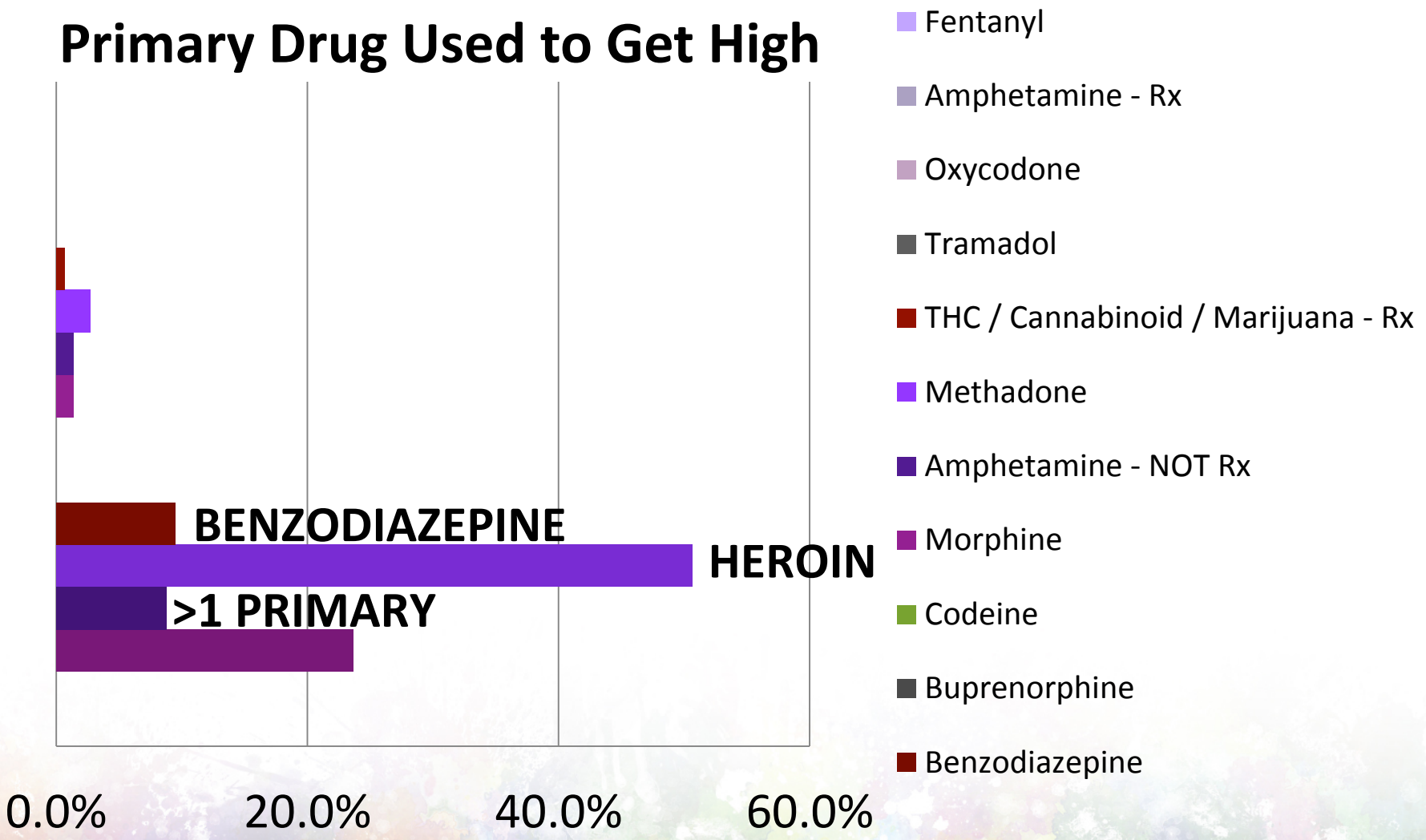
# Europe –Dosage Units per Population



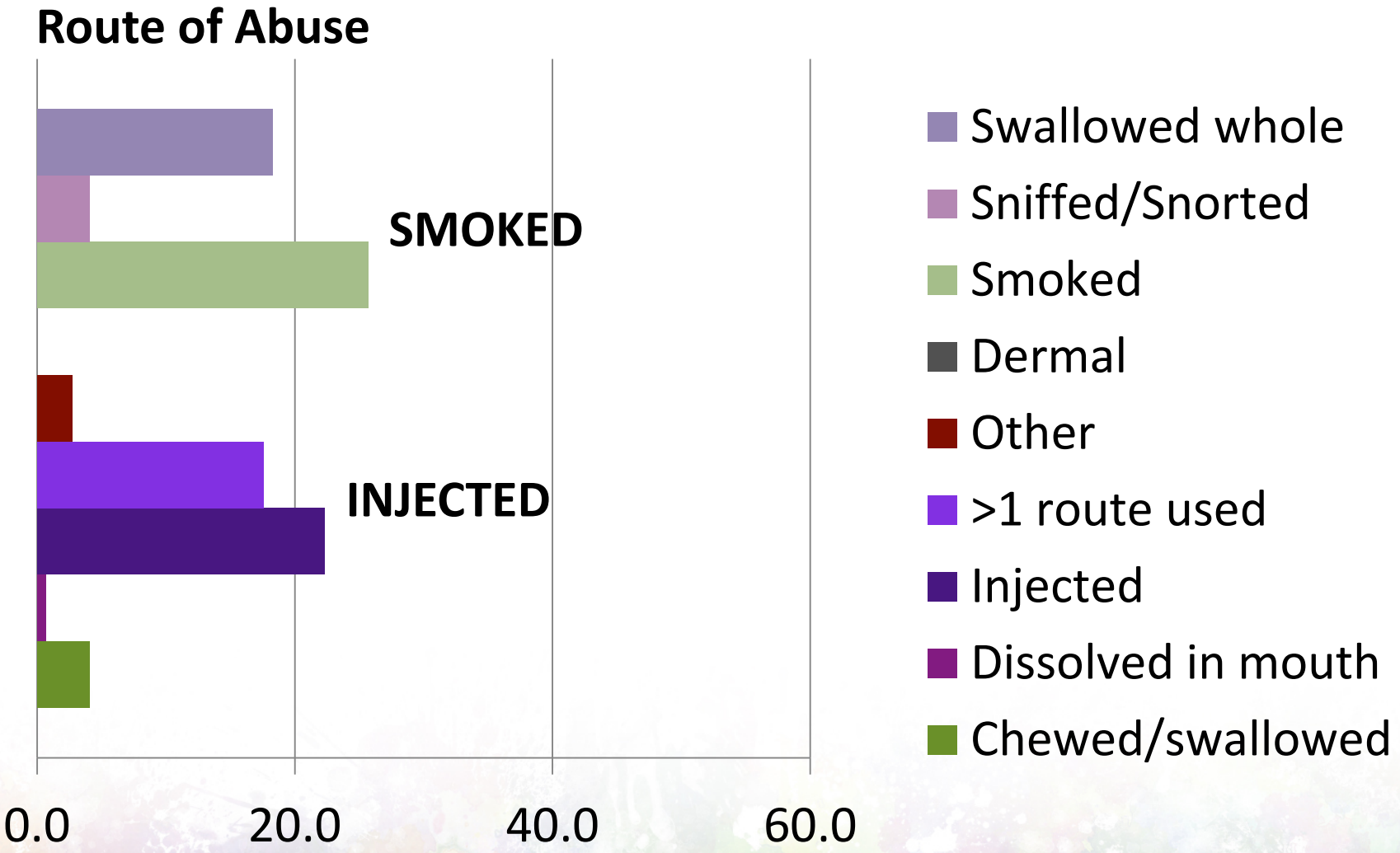
# Germany - EUROPAD

| | Germany n=148 | |
|---|---|---|
| **Age** | N | 148 |
| | Mean | 38.95 |
| | Median | 40 |
| **Gender** | Female | 33 (22.29) |
| | Male | 114 (77.03) |
| | Missing | 1 (0.68) |
| **Pregnant** | Yes | 1 (0.68) |

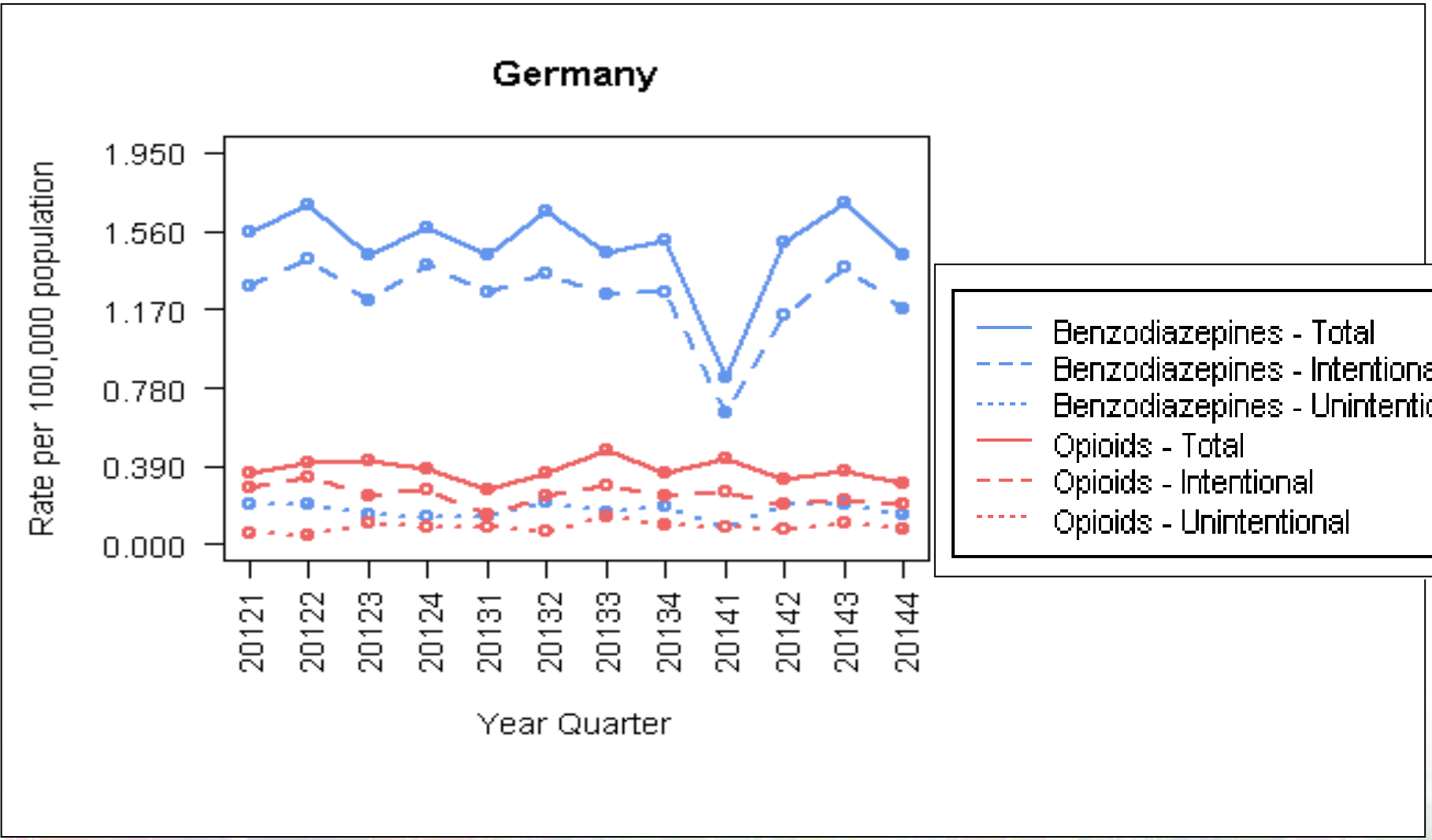
# Germany - EUROPAD



# Germany - EUROPAD



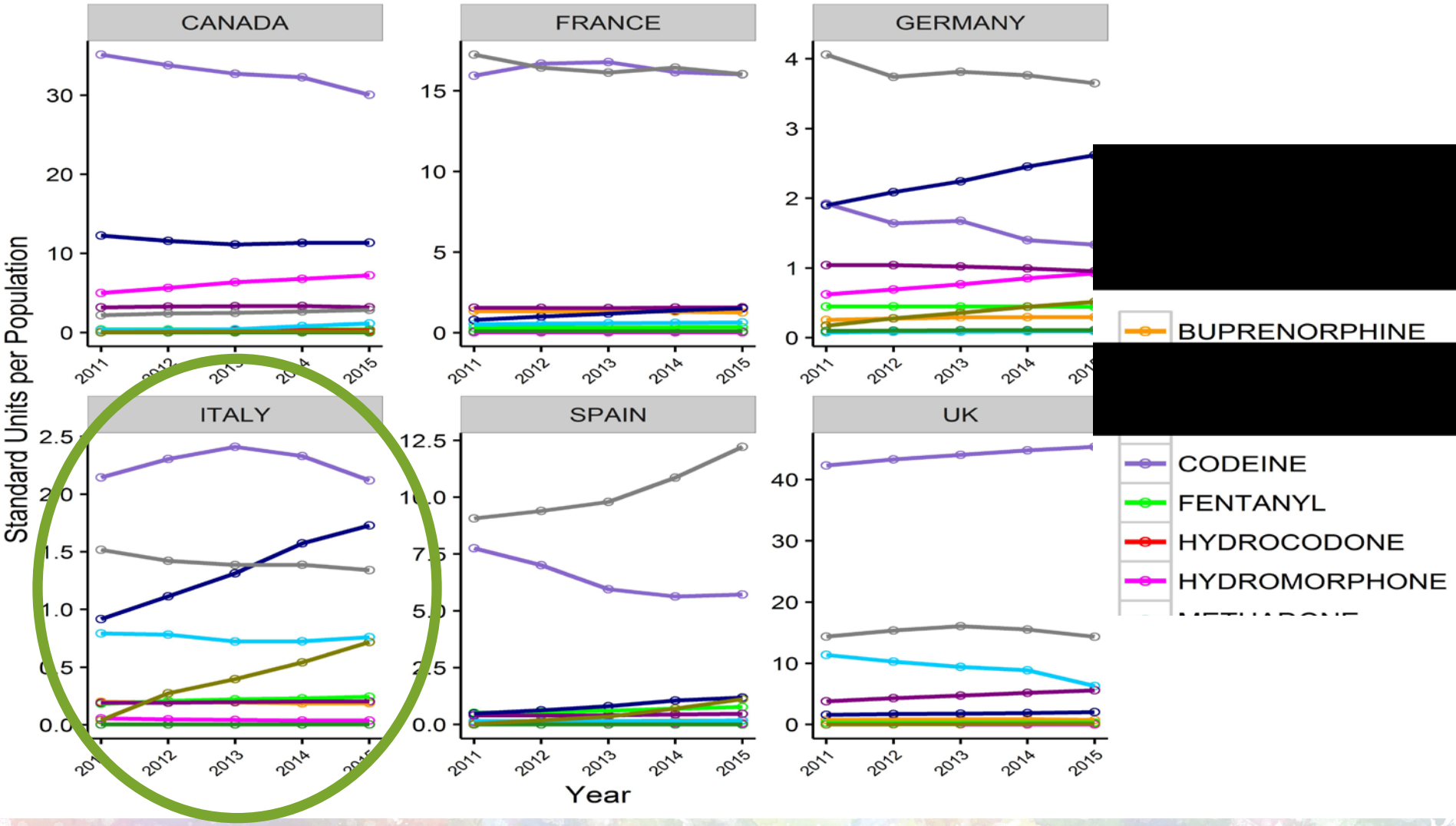
# Germany GTNet–Adult Human Exposures to Opioids and Benzodiazepines



# Germany Summary

- Oxycodone and hydromorphone utilization increasing
- Patients entering substance abuse treatment most often report heroin, benzodiazepines as their primary drug of abuse
  - Smoking and injection reported by ~22-26%
- Intentional abuse of benzodiazepines reported 4-5x more often than opioids to poison centre

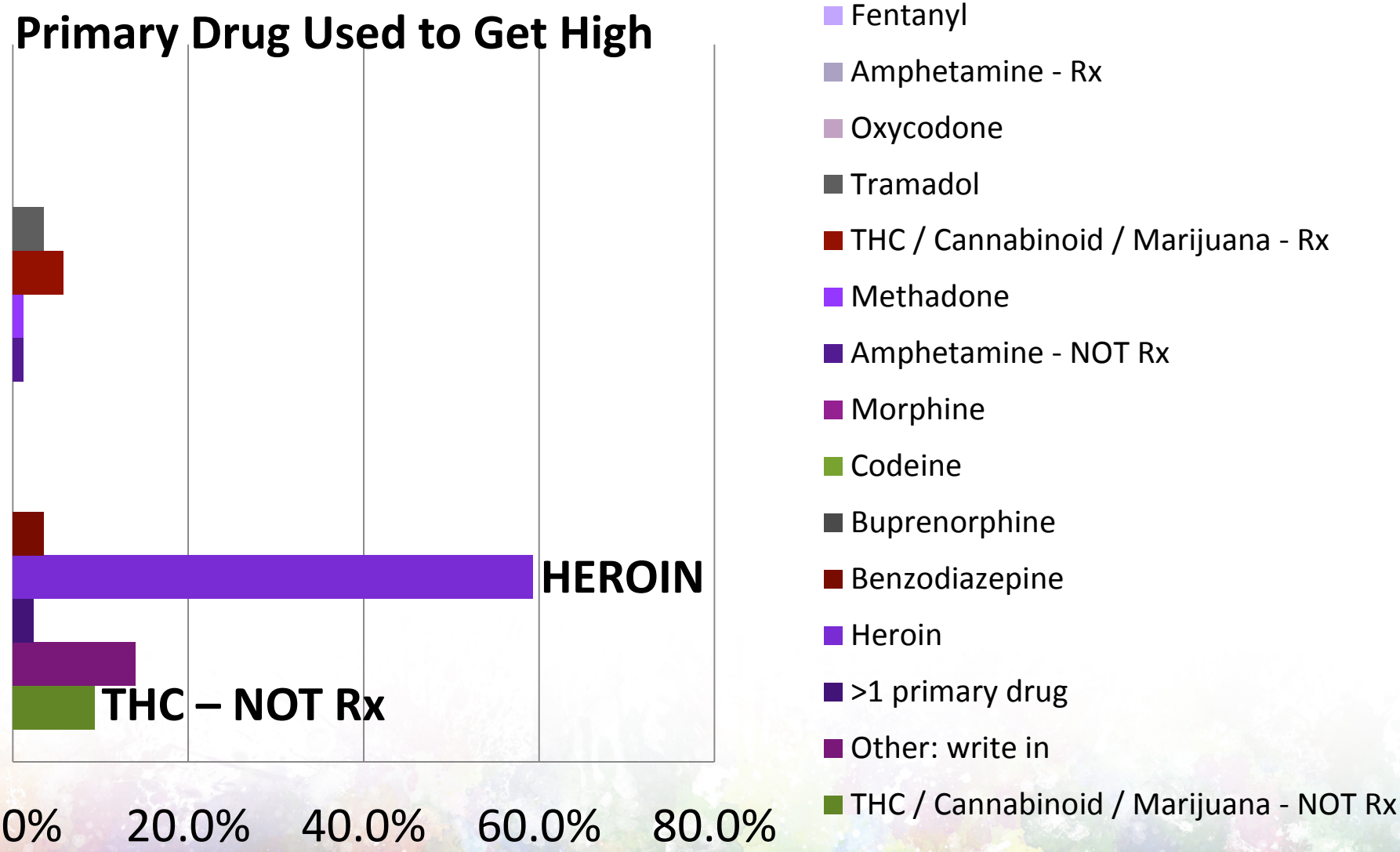
# Europe –Dosage Units per Population



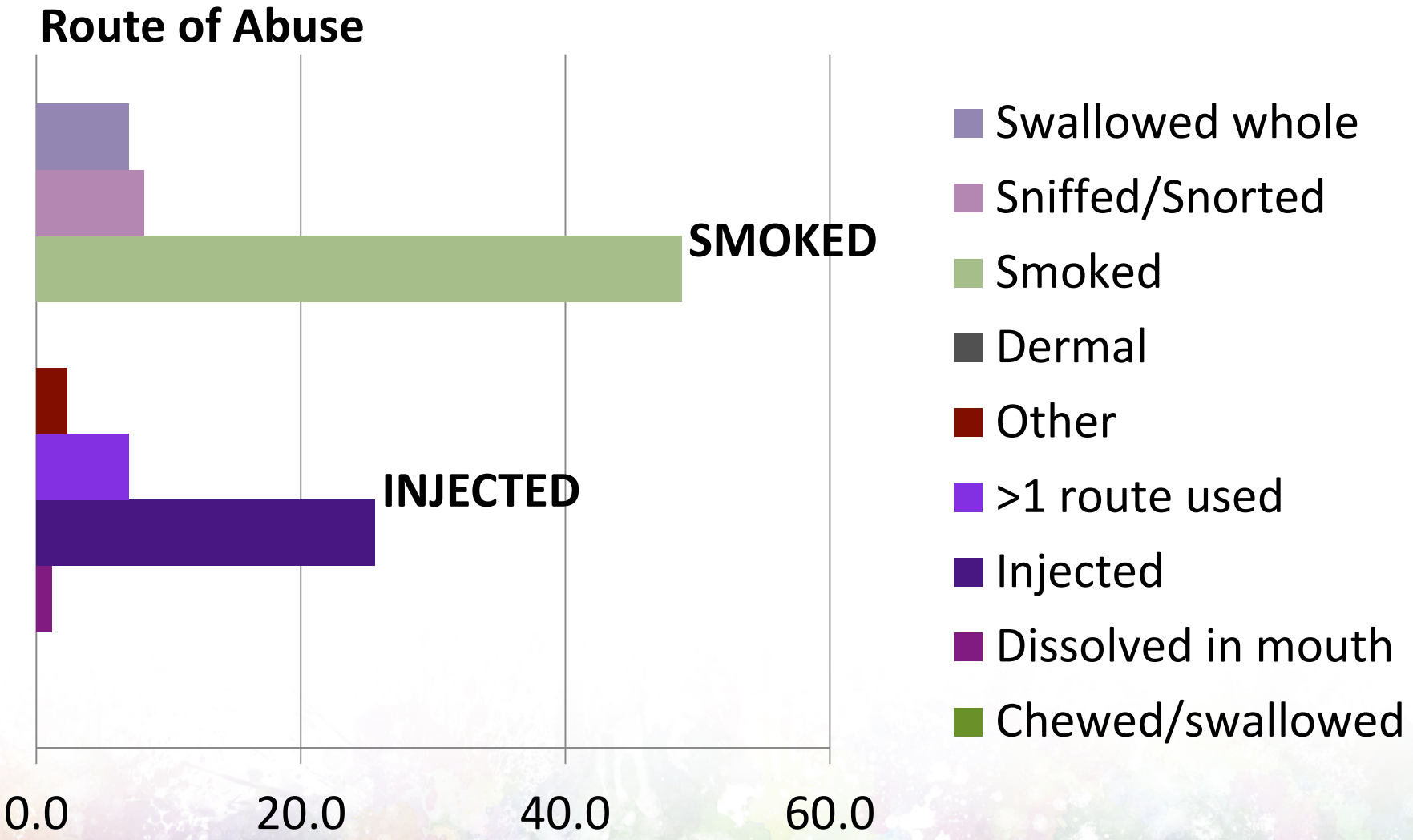
# Italy- EUROPAD

| | | Italy n=86 |
|---|---|---|
| **Age** | N | 86 |
| | Mean | 31.37 |
| | Median | 27 |
| **Gender** | Female | 23 (26.74) |
| | Male | 63 (73.26) |
| | Missing | 0 (0) |
| **Pregnant** | Yes | 1 (1.16) |

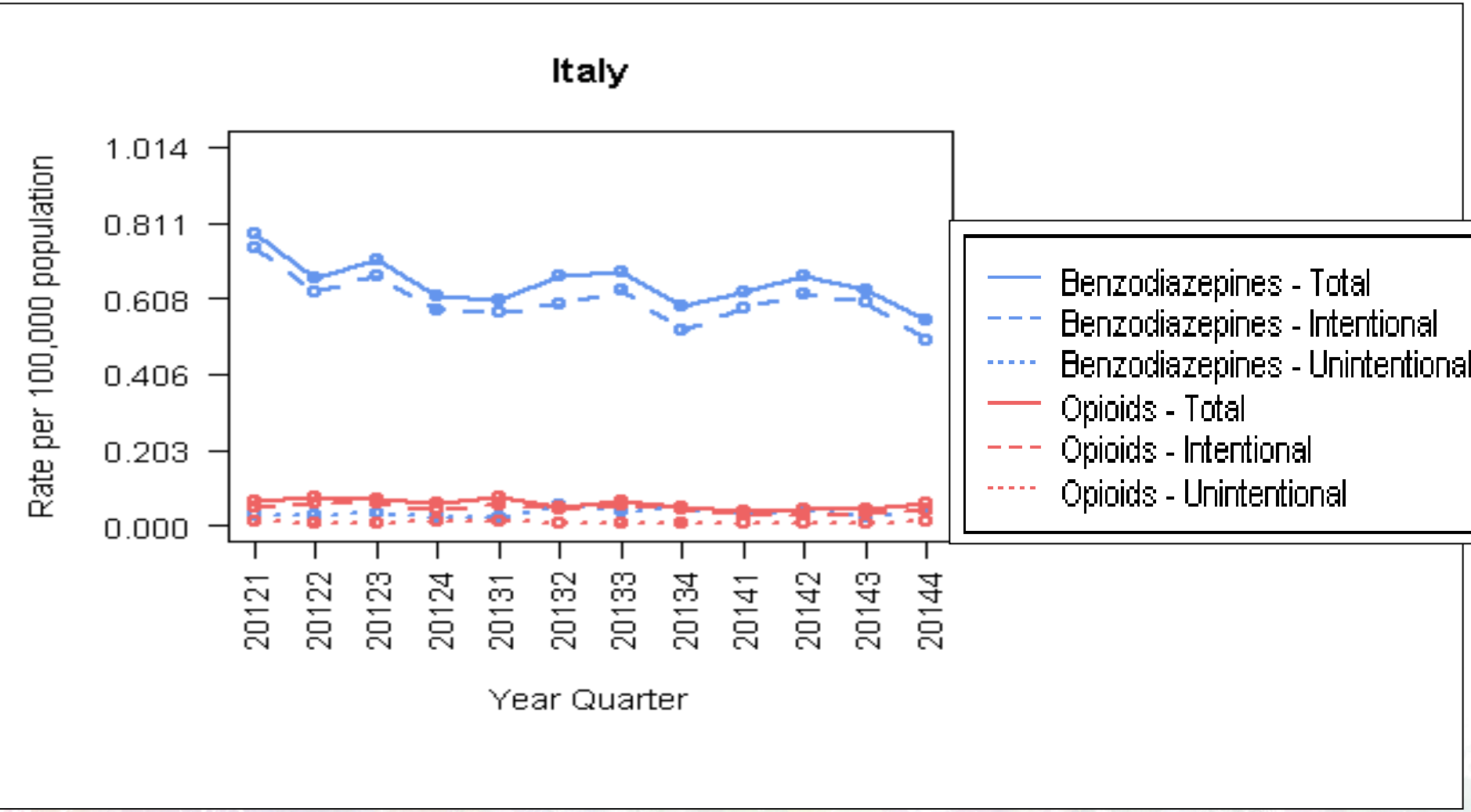
# Italy- EUROPAD



# Italy- EUROPAD



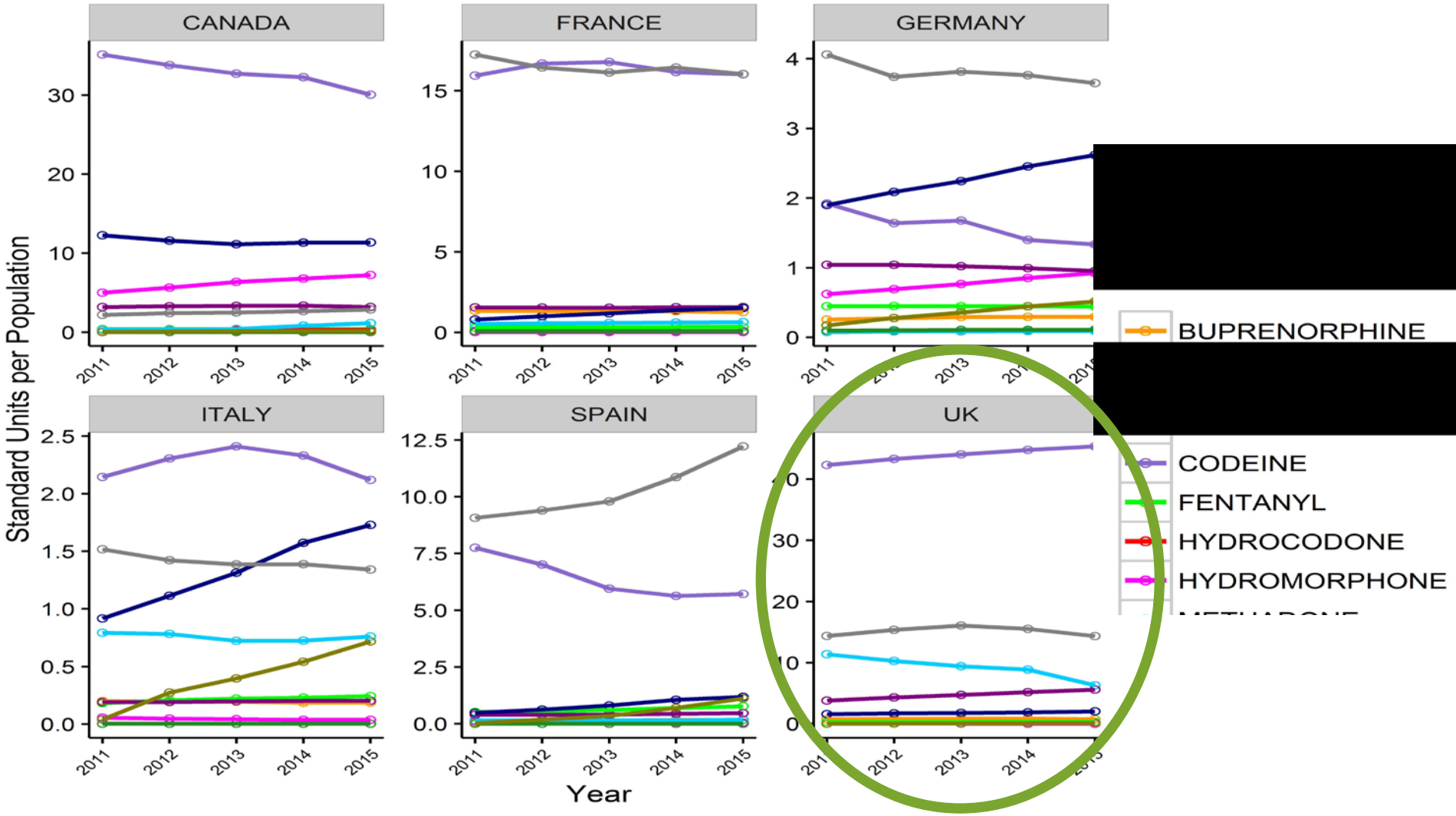
# Italy GTNet–Adult Human Exposures to Opioids and Benzodiazepines



# Italy Summary

- Codeine most commonly utilized opioid, oxycodone utilization increasing
- Patients entering substance abuse treatment most often report heroin and THC (not Rx) as their primary drug of abuse
  - Smoking reported most often (49%)
  - Injection reported by ~27%
- Exposures to benzodiazepines reported 7-8x more often than opioids to poison centre

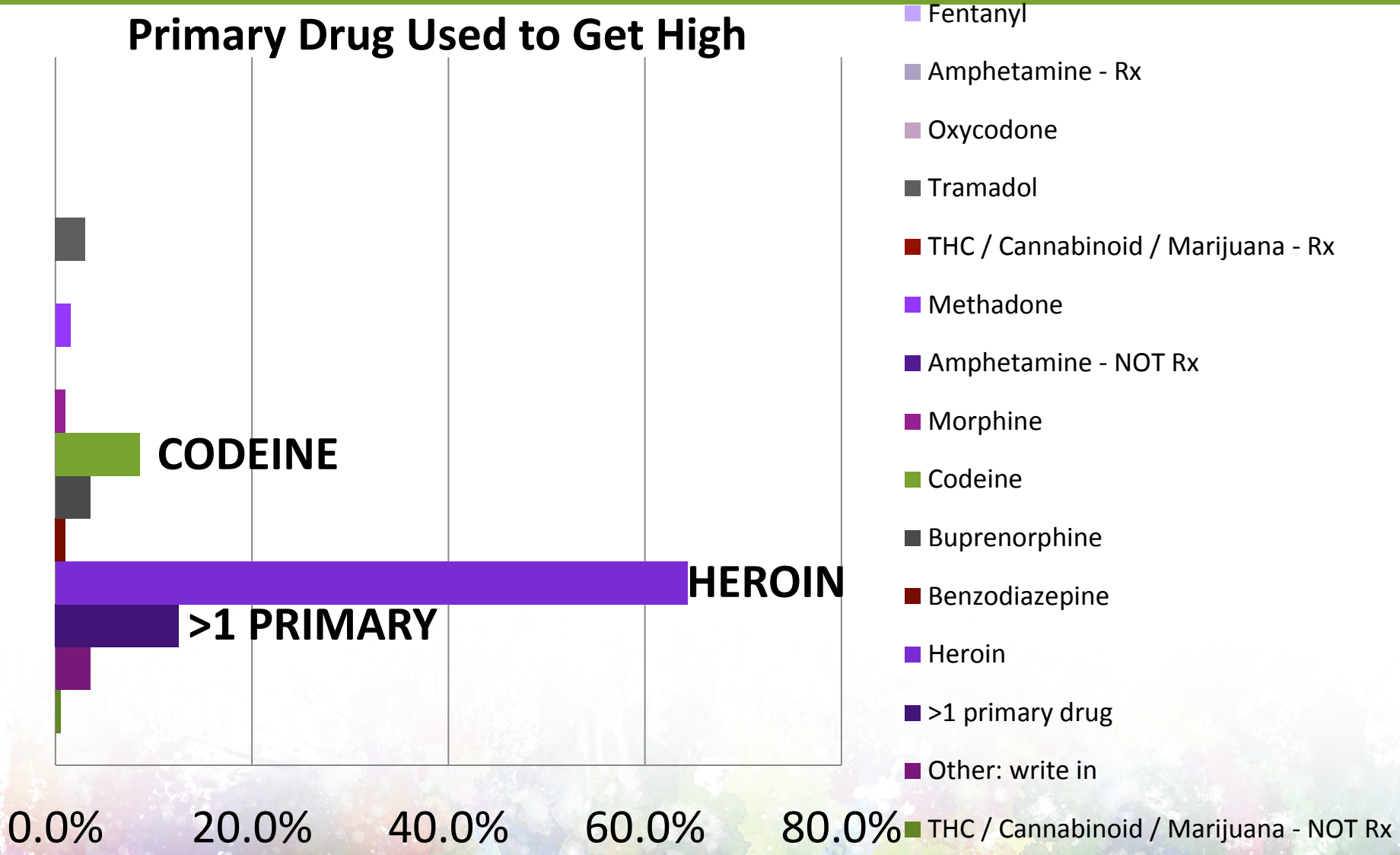
# Europe –Dosage Units per Population



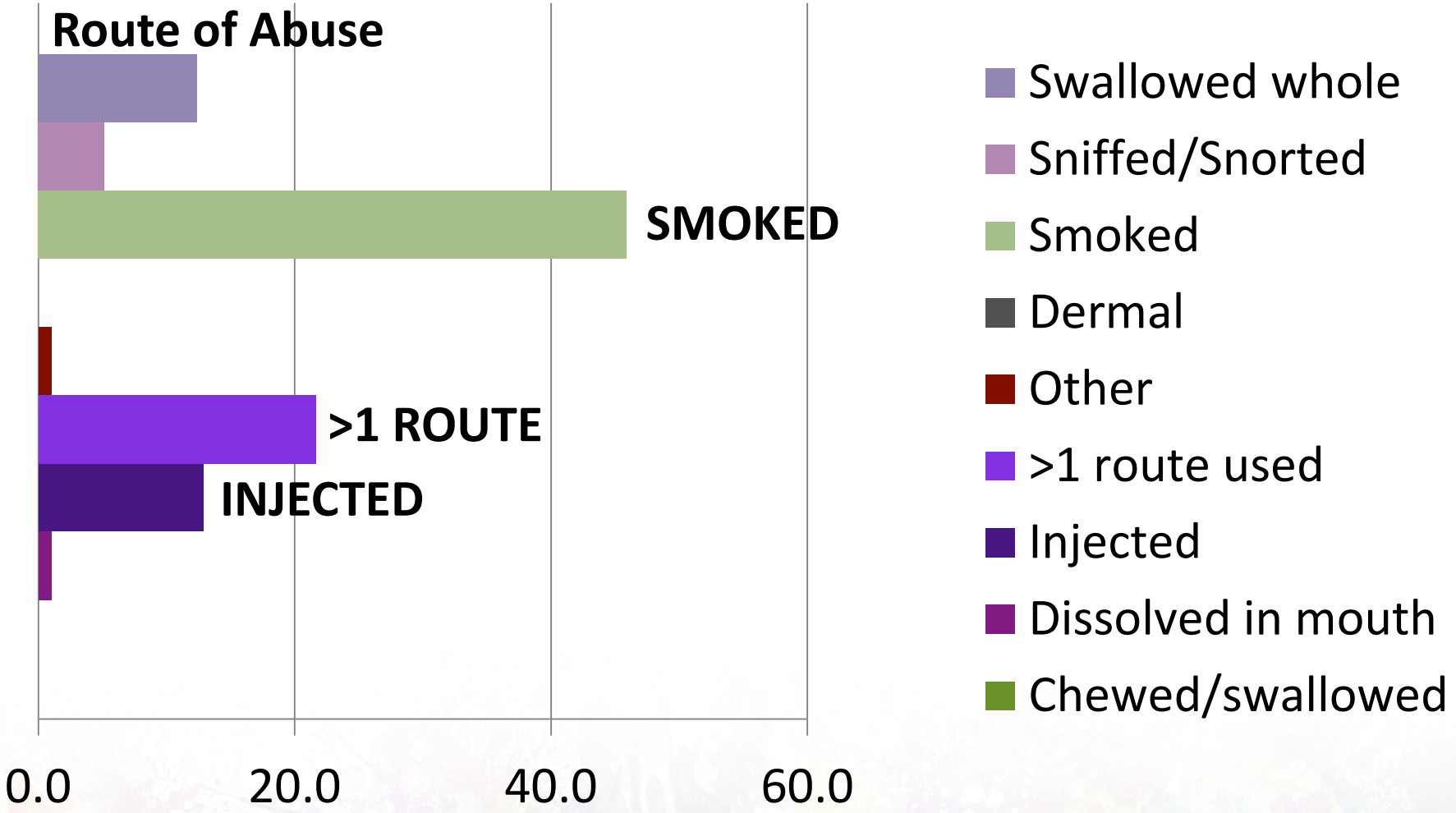
# United Kingdom - EUROPAD

| | United Kingdom n=199 | |
|---|---|---|
| **Age** | N | 199 |
| | Mean | 36.8 |
| | Median | 36 |
| **Gender** | Female | 50 (25.13) |
| | Male | 147 (73.87) |
| | Missing | 2 (1.01) |
| **Pregnant** | Yes | 0 (0.0) |

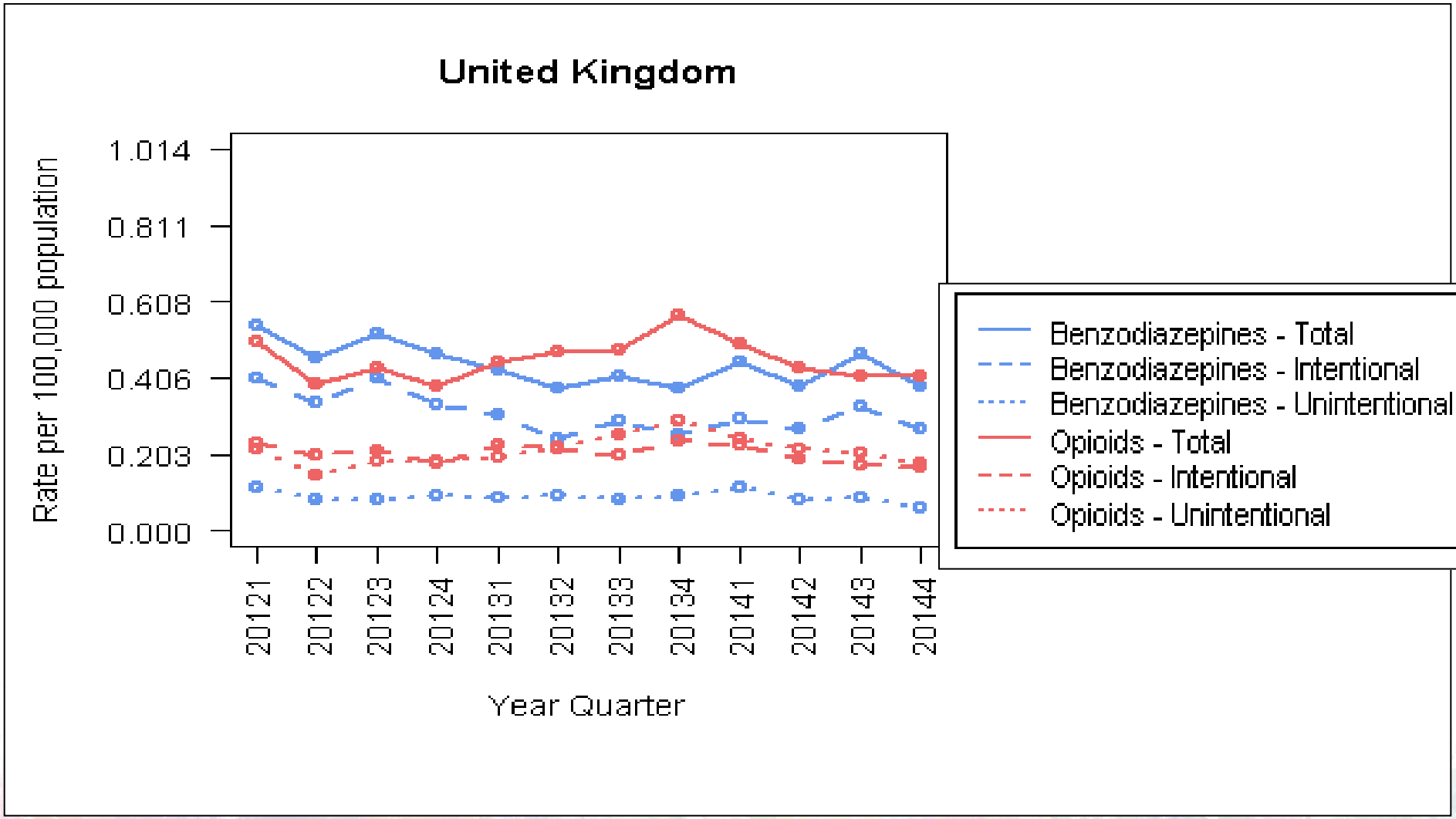
# United Kingdom - EUROPAD



# United Kingdom - EUROPAD



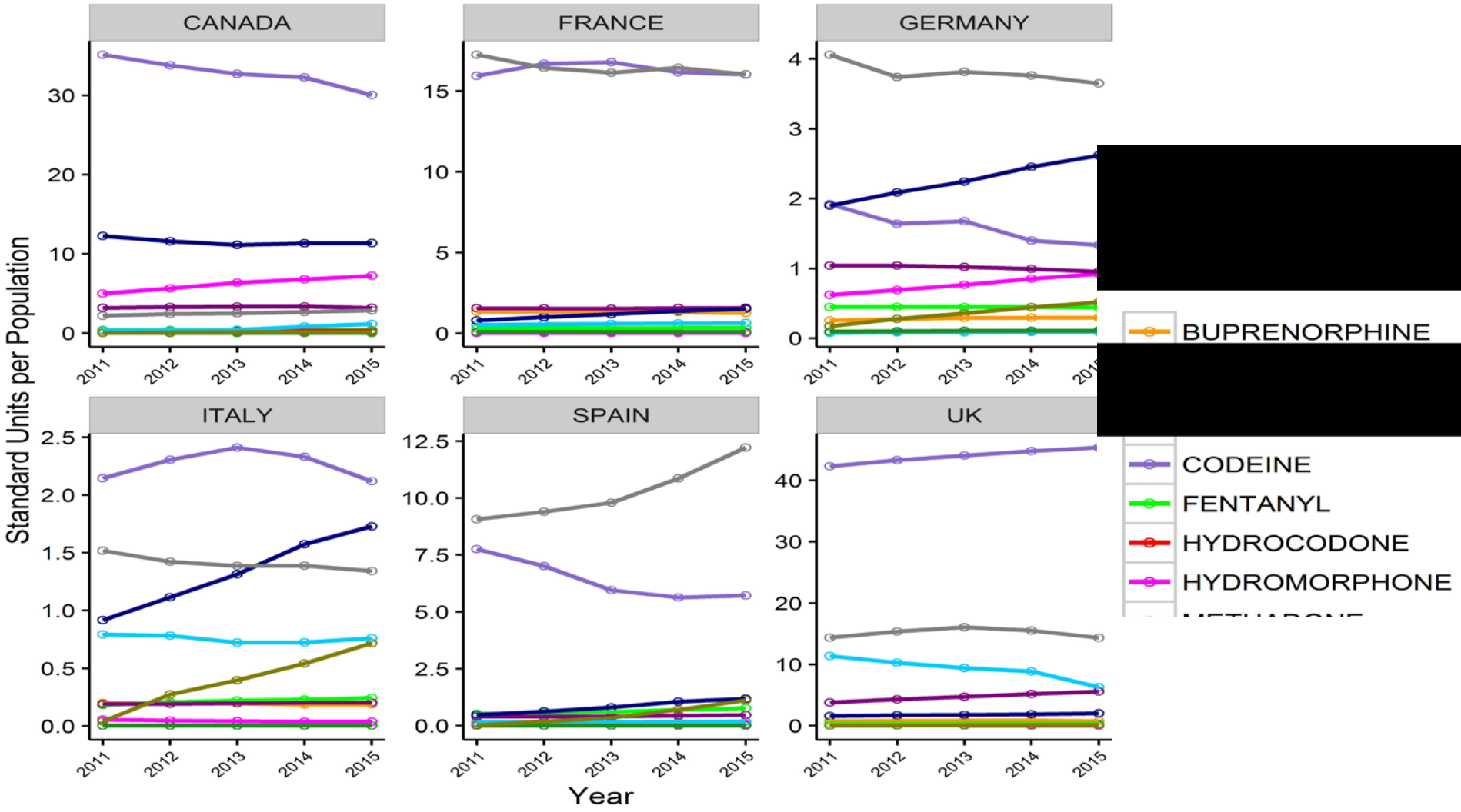
# UK GTNet–Adult Human Exposures to Opioids and Benzodiazepines



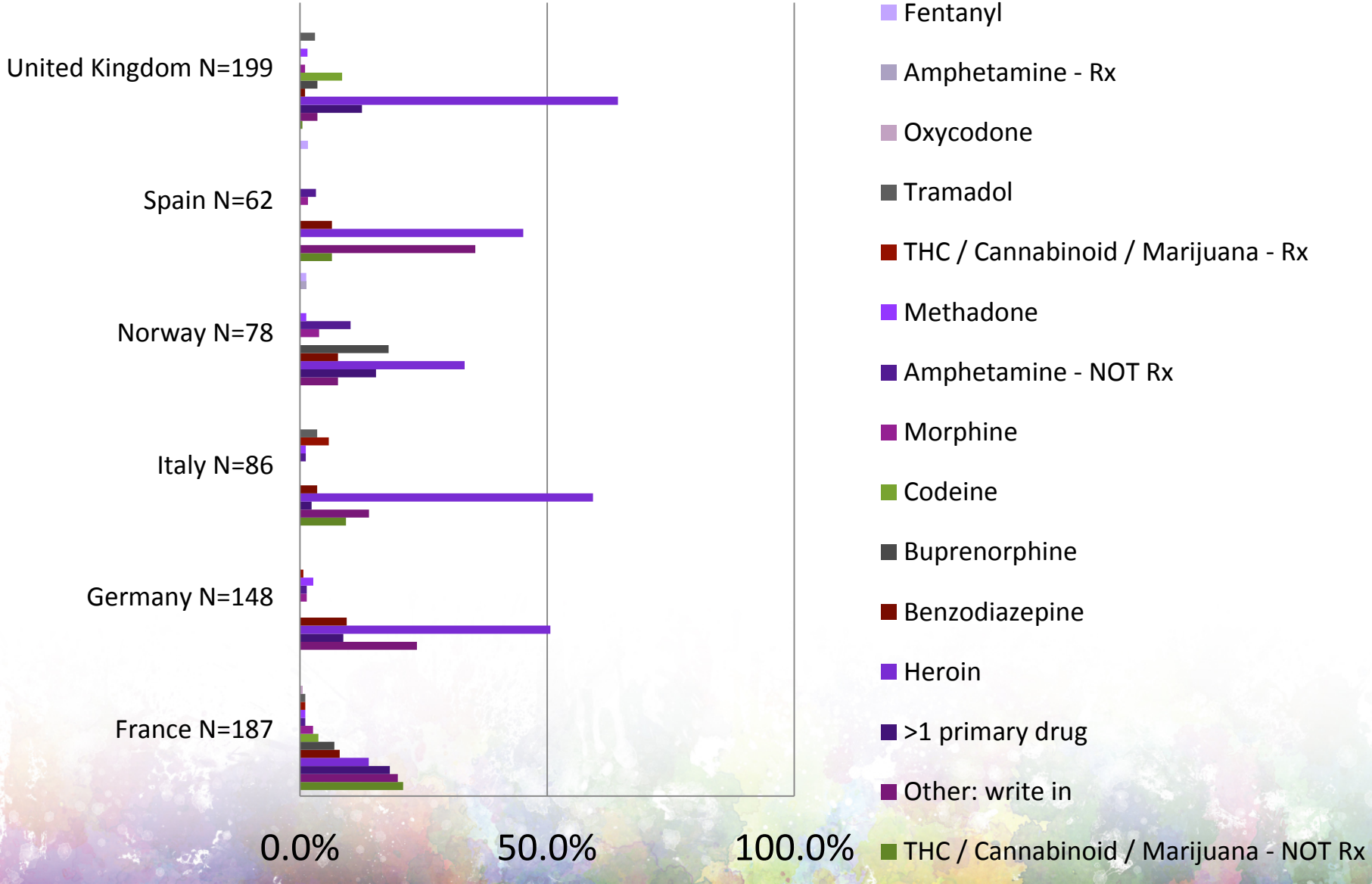
# United Kingdom Summary

- Codeine most commonly utilized opioid, morphine utilization increasing
- Patients entering substance abuse treatment most often report heroin and codeine as their primary drug of abuse
  - Smoking reported most often (46%)
- Exposures to benzodiazepines and opioids similar as reported to poison centre

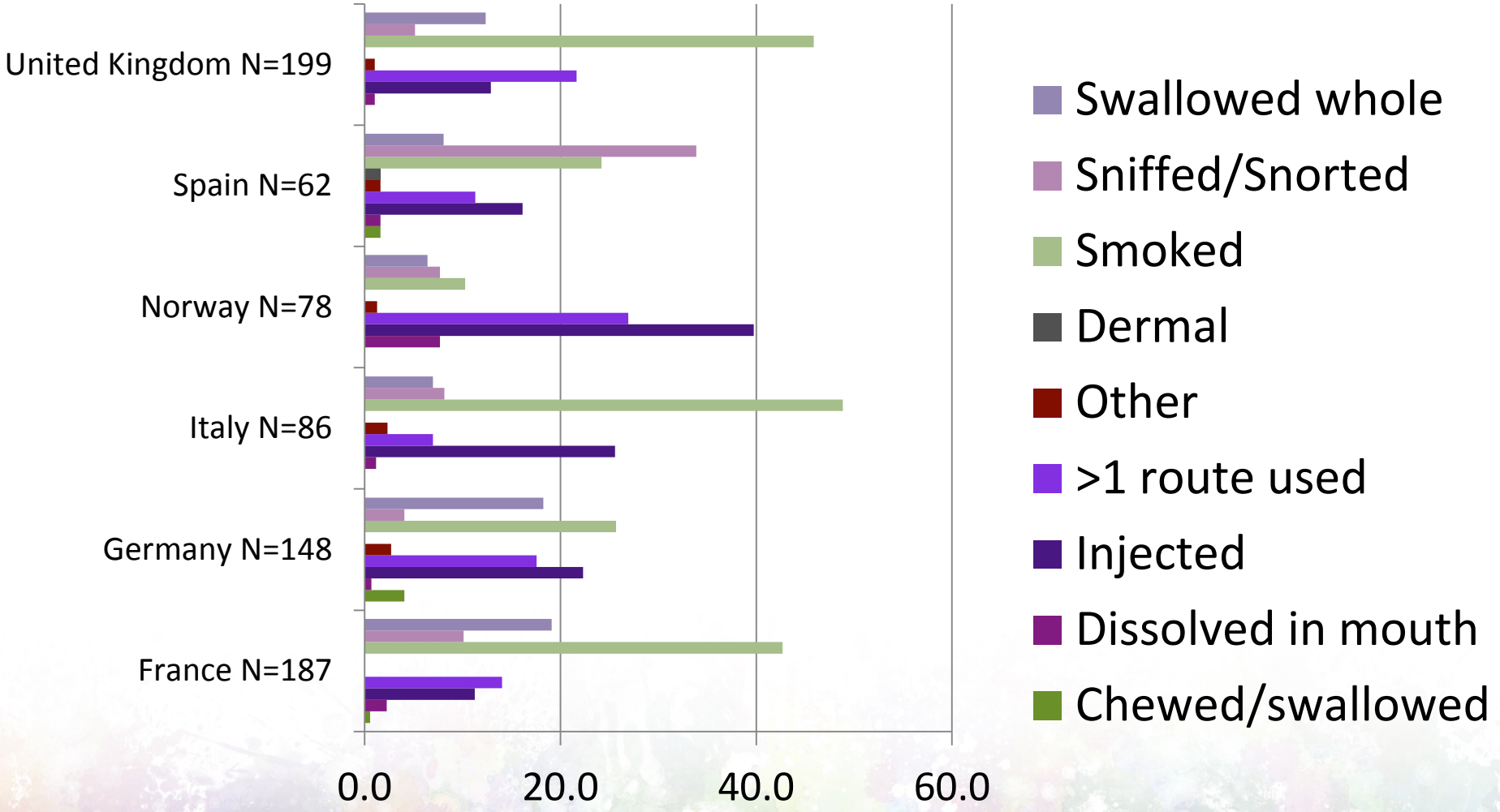
# Europe –Dosage Units per Population



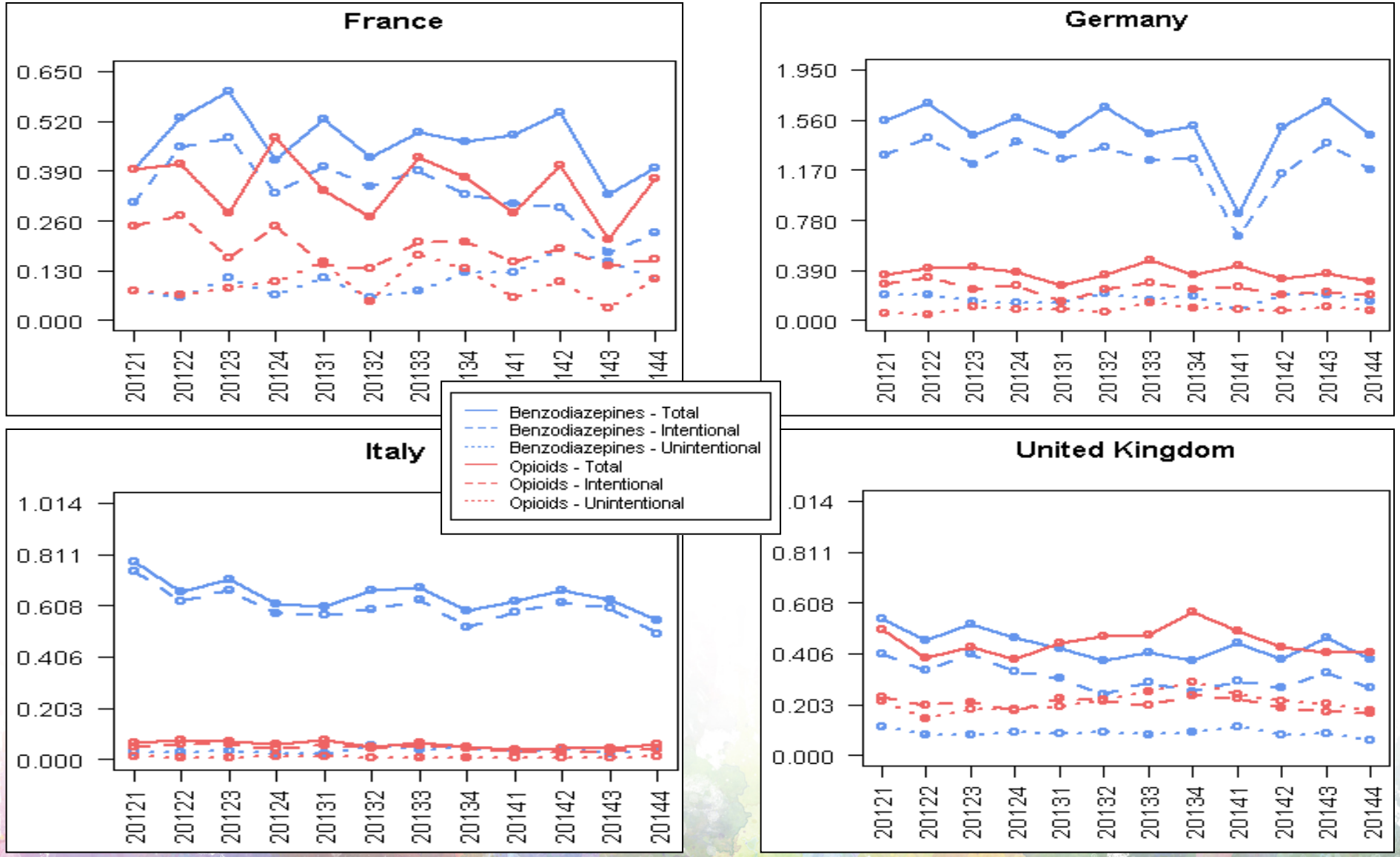
# EUROPAD – Primary Drug Used to Get High



# EUROPAD – Route of Abuse



# GTNet–Adult Human Exposures to Opioids and Benzodiazepines (per 100,000 population)



# Conclusion

- A mosaic approach to surveillance provides valuable insight from multi-dimensional perspectives
- Each of the programs presented target different facets of prescription opioid abuse, misuse, and diversion
- While magnitude and patterns vary, heroin, THC, prescription opioids and benzodiazepines commonly abused/misused in many countries

Questions?

Jody.Green@rmpdc.org