

Abuse of Pregabalin and Gabapentin in France, Germany, and Italy

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BACKGROUND

- Medications that affect the central nervous system are often abused, especially pain medications.¹
- Abuse and misuse of prescription and/or illicit drugs may involve unlawful activities. As such, accurate capture of information regarding abuse and misuse of prescription medications is hindered by its covert and illegal nature.
- Alpha2-delta ligands, eg, pregabalin and gabapentin, are recommended first-line therapies for some chronic pain conditions. However, these drugs are increasingly reported as drugs of abuse in different countries.²⁻⁶
 - However, studies that capture comparative information between countries are limited, and observations are largely based on anecdotal reports in single countries or regions.

OBJECTIVE

- To assess current rates of abuse of pregabalin and gabapentin compared with other medications with known abuse potential in France, Germany, and Italy.

METHODS

- The Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS[®]) System,⁷ an observational multicenter surveillance study in adults, collates multiple perspectives to obtain uniformly collected, timely, and reliable information on prescription drug abuse and misuse in the community. It uses the following resources to estimate prescription drug abuse in each country:

1. Survey of Non-Medical Use of Prescription Drugs (NMURx) program, a confidential and anonymous web-based survey that provides population-based estimates.

2. European Opiate Addiction Treatment Association (EUROPAD), a surveillance population of individuals seeking treatment for substance abuse disorders.

- Although no single data source adequately captures the existing breadth of experience with drug abuse, data from multiple perspectives can create a mosaic image.⁷

- Data were captured on pregabalin, gabapentin, opioid analgesics, and other drugs with known abuse potential:
 - “Opioids” included (depending on data set) buprenorphine, codeine (prescription and over-the-counter), fentanyl, hydromorphone, morphine, oxycodone, sufentanil, and tramadol.

- The Drug Abuse Screening Test (DAST-10)⁸ gave a measure of the degree of consequences of drug abuse/misuse.

- Data were collected from 2012 to 2017.

– NMURx survey data were weighted to the national adult populations in each respective country.

Definitions of Drug Abuse

- Drug “abuse” was defined as a report of non-medical use “for enjoyment/to get high” in the NMURx program.

RESULTS

Respondent Characteristics

- Ages ranged from 18 to >65 years; 30%–40% reported a history of chronic pain in the NMURx program.
 - At least 95% of respondents had a DAST-10 score of “low level” or “no abuse risk.”

Prevalence of Drug Abuse

- In NMURx, lifetime drug abuse rates of pregabalin or gabapentin were numerically lower in all countries than for opioids or other comparator drugs (Figure 1).
- In EUROPAD, cumulative rates of abuse were higher in Germany than in other countries for every drug (Figure 2).
- Lifetime abuse of pregabalin or gabapentin was predominantly reported with lifetime abuse of another drug group (Table 1).

Figure 1. Lifetime Abuse of Prescription Drugs by Country (NMURx)

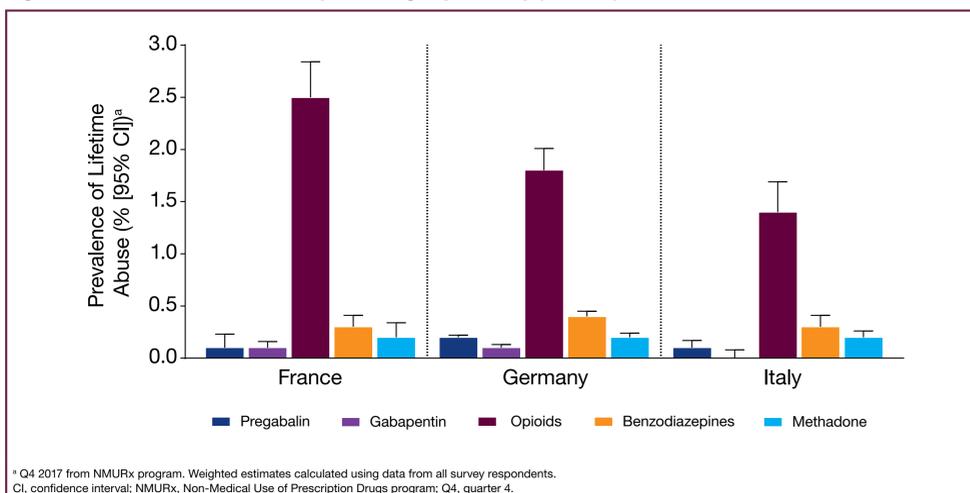
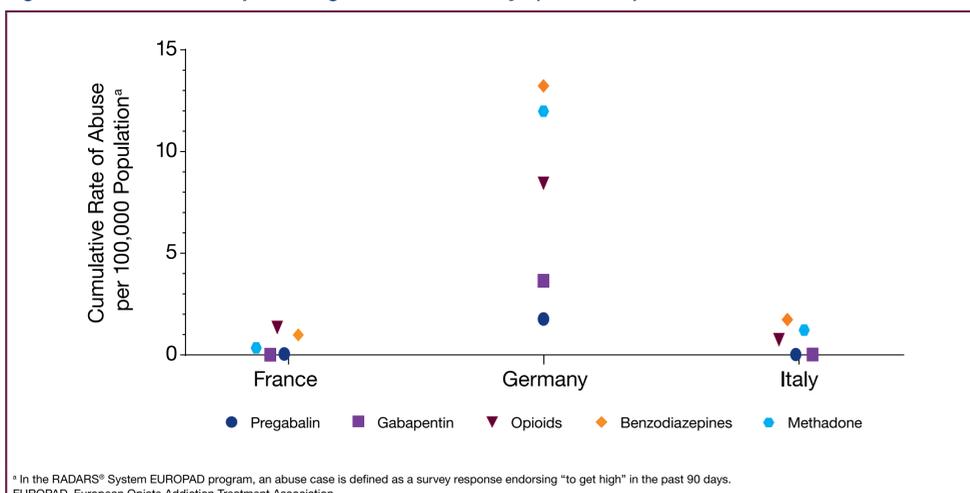


Figure 2. Abuse of Prescription Drugs in the Past 90 Days (EUROPAD)



^a In the RADARS[®] System EUROPAD program, an abuse case is defined as a survey response endorsing “to get high” in the past 90 days. EUROPAD, European Opiate Addiction Treatment Association.

Table 1. Case Counts of Lifetime Abuse in Q4 2017 (NMURx)^a

	France n (%)		Germany n (%)		Italy n (%)	
	Single	Multiple ^b	Single	Multiple ^b	Single	Multiple ^b
Pregabalin	1 (7.1)	13 (92.9)	4 (20.0)	16 (80.0)	2 (14.3)	12 (85.7)
Gabapentin	0 (0)	8 (100)	3 (21.4)	11 (78.6)	1 (20.0)	4 (80.0)
Opioid analgesics	122 (49.0)	127 (51.0)	114 (45.6)	136 (54.4)	70 (39.5)	107 (60.5)
Benzodiazepine	11 (33.3)	22 (66.7)	16 (29.6)	38 (70.4)	13 (33.3)	26 (66.7)
Baclofen	1 (11.1)	8 (88.9)	5 (29.4)	12 (70.6)	3 (30.0)	7 (70.0)
Methadone	7 (26.9)	19 (73.1)	7 (28.0)	18 (72.0)	3 (12.5)	21 (87.5)

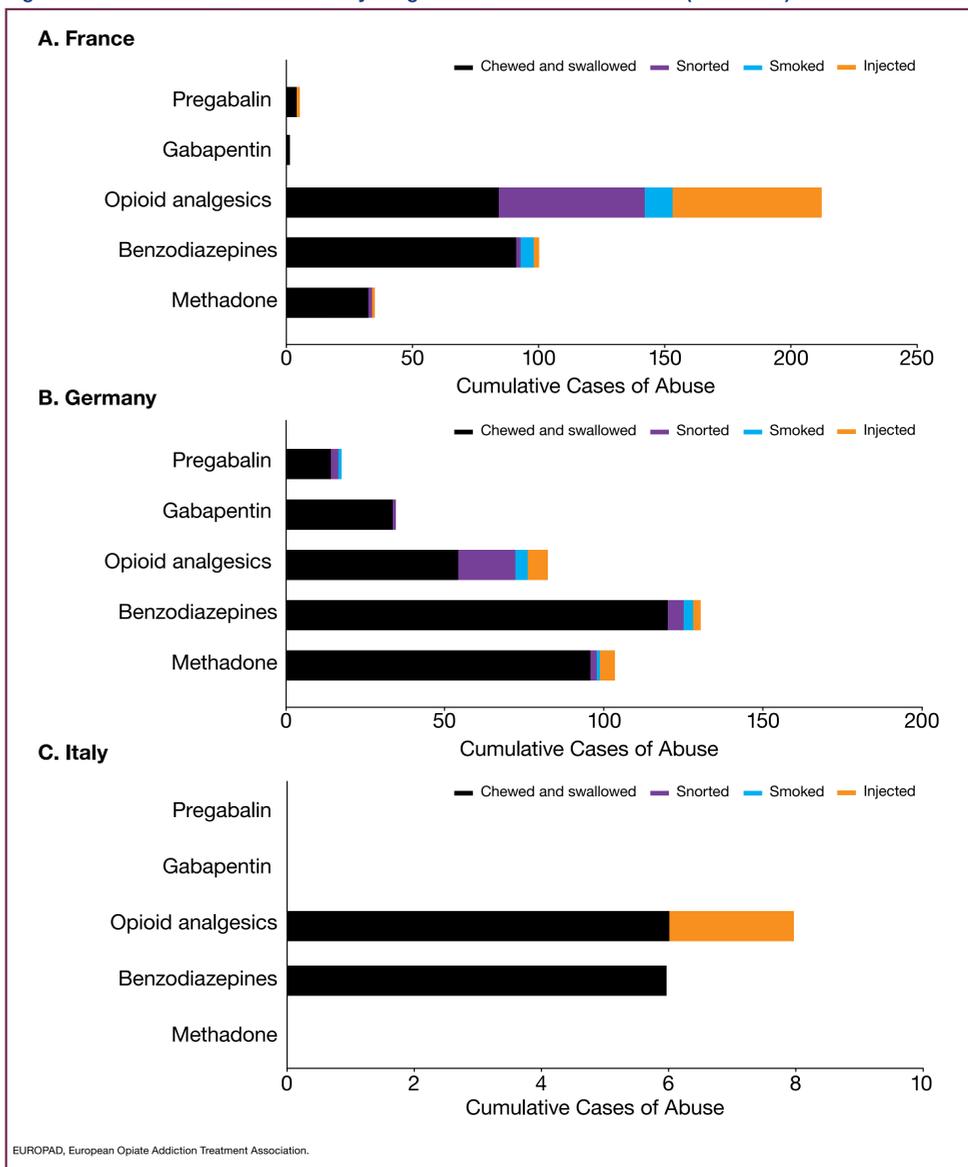
^a Case counts were too low to provide weighted estimates, and therefore they represent unweighted number of respondents who reported abuse.

^b Multiple drugs were classified as ≥1 endorsement from the given drug group and ≥1 other endorsement from another drug group. These do not imply concomitant abuse. NMURx, Non-Medical Use of Prescription Drugs program; Q4, quarter 4.

Route of Administration for Drug Abuse

- Non-oral routes of abuse were much more prevalent with opioids compared with other drugs, including pregabalin and gabapentin (Figure 3).

Figure 3. Cumulative Cases of Abuse by Drug and Route of Administration (EUROPAD)



EUROPAD, European Opiate Addiction Treatment Association.

- EUROPAD data may have limited generalizability in each country because of geographic distribution of participating treatment centers.

CONCLUSIONS

- The rates of abuse of pregabalin and gabapentin were low in relation to other drugs, including opioids, across France, Germany, and Italy.
 - Cumulative rate of lifetime abuse was highest in Germany (for all drugs).
- When pregabalin or gabapentin were abused, they were generally abused along with another drug, and rarely via non-oral routes of administration.
 - These observations are in line with studies conducted within individual countries,^{6,9,10} which indicate that pregabalin is particularly abused by patients with a history of opioid abuse.¹¹
- Prescribers should be aware of high-risk populations and monitor for signs of abuse.
 - Future research is needed to further investigate latent class analysis of each drug substance.

References

- Hernandez SH, Nelson LS. *Clin Pharmacol Ther.* 2010;88:307-17.
- Chiappini S, Schifano F. *CNS Drugs.* 2016;30:647-54.
- Evoy KE, et al. *Res Social Adm Pharm.* 2019;15:953-8.
- Snellgrove BJ, et al. *CNS Drugs.* 2017;31:891-8.
- Schwan S, et al. *Eur J Clin Pharmacol.* 2010;66:947-53.
- Papazisis G, Tzachanis D. *Int J Clin Pharmacol Ther.* 2014;52:709-16.
- Dart RC, et al. *N Engl J Med.* 2015;372:241-8.
- Addiction Research Foundation. <https://www.bu.edu/bniart/files/2012/04/DAST-10-Institute.pdf> (accessed Aug 8, 2019).
- Bossard JB, et al. *Clin Drug Investig.* 2016;36:735-42.
- Gahr M, et al. *Eur J Clin Pharmacol.* 2013;69:1335-42.
- Evoy KE, et al. *Drugs.* 2017;77:403-26.

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