

# Misuse of psychoactive prescription drugs in Portugal

## The MisuMedPT Project

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# Conflicts of interest

- The authors declare no conflicts of interest.

# Background

- Drug exposure is difficult to measure due to the specificity of the exposure and its socio-demographic-economic and clinical determinants.
- Estimating the potential for misuse and drug dependence is further complicated by the fact that it is a behaviour often concealed, which usually concerns a small number of individuals compared to the total number of patients exposed.
- Safety information, including data on misuse potential, is limited when a medicine is approved due to limitations of pre-authorisation clinical trials (narrow population, exclusion of concomitant therapies and diseases, short duration). Once the medicine is marketed, the benefit-risk profile can prove to be substantially different because the size of the exposed population is much larger, and patient characteristics are different, when compared to the population studied in clinical trials.

# Background

- Monitoring systems of medicines' misuse can be based on several sources of information:
  - Drug-related deaths
  - Drug-related emergency visits
  - Data from poison control centres (PCCs)
  - Prescription/reimbursement databases
  - Pharmacovigilance data - spontaneous reports and risk management plans
  - Electronic prescription monitoring programmes
- PCCs can thus act as near-real-time sentinel indicators of prescription drug misuse and be part of an active surveillance system with data collected from different sources.

# Background

- Prescription drug misuse is a public health problem in some countries worldwide.
- In Portugal, there are some statistics published by the General Directorate for Intervention on Addictive Behaviours and Dependencies (SICAD) on consumption of sedatives, tranquilizers and hypnotics, based on data from the National Survey on Psychoactive Substance Use in the General Population.
- However, in Portugal there are no published data on the health-related consequences of medicines' misuse, which is therefore a public health issue of unknown dimension in our country.

# The MisuMedPT Project

- Goal: To characterise the epidemiological pattern of misuse of psychoactive medicines in Portugal
- Therapeutic classes: opioid analgesics, antiepileptics, anxiolytics, hypnotics and sedatives, antidepressants and drugs used in opioid dependence – 69 active substances
- Sources of data:
  - ✓ Morbid consequences of misuse:
    - ⇒ Medicine-related poisonings communicated to the Poison Information Centre (CIAV)
    - ⇒ Medicine-related deaths - National Institute of Legal Medicine and Forensic Sciences (INMLCF)
    - ⇒ Medicine-related hospital admissions - National Database on Hospital Morbidity (ACSS)
    - ⇒ Pharmacovigilance data (misuse cases reported as adverse drug reactions) - National Authority of Medicines and Health Products (INFARMED)
  - ✓ Medicines sales data - Health Market Research Portugal (hmR Portugal)
  - ✓ Medicines reimbursement database – Regional Health Administration of Lisbon and Tagus Valley (ARSLVT)

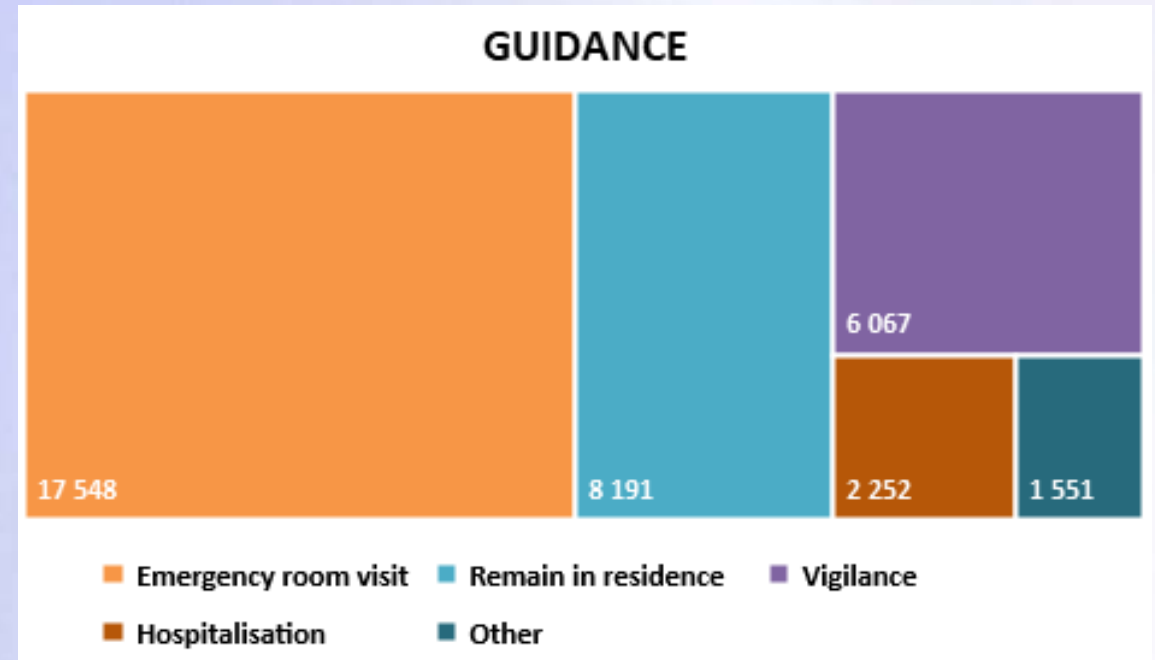
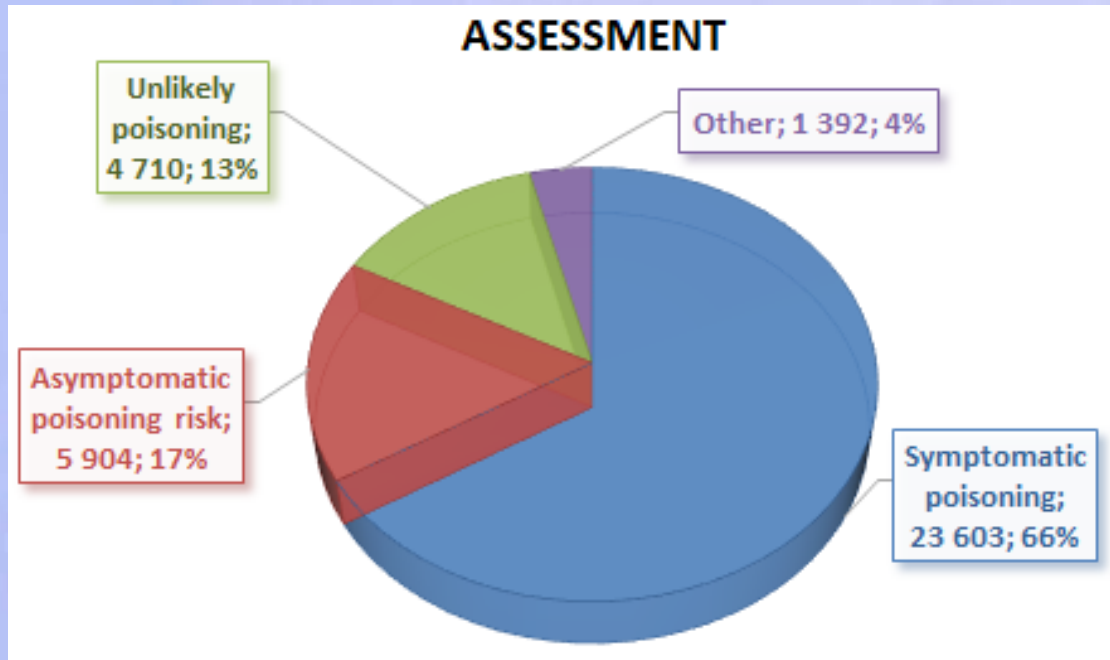


# Data so far...

- Data from CIAV (2014-2018): calls received reporting poisoning with medicines, illegal drugs or alcohol
  - ✓ Calls involving more than one medicine, illegal drug or alcohol – each substance considered as a unique exposure (or case mention)
  - ✓ Intentional exposure  $\Rightarrow$  possible misuse case
- Data from hmR (2014-2018): number of packages dispensed in community pharmacies of the medicinal products containing the 69 substances included in the study, used to estimate the number of patients receiving treatment with each medicine (population at risk)
- Data from INMLCF (2014-2018): deaths involving at least one of the studied active substances – ongoing
- Data from ARSLVT (2016-2018): dispensing data from ARSLVT medicines reimbursement database, allowing for characterisation of prescription and dispensing of the studied medicines - ongoing

# Preliminary results

- 27,308 calls were received at CIAV reporting 39,421 intentional exposures to any medicinal product, alcohol or illicit drug.
- Call characteristics:



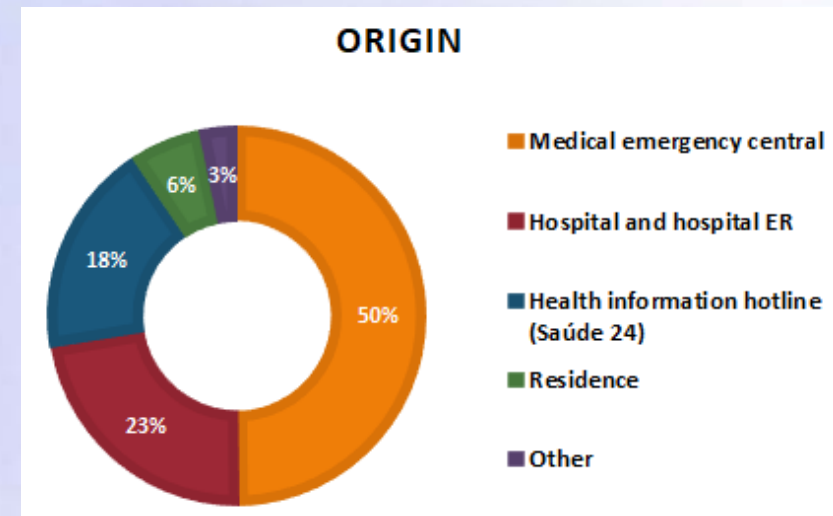
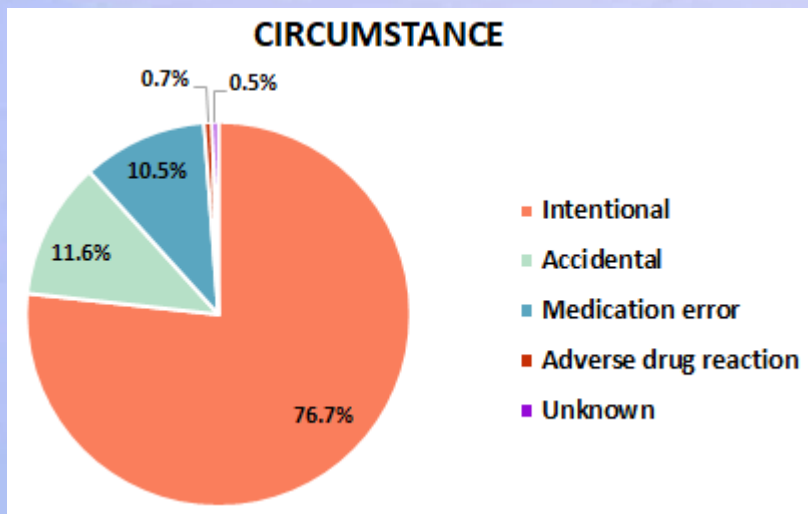
- Poisoning: 96% of calls
- 55% of calls with emergency room visit advice or effective hospitalisation.



# Call characteristics

Age group (years)	Number of calls		Mean number substances involved (SD)		Range of the number of substances involved	
	F	M	F	M	F	M
15-24	4 173	2 052	1.31 ( 0.61 )	1.30 ( 0.60 )	1 - 5	1 - 5
25-34	3 246	1 804	1.45 ( 0.76 )	1.41 ( 0.67 )	1 - 5	1 - 5
35-44	4870	1983	1.48 ( 0.77 )	1.47 ( 0.72 )	1 - 5	1 - 5
45-54	4918	1540	1.49 ( 0.76 )	1.46 ( 0.71 )	1 - 5	1 - 5
55-64	2 617	788	1.44 ( 0.73 )	1.47 ( 0.71 )	1 - 5	1 - 5
65-74	1 408	475	1.36 ( 0.64 )	1.31 ( 0.60 )	1 - 5	1 - 4
75-84	921	384	1.25 ( 0.55 )	1.28 ( 0.58 )	1 - 5	1 - 4
> 85	414	170	1.30 ( 0.59 )	1.24 ( 0.50 )	1 - 5	1 - 3
	63%	26%				

- 63% of calls refer to females and 37% to the 35-54 age group.
- Age group 35-54: higher mean number of substances mentioned per call and higher SD.
- 77% of calls refer to intentional poisonings.
- 68% of calls come from the medical emergency central (112) and health information hotline (Saúde 24).



# Intentional exposures - demography

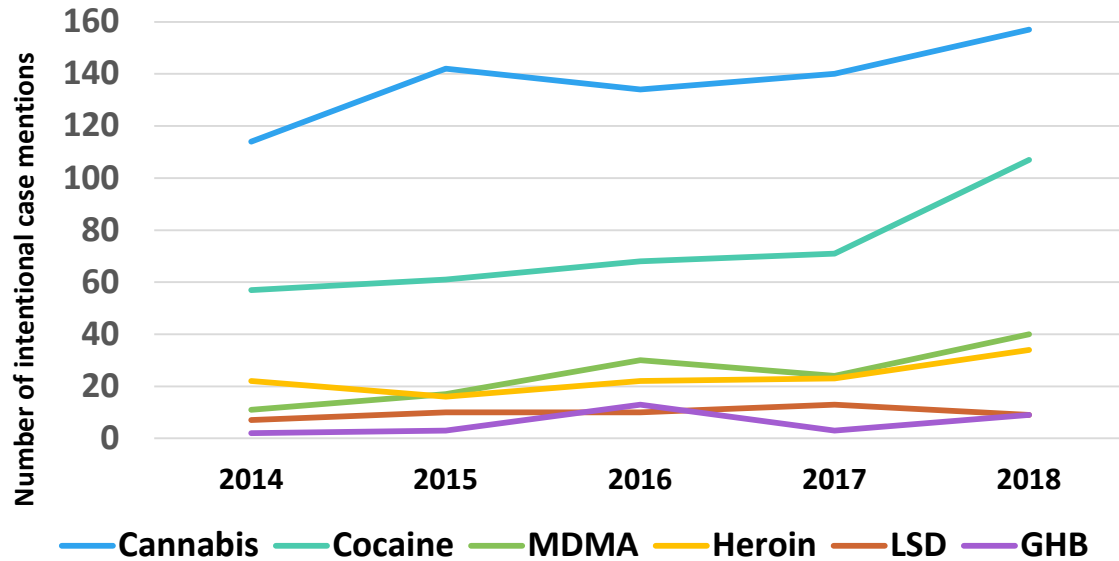
- The 27,308 calls received reported a total of 39,421 intentional exposures to any medicinal product (34,203), alcohol (3,512) or illicit drug (1,706).
- 31,169 exposures (91,1% of the total number of intentional exposures to any medicine) involving one of the psychoactive medicines included in the study.

Age group (years)	Prescription drugs		69 Prescription drugs		Alcohol		Illicit drugs	
	F	M	F	M	F	M	F	M
< 15	787	189	658	174	25	10	21	46
15 - 24	4 581	1 544	4 001	1 334	244	273	231	468
25 - 34	3 856	1 570	3 506	1 413	262	312	113	375
35 - 44	6 015	1 913	5 508	1 761	495	433	61	217
45 - 54	6 038	1 456	5 617	1 348	498	407	19	100
55 - 64	2 914	720	2 737	662	222	168	1	22
65 - 74	1 175	316	1 107	298	56	48	0	2
75 - 84	484	171	456	158	9	12	0	0
> 85	151	61	138	58	0	2	0	0
<b>Total</b>	<b>26 001</b>	<b>7 940</b>	<b>23 728</b>	<b>7 206</b>	<b>1 811</b>	<b>1 665</b>	<b>446</b>	<b>1 230</b>

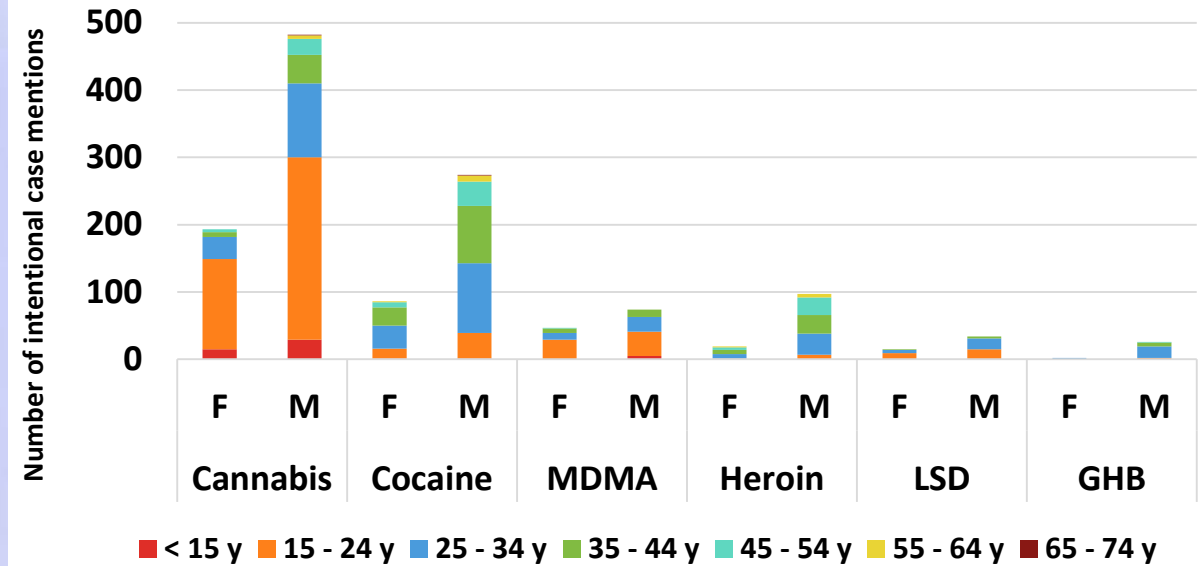
- Exposures to prescription drugs and alcohol: female and 35-54 age group predominance
- Exposures to illicit drugs: male and 15-34 age group predominance

# Intentional exposures – illegal drugs

## ILLEGAL DRUGS - TEMPORAL TRENDS



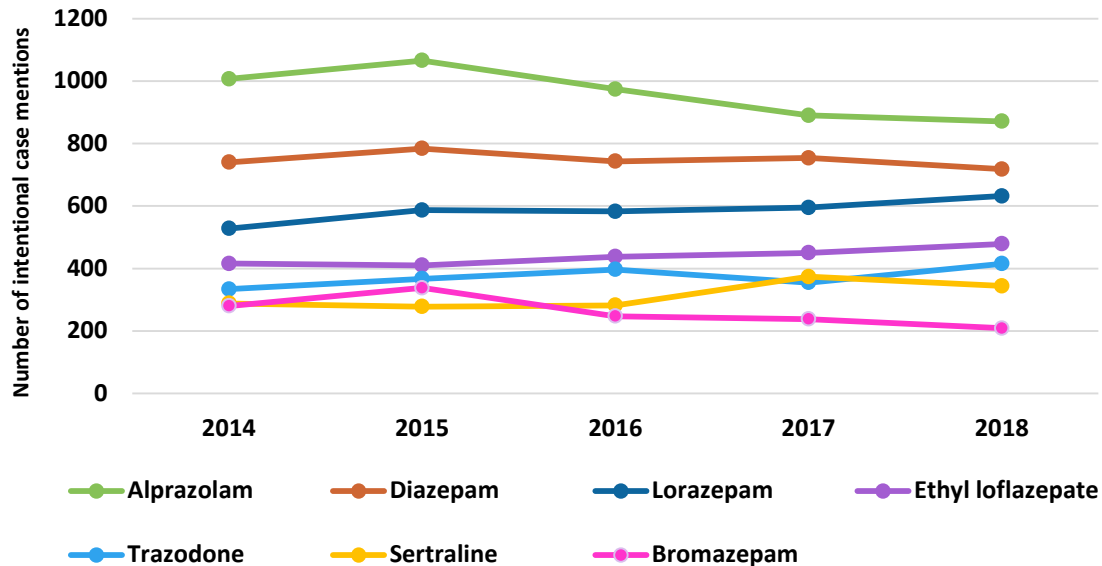
## ILLEGAL DRUGS - DEMOGRAPHICS



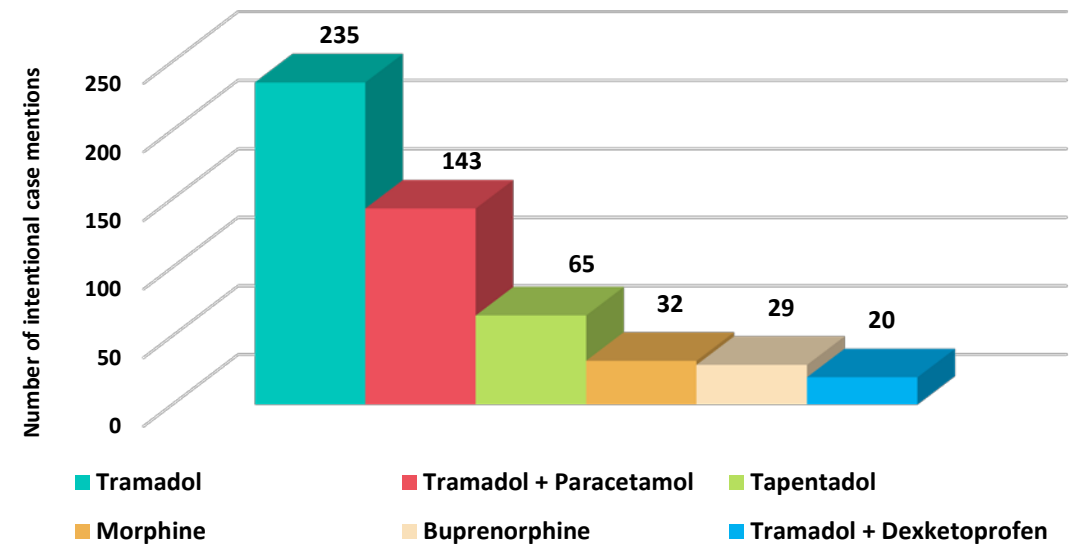
- Total of 1,706 intentional exposures to illegal drugs, with a positive trend throughout the research period. Cocaine had the highest increase (+50%) from 2017 to 2018.
- Cannabis, cocaine and ecstasy were the most frequently reported illegal drugs, mainly in men and in the 15-34 age group.
- This trends match drug use profiles in Portugal, according to published data from SICAD.

# Intentional exposures - prescription medicines

TOP 5 PRESCRIPTION MEDICINES



PRESCRIPTION OPIOIDS – 5-year period

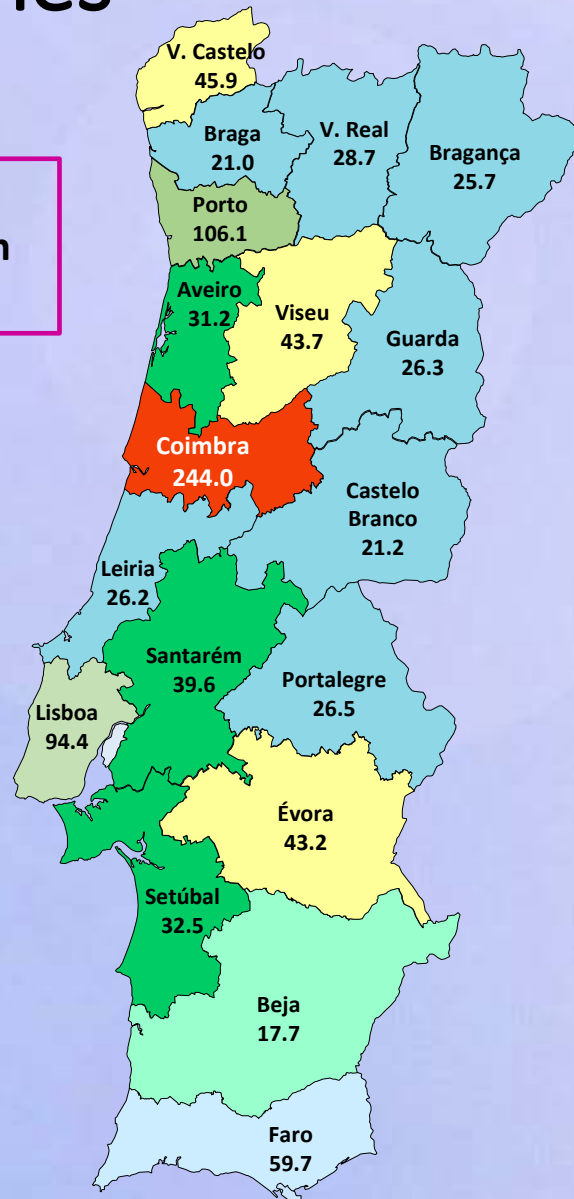


- Benzodiazepines and antidepressants are the most frequently involved prescription medicines in intentional exposures, with alprazolam on the top, declining since 2015.
- Prescription opioids are quite underrepresented, with tramadol being the 25th most frequently reported prescription medicine in intentional exposures.
- Tramadol and its associations represent 73% of the total case mentions reported involving prescription opioids during the study period (methadone was excluded from the analysis since it is not available in community pharmacies).

# Rates of intentional exposures to the studied prescription medicines

## Rates of intentional poisonings by region in 2018

- Population-based rates (Statistics Portugal)
- Highest incidence rates of intentional exposures to the medicines of interest in the districts of Coimbra, Oporto and Lisbon.

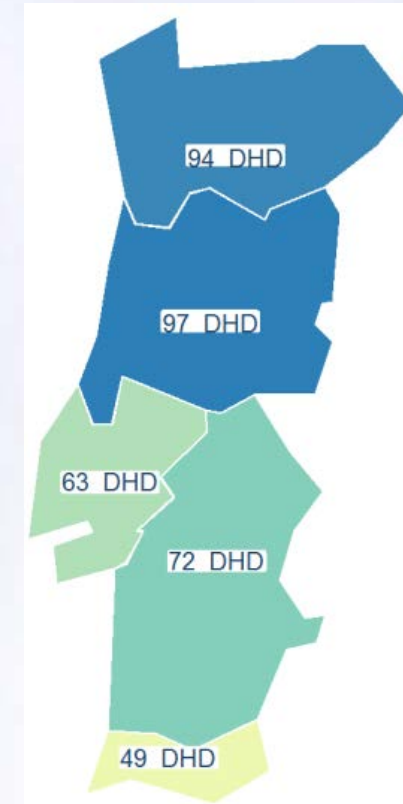


- Rates of intentional poisonings in accordance with benzodiazepines utilisation data in the central region of Portugal available in other studies



## Use of BZD by region in 2016 (INFARMED, I.P.)

- ✓ DHD: medicines utilisation metric to enable comparisons of medicine use between countries and regions, and to examine trends in drug use over time .
- ✓ DDD: assumed average maintenance dose per day for a medicine used for its main indication in adults.
- ✓ DHDs are used as surrogate for point prevalence of use of a medicine in the population and provide an estimate of the proportion of the study population treated daily with a particular medicine or group of medicines. DHD=10 means that 1% (10/1000) of the population is receiving the medicine each day in that year.



$$DHD/year = \frac{\text{total DDD consumed in each year}}{\text{Population} * \text{number of days in the year}} * 1,000$$



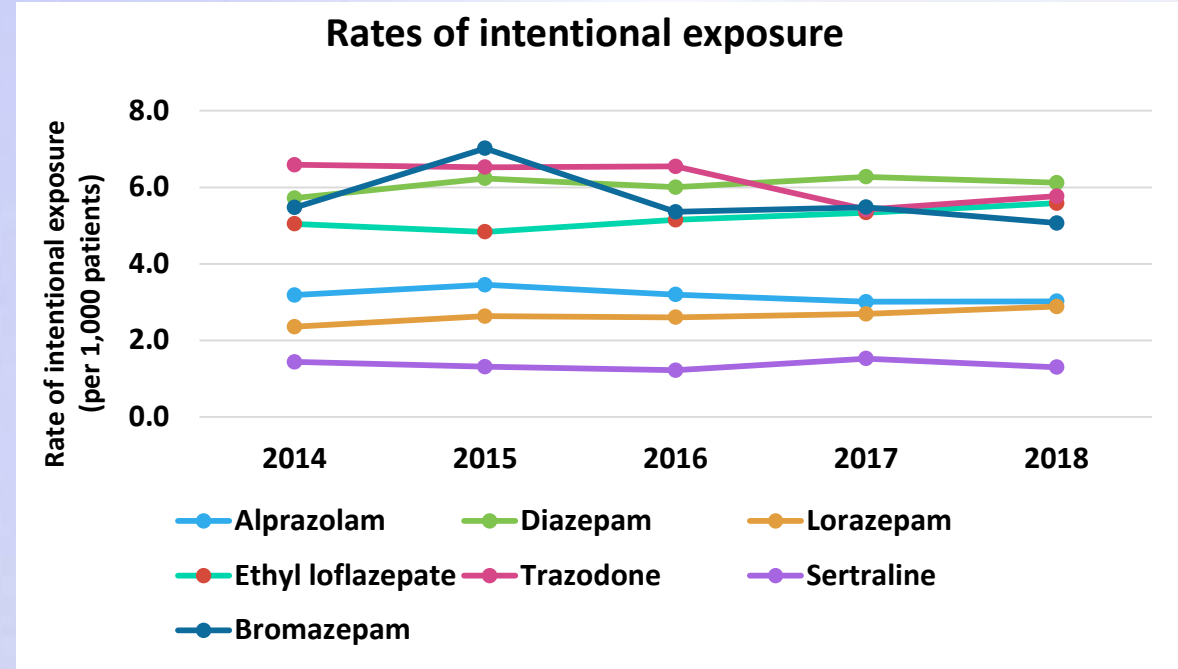
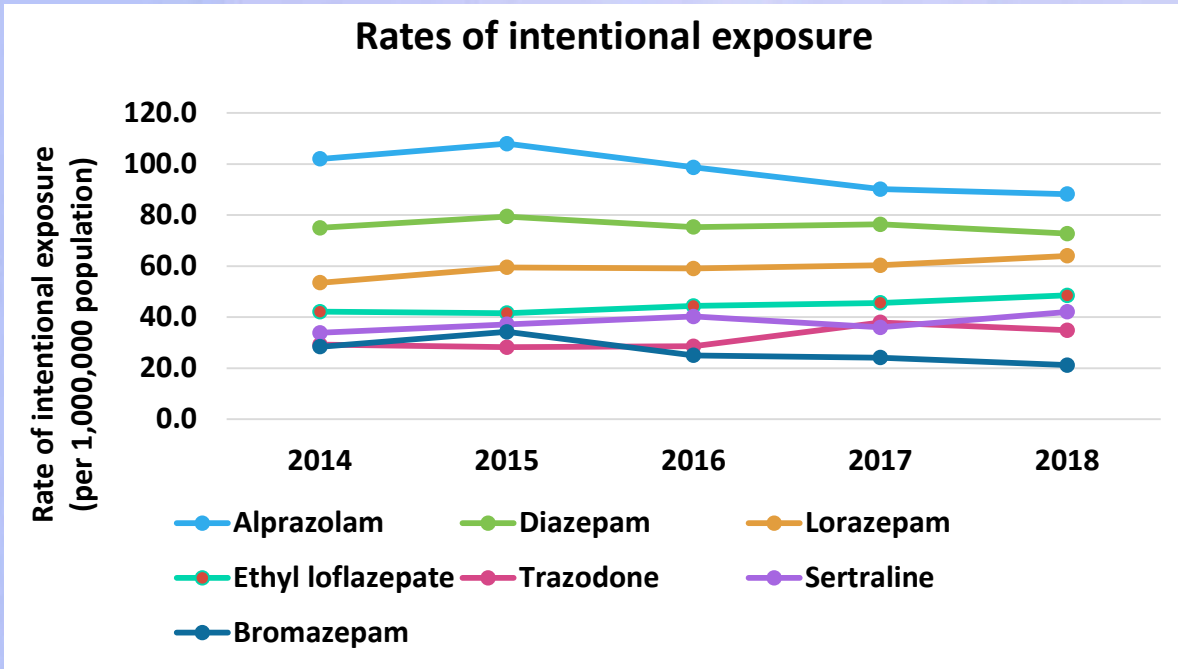
# Rates of intentional poisonings – Top 5 prescription medicines

## Population-based rates

## Patient-based rates



$$\# \text{ Treated patients/year} = \frac{\text{total DDD consumed in each year}}{\text{number of days in the year}}$$



- Alprazolam, which is the most consumed benzodiazepine in Portugal, has the highest rate of intentional poisoning per million inhabitants.
- However, considering the at-risk population (patients being treated with each medicine), the rate of intentional poisoning is higher for **diazepam** and **trazodone** (in 2018, 6.1 and 5.8 per thousand patients, respectively)



# Main findings

- Intentional poisonings reported to prescription drugs and alcohol: female and 35-54 age group predominance; intentional poisonings reported to illegal drugs: male and 15-34 age group predominance.
- Benzodiazepines and antidepressants are the most frequently reported prescription medicines in intentional poisonings, with alprazolam on the top.
- Prescription opioids are responsible for a very small number of intentional poisonings for which advice was sought from CIAV.
- The number of intentional poisonings to illegal drugs reported to CIAV has been increasing, especially for cocaine (+50% from 2017 to 2018).
- Patient-based rates, adjusting for differences in the level of medicinal dispensing associated with each medicinal product, provide a better estimate than population-based rates for quantifying the medicine's benefit-risk. Alprazolam has the highest rate of intentional poisoning per million inhabitants. However, considering the patient population, the rate of intentional poisoning is higher for diazepam and trazodone, with alprazolam coming down to the 5<sup>th</sup> position of the ranking.

# Limitations of the data analysed so far

- Data from CIAV:

- ✓ Due to the way information is registered in CIAV's database, no analysis is possible regarding administration route, which is an important aspect when studying poisoning data (IV route potentially has more harmful consequences than oral route).
- ✓ Limited information from each call is registered in CIAV's database and not all people who misuse substances will request the assistance of a poison centre.
- ✓ Information registered in the database does not include any identification of the patient (only sex and age), so no individual risk assessment is possible and no information can be retrieved later on the outcome of the patient. On the other hand, the same patient can contact CIAV more than once regarding the same exposure(s), which will be counted accordingly.
- ✓ Calls for which substance classification by CIAV has not been concluded have been excluded (7,560 calls during the study period).

- Medicines consumption data (hmR sales data):

- ✓ The metric used to estimate medicine consumption (WHO DDD methodology) has limitations, not necessarily reflecting the dose actually consumed daily. The estimates are only true if there is good agreement between the real consumed dose and the DDD.
- ✓ Data refer to medicines that are dispensed in community pharmacies. It is unknown if patients actually take the medicines they buy, nor is it known whether the dispensed packages have been prescribed by a medical doctor.
- ✓ No demographic characterisation of patients to whom the studied medicines were dispensed is possible.

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# Thank you!

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