

SHORT ORIGINAL

How is the use of opioid medicines in Spain? Analysis of data from the EDADES 2017 survey

¿Cómo es el uso de medicamentos opioides en España? Análisis de los datos de la encuesta EDADES 2017

ABSTRACT:

Objectives: Quantify the level of use of opioid medicines in this general population, the level of follow-up to prescribed guidelines, the reason for use, and the means of obtaining these medicines in Spain.

Methodology: Analysis of the raw data for the EDADES 2017 study that has been conducted in Spain every two years since 1995 among the general population (15 to 64 years of age). After categorizing and cleaning the data, several pivot tables were performed to extract the desired information.

Results: In Spain the prevalence of any opioid drug use at 12 months was 6.7 % of the population between 15 and 64 years of age. 87 % of this use was associated with weak opioids (tramadol or codeine) and the rest was related to major opioids, with morphine being the most widely used with 8% of total opioid users. 92 % of people obtained the medicine through their own prescription while 4 % obtained it at the pharmacy without a prescription and an additional 3 % obtained it through friends or family.

74 % of patients had followed the dose and duration of treatment guidelines prescribed by the doctor, while 19 % had used opioid medicines in lower doses or for less time than prescribed.

Conclusions: Use of strong opioids is low in Spain, most patients use it under medical supervision and following the guidelines prescribed by the doctor. Patients who obtain opioid medications without their own prescription as well as those who use it differently than the prescribed one need to be tracked.

RESUMEN:

Objetivos: Cuantificar el nivel de uso de los medicamentos opioides en esta encuesta de población general, el nivel de seguimiento de las pautas prescritas, el motivo de uso y el medio por el que se obtuvieron.

Metodología: Análisis de los datos brutos correspondientes al estudio EDADES 2017, así como los correspon-

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dientes cuestionarios. El estudio EDADES es una encuesta sobre alcohol, drogas y otras adicciones en España que se realiza cada dos años desde el año 1995 entre la población general residente en hogares (15 a 64 años de edad), siendo los datos representativos a nivel nacional. Se seleccionaron las preguntas relevantes al objeto de este análisis que correspondieron a 2,2 millones de datos. Tras la categorización y limpieza de datos de las variables elegidas se procedió a la realización de varias tablas dinámicas que permitieran extraer la información deseada.

Resultados: En España la prevalencia de uso de medicamentos opioides a 12 meses fue del 6,7 % de la población entre 15 y 64 años de edad. El 87 % de este uso se asoció a tramadol y el resto se relacionó con opioides mayores, siendo la morfina el más utilizado con un 8 % de los pacientes. La edad media de pacientes con opioides estuvo entre 39 y 53 años y el uso de medicamentos opioides fue ligeramente superior entre las mujeres. El 92 % de las personas obtuvieron el medicamento a través de receta médica propia, mientras que un 4 % lo obtuvieron en la farmacia sin receta y un 3 % adicional lo obtuvieron a través de amigos o familiares. El 74 % de los pacientes habían seguido las pautas de dosis y duración de tratamiento que habían sido prescritas por el médico, mientras que un 19 % había usado los medicamentos opioides en menor dosis o durante menos tiempo del prescrito y un 5 % lo habían usado en más dosis y más tiempo del prescrito.

Conclusiones: El uso de opioides en España es bajo. La mayoría de los pacientes lo usan bajo supervisión médica y siguiendo las pautas prescritas por el médico. Es necesario realizar seguimiento de los pacientes que obtienen medicamentos opioides sin receta propia, así como de aquellos que lo usan de forma diferente a la prescrita.

Introduction

The opioid drug epidemic has created a major health, economic and social burden in the United States (1-5). The situation in that country could have been reproduced in other countries around Europe, and although this does not seem to have been the case so far, it is important to maintain extreme vigilance and prudence in order to prevent it. To this end, the Delegation of the Spanish Government for the national drug plan introduced in 2017, for the first time, a series of questions related to the use of opioid drugs. In this work we present the main conclusions that we can draw from an in-depth analysis of the raw data. The data for the year 2019 are the most recent but that database will not be accessible to researchers until January 2022.

Objectives

Analyze data related to opioid painkillers from the EDADES study 2017 and quantify the level of use of opioid medicines in this general population survey, the level of follow-up of prescribed guidelines, the reason for use, and the means of obtaining these medicines.

Methodology

The Delegation of the Government of Spain of the National Drug Plan was requested to access the most recent raw data for the EDADES study (6) and provided us with the data for 2015 and 2017, as well as the corresponding questionnaires. The EDADES study (1) is a survey on alcohol, drugs and other addictions in Spain that has been conducted every two years since 1995 among the general population resident in households (15 to 64 years of age) being the nationally representative data being the sample framework the urban and rural population resident in Spain. The sampling procedure was performed by three-step clusters without substitution. The first stage units were the census tracts (36,215 in 2017) corresponding to 8,125 municipalities from which 2,147 census tracts corresponding to

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953 municipalities were selected. The units of second stage were the family dwellings (homes) being excluded: the population residing in institutions (quarts, convents, prisons, residences for students or the elderly, etc...), the population living in collective establishments (hotels, pensions, etc.) or the homeless population. In the third stage, an individual was selected within each household using ad hoc random number tables that allowed the probability of young people aged 15-39 years to be selected increased. A household was considered to be inhabited and habitual residence when a person aged 15-64 had lived in it for at least 8 of the last 12 months or intended to live in it for at least 8 months. In 2017 (7) the data collection was carried out between February 5 and April 27, 2018 and the sample had 21,249 valid questionnaires with a sample error of 0.8 % for a 95 % confidence level. The data file provided contained 11.36 million data corresponding to the responses obtained in both the questionnaire completed by the interviewer and the self-completed questionnaire by the interviewee. The interviewer remained present throughout the process and collected the completed questionnaires. In 2017 the response rate was 50.6 %. The EDADES survey programme is led by the Government Delegation for the National Drug Plan (DGPNSD) and has the collaboration of the autonomous communities. Once these questionnaires were reviewed, the relevant questions were selected for this analysis that corresponded to 2.2 million data related to participant profile data, questions about the use of opioid drugs, and questions related to the use of tranquilizers and sedative drugs. After categorizing and cleaning data of the chosen variables, several pivot tables were performed to extract the desired information.

Results

Of the 21,249 interviewees, 16.6 % (3,539) had ever used an opioid drug (18.1 % among women and 15.2 % among men), 6.7 % of all participants had used them in the last 12 months and 2.8 % had used them in the last 30 days. 12-month prevalence of strong opioids use was 0.87 %. Among people who had used opioid medicines in the last 12 months, the most widely used was codeine (59 % of respondents) followed by tramadol (28 %) while

major opioids were very little used with morphine being the most common with 7.8 % of all opioids (Table I).

Analyzing in detail the usage profile associated with the main molecules, we found that 944 people had ever used tramadol which equates to 1.9 % of the total sample and 43 % of them had used it in the last 12 months and, within this group, 58 % had been women with an average age of 43 years with a maximum period of continued use of 75 days on average while 42 % of use corresponded to men with an average age of 45 years and an average of 137 days continued at most (Table II).

Regarding morphine, use was relatively higher in women who were 61 % of those who used the drug in the last 12 months. The average age of morphine patients was 43 years and was used for a maximum of 113 continuous days (women) or 63 days (men).

Fentanyl was used only by 1.2 % of those who had used prescription opioids and only 0.08% of the total population with an average age of 47 years old, and a maximum number of days of continued use between 43 days (women) and 15 days (men).

Oxycodone was used by 0.8% of opioid users representing 0.06% of the total sample. The average age was 45 years higher among women (49 years) versus men (39 years). The maximum period of continued use of this medicine was on average 252 days in women and 370 days among men. Finally, tapentadol had been used by 1.2 % of those who used some opioid in the last 12 months being 0.08 % of the total population studied. The average age of tapentadol treatments was 47 years, higher among men (52 years) compared to women (44 years). The maximum period of continued use of this medicine was 290 days on average, being higher among women (463 days) than in men (79 days).

Table I. Percentage of respondents who had taken each of these opioid drugs in the last 12 months.

	Tramadol	Codeine	Morphine	Fentanyl	Oxycodone	Hydromorphone	Petidine	Tapentadol	Methadone	Buprenorphine
Women	29 %	58 %	8 %	1 %	1 %	0 %	0 %	1 %	0 %	1 %
Men	28 %	60 %	7 %	1 %	1 %	0 %	0 %	1 %	1 %	1 %
% of total opioids	28 %	59 %	7.8 %	1.2 %	0.8 %	0.1 %	0.4 %	1.2 %	0.6 %	0.8 %
% of total population	1.91 %	3.93 %	0.53 %	0.08 %	0.06 %	0.00 %	0.03 %	0.08 %	0.04 %	0.05 %

As for the follow-up to the guidelines prescribed by the doctor, data are available from 2,764 patients of which 74 % had used opioids following the amounts and times prescribed by the doctor while 24% had used it for more or less amount or more time than prescribed (Table III). The remaining 3 % had used it to increase or decrease the effect of other drugs, treat addiction or to get high, being this higher among men than among women (Table III).

Regarding the reason for initiation of opioid treatment, respondents mostly reported that the onset was to treat acute pain (56 %), for pain after surgery (14 %) or to treat chronic pain (13 %).

Finally, 92 % of those who had used an opioid drug had obtained it through a prescription issued to them, 3 % obtained it through friend or family and 4 % obtained it from the pharmacy without a prescription (Figure 1). The prevalence of opioid use without own prescription is 0.6 % and within this group, 57 % had obtained the drug at the pharmacy without a prescription while 36 % got it from the family.

Discussion

The EDADES (6) study has a nationally representative sample with a low margin of error, representing the reality of the Spanish population regarding the use of opioid medicines. In our analysis we note that the prevalence of opioid use in total is relatively high with 16.6 % of people who have ever used it and 6.7 % who have used it in the last year, but most of this use, 87 %, was related to minor opioids (tramadol or codeine) so the prevalence of strong opioids uses in 2017 was 0.87 % of the general population of between 15 and 64 years of age. The higher use of tramadol and codeine-based opioids found in our study is consistent with a registry published in 2019 (8).

Among the major opioids the most used by far has been morphine while fentanyl, in patch or immediate release formulation did not represent more than 1.2 % of the total opioids (similar to tapentadol), has been the focus of attention of the Spanish Medicines Agency, especially in relation to immediate release (9). On the other hand, it should also be noted that, unlike in the United States where oxycodone and hydromorphone (10-12) are the most widely used and abused medicines, in Spain in use of these

Table II. Sex, age and maximum number of days of continued use for each opioid drug.

	Once-in-a-lifetime use (% of all people who used an opioid)	Among those who have used the drug in the last 12 months				Average age (years)	% of those who have used in the last 30 days over the total ever used this molecule	Maximum number of days of continuous use (average)
		% of those who have used this molecule in the last 12 months over the total used	% Women	% Male				
Tramadol	27 %	43 %	58 %	42 %	44	21 %	102	
Codeine	55 %	43 %	56 %	44 %	39	16 %	13	
Morphine	11 %	29 %	61 %	39 %	43	13 %	90	
Fentanyl	1 %	35 %	47 %	53 %	47	16 %	29	
Oxycodone	1 %	25 %	67 %	33 %	45	13 %	306	
Hydromorphone	0 %	7 %	100 %	0 %	53	7 %	12	
Petidine	1 %	15 %	50 %	50 %	43	3 %	18	
Tapentadol	1 %	46 %	59 %	41 %	47	35 %	290	
Methadone	1 %	27 %	33 %	67 %	45	21 %	547	
Buprenorphine	1 %	33 %	64 %	36 %	41	24 %	72	

two molecules is also low according to this analysis representing together only 0.9 % of the total opioids.

In our analysis we also observed some relevant differences in the maximum duration of treatments, the longest being methadone, understanding that it refers to patients receiving treatment for addiction. Among the other molecules, the longest continuous time has been oxycodone with 306 days and here we can see an alarm signal that should be monitored since the longer treatments are those that are associated with an increased risk of dependence or abuse (13). Tapentadol use is also relatively long with maximum periods of up to 290 days of continuous use.

The average age of patients is between 39 years of codeine and 53 years of hydromorphone and, in terms of sex, the use is slightly higher in women for all molecules except fentanyl and methadone, which is consistent with other studies in Spain (8).

It is important to note that 92 % of patients had had their own prescription for this type of medicine and therefore only 8% had obtained this medicine outside of direct medical control. Although this figure is lower than what is observed in the United States (10,11), it is still an alarm signal since 4 % of people obtained the drug in the pharmacy without using their own prescription and

up to 3 % had obtained it from a friend or family member without their own prescription, situations that are high risk and that must be analyzed in depth. The use of opioid medications is safe and effective when performed under the prescription of a properly trained physician and within the health system (13). However, risks of adverse reactions, misuse and abuse grow when proper medical follow-up is lacking. Gross data from the EDADES 2019 study are not available for analysis of gross data by third parties, but the Ministry has recently published a summary of them (14). In the data published so far of the 2019 report, the full prevalence of opioid drug use without prescription was 1.7 % and 0.6 % prevalence in the past year. Of those who had used opioid without a prescription 53 % had obtained it through a friend or family member, 19 % through the over-the-counter pharmacy, 9.7 % prescription that was from someone else, 3.7 % through a drug dealer and 1.9 % over the internet (14). Although the available data from the 2019 study do not allow an analysis as deep as the one presented in this work for 2017, we can see some trend, such as the growth in the use of opioid analgesics without a prescription in the last year that has increased from 0.3 % in 2017 to 0.6 % in 2019. There is also an upward trend in the use of these analgesics in the last 12 months or in the last 30 days. These data are really alarming and should make us pay attention to this use of opioids without medical prescription as it is a non-medical use frequently identified in the United States where it has been associated with the development of abuse and addiction.

Finally, note that a majority of patients (74 %) they had used the medicine in the same amounts and time prescribed by the doctor however 19 % had used it less time or in lower doses than prescribed and 5 % had used it in higher doses or for longer than prescribed. Dose and time reduction may be appropriate depending on the type of prescription or indications given by the doctor, although there is a risk that poor acute pain management will lead to a chronification of pain by central sensitization mechanisms (15,16), so patients should always follow prescribed guidelines. In the case of increasing dose or duration of treatment we are faced with a situation of abuse by the patient that should be addressed as soon as possible to avoid risks of dependence or addiction. It is important to note that most deviations occur down, i.e. by reducing dose or time, while upward usage devia-

Table III. Percentage of people who had followed or modified the guidelines prescribed by the doctor.

	Higher dose	Lower doses	More time	Less time	Prescribed amount and time	Increase effect other drugs	Treat addiction	Get high
Women	3 %	8 %	2 %	12 %	74 %	1 %	0 %	0 %
Men	4 %	7 %	3 %	10 %	74 %	1 %	1 %	1 %
Total	3 %	8 %	2 %	11 %	74 %	1 %	0 %	1 %

tions are much lower and much lower than the rates observed in the United States. In this country the National Survey on Drug Use and Health published in 2013 (17) estimated that more than 1.8 million people were dependent or had abuse of prescription opioids. However, other references from 2013 (18) show that there are over 2 million people with addiction associated with prescription opioids in the United States of America. In the same sense as the previous other study (19) provides figures for opioid abuse, dependence and overdoses from a sample of 117 million American beneficiaries. Their study shows an increase in the incidence of combined outcome (abuse + dependence + overdose) from 1.4 % in 2010 to 2.46 % in 2014, while the prevalence went from 2 % to 4 % in the same period. The 2016 National Study on Drug

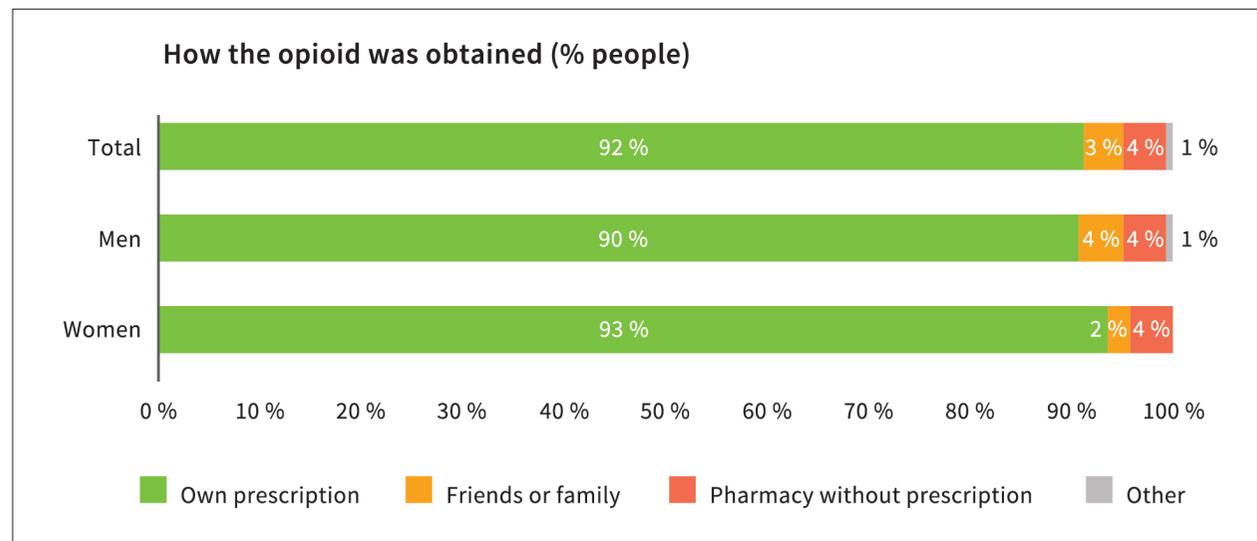


Figure 1. Percentage of people depending on how they got the opioid medication. Total sample and by sex.

Use and Health in the United States (20) gave the following data: 11.5 million people who misused opioid prescriptions; 2.1 million people who misused an opioid prescription for the first time; 2.1 million people who had an opioid use disorder; 948,000 people used heroin and 170,000 used heroin for the first time

Other publications on the United States are available indicating that the misuse of prescriptions by patients is higher in that country versus that detected in Spain.

One limitation of our analysis is that it is based on data from EDADES study in which the interviewer collects part of the data that is referred by the interviewee voluntarily and therefore it cannot be checked or confirmed properly. Another limitation is that EDADES data is collected only for people between 15 and 64 years of age. The group of patients over the age of 65 may be associated with increased use of analgesics in general and of opioids in particular as seen in previous studies (21) mainly due to higher prevalence of diseases and co-morbidities that are associated with pain.

As a result of these limitations, it would be desirable to analyze in detail how the prescriptions of opioid medicines have been made and how many of the patients treated in Spain have developed abuse or addiction to opioid medicines, data that is not possible to obtain in this study. It would also be necessary to study, for that 4 % of the patients who obtained the treatment in the pharmacy without a prescription, what drug was dispensed and whether or not they had had an earlier prescription. Unlike in the United States, the diversion of official prescriptions to illegal use is non-existent in Spain, as demonstrated in this study, probably due to the strength of the Spanish narcotics prescription control system that allows to obtain a complete traceability of all the prescriptions performed and all narcotics dispensed in the pharmacy versus a lack of control of the dispensation in the United States, where the PDMP (Prescription Drug Monitoring Program) was not implemented until 2010 unequally by states and without centralized prescription control systems.

The EDADES study is assimilated to the US NSDUH study, the latter being much more comprehensive in terms (10,11) of analgesic drugs and opioids, but it is certainly a first step in the right direction. In any case, it would be necessary to delve into the type of questions being asked and to conduct broader studies among patients treated with opioids in the medical environment

to understand how these patients are following medical guidelines in order to identify the alarm signals that allow the doctor or pharmacist to address potential situations of risk of abuse or addiction.

Conclusions

In Spain the prevalence of opioid drug use at 12 months was 6.7 % of the population between 15 and 64 years of age. 87 % of this use was associated with tramadol and the rest was related to major opioids, with morphine being the most widely used with 8 % of patients. The average age of opioid patients was between 39 and 53 years old and the use of opioid medications was slightly higher among women. 92 % of people obtained the drug through their own prescription while 4 % obtained it at the pharmacy without a prescription and an additional 3 % obtained it through friends or family. 74 % of patients had followed the dose and duration of prescribed opioids indicated by the doctor, while 19 % had used these medicines in lower doses or for less time than prescribed and 5 % had used it in more doses and longer than prescribed.

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Conflict of interest

None.

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