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Indications related to antidepressant prescribing in the Nivel-PCD database and the SIDIAP database

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A B S T R A C T

Background: Antidepressant drug consumption has increased, mainly in the elderly. This trend could be explained by the use for indications other than depression. We aimed to describe the indications related to antidepressant drug new users in two primary care settings.
Methods: A longitudinal study of new antidepressant users aged ≥65 was conducted, with data from the Nivel-PCD (The Netherlands) and SIDIAP (Catalonia) databases (2010–2015). As a proxy for indication, diagnoses registered around the 3 months of antidepressant prescribing were collected. Indications were classified in seven categories and an additional one of *non-selected indications*. The percentage and incidence calculated over the total population registered was described.
Results: A total of 16,537 and 199,168 new antidepressant users were identified in the Nivel-PCD and SIDIAP databases, respectively (women aged 65–69 were the most prevalent). *Depression* was the most frequent indication (24.0% and 31.3%), followed by *anxiety* (12.5% and 19.5%) and *sleep disorders (10.2% and 26.4%)*. Tricyclic antidepressants were the most commonly prescribed in Nivel-PCD (48.7%), mainly associated with *neuropathic pain*, and selective serotonin reuptake inhibitor antidepressants in SIDIAP (63.1%), associated with *depression*. The *non-selected indications* category showed an upward trend in the Nivel-PCD database while in the SIDIAP database it decreased.
Limitations: It is not mandatory for physicians to register a diagnosis with each prescription.
Conclusions: Depression was the most common prescribing indication in The Netherlands and Spain, followed by *anxiety* and *sleep disorders*. The most commonly prescribed antidepressant differed between the countries and is likely explained by differences in local guidelines.

1. Introduction

Prescribing of antidepressant drugs has increased immensely in the last years. Antidepressant prescribing in five European countries (PROTECT project) during 2001 and 2009 (Abbing-Karahagopian et al., 2014), showed an increasing trend in almost all participant countries (Spain, Germany, Denmark, the United Kingdom, and The Netherlands). The highest prevalence was described in the United Kingdom in 2008, with around 920 users per 10,000 person-years (PYs), followed by the Spanish, Danish and German populations with 644, 637, 618 users per

10,000 PYs, respectively. In addition, a study on antidepressant drug consumption in 18 European countries (including The Netherlands and Spain) by the organization for Economic Co-operation and Development (OECD) (OECD, 2014) reported that antidepressant consumption almost doubled between 2000 and 2012, from 28 defined daily doses (DDD) to 56 DDD/1000 people per day.

In Spain, The Spanish Agency of Medicines and Medical Devices revealed an increase from 26.5 DDD per 1.000 inhabitants per day to 79.5 DDD per 1.000 inhabitants per day of antidepressant drug consumption in the period 2000–2013 (Agencia Española de Medicamentos y Productos Sanitarios, 2015). This has further been confirmed in other studies on consumption of antidepressants in Europe (Forns et al., 2019; Serna et al., 2010; Noordam et al., 2015).

The PROTECT study (Abbing-Karahagopian et al., 2014) showed two times higher prevalence of antidepressant use in patients >80 years in 2008 when compared with those aged 60–69 years in Denmark, while the rest of the countries showed a constant rise in prevalence of users in older age groups.

Additionally, the pattern of use of antidepressant drugs has changed. They are prescribed for a variety of diseases and symptoms, including depression and anxiety but also for treating somatic diseases and symptoms such as neuropathic pain and headache, as shown in a Dutch study (Aarts et al., 2016) performed between 1997 and 2013 on a population of 45 years or older that received an antidepressant prescription. This research showed that antidepressant drugs were most commonly used to treat depression (52.4%), followed by stress, anxiety, pain and sleep disorders. Some of the reasons reported by patients are "clinically-accepted" but off-label indications, like neuropathic pain or sleep disorders in The Netherlands.

Changes in indications for antidepressant prescribing over time have been reported. A Canadian (Patten et al., 2007) study evaluated prescribing practices of 652 physicians during 2000–2005 and found a rise in prescriptions of antidepressants for anxiety conditions, with just slight changes in serotonin reuptake inhibitors recommendation for depression. The proportion of tricyclic antidepressant (TCA) prescriptions for depression decreased from 32.6% in 2000 to 19.4% in 2005. Furthermore, TCA prescriptions for non-psychiatric indications increased markedly from 2000 to 2005: musculoskeletal conditions, migraine headaches and sleep disturbances were the most frequent associated indications.

To our knowledge, there are few cross national comparative studies about indications with antidepressant drugs in the elderly. The elderly population was chosen because of their frequent antidepressant use. Additionally, The Netherlands and Catalonia have populations of similar magnitude and their teams have experience with antidepressant investigation, and for these reasons this research was set-up.

We aimed to assess the incidence of indications for antidepressant prescribing in the elderly (≥65 years) population in Catalonia (Spain) and The Netherlands during 2010–2015 and how it changed over time.

2. Methods

2.1. Setting and study population

Information about antidepressant prescribing and indications in Catalonia, Spain was collected from the clinical SIDIAP database (Information System for Research in Primary Care from Catalan Institute of Health, http://www.sidiap.org/), which includes electronic medical records of 5,8 million primary care patients (approximately 80% of the population of Catalonia) recorded by Primary Care Teams (PCT) which are managed by the Catalan Institute of Health (CIH). The SIDIAP database provides coded demographic information, ICD-10 diagnosis codes provided by General Practitioners (GPs) in consultations and prescribing information (Table 1S). Prescribing data contains medication class (coded according to the ATC classification), prescribing date, prescribed dosage regimen and prescribing professional code. All

SIDIAP variables have been validated in other studies (Ramos et al., 2012; Simó et al., 2013; Barrecheguren et al., 2016; García-Gil et al., 2014; Brookhart et al., 2010).

Information about antidepressant prescribing and indications in the Dutch population was collected from Nivel Primary Care Database (Nivel-PCD) (Nivel-PCD, 2014; van Oostrom et al., 2014; Heins et al., 2016; Ivanovska et al., 2017). Nivel-PCD obtains routinely recorded data including diagnoses, prescription information and referrals to medical specialists from around 500 GPs across the Netherlands. GPs register coded diagnoses during consultations using the International Classification of Primary Care (ICPC) (Table 2S). Prescription data includes information about the prescribed drug (ATC classification), prescribing date, amount prescribed and the prescribed dosage regimen (Table 3S).

Information on antidepressant prescribing and indications were obtained from both databases for the period between 2010 and 2015. To compare diagnoses between both databases, diagnosis mapping created by The Spain's Ministry of Health which link ICPC and ICD-10 diagnoses was used (https://www.mscbs.gob.es/estadEstudios/estadisticas/estadisticas/estMinisterio/SIAP/home.htm). In both databases diagnoses are registered at the specific date that GPs recorded them on electronical patient chart.

Antidepressants included in the study were those with an ATC code of N06A, excluding N06AF and N06AG (non-selective and selective monoamine oxidase inhibitors) (Table 4S).

The study population included all new users of antidepressant drugs aged 65 or older for the period 2010–2015. The date of the first antidepressant prescribed during the study period was defined as the index date. Only new users were included, which were defined as those who did not have an antidepressant prescription during the year before the index date.

2.2. Outcome

The primary outcome in this study was indication for antidepressant prescribing. Diagnoses available ±3 months around the index date were identified as a proxy for indications. This time window was chosen based on the results of a previous study of antidepressant indications in The Netherlands (Gardarsdottir et al., 2007), which showed that most antidepressant indications can be captured using this definition.

Indications were divided into selected and *non-selected* categories. The selected category included the following diagnoses *depression, anxiety, sleep disorders, migraine/headache, neuropathic pain, fibromyalgia*, and *other mental and behavioral disorders*. These indications were selected based on licensed indications by National Regulatories Agencies (Healthcare Institute Netherlands 2017 and Agencia Española de Medicamentos y Productos Sanitarios 2017), clinically accepted use (local medical guidelines in depression) and findings of other studies (Aarts et al., 2016; Patten et al., 2007) about antidepressant drug use (Table 5S).

The "*non-selected indications*" category included those diagnoses none considered in the aforementioned indication groups. (Tables 1S and 2S). Patients could have more than one indication registered in their electronic patient file, but only if they did not have at least one of the diagnoses of selected categories they were included in "*non-selected indications*" category. All the registered diagnoses were considered in the analysis.

A sensitivity analysis was performed extending the time window to 6 months before and after the index date.

2.3. Use of antidepressants

Antidepressant use was defined as having a first antidepressant drug prescribed during the study period, without any use in the previous 12 months to the index date (the day of the first antidepressant prescription in each patient follow-up). The antidepressants were divided into the

following groups according to the ATC classification system: tricyclic antidepressants (N06AA), selective serotonin reuptake inhibitors (N06AB) and other antidepressants (N06AX) (Table 4S). Patients could have more than one antidepressant drug prescribed at index date.

Monoamine oxidase A inhibitors were excluded because it is a group usually prescribed by specialists, who are not registered in the study databases.

2.4. Data analysis

Descriptive analysis was performed. Sex (percentage) and age (mean and standard deviation) was stratified by database, antidepressant group and active substance. Additionally, distribution by 10 year age bands was calculated.

For each indication category, the percentages over total number of new antidepressant users were calculated for the study period. In addition, the incidence of each indication was calculated over the population aged 65 and older registered in the database on 1st July of each year in SIDIAP database, and over the patients aged 65 years and older listed in the database for at least one quartile during that year in Nivel-PCD database.

The change of yearly incidence in indications was described and graphed for each database and expressed in proportions. Standardization by age and sex in older than 64 years was performed per person year using the distribution of the Eurostat (https://ec.europa.eu/eurostat) population in 2014.

Data extraction and analysis were done using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

2.5. Ethical approval of the study protocol

The protocol was approved by the Investigational Ethic Committee of IDIAP Jordi Gol before SIDIAP information was provided.

According to Dutch legislation, neither obtaining informed consent from patients nor approval of a medical ethics committee is obligatory for this type of observational studies containing no directly identifiable data (Dutch Civil Law, Article 7:458). This study has been approved by the applicable governance bodies of Nivel Primary Care Database under number NZR00317.039.

3. Results

We identified 16,537 and 199,168 new users of antidepressants in Nivel-PCD and SIDIAP databases, respectively during 2010–2015. This represents 1.3% (Nivel-PCD) and 3.2% (SIDIAP) of the population older than 64 years per each study year. The majority were women, 63.5% in Nivel-PCD database and 67.4% in the SIDIAP database. Most were aged 65–74 years (47.4% and 40.3%) (Table 1).

Half of patients received a TCA (48.7%) in the Nivel-PCD database, in contrast to the SIDIAP database where most received SSRIs (63.1%)

Table 1
Demographic characteristics in index date.

	The Netherlands		Catalonia	
	n	%	*n*	%
TOTAL	16,537		199,168	
GENDER				
Female	10,495	63.5	134,157	67.4
Male	6042	36.5	65,011	32.6
AGE (years)				
65–74	7833	47.4	80,357	40.3
75–84	6052	36.6	80,445	40.4
85–94	2502	15.1	35,943	18.0
≥95	150	0.9	2423	1.2
Missing	0.0	0.0	0.0	0.0
Mean age (SD)	75.9 (7.72)		77.06 (7.84)	

Table 2
Antidepressant use by group and by gender.

	The Netherlands			Catalonia		
	n (%)	Female *n* (%)	Male *n* (%)	*n* (%)	Female *n* (%)	Male *n* (%)
TOTAL*	16,590	10,534	6056	203,021	136,703	66,318
TCA	8075 (48.7)	5212 (49.7)	2863 (47.4)	21,574 (10.8)	14,715 (11.0)	6859 (10.6)
SSRI	4848 (29.2)	3073 (29.3)	1775 (29.4)	125,603 (63.1)	87,461 (65.2)	38,142 (58.7)
OTHER	3667 (22.1)	2249 (21.4)	1418 (23.5)	55,844 (28)	34,527 (25.7)	21,317 (32.8)

* Total antidepressant users exceed the total number of new users as the patients can have prescribed more than one antidepressant drug.

TCA: tricyclic antidepressants. SSRI: selective serotonin reuptake inhibitors.

(Table 2).

Amitriptyline was the most frequently prescribed antidepressant in Nivel-PCD database (39.9%), followed by citalopram (16.1%) and mirtazapine (13.5%), whereas citalopram was the most frequently prescribed drug (24%), followed by sertraline (15.3%) and trazodone (13.6%) in SIDIAP database.

Depression was the most often recorded indication in Nivel-PCD and SIDIAP databases (24% and 31.3%, respectively). *Anxiety* was the second most common indication (12.5%), followed by *sleep disorders* (10.2%) in the Nivel-PCD database, while it was *sleep disorders* (26.4%), followed by *anxiety* (19.5%) in the SIDIAP database (Table 3). However the *non-selected indication* category represented about one half of all the indications in the Nivel-PCD database.

The antidepressant group most prescribed for the *non-selected indication* category was TCA in Nivel-PCD and SSRIs in SIDIAP.

In the Nivel-PCD database, the *non-selected indication category*, 54% of indications were related to Musculoskeletal and Skin problems (Table 6S). For the SIDIAP database this identification was not possible because we asked for only certain CIE-10 diagnoses related to antidepressant drugs.

Regarding the indication change over time, the percentage of selected indications over new antidepressant users, decreased in Nivel-PCD database in comparison to initial years, with the exception of *fibromyalgia*, which showed a greater percentage in the last study year. Conversely, the prescription proportion for all the selected indications increased from 2010 to 2015 in SIDIAP database (Table 4).

In the same way, the *non-selected indications* category showed an increase (8.3%) in Nivel-PCD database during the study period, while an important proportion of *non-selected indications* category showed a decrease (19.1%) in SIDIAP database.

Additionally, the change over time during the study period in the yearly incidence of the indications for antidepressant use showed an

Table 3
Distribution of chosen indications during all period.

	The Netherlands		Catalonia	
	*N**	%	*N**	%
Depression	3963	24.0	62,360	31.3
Anxiety	2067	12.5	38,846	19.5
Sleep disorders	1680	10.2	52,503	26.4
Neuropathic pain	1339	8.1	2111	1.1
Migraine/headache	792	4.8	7607	3.8
Fibromyalgia	565	3.4	2140	1.1
Other mental and behavioral disorders	514	3.1	10,401	5.2
Non-selected indications	7695	46.5	76,897	38.6

* Total exceed the total number of antidepressant drug users as the patients can have more than one indication registered in the patient contact file.

Table 4
Percentage indications over new users* 2010 and 2015.

	The Netherlands *n* (%)		Catalonia *n* (%)	
	2010	2015	2010	2015
Depression	175 (28.5)	1033 (21.9)	9160 (27.7)	10,336 (32.9)
Anxiety	78 (12.7)	527 (11.2)	4712 (14.2)	8051 (25.6)
Sleep disorders	76 (12.4)	383 (8.1)	7780 (23.5)	8963 (28.5)
Neurophatic pain	59 (9.6)	321 (6.8)	208 (0.6)	574 (1.8)
Migraine/headache	32 (5.2)	210 (4.5)	978 (3)	1327 (4.2)
Fibromyalgia	12 (2)	171 (3.6)	249 (0.8)	408 (1.3)
Other mental and behavioural disorders	24 (3.9)	119 (2.5)	1129 (3.4)	2158 (6.8)
Non-selected indications	261 (42.6)	2399 (50.9)	16,083 (48.6)	9273 (29.5)

* Antidepressant new users per year.

upward trend of 38.53 PYs in the *non-selected indications* category in the Nivel-PCD database population, while in SIDIAP database the trend for this category showed an overall decrease of 79.24 PYs in the whole study period. Figs. 1 and 2 show the incidence of the indications quarterly. In 2012, the incidence of *depression* had a peak in both databases, with a concomitant peak for *anxiety* in the Nivel-PCD database. The remaining indications tended to increase during the whole period in the SIDIAP database.

The age and sex standardized rates were not essentially different from the non-standardized ones (Table 7S, Figs. 1S and 2S).

The results on the sensitivity analysis (Table 8S), in which the time window for identifying indications was increased to 6 months before and after the index date, showed a 4.6% decrease in the proportion of the *non-selected indications* category in the Dutch database and of 1.3% in the Spanish database, compared to the time window definition of 3 months before and after index day. The detection of diagnoses did not show any improvement for the remaining indications.

4. Discussion

Our research used two primary care databases from The Netherlands and Catalonia (Spain) to describe antidepressant use in the elderly. To the best of our knowledge this is the first cross national study investigating the indications for antidepressant prescribing specially in the elder population, an area of research that could help explain the patterns of use of antidepressant drugs in this population.

This study found that TCAs represented almost 50% of prescribing in Nivel-PCD and 11% in SIDIAP while SSRIs represented 62% in SIDIAP and 29% in Nivel-PCD in 2010–2015. Amitriptyline was the most prescribed antidepressant in the Nivel-PCD while citalopram was the most prescribed SSRI in both databases. *Depression* and *anxiety* were the most frequently associated indications in both databases across the study period. However, the *non-selected indications* category had the highest percentage among all diagnosis categories, representing almost half of percentage of all indications in the Nivel-PCD database.

The finding on SSRIs as the most prescribed antidepressant group in the SIDIAP database is similar to that observed in a previous study in the Spanish database BIFAP (of several Spanish regions excluding Catalonia), where a standardized annual prevalence in 2008 of SSRIs higher than TCAs was observed (553/10,000PY vs 115/10,000PY) (Abbing-Karahagopian et al., 2014). And in a previous investigation about the patterns use in initiators of 10 antidepressant drugs in the SIDIAP database for the period 2009–2014 (Forns et al., 2019), where the SSRIs and citalopram were the most prescribed antidepressant group and individual drug, respectively.

A primary care study in the general population older than 10 years in The Netherlands (Noordam et al., 2015), embedded in the Integrated Primary Care Information database, found that SSRIs were the most frequently prescribed group in 2006–2012. The rate of TCA prescribing increased during the study period. This was also observed in the present research. The fact that the included population was younger than the one for the present research could explain the observed differences between both studies.
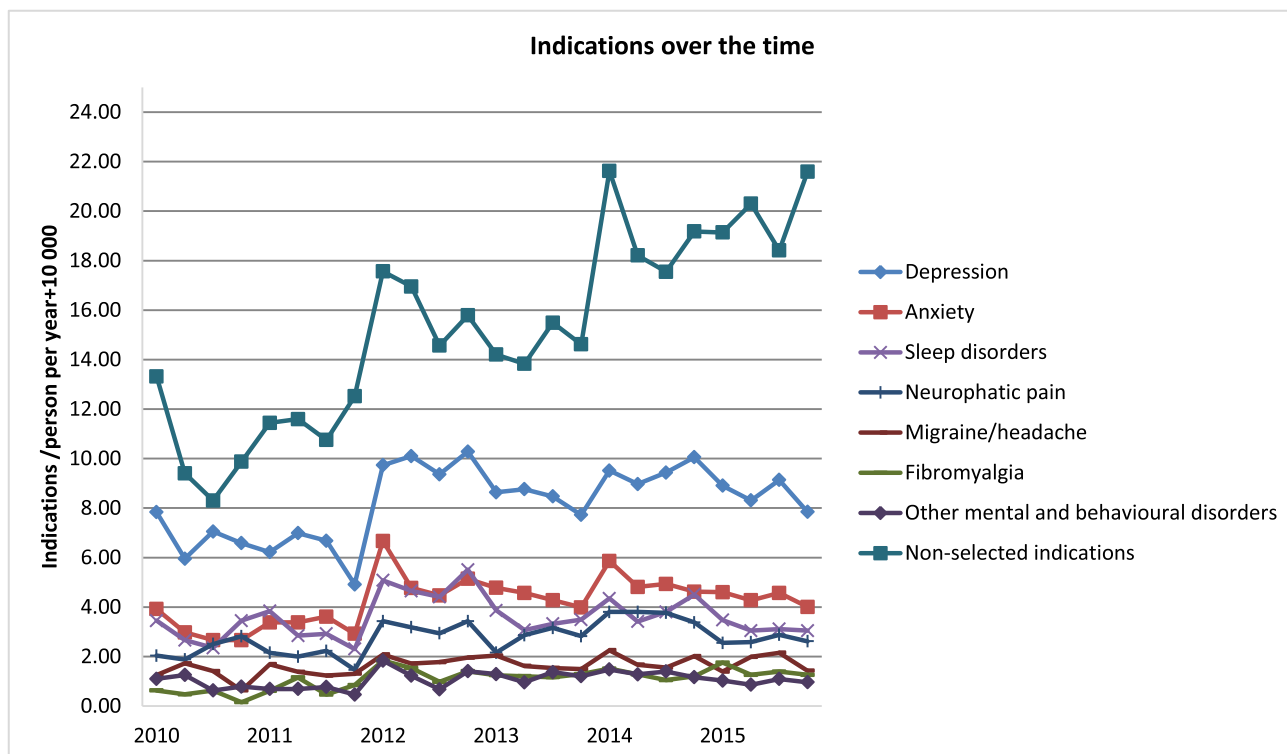

Fig. 1. Indications over the time, per quarter. THE NETHERLANDS.

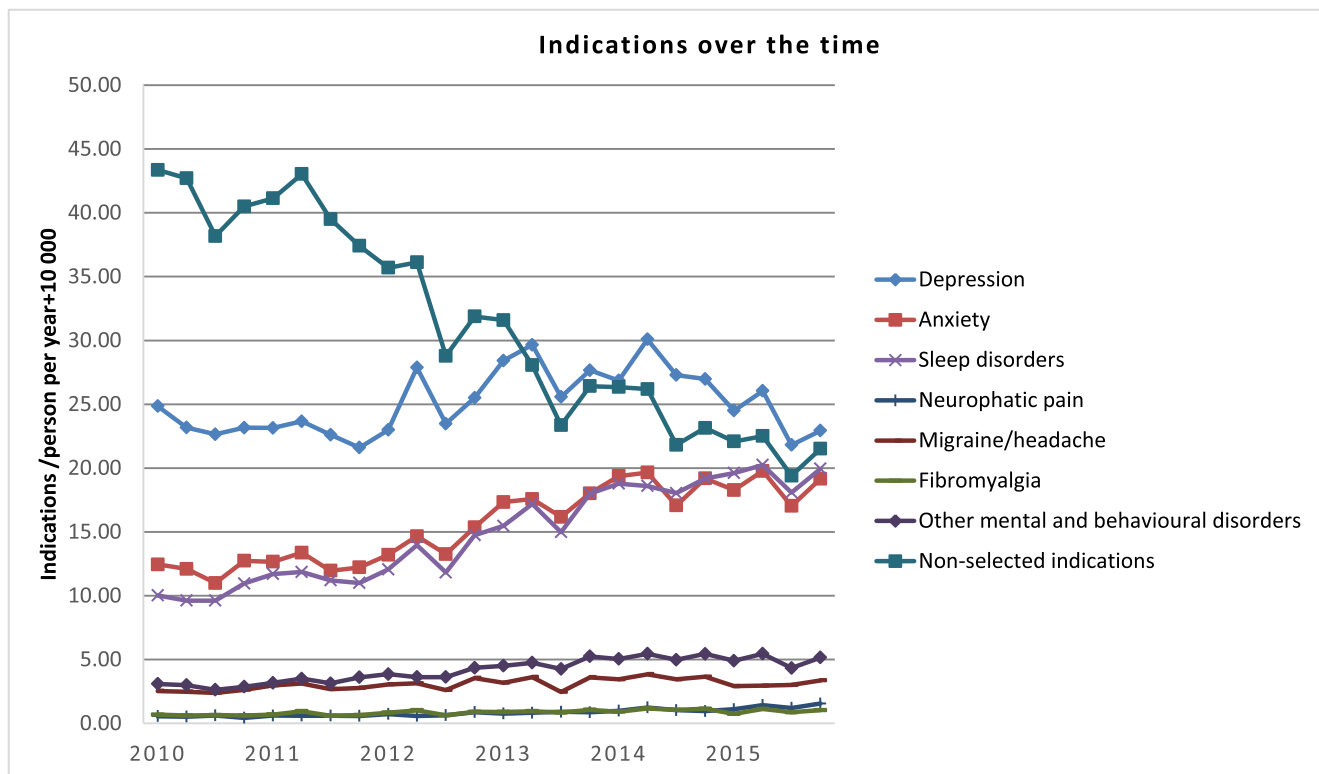## Indications over the time

Fig. 2. Indications over the time, per quarter. CATALONIA.

Similar results were found in the PROTECT study, where two participating Dutch databases, Nivel-PCD and the Almere Health Care group (Mondriaan-AHC) (Abbing-Karahagopian et al., 2014), showed a higher prevalence for SSRIs use (271 and 311/10,000PY, respectively) when compared to TCAs (128/10,000 PY in both databases) in 2008. However, it should be noted that, the antidepressant use was measured as a period prevalence, the Mondriaan-AHC database has information on dispensing drugs, all age populations were considered and the study was performed in a different time period. All these factors could explain the observed differences when comparing with the present study results. These Dutch databases are electronic medical record databases based on general practitioner registers.

On the other hand, the GIP databank, a database with drug reimbursement information of the whole Dutch population, (GIP databank 1988) showed an increased amitriptyline dispensing in 2010–2015, being amitriptyline the most dispensed antidepressant drug among the total population in 2015. Although this data is based on reimbursement data the results on amitriptyline use are similar to ours.

Regarding indications, these results have been also shown by others (Gardarsdottir et al., 2007; Abbing-Karahagopian et al., 2014), despite the fact that the study periods are different from ours, between 2001 and 2009.

Interestingly, the overall *non-selected indications* category in the Nivel-PCD database, not approved or not accepted in clinical practice for depression, were second most commonly registered after *depression*. A study carried out in patients 18 years and older in the Nivel-PCD database in 2001 (Gardarsdottir et al., 2007), showed that *none of above category* (not approved or not accepted in clinical practice) showed the second largest proportion, after depression, and the *none of above category* had major percentage in TCAs prescribing patients. They suggested that there could be some degree of misclassification for the prescription associated diagnosis. To evaluate this we performed a sensitivity analysis, with a widened time window to 6 months before and after the index date, however the results did not show noteworthy changes in any database.

In the Integrated Primary Care Information database based study from The Netherlands between 1996 and 2012 (Noordam et al., 2015), they determined that the percentage of *depression* diagnosis tended to decrease, at the expense of an increase of *anxiety*, *sleep disorders* and *neuropathic pain*. Contrasting results about the increase of *sleep disorders* and *neuropathic pain* compared to our research that could be explained by a younger study population.

Another study evaluated diagnoses related to antidepressant drug prescribing in chronic users in the population older than 18 years between 2011 and 2015 in the Nivel-PCD database (Verhaak et al., 2019). Overall results described depression (38%) as the most frequent diagnosis, somatic symptoms (25%) as second and other psychological diagnoses (20%) in third position. We did not have a somatic symptoms category, although in the *non-selected indication* category many somatic symptoms were found. Unfortunately, the provided data did not allow us to calculate the frequency of the *non-selected indication* category.

There are some differences in the local guidelines for depression in the elderly between The Netherlands and Catalonia that could explain the differences in the results among the two databases (Van Weel-Baumgarten et al., 2012; Departament de Salut. Generalitat de Catalunya 2014Pautes per a l'harmonització del tractament farmacològic de la depressió major en adults, 2014). Both guidelines recommend SSRIs as the first antidepressant drug to be used in the elder, but in the Dutch guideline TCAs can be a second option when persistent hyponatremia appears, while in the Catalonian guideline is not an option considered for this population. Comorbidities have not been taken into account in our research, it could be possible that our sample in the Nivel-PCD database would have had more risk factors to develop sodium disorders, with a consequently major use of TCAs as their guidelines recommended. At the same time, in the SIDIAP database, Other antidepressant is the second most frequently used group as their clinical guidelines advised.

A comparative research between three western countries and an Asian country was carried on six databases (Canada, Taiwan, UK and USA). This research evaluated electronic health records and population-

based administrative data of new users of antidepressant drugs in a population older than 64 years in a period between 2009 and 2014 (Tamblyn et al., 2018). These investigators found the highest overall incidence of antidepressant use (18.6%) in Taiwan and the lowest (4.7%) in Quebec-Montreal. TCA was the most prescribed antidepressant group in Taiwan and UK, while SSRI group was in Canada and USA. In contrast with our results, when they described the prevalence of potential therapeutic indications for new antidepressant use, chronic pain was the major reason in all the countries. Anxiety was the second diagnosis for five databases, only in Quebec City and Montreal depression diagnosis appeared as second in frequency.

The strengths of this study are, first, data was used from two different European databases with representative sample populations despite the fact that they do not cover the whole population (Table 3S) (http s://www.nivel.nl/en; Garcia-Gil et al., 2014). It focused on indications related to prescription in the elder population. Little published information is available in this age group. In addition a sensitivity analysis widening the time window for diagnosis was performed. It showed that a 3 months time window for diagnosis capture had similar results to a 6 months window supporting our main analysis.

Second, the health system in Spain and in The Netherlands has as a first step of their medical attention the general physician (Generalitat de Catalunya 2021). Therefore, the research in the primary care setting provides a wide view of patient drug use in the population (Ministry of Health, 2021; Ministry of Public Health, Welfare and Sport, 2016). The Nivel-PCD and SIDIAP databases have similarities, both are clinical databases that contain multiple variables registered by the primary care team in their routine attention. Both databases include demographic, health problems and prescription information. A common protocol was applied with the objective of harmonizing their information to perform the study (Vlahović-Palcevski et al., 2016).

On the other hand, our research has some limitations, all information has been collected from the prescription information of two Primary Care Databases, in which it is not mandatory for physicians to register a diagnosis with each prescription. Only active diagnosis codes at the time of the antidepressant prescription were selected in both databases, therefore these codes may not always reflect the actual reason for prescription. And the selected diagnoses categories were chosen by study investigator based either approved indications in each country, clinical acceptance, or use in published research, however not all diagnoses could be considered licensed indications.

Also each database has different code dictionaries with distinct granularity. ICPC (Nivel-PCD) has fewer health problem codes than CIE-10 (SIDIAP), however the codes were harmonized in both databases where a common protocol was applied. Nevertheless this difference in coding might have some influence in the diagnosis classification and therefore in the attributed indication for antidepressant use. It is also a limitation the fact that we did not analyze the influence of patient comorbidities as determinants for indication of use. We would like to point out the need of a prescription or dispensing link with diagnosis to be available in the healthcare databases to help perform adequate pharmacoepidemiological studies.

Moreover, the available in-house information for the SIDIAP database in this study is incomplete, so we cannot describe the codes included in the *non-selected indications* category as we do for Nivel-PCD (Table 6S).

Additionally, the Nivel-PCD database just includes selected general practitioners who fulfill data based on particular requirements including completeness. According these requirements, the number of physicians increased during the study period from 48 to 312. This increase could represent an inclusion of different physician populations with distinct prescribing practices. This fact may help explain some of the observed differences in several indication incidences across time.

In conclusion, the results presented in this study have shown that *depression* was the main indication for antidepressant drug prescription followed by *anxiety* and *sleep disorders* in the elder population during the whole study period in Catalonia and The Netherlands. This fact is reassuring since these are the approved indications for these groups of medicines. However, the selection of the appropriate type of antidepressant looks to be in more agreement with the national guidelines for depression in Catalonia than in The Netherlands where a TCA was more commonly prescribed instead of a SSRI. Other diagnoses could have more agreement with the guidelines. This could have clinical implications in the elder, it is known that this antidepressant group should be restricted in this population due to anticholinergic adverse effects and cardiac risk of arrhythmia.

This cross national drug utilization study helps understand the patterns of use of antidepressant drugs in two European countries and raises some questions that could be clinically important for the elder.

CRediT authorship contribution statement

L.F. Camacho-Arteaga: Conceptualization, Formal analysis, Data curation, Writing – original draft, Writing – review & editing. **H. Gardarsdottir:** Visualization, Formal analysis, Data curation, Writing – review & editing. **L. Ibañez:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **P.C. Souverein:** Visualization, Formal analysis. **L. van Dijk:** Visualization, Formal analysis, Writing – review & editing. **K. Hek:** Visualization, Formal analysis, Writing – review & editing. **X. Vidal:** Visualization, Formal analysis, Writing – review & editing. **E. Ballarín:** Conceptualization, Data curation, Writing – review & editing. **M. Sabaté:** Conceptualization, Data curation, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no conflict of interest

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2022.02.001.

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