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**Use and prescription of psychiatric
medication in our health environment:**
influence of new clinical guidelines

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"There's always soma to give you a holiday from the facts. And there's always soma to calm your anger, to reconcile you to your enemies, to make you patient and long-suffering. In the past you could only accomplish these things by making a great effort and after years of hard moral training. Now, you swallow two or three half-gramme tablets, and there you are. Anybody can be virtuous now. You can carry at least half your morality about in a bottle. Christianity without tears—that's what soma is."

Brave New World, Aldous Huxley

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ABSTRACT

Introduction: use of psychiatric drugs has evolved according to the new clinical guidelines that have been published for mental diseases. Among these, the recent release of DSM-5 has risen some authors' critical voices claiming the new diagnostic criteria for depression leads to an overdiagnosis of this disease and its subsequent overtreatment with antidepressants.

Objectives: the aim of this project was to analyse the influence of DSM-5 in the prescription of drug treatments for mental illnesses, focusing on the consumption of antidepressants internationally and in our health territory.

Methods and materials: a bibliographical review and a field, transversal research were performed in order to learn about the antidepressant consumption before and after the release of DSM-5 in May 2013.

Results: the information obtained from the bibliographic research showed an ongoing international increase in the antidepressant consumption. Besides, the statistical analysis of our environment stated the consumption in the Basque Autonomous Community increased by a 6,7 % ($p < 0,0001$) after the release of the DSM-5 manual. This rise was statistically significant when compared to the control group with an OR of 1.005 (95% CI 1.003-1.007).

Conclusion: although given the multifactorial motivation of antidepressant usage no direct relationship can be stated, antidepressant consumption is experiencing a gradual increase which became consolidated after the DSM-5 release in May 2013.

1. INTRODUCTION

1.1. HISTORICAL CONTEXT OF PSYCHOPHARMACOLOGY

Since the dawn of time, the human species has been able to conquer and rule over every single habitat on Earth and beyond, fighting in its way against the forces of nature, other species and other human beings. However, we are still helpless when it comes to understanding our own mind, for it is mysterious as it is fickle and its insanity brings as much suffering for the individual as any other pathologic physical condition.

Those troubled by their own mind have historically faced a dual torment, since incomprehension and fear are as closely related as mental illness and stigma. Already in the time of the ancient Egyptian Pharaohs, the Ebers Papyrus (1), one of the first known medical texts, devoted a whole chapter to their description, blaming this mental conditions on demonic possessions or divine punishment. The same path was followed by many other cultures, like the Chinese or the Indus Valley civilization.

When it comes to psychopharmacology, the use of drugs in order to obtain behavioural modifications is as old as human history itself. Ancient Egyptian and Babylonian texts recorded the medical administration of cannabis while Pre-Columbian American civilizations followed the same tendencies with coca leafs and peyote (2).

The first medical model of mental illness was born in Classical Greece by Hippocrates, whose Humour Theory saw this pathological processes as the decompensation of the black humour, in Greek *melania chole*, which gave us the word melancholy (3). These advances were totally disregarded during the Dark Ages, where divine punishment and demonic possessions prevailed. Even throughout these times some little advances in the field of psychopharmacology were made when Thomas Sydenham studied the use of belladonna, zinc, copper and, distinctively, opium (4).

In spite of these steps forward, it was not until the times of the French Revolution that the magical and theological vision of the ancient psychiatry was left behind. The turning point came in 1793 when, infatuated with the ideas of the Illustration, the doctor Philippe Pinel symbolically broke the chains that held the inmates of *La Salpêtrière* Hospital tied to their cells (**Figure 1**) (5).



**Figure 1: Citoyen Pinel, médecin en chef de la Salpêtrière délivrant les aliénés de leurs chaînes en 1876
(Tony Robert-Fleury) (5)**

This subversive act triggered a revolution that changed drastically the history of psychiatry. For the very first time, insane people ceased to be social outcasts or evil pariahs in order to be recognised as patients. *Id est*, they were finally seen as humans who needed care, attention and treatment for their condition. The first classifications of mental illnesses and specific treatments started to appear in the early 19th century by the hand of Pinel himself. Note that other eminent names of this new era include Bleuler and Bönhoffe, under whose direction the first clinical trials with bromide, trional, alcohol and caffeine were performed (2).

Most authors agree on dating the birth of modern psychopharmacology in the mid-20th century's context of constant avant-garde innovative discoveries. The first attempts date back to 1949 (6), when lithium was found to be useful as a mood stabiliser and started to be prescribed for maniac disorders. However, it is internationally regarded as serendipity what made Deniker and Delay discover in 1952 that chlorpromazine, a recently synthesised antihistaminic, turned out to show neuroleptic features (7).

From that moment on, an unstoppable waterfall of new psychotropic molecules started to be synthesised, which lead to the development of the six big groups in which modern psychopharmacology is based on: antipsychotics (N05A), anxiolytics (N05B), hypnotics (N05C), antidepressants (N06A), psychostimulants – nootropics (N06B) and anti-dementia drugs (N06D). Among all the previously mentioned drugs, antidepressants are one of the most intriguing ones and, therefore, the subject of this work.

1.2. DEPRESSION AND PHARMACOTHERAPY

Depression is a cognitive and behavioural disorder that causes feelings of sadness and anhedonia or inability to feel pleasure in normally pleasurable activities. It can lead to a variety of emotional and physical problems which can affect and eventually obliterate the individual's ability to perform everyday activities (8). This disorder can be potentially life-threatening, affecting more than 350 million of people of all ages across the globe. Nowadays it is the leading cause of disability worldwide and a major contributor to the overall global burden of disease (9). The treatment for this condition disease is not easy neither infallible and it is based on two major pillars: psychotherapy and drug therapy or antidepressants.

This last pharmacologic groups act according to the chemical imbalance theory, which claims that in depressive patients the availability of the neurotransmitters involved in mood regulation is characteristically low. These neurotransmitters or monoamines include:

- Serotonin: its role is to regulate mood, appetite, sleep, memory, social behaviour and sexual desire.
- Noradrenaline: involved in the regulation of alertness and motor function.
- Dopamine: it is not only a key molecule in the signalling of pleasure and reward, but also in motivation and arousal.

The aim of the drugs is to increase the availability of one or several of these neurotransmitters in different ways according to which they are classified. The main antidepressant groups are:

- Selective Serotonin Reuptake Inhibitors (SSRIs): they work by specifically inhibiting the reuptake of serotonin. Developed in the 70s, they are the newest and most commonly prescribed antidepressants (10).
 - E.g. fluoxetine (Prozac®) and sertraline.
- Serotonin and Noradrenaline Reuptake Inhibitors (SNRIs): they work in a similar way to SSRIs inhibiting the reuptake of both serotonin and noradrenaline, which can be helpful for psychomotor retardation (11).
 - E.g. duloxetine and venlafaxine.

- Tricyclic Antidepressants (TCAs): being discovered in the 50s, they are the oldest kind of antidepressants. Their mechanism of action is similar to the previous ones, they inhibit the absorption of serotonin and norepinephrine, as well as blocking acetylcholine receptors. Although once commonly used, they have been replaced by more effective drug agents with fewer side effects.
 - E.g. imipramine and amitriptyline.
- Monoamine Oxidase Inhibitors (MAOIs): also developed in the 50s, they inhibit the action of an enzyme called monoamine oxidase, whose role is to break down monoamines. They are not often used due to their dangerous interactions with foods rich in tyramine like wine or cheese.
 - E.g. selegiline and phenelzine.
- Atypical Antidepressants: they are rather new and do not fit into any of the above-listed categories. They affect serotonin, norepinephrine, and dopamine levels in unique ways.
 - E.g. bupropion (dopamine reuptake inhibitor), mirtazapine (noradrenergic antagonist) and trazodone (serotonin antagonist and reuptake inhibitors)

Since the serendipitous discovery of imipramine in 1955, antidepressants have revolutionised both our understanding and management of depression. As listed above, currently there are five major groups of antidepressants that are mainly intended to treat depression and mood disorders. Anyhow, nowadays they are also used in a much wider variety of disorders, such as attention deficit hyperactivity disorder, obsessive-compulsive disorder, anxiety disorders, menopausal symptoms, fibromyalgia and chronic neuropathic pain.

However, their role in the treatment of depression has long been discussed, for their supposed effectiveness is the primary evidence for the chemical imbalance theory. Moreover, many controversial studies have shaken the foundations of this theory by highlighting the role of placebo response in antidepressant efficacy trials (12). In any case, even the studies backing up the benefits of these drugs cannot dodge some important negative features, such as the several weeks delayed therapeutic onset, intolerability and arguable efficacy in milder depression or treatment-resistant one (13).

It is worth mentioning that in the past few months, one of the biggest network meta-analysis, which compares the efficacy and acceptability of 21 antidepressants, has indisputably confirmed the efficacy of these drugs against placebo (14). Nonetheless, many specialists have reported that most of the analysed studies (78%) were funded by the pharmaceutical industry, threatening their truthfulness. Furthermore, the trials often included people who were already on antidepressants, which means they may predictably have experienced withdrawal symptoms when randomised to placebo. As this phenomenon is highly likely to be classified as a relapse, it supposes a great bias risk (15). In conclusion, the debate is still on.

1.3. DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS

The Diagnostic and Statistical Manual of Mental Disorders (DSM) is a standard classification of mental disorders intended to be applicable in a wide array of contexts with both clinic and research purposes. It is regarded as the authoritative guide to the diagnosis of mental disorders worldwide and contains descriptions, symptoms and, most importantly, regularly updated criteria for diagnosing mental disorders. (16)

The DSM-I was first published in 1952, but since medicine is a dynamic science, it underwent a great evolution. As a key tool to the legitimate performance of psychiatry, the manual needed to be updated four more times to keep up to the constant discoveries. Under this process some diagnoses were further analysed and described and some others were removed. A really well known case was the one of homosexuality which was removed in the sixth printing of DSM-II in 1974 (17).

Although always polemic, the publication of the fifth edition of this manual, the DSM-5, in May 2013 unleashed the uprising of many critical voices. A case of conflicts of interest was reported just before the manual was released claiming that the DSM-5 panel members had strong financial ties to drug companies (18). Additionally, a former member of the group in charge of reviewing DSM-IV published a book detailing the pressure and influence of the pharmaceutical lobby in their job (19).

In this new version, even if some widely accepted conditions as transexuality (gender identity disorder) have been de-pathologised, some suspicious changes have appeared

too. New diagnoses have been added, old ones have changed their names and, maybe most polemically, some diagnostic criteria have been revised.

This is the case of depression, since in the latest manual, grief is not considered to be an excluding criteria for its diagnosis, which opens a new way for the unnecessary medicalisation of one of the most commonly experienced processes of human beings (20). This sounds obviously counter-productive when it comes to tearing down the stigma surrounding mental illness, as pathologising normal and healthy processes is definitely not the best way to make it disappear.

2. HYPOTHESIS AND OBJECTIVES

Once the background has been set and the controversy surrounding the DSM and its relationship with the interests of the drug industry introduced, one cannot but wonder if the last update of this manual has had an effect on the consumption of psychotropic drugs. Therefore, our study is a field, transversal research which aims to analyse the influence of the release of DSM-5 in the prescription of drug treatments for mental illnesses in our health territory. As among these drugs antidepressants happen to be the most contentious ones, the objectives are the following:

1. Perform a review of the available bibliography so as to discover if the release of the DSM-5 in 2013 has had any effect in the consumption and prescription of antidepressants which have been noticed in other regions of the world.
2. Obtain and analyse the data concerning the prescription and consumption of antidepressants in our health environment.
 - 2.1. Study the trends of consumption of antidepressants over the years in the Basque Autonomous Region and its three different Historical Territories.
 - 2.2. Compare it to the consumption of other psychotropic drugs to find out if there is a statistically significant difference between the values previous to the publication of the DSM-5 and the current ones.

For these purposes, we will make use of global official databases about medication use and prescription information. In addition to that, we will have access to key information about the psychotropic drug consumption in our region, provided by the Health Office of the Government of the Basque Country.

3. METHODS AND MATERIALS

3.1. FIRST OBJECTIVE: BIBLIOGRAPHICAL REVIEW

For the fulfilment of this objective, three global official databases were consulted: PubMed, TripDatabase and AskMedline. The intention was to find similar studies to the one we expected to perform in our health region. For that purpose, the PICO method was the chosen one, the following one being the distribution:

- P (Population): people taking antidepressants, the group in which a change to happen was expected. We intended to analyse the use of antidepressant drugs, that is to say, the prevalence of their consumption in our society independent from the characteristics of those consuming them.
- I (Intervention): the hypothesis stated the release of DSM-5 had an influence on our P group. As this manual was published in May 2013, this date will be the intervention turning point of our work.
- C (Comparison): not pertinent taking in to account the objective of our work.
- O (Outcome): the prescription and consumption trends of antidepressants.

The filters applied to ease the correct selection of the articles to be analysed were the ones described below:

- Articles concerning humans (P group).
- Articles published from 2014 on. The intervention (I) expected to make a difference in the people taking antidepressants was the release of DSM-5. As this manual was published in May 2013, we used this publication time filter to find the articles subsequent to its release.
- Articles whose full text was available.
- Articles written in English, French, Spanish and Basque.

We looked for the articles analysing statistically any change of prevalence in the consumption of antidepressants all over the world. As the overall consumption was the key data, the characteristics of the population were not taken into account.

The resulting articles were sorted by their correspondence with the objective of this paper first by reading the title and rejecting the obviously unrelated ones, then by

reading the abstract and finally by deliberating their suitability when reading the whole article.

In order to obtain further international data, another database was consulted: OECD iLibrary, in which the key words “antidepressant” and “consumption” were used.

3.2. SECOND OBJECTIVE: FIELD RESEARCH

Consumption data concerning psychotropic drugs was gathered from the Health Office of the Basque Government, which keeps a detailed record of the prescription drugs purchased and consumed within the Autonomous Community of the Basque Country and its three Historical Territories. These data were completely anonymous, being only accessible the information about the amount of psychotropic drug packages prescribed and consumed in our region.

The data were displayed in a detailed and organised way which highlighted the number of packages consumed for every marketed psychotropic drug. These data were added in order to obtain the total amount of each pharmacological group consumed every year.

From that moment on, the consumed packages were analysed in two time periods: one period in which the total consumed packages for the four years that came before the release of DSM-5 (2010-2013) were added and the other, in which the consumption for the four years that came afterwards (2014-2017) were added. This design was taken in order to perform the statistical comparison of two identical number of years regarding the influence of the DSM manual. Moreover, the obtained quantity was adjusted with the corresponding population for whom the drugs were available. Therefore the units used henceforward are displayed as number of packages per inhabitant.

Information relative the population at the given periods was taken from the records of the Spanish Statistic Office (*INE*). The demographic data corresponding to each analysed period was obtained by adding the populations of the years they comprised and dividing them by four, thus getting the arithmetic mean. The number of consumed packages, the demographic means and the results of adjusting the first one to the second, are displayed in **Tables 1 to 3** using the antidepressants as example.

Table 1. Data concerning the arithmetic means of the population of the fields of study when arranged in two time periods.

Demographic means	BAC	Bizkaia	Gipuzkoa	Araba
First Period: 2010-2013	2,186,930	1,156,096	710,696	320,138
Second Period: 2014-17	2,190,484	1,149,140	717,274	324,070

Table 2. Overall gross quantity of antidepressant packages consumed in both periods.

Consumed Antidepressant packages	BAC	Bizkaia	Gipuzkoa	Araba
First Period: 2010-2013	5,980,532	3,221,661	1,955,823	582,586
Second Period: 2014-17	6,391,215	3,295,005	2,086,463	640,584

Table 3. Consumed antidepressant packages adjusted to the population of every territory.

Antidepressant consumption (packages/inhabitant)	BAC	Bizkaia	Gipuzkoa	Araba
First Period: 2010-2013	2.734670063	2.78667256	2.751982564	1.819796463
Second Period: 2014-17	2.917718185	2.86736603	2.908878615	1.97668405

The outcomes from the periods previous and subsequent to the release of the manual were statistically compared with the help of GraphPad Prism® program: they were displayed in a contingency table and analysed by using the χ^2 and Fisher's exact test.

Right after getting the results about the antidepressant prescription patterns, the exact same procedure was carried on with the consumption of antipsychotics, anti-dementia drugs and psychostimulants. The obtained quantities for every psychopharmacological group are displayed in the **Tables 9 to 14** of the appendix.

Finally, the relevance in the variation in the overall antidepressant consumption and in the four most popular antidepressants was compared to the variation of a control group. For this purpose, the antipsychotics were chosen. GraphPad Prism® was the software in charge of carrying on the statistical procedures. The data were displayed in a contingency table and analysed by using the χ^2 and Fisher's exact test.

4. RESULTS

4.1. BIBLIOGRAPHICAL REVIEW

As detailed above, three international databases were consulted to obtain the desired information. The result of that process is described in the **Table 4** and the following algorithms beneath this lines:

- **Global Official Databases**

Table 4. This table displays the PICO method followed for the obtaining of the information needed to fulfil objective number one.

<u>P (population)</u>		<u>I</u> <u>intervention</u>	<u>O (outcome)</u>	
Free Terms #1	MeSH Terms #2		Free Terms #3	MeSH Terms #4
Antidepressant (41135)	Antidepressive agents (55890)		Trend (205127)	prescriptions (32672)
Antidepressants (32303)	Depression/drug therapy (14725)		Prescription (76818)	drug prescriptions (31302)
Antidepressive (57291)	Depressive disorder/drug therapy (25046)	<i>The release of DSM-5 (time filters were used)</i>	Consumption (337957)	Drug industry/trends (3000)
Antidepressive agents (147332)				Consumer behaviour (20355)
Depression/drug therapy (5017)				Drug therapy/trends (6931)

As showed above, Free and MeSH Terms were used and classified according to the PICO method. It is worth mentioning that, even if the P group made reference to the people consuming the drugs, we used the antidepressant related terms themselves for the strategic research and later the human filter was applied. The number of results available in the PubMed database for each term is shown inside the brackets.

The following algorithm represented by **Figure 2** shows the strategies and filters used for the search in the a) PubMed database and the ones browsed after it: b) Trip Database and c) AskMedline.

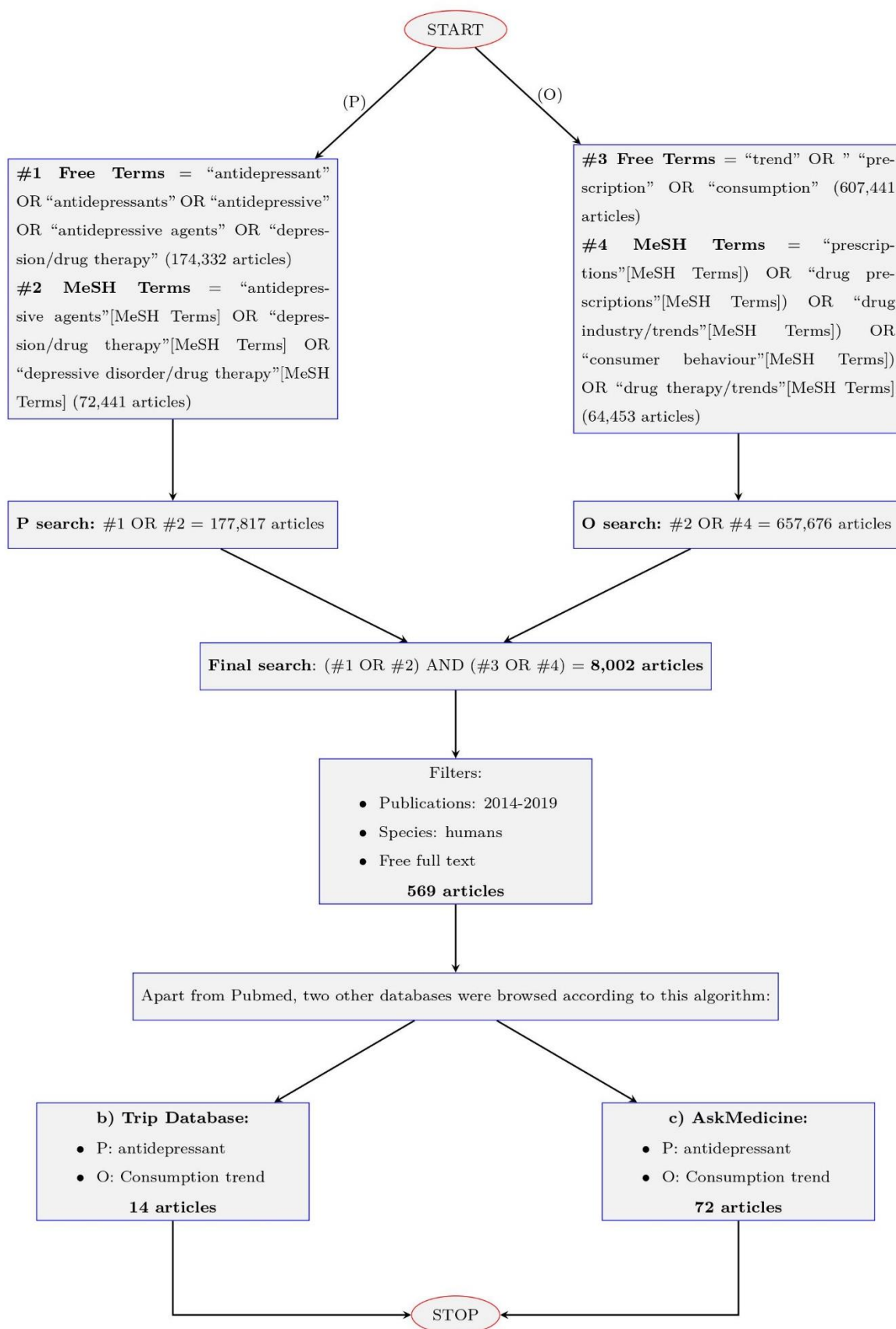


Figure 2. Algorithm portraying the search strategies followed to browse the global official databases.

- **OECD iLibrary**

By typing the words “antidepressant” (P) and “consumption” (O) four results popped up which consisted on four graphs or data tables displaying the DDD per 1000 people per day in the member countries of this organisation during the period 2011-2015.

- **Article selection**

The results obtained by searching in the first mentioned three databases add up 655 articles, which were selected and discarded by the following criteria displayed in the algorithm of **Figure 3**:

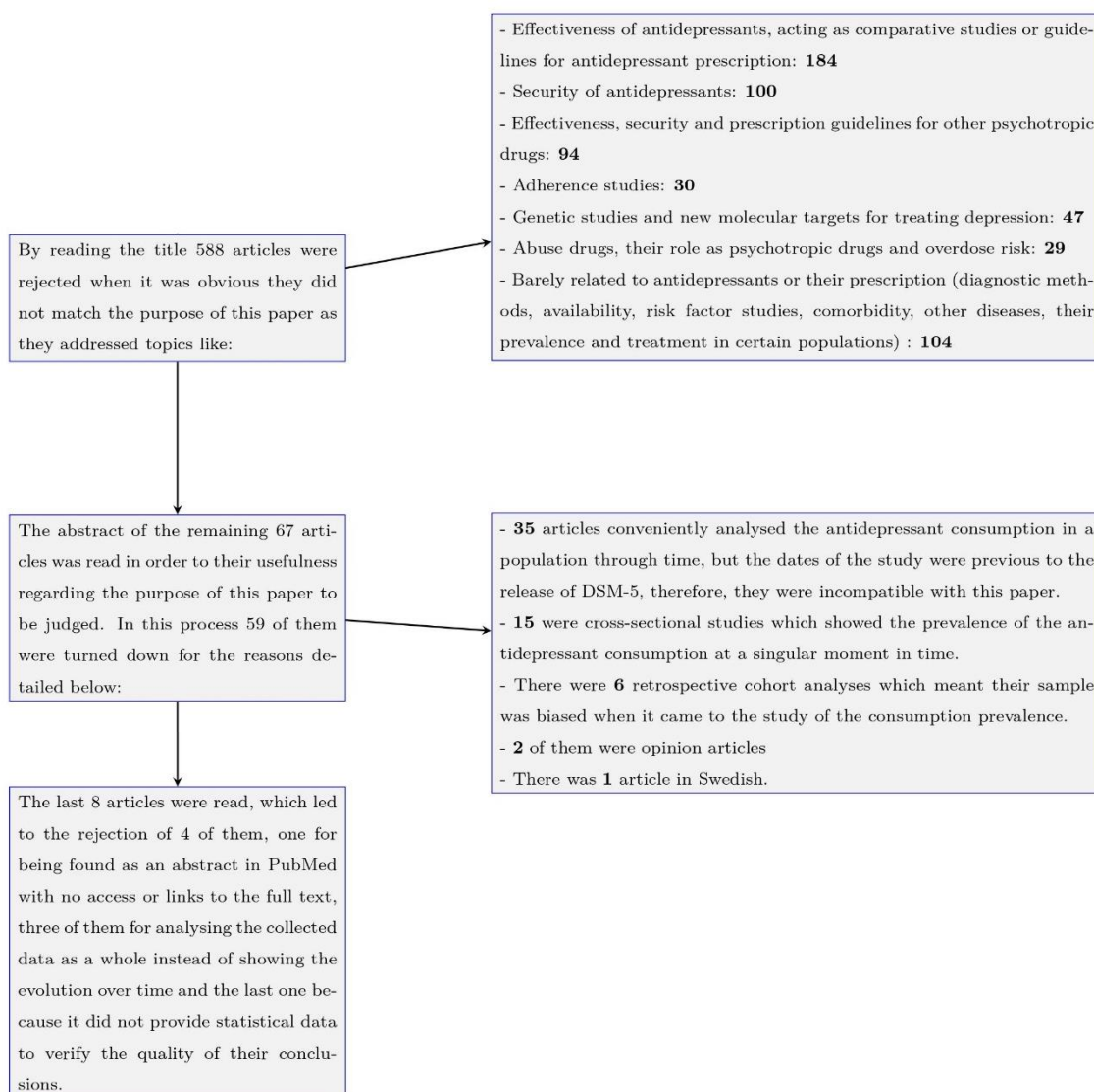


Figure 3. Algorithm displaying the strategies followed to select and discard the obtained articles.

In the end, the 4 remaining articles are analysed and discussed in the next pages, after that, the data obtained from the OECD iLibrary are disclosed.

4.1.1. Antidepressant prescriptions and mental health nurses: an observational study in Dutch general practice from 2011 to 2015 (21)

This article published on March 2018 attempted to evidence a reduction in the antidepressant prescription of general practitioners in the Netherlands as a consequence of the introduction of the so called Mental Health Nurses. These professionals provide short-term psychological treatment and perform diagnostic assessments thanks to their training as psychiatric nurses, psychologists or social workers.

197,512 patients aging 10 to 65 were registered during the full study period, from which 27,044 had at least one episode of anxiety or depression (13.7%). Taking into account that some of the patients suffered two (23.2%), three (7.7%) or even four (5.0%) episodes, a total of 42,423 episodes of anxiety or depression were recorded. 30,3% of the recorded episodes led to an antidepressant prescription which, adjusted to the number of episodes each patient had, entails an overall of 8,217 patients with at least one episode of anxiety or depression with at least one prescription of antidepressants.

When it comes to the distribution of this prescriptions over the development of the study, the data show a significant linear effect. Each year, from 2011 to 2015, more antidepressants were prescribed despite the inclusion of the Mental Health Nurses. Taking the 2011 prescriptions as the control group, statistical comparison were held with the following years. Even adjusted to the number of episodes taking place in that period, all of them showed a slight increase in prescriptions, with 2015 being the most statistically significant one (OR 1.17; 95% CI= 1.07–1.28).

In spite of these results which clearly rejected the hypothesis of the article, there was still a positive finding: an immediate antidepressant prescription after an episode was less likely in 2015 than in 2011 (OR = 0.76; 95% CI= 0.70–0.83).

In conclusion, antidepressant prescriptions increased over time regardless of the job of the nurses, which brings us to think that there were other variables influencing the number of antidepressant prescriptions.

4.1.2. Trends in General Practitioner prescribing of psychotropic medications among young patients aged 16–24 years: a case study analysis (22)

This article was born as an answer for the concern raised in Australia by the high number of General Practitioner's psychotropic prescriptions for young patients aged 16-24. As a matter of fact, 89% of antidepressants for this age group in that country were prescribed by these professionals in 2012.

To verify and quantify this worrying facts, this Australian retrospective analysis recorded data from 9112 patients from the Melbourne East region with a mental health condition, which does not compulsorily imply a diagnosis. For instance, from the overall sample, 2747 patients (30.1%) had been officially diagnosed and had already received psychotropic prescription, 5145 of them (56.5%) had been diagnosed but not prescribed and 1220 (13.4%) had been prescribed psychotropic drugs with no diagnosis supporting it.

During the recorded period, 11,934 psychotropic prescriptions were provided, from which antidepressants were the most usual ones (81.4%). However, when it comes to the distribution of this prescriptions over time, the findings turn out to be rather remarkable. This is so, because even if the number of patients significantly dropped from 4394 in 2009 to 3816 in 2014, the number of psychotropic prescriptions kept rising from 1791 in 2009 to 2182 in 2013, before discretely decreasing to 2100 in 2014.

Being the prescriptions of the year 2009 the reference to which the rest of the years were statistically compared, we can see a constant significant growth in the number of prescriptions (from OR 1.04, 95% CI: 0.93–1.15 in 2010 to 1.35, 95% CI: 1.21–1.50 in 2014).

One last interesting result was obtained from this article: among all the antidepressants prescribed, SSRIs were 75.1%, from which citalopram and sertraline altogether made the 70.6%. This would be a totally harmless curiosity, were it not for the fact that ongoing clinical guidelines solely recommend the prescription of fluoxetine for patients the age of the recorded ones. For the time being, there is not sufficient evidence to support the use of neither escitalopram nor sertraline in patients under 18 years old.

4.1.3. Psychotropic drug use among 0-17 year olds during 2004-2014: a nationwide prescription database study (23)

Time trends in psychotropic drug prescriptions show great variability among different countries. This difference is remarkable when the studied population is younger than 18 years old. To examine the situation in Norway, data regarding the prescription of these drugs during the 2004-2014 period were drawn from the Norwegian Prescription Database.

Variations concerning the consumption trends of every drug were studied, resulting in an overall increase in the prescriptions. The prescriptions became increased among boys and girls from 30.6 to 35.3 and from 19.2 to 25.0 per thousand inhabitants respectively. As mentioned, boys consumed quite more psychotropic drugs than girls, which is attributable to the prescription of stimulants as a therapy for ADHD. However these results rely on the youngest population groups, and when it comes to adolescents the burden of the psychotropic drugs consumed falls to the hypnotics and antidepressants. These last ones being specially popular among adolescent girls.

With regard to these last psychotropic drugs, the article confirms an annual rising trend in the consumption of antidepressants, which is more pronounced in girls over 15 years. For instance when it comes to 17-year old adolescents, the antidepressant consumption in 2014 got to 27.9 prescriptions/1000 girls compared to 11.5/1000 boys. This prevalence showed a 70% increase between 2006 and 2013, which the article justifies by an increasing prevalence of depression or a more liberal prescription dosage.

In conclusion, the common use of stimulant drugs in the youngest population groups overshadows the relevance of the consumption of other psychotropic drugs, such as the antidepressants. These drugs showed a moderate increase in the recorded years, which was particularly visual in the case of adolescent girls.

4.1.4. Psychotropic medication in children and adolescents in the United States in the year 2004 vs 2014 (24)

This American study intended to challenge the global perception of children overtreatment on psychotropic drugs. To prove the point, they estimated the prevalence of use of this pharmacological group in the USA in the years 2004 and

2014. The gathered data showed the consumption of stimulants, anxiolytics, antidepressants, antipsychotics, mood stabilisers and drugs to treat drug dependence in children aged 2 to 18.

In both years, the most consumed drugs were hydroxyzine, methylphenidate and sertraline (followed by fluoxetine) for individuals aged 2 to 5, 6 to 16 and 17 to 18 respectively. Overall, the most consumed drug was methylphenidate. The results show the percentage of children receiving psychotropic drugs increased slightly from 8.55% in 2004 to 9.00% in 2014.

When it comes to the age of the patients, prescription prevalence showed a decrease in the period of 2004-2014 for preschool children younger than 5 years and 5 to 12 year-old children, from 3.08% to 2.63% and from 8.74% to 8.73% respectively. Nonetheless, the prescription prevalence became increased in adolescents from 10.89% to 12.11%, just in the group where the most usually prescribed drugs are the antidepressants.

Overall, the antidepressant prescription prevalence dropped from a 2.81% in 2004 to a 2.69% in 2014, decrease that was driven by the younger age groups, in which antidepressants are not often prescribed. On the contrary, as previously stated, prescriptions in adolescents rose nearly two percentage points.

The article concludes that the perception on the increasing psychotropic use in all children ages is false, since the overall prescription of psychotropics has decreased, a goal for which the article thanks new guidelines and box warnings.

4.1.5. **OECD records** (25-27)

The Organisation for Economic Co-operation and Development issues every 2 years its “Health at a Glance” manual. This biennial dossier offers a wide variety of international health status indicators, determinants of health and health expenditure and financing in its member countries.

Among the contents of this kind of document, key data about several countries’ antidepressant consumption can be found. The following **Table 5** presents the mentioned statistics regarding antidepressants (N06A in ATC classification) in

Defined Daily Dose per 1000 people units. The information was collected from the publications dating from 2012 to 2016. (25, 26, 27)

Table 5. Annual antidepressant consumption displayed in DDD per 1000 people units for the period 2011-2015

N06A DDD per 1000 people per day	2011	2012	2013	2014	2015
Australia	89	X	96	101	104
Belgium	70	70	72	75	78
Canada	86	X	85	87	90
Chile	13	X	13	13	37
Czech Republic	44	46	49	53	55
Denmark	85	83	80	77	77
Finland	70	70	69	69	68
Estonia	18	21	21	23	25
France	50	50	50	49	50
Germany	50	52	53	55	56
Hungary	27	27	28	28	28
Iceland	106	109	118	118	130
Italy	42	42	43	43	47
Korea	13	X	20	18	20
Luxembourg	51	52	54	56	54
Netherlands	42	42	43	44	45
Norway	58	57	56	56	57
Portugal	78	85	88	92	95
Slovakia	31	30	35	38	40
Slovenia	50	51	53	55	57
Spain	64	64	65	71	73
Sweden	79	81	84	88	93
United Kingdom	71	75	82	87	94

Note: the quantities were originally rounded to units when retrieved from the source. Some countries' 2012 data was also omitted in the 2014 publication but recovered in posterior releases.

The data show a general increase in the consumption of antidepressants all over the world. There are some countries such as France, Luxembourg, Norway and Hungary in which DDD numbers stay stable to a certain extent. Also there are two remarkable exceptions, Denmark and Finland, the only countries reducing their antidepressant consumption.

On the other hand we have those countries matching the general increasing trend, a group in which Portugal, the United Kingdom, Australia, and specially Iceland stand out. This latter country, increased its antidepressant consumption by a 22'6%.

In order to make the interpretation of **Table 5** easier, **Figure 4** displays the consumption of antidepressants during the period from 2011 to 2015 for Denmark, Portugal, France, Spain and Iceland. As we can see, even though the consumption in Spain is not the highest, it keeps rising through the years.

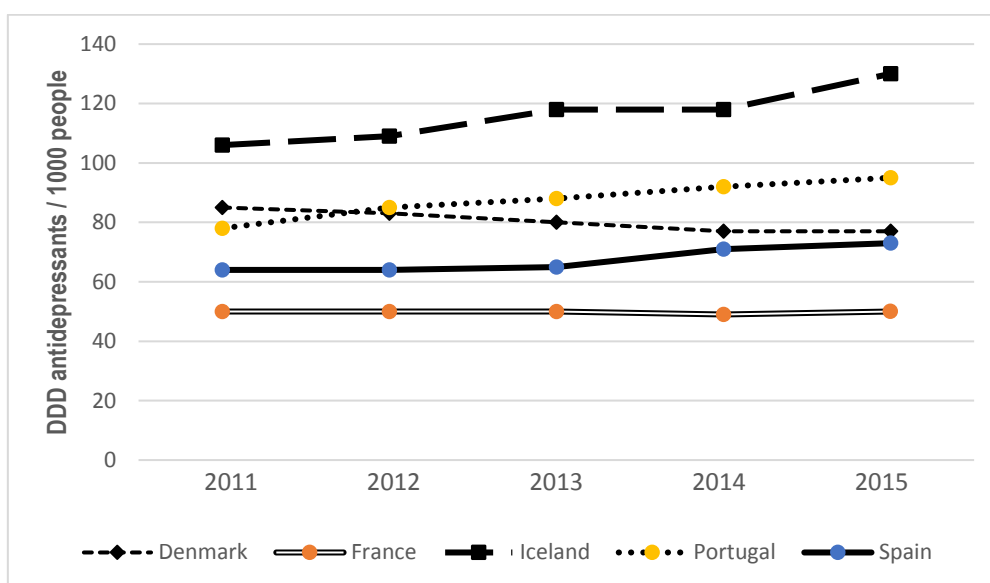


Figure 4. Trends of antidepressant consumption through the years in DDD per 1000 people units, five of the countries from table 5 are represented.

4.2. FIELD RESEARCH

As previously stated, the data regarding the psychotropic drug consumption in the Basque Autonomous Community (BAC) were drawn from the Health Office of our government and rearranged to obtain the overall amount of consumption of each psychopharmacological group. The studied period covers the years 2010 to 2017. There are six psychotropic drug groups which were analysed over eight years. However, in order to ease the comprehension of the reader, the following graphics and comments will include data regarding only antidepressants and the other psychotropic drugs which were expected to be used as a reference control for comparison purposes: antipsychotics, anti-dementia drugs and psychostimulants.

As a whole picture, the following data displayed in **Table 6** represent the total package consumption of psychotropic drugs during the recorded eight years:

Table 6. Annual consumption of antidepressant, antipsychotic, anti-dementia drugs and stimulant packages in the Basque Autonomous Community (BAC) for the period 2010-2017

Total regional consumption	Antipsychotics	Antidepressants	Anti-dementia drugs N06D	Stimulants
	N05A	N06A		N06B
2017	649,903	1,665,157	133,231	141,598
2016	641,393	1,627,944	134,484	176,160
2015	618,328	1,570,087	132,824	234,508
2014	598,347	1,528,027	130,381	245,142
2013	585,384	1,531,836	129,820	271,407
2012	586,288	1,512,835	179,276	271,407
2011	591,737	1,505,319	202,471	278,818
2010	594,831	1,430,188	199,796	266,552

4.2.1. Psychotropic drug consumption variations in the BAC and its territories before and after DSM-5

The aim of this section is to observe the modification in the consumption of antidepressants that took place after the release of DSM-5. Four fields will be subject of this analysis: the BAC as a whole and the three Historical Territories in which the BAC is divided. Later on, the same analysis will be held with antipsychotics, anti-dementia drugs and stimulants.

4.2.1.1. Antidepressant consumption variations in the BAC and its territories

As seen in **Figure 5**, a statistically significant difference was noticed between the periods compressing 2010-2013 and 2014-2017, which means that the antidepressant consumption rose in the four fields of study. However, the magnitude of this increase was not the same in every result. In fact, the percentages in which the consumption of antidepressants increased are the following:

- The antidepressant consumption in the BAC rose by a 6.7% ($p < 0.0001$).
- The antidepressant consumption in Bizkaia rose by a 2.9% ($p < 0.0001$).
- The antidepressant consumption in Gipuzkoa rose by a 5.7% ($p < 0.0001$).
- The antidepressant consumption in Araba rose by an 8.6% ($p < 0.0001$).

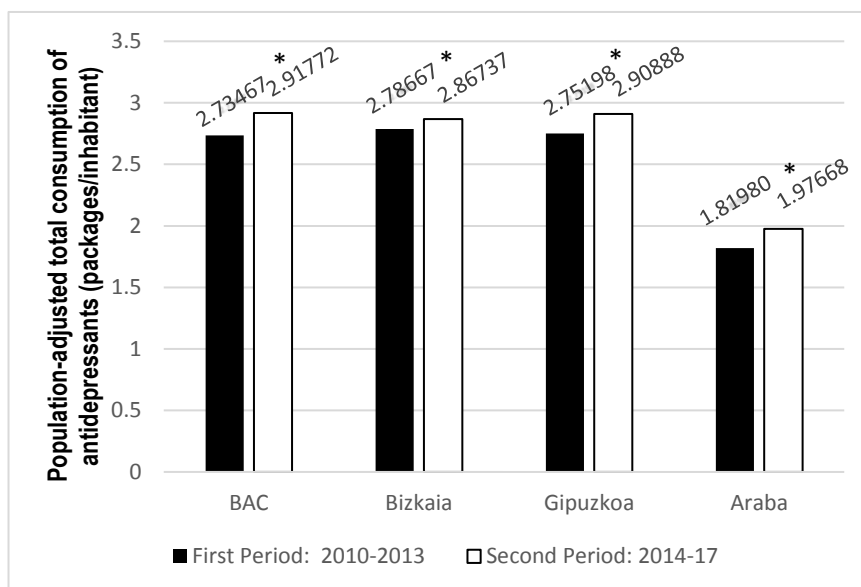


Figure 5. Overall antidepressant package consumption adjusted to the population
Note: * = $p < 0.0001$ vs first period by Fisher test

4.2.1.2. Antipsychotic consumption variations in the BAC and its territories

The difference between the periods compressing 2010-2013 and 2014-2017, as shown in **Figure 6**, turned out to be statistically significant, meaning there was a noticeable increase in the antipsychotic consumption. The percentages of the consumption shift are the following:

- The antipsychotic consumption in the BAC rose by a 6.2% ($p < 0.0001$).
- The antipsychotic consumption in Bizkaia rose by a 1.8% ($p < 0.0001$).
- The antipsychotic consumption in Gipuzkoa rose by a 7.9% ($p < 0.0001$).
- The antipsychotic consumption in Araba rose by a 12.7% ($p < 0.0001$).

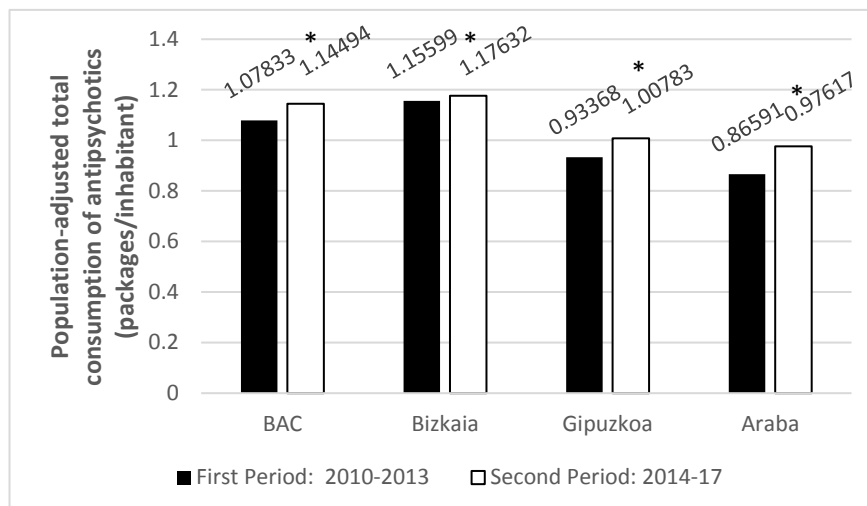


Figure 6. Overall antipsychotic package consumption adjusted to the population
Note: * = $p < 0.0001$ vs first period by Fisher Test

4.2.1.3. Anti-dementia drug consumption variations in the BAC and its territories

As displayed in **Figure 7**, a statistically significant reduction was observed. After analysing the difference statistically and obtaining the exact proportions, these were the results:

- The anti-dementia drug consumption in the BAC dropped by a 25.5% ($p < 0.0001$).
- The anti-dementia drug consumption in Bizkaia dropped by a 30.7% ($p < 0.0001$).
- The anti-dementia drug consumption in Gipuzkoa dropped by a 23.4% ($p < 0.0001$).
- The anti-dementia drug consumption in Araba dropped by a 32.4% ($p < 0.0001$).

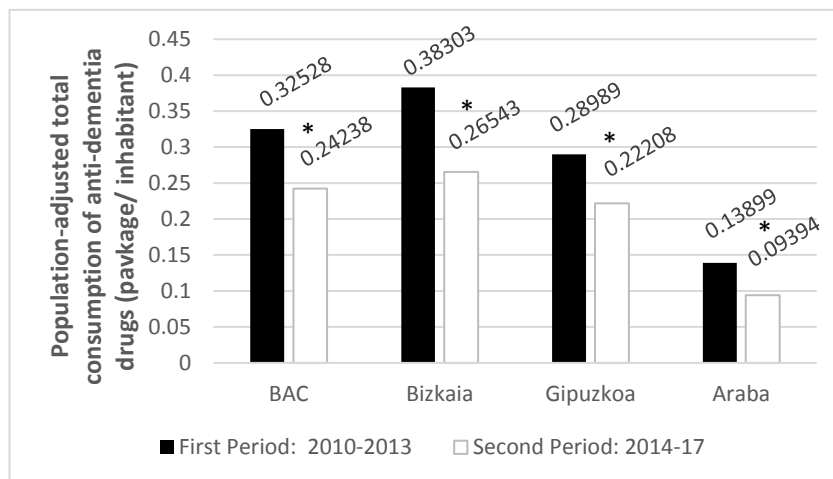


Figure 7. Overall anti-dementia drug package consumption adjusted to the population
Note: * = $p < 0.0001$ vs first period by Fisher Test

4.2.1.4. Psychostimulant consumption variations in the BAC and its territories

Regarding the psychostimulant data in **Figure 8**, we see the consumption drastically decreased from the period comprising the 2010-2013 data to the one from 2014-2017. The performed statistical analysis gave us the following data:

- The psychostimulant consumption in the BAC dropped by a 34.2% ($p < 0.0001$).
- The psychostimulant consumption in Bizkaia dropped by a 25.5% ($p < 0.0001$).
- The psychostimulant consumption in Gipuzkoa dropped by a 31.1% ($p < 0.0001$).
- The psychostimulant consumption in Araba dropped by a 30.6% ($p < 0.0001$).

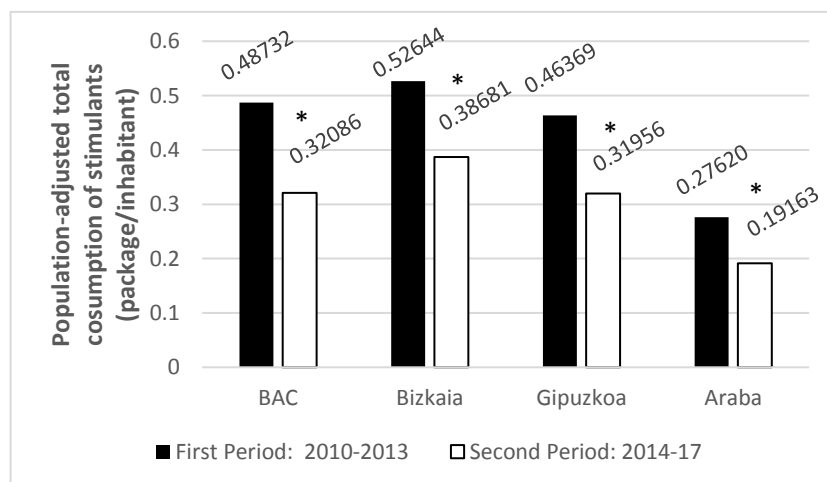


Figure 8. Overall psychostimulant package consumption adjusted to the population
Note: * = $p < 0.0001$ vs first period by Fisher Test

4.2.2. Antidepressant consumption variations before and after DSM-5 compared to the control group

As the first results of the former section confirm a general increase in the consumption of antidepressants in the whole territory, the next analysis intended to compare the increment in antidepressant consumption with the trend variation of the antipsychotics as a control group. This would allow us to explore whether the effect on antidepressants was specific or general for all psychotropics.

The selection of antipsychotic drugs as a suitable control group was based on the fact that no impact existed related to the release DSM-5, with a similar general evolution related with the environment. In fact, the consumption pattern of antipsychotics was somewhat similar to the antidepressants' one, while the other two classes, the stimulants and anti-dementia drugs, presented a drastic decrease in the second period. In a similar way to the previous section, the data regarding the drug package consumption of the experimental and control drugs, antidepressants and antipsychotics, were divided into two time periods four years long before and after the release of the DSM-5 manual. However, in this case, the values are obtained as Odds Ratios, that is, the consumption of antidepressants respect to antipsychotics (control) in the post DSM period compared to that in the pre-DSM period.

The meaning of the results displayed in **Figure 9** will be explained in an independent way for every region studied:

- The BAC
 - When the overall gross quantities of antidepressants from both periods were adjusted with the consumed antipsychotics, the outcome turned out to be statistically significant with an OR of 1.005 (95% CI 1.003-1.007). This corroborates an increase in the consumption of antidepressants which is even bigger than the increase of the antipsychotic consumption.
- Bizkaia
 - In a similar way to the previous point, the increase in the antidepressant consumption respect the control proved to be significantly bigger in the

post DSM period than the one in the pre DSM period (OR = 1.011, 95% CI 1.008-1.014).

- Gipuzkoa
 - The difference between the consumption trends of both pharmacological groups was proved to be statistically significant too. Nonetheless, an OR value of 0.979 (95% CI 0.975-0.983) meant that, even if the antidepressant consumption had increased after DSM-5, as demonstrated in the 4.2.1.1 section, its increase was not as sharp as the one of the antipsychotics.
- Araba
 - The outcome of the comparison, analogous to the one above, turned out to be statistically significant, yet with an OR of 0.963 (95% CI 0.957 – 0.969). The meaning was identical, the antidepressant consumption increase after DSM-5 was not as big as the antipsychotics' one.

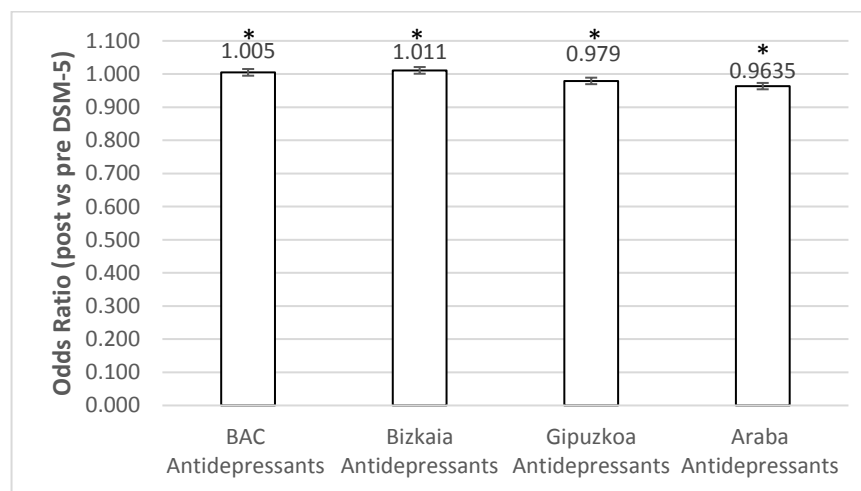


Figure 9. Odds Ratio resulting from the statistical comparison of the Antidepressant consumption adjusted with antipsychotic control after vs before DSM-5.
Note: * = $p < 0.0001$ vs first period by Fisher Test

4.2.3. Most popular antidepressants' consumption variations before and after DSM-5 compared to the antipsychotics as a control group

As a final statistical analysis of the data obtained from the Basque Health Office, the consumption trends of the most used antidepressants were adjusted to the control

group: the antipsychotics. The normalised data of the most consumed antidepressants were compared in the two analysed periods of this study: 2010-2013 and 2014-2017.

First, to select the most prevalent antidepressant drugs, the consumption of every single antidepressant was estimated as percentages over the total amount of antidepressants. During the first period the most popular drugs happened to be escitalopram (17.37%), duloxetine (10.72%) and venlafaxine (8.84%). Similarly, during the second period the most prevalent antidepressants were again escitalopram (13.44%) and duloxetine (12.6%), but another drug was more prevalent than venlafaxine: trazodone (9.65%). The gross overall package consumption and the percentage it represents over the total antidepressant consumption are displayed on **Table 7 and 8**.

Table 7. Overall gross package consumption of the most popular drugs.

Most Consumed drugs	Escitalopram	Trazodone	Duloxetine	Venlafaxine
First Period: 2010-2013	1,038,993	452,597	641,382	528,932
Second Period: 2014-2017	859,169	616,498	805,339	523,696

Table 8. The proportion each single drug makes over the total consumption of antidepressants

Single antidepressant consumption % over total	Escitalopram	Trazodone	Duloxetine	Venlafaxine	Total
First Period: 2010-2013	17.3729193%	7.567838%	10.72449%	8.84423%	44.50949%
Second Period: 2014-2017	13.4429682%	9.646022%	12.60072%	8.19399%	43.88371%

The previously mentioned four drugs are explored in **Figure 10** by comparing their consumption adjusted to a control group (antipsychotics), before and after the release of DSM-5. The outcome is displayed in Odds Ratios values.

The results represent the statistical differences for the variations of these single antidepressants before DSM-5 compared to the one after its release. The meaning of those differences is the following:

- Escitalopram
 - The difference between the consumption trends of escitalopram adjusted to the control group between the two periods was statistically significant with an OR of 0.775 (95% CI 0.772 - 0.777). This means the variation in the consumption of antipsychotics was bigger than the one of escitalopram. Besides, if we look at the gross data, escitalopram was far less prescribed during the second period.
- Trazodone
 - In the opposite way to the previous case, trazodone turned out to be more prescribed in the second period than in the first one. The comparison to the control group gave an OR of 1.281 (95% CI 1.275 – 1.287). This means the growth in the consumption of trazodone was proportionally bigger than the one of the control group.
- Venlafaxine
 - This time the difference between the consumption trends of both groups was proved to be statistically significant too. Nonetheless, an OR value of 0.931 (95% CI 0.927-0.935) means that the variation in the consumption was bigger in the case of the antipsychotics. In addition to that, the consumption of venlafaxine decreased from the first period to the second, being moved to the fourth position of the most consumed antidepressants.
- Duloxetine
 - The outcome of this comparison turned out to be statistically significant too. The fact of the OR value being 1.181 (95% CI 1.176 - 1.186) means the increase in duloxetine consumption was more considerable than the one of antipsychotics.

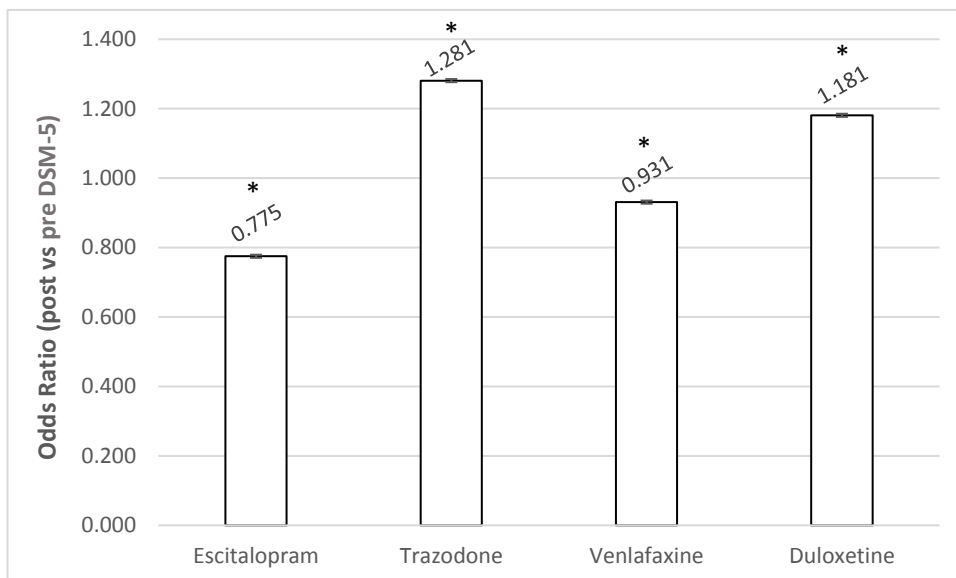


Figure 10. Odds Ratio resulting from the statistical comparison of each of the most popular antidepressant consumption adjusted to antipsychotic control after vs before DSM-5.

Note: * = $p < 0.0001$ vs first period by Fisher Test

5. DISCUSSION

The results of this study show, among others, an overall worldwide increase in the consumption of antidepressants, a kind of drug which never ceases to raise controversy. In fact, in the very moment imipramine was discovered in the 1950s (28), the novel pharmacological group of the antidepressants began a rising visibility which would place them among the most renowned drugs in history. Yet, the historical milestone came in January 1988, when fluoxetine was launched to the market under the name of Prozac (29).

This initial context of success and high profit for the drug industry was soon enough tarnished with news about adverse reactions (30), delayed effects and dubious efficacy (13). Nevertheless, the consumption of this kind of drugs did not stop rising every year (31, 32, 33), thus awakening the concern of researchers, who did not hesitate to write about the presence of antidepressants in our society. It were these writings the ones inspiring this study and its objectives, which led us to the results discussed below.

5.1. BIBLIOGRAPHICAL REVIEW

As stated before, a big array of papers have come out to record and analyse the consumption trends of these drugs, trying to find a link between the consumption and the unemployment (34), the economic crisis (35, 36), or the way they are universally advertised in mass media (37, 38). However, studies have seldom wondered about the role of current guidelines like the DSM. In fact, finding the right articles for the bibliographical research was not easy, and terms like “antidepressants” and “prescription trends” have turned out to be multi-purpose words with a wide range of results in every global database.

A good number of articles had to be discarded in the searching process, most of which recorded the antidepressant consumption over the years, because the dates of most of those studies gathered data concerning periods prior to the release of DSM. In any case, the eventually chosen articles were analysed, resumed in the previous section and are discussed beneath this lines.

5.1.1. Antidepressant prescriptions and mental health nurses: an observational study in Dutch general practice from 2011 to 2015 (21)

The fact that during the years of the study the efforts made to improve mental health in the population by the program of mental health nursing were not able to make a difference in the antidepressant consumption gives us an insight about the seriousness of the problem. Even if the hypothesis expected this mentioned program to reduce the amount of antidepressants consumed in the Netherlands, the sales were proven to unstopably increase.

The statistic outcome regarding the difference in prescriptions between 2011 and 2015 is somewhat compatible with the results obtained in section 4.2.1.1 of our analysis for the consumption in the BAC. The difference in our study was smaller, but we must bear in mind that the Dutch study was comparing year-to-year data and we decided to compare a gathered period of four year, where results can be diluted.

5.1.2. Trends in GP prescribing of psychotropic medications among young patients aged 16–24 years: a case study analysis (22)

In a similar way to the previous one, this Australian article confirmed an increase in the antidepressant consumption during the period in which the data were recorded. Furthermore, even after the number of observed people significantly decreased, the number of psychotropic prescriptions kept rising, thus giving us a glance at the magnitude of the problem regarding the current antidepressant consumption. The consumption results are worrying, but not as much as the fact regarding the drugs prescribed, which clearly went against the recommendations.

The controversy surrounding General Practitioners' antidepressant prescriptions has long been subject of study (39, 40) to the point where two of the analysed articles address this topic. Indeed, an 89% of antidepressant prescriptions issued by GPs in Australia is a high proportion, far larger than the rates of European countries (41).

When it comes to the characteristics of this study, we can see there are some differences when compared to our field research. In the Australian study, the sample size does not correspond to the whole population, but to a selected group of patients prone to psychotropic prescriptions. Therefore, it is not possible to estimate the actual prevalence of antidepressant consumption in the country, but it plausibly gives an idea about the prescription trends.

5.1.3. Psychotropic drug use among 0-17 year olds during 2004-2014: a nationwide prescription database study (23)

This Norwegian article, exploring the psychotropic consumption of children younger than 17 years gives us enough information to understand how unique the relationship with psychotropic drugs is at that age. The prescriptions of psychotropic drugs increased gradually with age, however, in children younger than 13 years those prescriptions rely on the stimulants as a therapy for ADHD. On the contrary, adolescents show a totally different consumption pattern, more similar to that of the adults in which the most important drugs are anxiolytics and antidepressants, specially in girls.

This consumption of antidepressants is in compliance with the prevalence of depression at the studied patients' age (42). Although often sorted into the same

population group, depression in children and adolescents follows totally different prevalence patterns: it does not reach a 1% among children but it can achieve an outstanding 25% in adolescents (43). Most studies attribute this phenomenon to certain age-related changes such as acquired self-awareness, social understanding, organic brain maturation or increased levels of stress, especially in the case of the girls (44).

5.1.4. Psychotropic medication in children and adolescents in the United States in the year 2004 vs 2014 (24)

This was the most contentious article of the revised work, for it calls the perception about the growing utilisation of psychotropic medication in children and adolescents into question. According to their results, there is a general decrease of prescription for every pharmacological group. Nevertheless, if the age groups are independently analysed, we can only see a decrease in the prevalence of people with prescriptions in the toddler group, from a 3.08% in 2004 to 2.63% in 2014, while the prevalence of adolescents with a psychotropic prescription rose nearly two percentage points. In contrast to the claimed prevalence decrease in toddlers, this latter increment was presented as a “slight increase”.

One remarkable data from the study was the one regarding the most prescribed antidepressant: sertraline. This is a singular fact because, as stated in the previous section, only fluoxetine is recommended for this age group (22). It seems to be worth mentioning that in the acknowledgements section, three of the authors recognised to be employees of Novartis Pharmaceuticals Corporation.

To close this section, the suitability of the variable used must be discussed. It is true that the prevalence of prescribed people can express the changes in prescription trends. However, it is not possible to compare these values with the data from the field research performed in our study. In fact, the values of prevalence of prescribed people may differ from data of consumption, as the concomitant use of more than one antidepressant or dosage differences from one patient to another can interfere.

5.1.5. OECD records

The Organisation for Economic Co-operation and Development (OECD) is an international economical organisation financed by its member countries, which happen

to be the wealthiest countries of the world (45). They intend to measure productivity and global flows of trade and investment by analysing and comparing data to predict future trends (46).

The table drafted from the records of this organisation was used to understand the international panorama regarding the antidepressant consumption. However, we should not forget this consumption is not actually the direct consequence of one aetiology, but the result of a complicated mix of depression rates, stigma, wealth, health coverage and availability of treatment (47).

The general increase in the consumption of antidepressants observed in the bibliographic research was also confirmed in this section for most of the countries, but overall there were three different behaviours. In most countries such as the UK, Portugal and, to lesser degree, Spain, antidepressant consumption rose along the 2011-2015 period. In France Hungary or Norway, consumption values stayed quite stable. Finally, in some Nordic countries such as Finland and Denmark, the consumption rates were decreased in this period.

It is not easy to reveal the underlying reasons driving Finland and Denmark's behaviour, but it does not seem to be cultural or based on the health system model, since other Nordic countries with similar conditions (e.g. Iceland) not only did not decrease but increased their antidepressant consumption over the years.

The Health at a Glance dossiers of OECD usually keep a detailed record of government health expenditure and devotes itself to come up with different strategies to cut it back. The drug consumption, as it is at least partially funded by the government in many countries, was a pertinent piece of information which, in the last release of the dossier in 2018 was unreasonably cut out of the records (48).

5.2. FIELD RESEARCH

5.2.1. General tendency

The data obtained from the Health Office of the Basque Government show a significant increase in the consumption of the psychotropic drugs used in psychiatric diseases' therapy (antidepressants and antipsychotics) and a decrease in the ones used

in the field of neurology (anti-dementia drugs) or paediatrics (psychostimulants). In the case of the antipsychotics, the increase can be observed from 2014 on, but when it comes to the antidepressants, consumption keeps rising from the beginning of the recorded data in 2011, although it becomes clearer since 2014. Additionally, the decrease in the anti-dementia drug consumption can only be noticed in the first period, dating from 2010 to 2013, while their consumption becomes stable from that moment on. Psychostimulant consumption starts dropping in 2014, surely as a result of a more severe control of the management of ADHD in childhood.

5.2.2. Specific tendency

If we focus on the comparison in the consumption concerning the periods previous and posterior to the release of the DSM manual, the increase in the drug consumption all over the Basque Country turned out to be significant when it came to the antipsychotics and the antidepressants. In the case of the latter ones, as demonstrated in the point 4.2.1.1, Araba was the region where consumption rose more sharply from the first to the second period. But anyway, it was Gipuzkoa the region where the antidepressant packages consumed per inhabitant turned out to be the highest during the second period (2.91 packages / inhabitant). Bizkaia, the most populated of the three Historical Territories, was also the one where the increase in the consumption of antidepressants was more modest. The decrease in the consumption of anti-dementia drugs and psychostimulants was also significant between both periods, being this tendency more patent in Araba and Gipuzkoa respectively.

Therefore, we could say that, even if the consumption of psychotropic drugs used to treat psychiatric diseases has been rising in the BAC since 2011, it was strengthened after the release of the new mental disease criteria of DSM-5. This increase goes along the same lines as the international results of section 4.2. Since antidepressants and, particularly, SSRI were launched to the market, their consumption does nothing but enlarge (32). It is essential to see the danger in this universal trend, for they are medical drugs whose usage implies as much risk as any other. Antidepressants cause a wide variety of adverse phenomena, some of them can even be life threatening (49) and by increasing their usage we are inevitably increasing the odds for the appearance of unwanted reactions.

5.2.3. Comparison with the control group

Bearing in mind that the new DSM criteria does not affect every mental illness the same way, we decided to assess the probability of a consumption increase in antidepressants as a result of the release of DSM by comparing them to the antipsychotics using an Odds Ratio analysis. The decision of choosing these drugs as a control group was not easy. Stimulants and anti-dementia drugs were also considered, but their circumstances tipped the scales in favour of the antipsychotics. To begin with, stimulants and anti-dementia drugs are mostly used in a specific kind of patients of a very narrow age range and, besides, both pharmacological groups showed an evident decrease in their consumption over the years. As this suggested the existence of external forces influencing the consumptions of these drugs, there was no other choice but to dismiss them.

The OR results show a relative increment of the antidepressant consumption in the BAC with respect to the antipsychotics after the appearance of DSM-5. This increase was specifically noteworthy in the case of Bizkaia. This conclusion reinforces the hypothesis which suggested that the new specific criteria for the diagnosis of depression has led to an overdiagnosis of this illness and its subsequent treatment with antidepressants.

Notwithstanding the clear evidence reinforcing our hypothesis in the whole territory, the statistical significance endorsing the antidepressant consumption increase was not observed in two of the Historical Territories of the BAC: Araba and Gipuzkoa. This suggests the results of this study should be interpreted with the utmost caution, considering other alternatives to the consumption increase. In fact, we should not forget that antidepressant consumption is a multifactorial reality (45) and it cannot be easily judged despite the results of this study.

5.2.4. Most consumed antidepressants' analysis

The final results, concerning the analysis of the most popular antidepressants, give us some substantial information regarding escitalopram. In fact, it was the most prescribed antidepressant during the 2010-2013 period and even though it showed the most significant decrease between both periods, it currently maintains its privileged

position. Trazodone, on his behalf, was the antidepressant presenting the biggest growth.

Finally, the fact that the four most consumed antidepressants only made 43.89% of the total consumption entails a transversal and balanced use of the current available drugs.

6. CONCLUSION

Antidepressants are widely consumed drugs, a consumption which has been constantly rising since they were launched to the market. The results of this study have objectified this increase in all the analysed aspects.

- The available bibliography showed an ongoing international increase in the antidepressant consumption. However, this evidence is still scarce and we may have to wait more for the number of articles analysing the influence of DSM-5 to enlarge.
- The statistical analysis of our health environment consumption data demonstrated an overall antidepressant consumption increase in the BAC which became consolidated after the release of the mentioned manual. This increase was still significant when compared to the antipsychotics as a control group.

At any rate, given the multifactorial motivation of antidepressant usage, it was not possible to fully prove a direct relationship between the DSM and this increasing tendency. Nevertheless, due to the present inaction and complacency against this rising trend, our society may be facing a complex situation with not only medical but also political and philosophical implications that may shake its foundations in the future.

7. ACKNOWLEDGEMENTS

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8. CONFLICTS OF INTEREST

There is no conflict of interests in this work.

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10. APPENDIX

Table 9. Overall gross quantity of antipsychotic drug packages consumed in both periods.

Consumed antipsychotic packages	BAC	Bizkaia	Gipuzkoa	Araba
First Period: 2010-2013	2,358,240	1,336,436	663,563	277,210
Second Period: 2014-17	2,507,971	1,351,757	722,890	316,349

Table 10. Consumed antipsychotic drug packages adjusted to the population of every territory.

Antipsychotic consumption (packages/inhabitant)	BAC	Bizkaia	Gipuzkoa	Araba
First Period: 2010-2013	1.078333554	1.155990506	0.933680505	0.865907827
Second Period: 2014-17	1.144939201	1.176320553	1.007829644	0.9761749

Table 11. Overall gross quantity of anti-dementia drug packages consumed in both periods.

Consumed Anti-dementia drug packages	BAC	Bizkaia	Gipuzkoa	Araba
First Period: 2010-2013	711,363	442,823	206,021	44,495
Second Period: 2014-17	530,920	305,011	159,290	30,442

Table 12. Consumed anti-dementia drug packages adjusted to the population of every territory.

Anti-dementia drug consumption (packages/inhabitant)	BAC	Bizkaia	Gipuzkoa	Araba
First Period: 2010-2013	0.325279273	0.383033070	0.289886252	0.138986937
Second Period: 2014-17	0.242375658	0.265425449	0.222076919	0.093936495

Table 13. Overall gross quantity of stimulant drug packages consumed in both periods.

Consumed Stimulant packages	BAC	Bizkaia	Gipuzkoa	Araba
First Period: 2010-2013	1,065,729	608,614	329,544	88,423
Second Period: 2014-17	702,843	444,498	229,212	62,100

Table 14. Consumed stimulant drug packages adjusted to the population of every territory.

Stimulant (packages/inhabitant)	BAC	Bizkaia	Gipuzkoa	Araba
First Period: 2010-2013	0.487317381	0.526438981	0.46369193	0.276202763
Second Period: 2014-17	0.320861965	0.386809266	0.319559889	0.191625266