Cardiovascular risk factors in chronic treatment with antipsychotic agents used in primary care

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Aim. To compare the prevalence of cardiovascular risk factors (CVRF) and vascular events, between patients treated and untreated with antipsychotic drugs.

Subjects and methods. A cross-sectional study was done in Barcelona. We compared patients attended in Primary Health Care Centres, treated with or without antipsychotics between 2008 and 2010. Anthropometric measurements, clinical variables, and CVRF were assessed. Adult and elderly patients, typical and atypical antipsychotics, were studied separately.

Results. 14,087 patients had been prescribed antipsychotics (63.4% atypical), the most common being risperidone. We selected 13,724 patients with the same age and gender but not treated (total of 27,811 patients). Patients receiving antipsychotic had higher prevalence of obesity (16.9% vs. 11.9%), smoking (22.2% vs. 11.1%), diabetes mellitus (16% vs. 11.9%), and dyslipidemia (32.8% vs. 25.8%) ($p < 0.001$). The prevalence of stroke was significantly higher in the treated patients, both in adults (odds ratio = 2.33) and the elderly (odds ratio = 1.64). The prevalence of coronary heart disease was similar in both groups (odds ratio = 0.97). Among patients treated with antipsychotic, differences were not observed depending typical or atypical ones.

Conclusions. Patients treated with antipsychotic drugs had a greater prevalence of several CVRF (diabetes mellitus, obesity, and smoking). The presence of stroke was higher in those treated with antipsychotics. No relevant differences were observed between patients receiving typical or atypical antipsychotics.

Key words. After treatment. Antipsychotic agents. Antipsychotic effect. Cardiovascular disease. Cerebrovascular disorder. Primary care.

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Introduction

Over the last decade the consumption of antipsychotic drugs in Spain has increased considerably from 1.5 to 8.7 DHD (defined daily dose 1000 inhabitants/day) [1]. The principal indications for this pharmacological group are the treatment of schizophrenia, acute and chronic psychosis, generalized anxiety, and bipolar disorder amongst others. The use of antipsychotics in the elderly, a practice widely extended in Spain and other European countries, is controversial due to their secondary effects which are particularly evident in patients suffering from dementia. In fact, the risk of an elderly patient suffering a severe secondary effect is tripled when taking antipsychotics [1].

Antipsychotics are classified into two groups: the classic or typical ones (TAD), dating back to more than fifty years, and which include haloperidol and chlorpromazine amongst others; and the atypical (AAD), such as risperidone, olanzapine, quetiapine, clozapine, and ziprasidone, which have appeared more recently on the market. The TAD are frequently associated with such secondary effects as extrapyramidal disorders (Parkinson's disease, dystonia, tardive dyskinesia, and neuroleptic malignant syndrome), anticholinergic effects, confusion, somnolence, and blood dyscrasia. The main argument for the utilization of the AAD was to improve the security profile of the TAD. However, secondary effects resulting from the AAD have been observed and include cardiovascular diseases and metabolic alterations such as diabetes mellitus, weight increase, and changes in the lipid profile [2]. The frequency of these secondary effects varies according to the drug. For example, weight increase is associated with cloropromazine, olanzapine, and clozapine [3].

Cardiovascular risk factors are, moreover, already common in patients receiving antipsychotic treatment, the most prevalent being smoking, high blood pressure, dyslipidemia, and diabetes mellitus [4]. The impact of these risk factors can be increased by problems with treatment compliance and non-pharmacological measures adopted by psychiatric patients. In addition, the commencement of antipsy-

chotic medication can worsen the evolution of patients with baseline hyperglycemia and increase the risk of hospitalization [5]. More serious effects such as stroke and increased risk of mortality have been reported in patients treated with both TAD [6] and AAD [7] for symptoms associated with dementia. Because of the above, the European Medication Agency recently included within its Seventh Framework Program the long-term evaluation of the secondary effects of this type of drug, with particular interest in elderly patient mortality and associated risk factors, as a research priority [8]. Due to their brief duration and the type of population included, clinical trials present limitations for detecting secondary effects arising from antipsychotics. It is, therefore, useful to draw on other kinds of studies such as case control ones or examine registers from health workers [9].

The increasing implementation of electronic health record (EHR) has permitted the creation of large, clinical population databases which can be used for research. One of the fields in which these data bases have been employed is for the detection of disturbances associated to the use of drugs.

The Institut Català de la Salut (ICS) provides coverage for 80% of the population of Barcelona. All of its centers use the same EHR (known as eCAP) which began in 2005. EHR permit the carrying out of baseline population studies with data gathered by healthcare professionals.

The objective of our study is to describe the prevalence of cardiovascular risk factors, through the comparison of patients with similar characteristics who are either receiving or not antipsychotic drugs. A secondary objective is to compare whether the profile of those cardiovascular risk factors differs between patients treated with TAD and those receiving AAD.

Patients and methods

Study design

A cross-sectional study of a database from a patient population with and without prescribed antipsychotic drugs as registered from 1st January, 2008, to 31st December, 2010, in the EHR.

Selection of study subjects

The population was made up of patients aged between 18 and 95 years who had been prescribed one or more antipsychotic drug for a period of at least 12 months during the study period. Their inclusion was on the 31st December, 2010, from the 51 Primary Health Care Centers (PHC) of the ICS in Barcelona (970, 000 inhabitants). For each patient treated with antipsychotics (TP), a non-treated patient (NTP) with matching age, gender, and assigned General Practitioner was randomly paired. Those patients classified as deceased or who had moved away from the city were excluded.

Measurements and outcomes

The following variables were studied using anonymous data obtained from the EHR:

Socio-demographics variables

Age, gender, assigned general practitioner and PHC.

Antipsychotic drugs

Categorized according to the Anatomical Therapeutic Chemical classification system: N05AA; N05AB; N05AC; N05AD; N05AF; N05AG; N05AL; N05AE; N05AH; N05AX. If the following drugs had been prescribed for more than one year they were grouped as:

- *TAD:* cloropromazine, levomepromazine, flufenazine, perfenazine, trifluoperazine, periciazine, pipotiazine, droperidol, haloperidol, zuclopentixol, pimozide, sulpiride, tiapride, clotiapine.
- *AAD:* sertindol, ziprasidone, clozapine, olanzapine, quetiapine, amisulpride, paliperidone, risperidone, aripiprazol.
- *Mixed:* antipsychotic drugs from the previous two groups prescribed for more than one year.

Data concerning health

Data concerning health according to the Tenth Edition of the International Classification of Diseases (CIE-10) was obtained in relation to the following diagnoses: psychotic disorders (F20, F21, F22, F23, F24, F25, F28, F29, F30, F31), behavioral disorders (F05, F06, F07, F08, F09), stroke (I64, I65, I66, I67), peripheral vascular diseases (I73), transitory cerebral ischemia attacks (G45), dementia (G46), Alzheimer's disease (G30), and cerebrovascular disease (F00, F01, F02 and F03), convulsions (G40), extrapyramidal events (G25, G26, R25, R56), amenorrhea (N91.1, N91.2), erectile dysfunction (F52.2), drug-induced cataracts (H25, H26.9), blood dyscrasia (D60, D61.1), psychotropic intoxication (T43), high blood pressure (I10, I11, I12, I13, I14, I15), coronary heart disease (I20, I21, I22, I24, I25), diabetes mellitus (E10, E11, E12, E13, E14), and dyslipidemia (E78).

Clinical and analytical variables

Anthropometric variables –weight, height, waist circumference, body mass index (BMI) as registered in the clinical records or calculated by dividing weight in kilos by squared height in meters–, smoking habits, blood pressure, glycaemia, total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides, and Hb_{A1c}. With the exception of height, a reasonably stable variable in adulthood, and which was calculated as an average of all the values registered in the EHR, the remaining variants were calculated as an average taken from the values registered during the study period.

Statistical analysis

Analysis was performed separately for the two age groups: patients aged between 18 and 64 years and those aged 65 and older. The chi-square test was employed in order to compare the percentage of information on cardiovascular factors in clinical records, between TP and NTP. Logistic regression was used to compare the prevalence of risk factors and clinical and analytical variables between TP and NTP, and between patients treated with AAD and TAD. The dependent variable was the presence or not of a risk factor (or change in parameter) whilst the independent variable was the group the patient belonged to (TP vs. NTP and AAD vs. TAD). Age and gender were included in the model as possible confounding variables. The odds ratio (OR) are shown with their 95% confidence intervals.

Results

14,087 TP met the inclusion criteria; 13,724 NTP adjusted for date of birth, gender, and assigned General Practitioner were matched. The total number of study participants was, therefore, 27,811.

No important differences in demographic characteristics were observed between the TP and NTP groups (Table 1). 53.4% of the participants were women. 27.5% of the TP had received only TAD, 63.4% only AAD, and 9. 1% both types of antipsychotics. This last group was excluded from the analysis of comparison because they could not be included into either of the two groups (AAD or TAD).

Globally, the antipsychotics most prescribed were: risperidone (26.5%) olanzapine (24.7%), quetiapine (22.7%), and haloperidol (10.3%). Distribution varied according to age. Patients younger than 65 received: olanzapine (32.7%), risperidone (24.1%), quetiapine (20.6%), and much less frequently haloperidol (3.9%). In contrast, patients aged over 65 were prescribed: risperidone (30.0%), quetiapine (25.8%), olanzapine (12.6%), and haloperidol (7.2%).

Significant differences were observed ($p < 0.001$) between the TP and NTP groups with respect to the prevalence of obesity (16.9% vs. 10.6%), smoking (22.2% vs. 11.1%), diabetes (16% vs. 11.9%), and dyslipidemia (32.8 vs. 25.8%) (Table I).

Regarding symptoms classically considered as adverse effects of antipsychotic drugs, statistically significant differences were reported between TP (8.5%) and NTP (3.1%) aged less than 65 years. Differences were not, however, observed in elderly patients (around 19.5%). The most common were convulsions (3.2%), extrapyramidal events (2.4%), and amenorrhea (1%).

Differences in the spectrum of registered diagnoses and the type of treatment according to the age of the patient (over or under 65 years) were reported.

Psychiatric diseases (51.4%) were more frequent than neurological ones (2.2%) in adult patients whilst in those aged 65 or more neurological diseases (35.8%) were more commonly found. With respect to the type of drug used, the AAD were more frequently prescribed in patients aged less than 65 years (75.4% vs. 62%) and TAD in the elderly (38% vs. 24.6%). For this reason, a stratified analysis was performed for age groups assuming that the profile of the patient being prescribed an-

Table I. General characteristics of the patients.

		Treated patients (n = 14,087)	Non-treated patients (n = 13,724)	p
Age	18-64 years	8,440 (59.9%)	8,424 (61.4)	0.012
	≥ 65 years	5,647 (40.1%)	5,300 (38.6)	
Female		7,522 (53.4%)	7,337 (53.5%)	NS
Obesity		2,381 (16.9%)	1,455 (10.6%)	< 0.001
Smoking		3,127 (22.2%)	1,523 (11.1%)	< 0.001
Hypertension		4,663 (33.1%)	4,611 (33.6%)	NS
Coronary heart disease		747 (5.3%)	686 (5.0%)	NS
Diabetes mellitus		2,254 (16.0%)	1,633 (11.9%)	< 0.001
Dyslipidemia		4,550 (32.3%)	3,541 (25.8%)	< 0.001

Percentages are calculated from the total of the column. NS: non-significant.

Table II. Percentage of each variable log in electronic health records.

	18-64 years			≥ 65 years		
	Treated patients (*n* = 8,440)	Non-treated patients (*n* = 8,424)	*p*	Treated patients (*n* = 5,647)	Non-treated patients (*n* = 5,300)	*p*
Smoking status	65.7	43.0	< 0.001	66.4	70.4	< 0.001
Body mass index	41.4	26.5	< 0.001	47.3	57.2	< 0.001
Weight	42.7	27.6	< 0.001	49.4	58.6	< 0.001
Height [a]	60.4	42.8	< 0.001	67.3	73.1	< 0.001
Waist abdominal circumference	6.2	2.0	< 0.001	91.4	90.0	0.012
Systolic blood pressure	59.6	41.6	< 0.001	79.5	79.2	0.741
Diastolic blood pressure	59.6	41.6	< 0.001	79.6	79.2	0.620
Total cholesterol	63.3	42.5	< 0.001	71.8	69.8	0.027
LDL cholesterol	50.0	32.1	< 0.001	62.8	63.4	0.566
HDL cholesterol	50.9	32.7	< 0.001	63.1	63.5	0.706
Triglycerides	54.9	35.4	< 0.001	65.9	65.2	0.444
Glycaemia	63.5	42.7	< 0.001	72.2	70.1	0.016

Percentages are calculated from the total of the column. HDL: high density lipoprotein; LDL: low density lipoprotein. [a] Height measured from start-up of the patient's clinical record.

tipsychotics differed according to whether the patient was an adult (18 to 64 years) or an elderly individual (65 years or more).

Differences between TP and NTP

Adults (18-64 years)

The TP presented a higher percentage of all the analyzed variables registered in EHR than the NTP ($p < 0.001$) (Table II).

Amongst the TP the prevalence of smoking status (OR = 1.98), dyslipidemia (OR = 1.81) and diabetes mellitus (OR = 1.71) was higher than the NTP (Table III). In a similar manner, a higher percentage of individuals with hypertriglycemia (OR = 1.80), low HDL (OR = 1.95), and BMI > 30 (OR = 1.64) (Table III) was observed. However, in the NTP group, the percentages of patients with poorly controlled blood pressure (≥ 140/90 mmHg) and diabetic patients with bad control of Hb_{A1c} (> 7 %) were higher than in the TP (Table IV).

Regarding vascular diseases, in general, a greater prevalence of cerebrovascular events were observed, particularly stroke (OR = 2.33). The frequency of coronary heart disease (CHD) was similar for both groups (Table III).

Elderly patients (≥ 65 years)

In this age group the registered anthropometric variables and smoking habits were higher in the NTP than the TP. In contrast, glycaemia recording was higher in the TP (Table II). Only smoking (OR = 1.36) and diabetes mellitus (OR = 1.28) were more commonly observed in the TP than in the NTP. This was not the case with HBP and dyslipidemia: as with the adult patients, a higher percentage of hypertriglycemia, low HDL cholesterol, and BMI > 30 was reported. The percentage of poorly controlled blood pressure, and Hb_{A1c} in diabetic patients, was similar to the adult group (Table IB). In the elderly group a greater prevalence of stroke (OR = 1. 64), but not CHD, was observed in the TP (Table III).

Table III. Distribution of diagnosis between treated and non-treated patients according to age.

	18-64 years			≥ 65 years		
	Treated patients (*n* = 8,440)	Non-treated patients (*n* = 8,424)	*Odds ratio* [a] (95% CI)	Treated patients (*n* = 5,647)	Non-treated patients (*n* = 5,300)	*Odds ratio* [a] (95% CI)
Cerebrovascular disease	2.2%	1.3%	1.70 (1.34-2.16)	15.8%	11.1%	1.46 (1.29-1.62)
Stroke	1.4%	0.6%	2.33 (1.67-3.26)	10.3%	6.3%	1.64 (1.42-1.89)
Smoking	62.3%	45.0%	1.98 (1.81-2.16)	12.4%	9.5%	1.36 (1.16-1.58)
Hypertension	13.8%	12.9%	1.09 (0.99-1.20)	57.2%	63.0%	0.77 (0.71-0.83)
Coronary heart disease	1.5%	1.6%	0.97 (0.76-1.25)	10.5%	10.4%	0.97 (0.85-1.09)
Dyslipidemia	23.1%	14.9%	1.81 (1.68-1.98)	37.8%	38.6%	0.99 (0.91-1.07)
Diabetes mellitus	8.2%	4.9%	1.71 (1.50-1.95)	24.3%	21.3%	1.28 (1.17-1.41)

Percentages are calculated from the total of the column (reference category: non-treated patients). 95% CI: 95% confidence interval. [a] Adjusted for age and gender.

Differences observed between TAD and AAD

Adults (18-64 years)

No statistically significant differences were observed between the two groups with respect to the prevalence of clinical variables, vascular diseases or cardiovascular risk factors with the exception of smoking which was higher in those treated with AAD (Tables V and VI). Neither were differences observed amongst the core components when analyzed separately.

Elderly patients (≥ 65 years)

In this group, patients treated with AAD presented a higher percentage of dyslipidemia and HBP (Table V), lower levels of HDL cholesterol (Table VI), and well-controlled BP. The rest of the variables did not differ between TAD and AAD.

No statistically significant differences were observed when analyzing the same variables with respect to a specific AAD (risperidone, olanzapine, and quetiapine).

Discussion

In our study it was observed that individuals treated with antipsychotics presented metabolic alterations such as obesity and an unfavorable lipid profile (high levels of triglycerides and low HDL cholesterol) more frequently, and a greater prevalence of smoking and diabetes mellitus (although with a better glycemic control), than untreated ones. In contrast, high blood pressure was more common in those not receiving antipsychotic drugs.

The comparison between AAD and TAD revealed fewer differences: a higher prevalence of smoking in adults treated only with AAD, and a greater proportion of patients with HBP and dyslipidemia in elderly patients receiving TAD.

There has been a recent, marked increase in the prescription of AAD which were originally commercialized as presenting a more favorable profile with respect to secondary effects, particularly extrapyramidal ones, than the TAD. Shortly after the introduction of the AAD, a number of studies were published which drew attention to their metabolic effects and how they could influence cardiovascular morbi-mortality. In one study which compared the effects of the two groups of drugs, TAD and AAD, it was reported that use of the AAD was also associated with an unfavorable metabolic profile.

Our study has been performed with data from the EHR (named eCAP) of a considerable number of patients which has permitted the detection of relations that could have been otherwise missed in a smaller sample size. Moreover, the characteristics of the individuals included has meant that biases found in clinical trials, which have far more rigorous inclusion criteria which can affect the external validity of the results, have been avoided. However,

Table IV. Percentage of patients presenting clinical or metabolic alterations according to age.

	18-64 years			≥ 65 years		
	Treated patients	Non-treated patients	*Odds ratio* [a] (95% CI)	Treated patients	Non-treated patients	*Odds ratio* [a] (95% CI)
Glycaemia ≥ 6.99 mmol/L	5,348 (7.7%)	3,592 (7.7%)	1.07 (0.91-1.26)	4,068 (17.2%)	3,703 (17.1%)	1.01 (0.90-1.14)
Triglycerides ≥ 1.71 mmol/L	4,625 (38.8%)	2,979 (26.3%)	1.80 (1.62-2.00)	3,716 (27.5%)	3,448 (22.4%)	1.32 (1.18-1.47)
Total cholesterol > 6.22 mmol/L	5,313 (20.0%)	3,559 (20.8%)	1.02 (0.91-1.13)	4,034 (15.6%)	3,676 (16.9%)	0.92 (0.82-1.05)
LDL cholesterol > 4.14 mmol/L	4,210 (18.6%)	2,687 (20.6%)	0.92 (0.82-1.04)	3,533 (12.9%)	3,337 (13.1%)	0.99 (0.86-1.14)
HDL cholesterol < 1.27 mmol/L (F) < 1.01 mmol/L (M)	2,022 (37.6%)	1,407 (23.3%)	1.95 (1.67-2.27)	2,353 (35.0%)	2,239 (24.7%)	1.65 (1.45-1.88)
Blood pressure > 140/90 mmHg	4,992 (14.9%)	3,465 (19.5%)	0.73 (0.65-0.82)	4,418 (24.2%)	4,098 (35.8%)	0.57 (0.52-0.63)
Body mass index > 30	3,247 (40.0%)	2,090 (35.3%)	1.64 (1.45-1.84)	2,467 (43.7%)	2,791 (39.2%)	1.17 (1.05-1.32)
Hb_{A1c} > 7% in diabetic patients	514 (36.2%)	285 (54.7%)	0.46 (0.34-0.61)	1,039 (33.7%)	898 (39.9%)	0.76 (0.63-0.92)

Percentages are calculated from the total of the column (reference category: non-treated patients). F: females; M: males; 95% CI: 95% confidence interval; HDL: high density lipoprotein; LDL: low density lipoprotein. [a] Adjusted for age and gender.

the design of our study does not allow establish causality.

It is noteworthy that diagnosis varied with age. Psychiatric diagnoses were predominant in the younger patients whilst neurologic ones were more common in older individuals. For this reason we carried out analysis stratified by age groups with a cut-off of 65 years.

The prevalence of diabetes mellitus was significantly higher in the TP than in the NTP although it was lower than that observed in the general population (13.8%) [10] and similar to other previously published studies [11]. The possible relationship between antipsychotics and diabetes mellitus is controversial. Changes in glucose regulation in psychiatric patients, irrespective of antipsychotic treatment [12,13], have been reported which indicate a resistance to insulin. It has been speculated that the two disorders, diabetes mellitus and psychosis, might share a common genetic base [14]. Nevertheless, weight gain and worsening of glucose metabolism associated with antipsychotic treatment could favor the development of diabetes mellitus [15]. In spite of the fact that some authors had detected an increase of diabetes mellitus in patients treated with AAD, particularly olanzapine [16], we did not observe differences in its prevalence between the two kinds of antipsychotics.

As observed in previous studies, a greater prevalence of obesity (BMI > 30) was reported in the TP than in the NTP (without observing differences among the various antipsychotics), particularly in the adult group [17,18]. Such observation has been related to the increase in leptin levels caused by AAD (especially clozapine and olanzapine, and to a lesser degree quetiapine and risperidone) and less frequently by TAP such as haloperidol [19].

A greater prevalence of dyslipidemia was reported in adult patients treated with antipsychotics compared to elderly ones. Both age groups presented high levels of triglycerides and low ones of HDL cholesterol, but not high total cholesterol and LDL cholesterol.

The studies available concerning the lipid metabolism of antipsychotics have a small sample size and are of short duration. Some case control studies have detected a greater risk of hypercholesterolemia developing in patients treated with most of the antipsychotics. In contrast, others have not found any relationship between the type of antipsychotic drug and the diagnosis of dyslipidemia [20,21].

The predominant pattern appears to depend more on the kind of antipsychotic prescribed: for example, olazapine and clozapine have been associated with higher levels of cholesterol and triglycerides than haloperidol and risperidone [22-24].

Concerning HBP, prevalence was only lower in elderly treated patients receiving AAD. The percentage of poorly controlled patients was higher in the TP irrespective of age.

The effects of antipsychotics on blood pressure are controversial and barely mentioned in the literature, although falls due to orthostatic hypotension and hypertensive crisis have been described associated with the treatment with risperidone [17,25]. The prevalence of smoking was higher in the TP, particularly in adult patients, although slightly inferior to that found in other studies with psychotic populations (65-85%) [26]. This could be explained by the fact that the TP group included psychiatric pathologies besides schizophrenia, or that different methodologies were employed. The percentage of smoking in the NTP group was less than the general Spanish population (31.4%) [27] which was probably due to the fact that they were being attended

Table V. Percentage of patients presenting health problems according to age group and type of antipsychotic they are receiving.

	18-64 years			≥ 65 years		
	Atypical (*n* = 5,603)	Typical (*n* = 1,831)	*Odds ratio* [a] (95% CI)	Atypical (*n* = 3,332)	Typical (*n* = 2,039)	*Odds ratio* [a] (95% CI)
Stroke	1.4	1.7	1.15 (0.75-1.77)	10.9	9.3	1.04 (0.86-1.26)
Smoking	63.6	55.5	1.15 (1.01-1.33)	12.3	12.0	0.97 (0.78-1.21)
Hypertension	12.0	19.2	0.87 (0.75-1.01)	55.3	61.5	0.74 (0.66-0.83)
Coronary heart disease	1.4	2.1	0.99 (0.66-1.47)	10.6	10.2	0.93 (0.77-1.11)
Dyslipidemia	21.4	28.6	0.93 (0.82-1.06)	36.2	41.3	0.88 (0.79-0.99)
Diabetes mellitus	7.1	10.8	0.90 (0.74-1.08)	24.2	24.6	0.97 (0.85-1.11)

Percentages are calculated from the total of the column (reference category: typical antipsychotic drugs). 95% CI: 95% confidence interval. [a] Adjusted for age and gender.

by a General Practitioner. Among the treated adult patients, but not the elderly ones, smoking was higher in those receiving AAD.

A positive relationship has been described, in both psychiatric and other pathological disorders, between treatment with haloperidol or risperidone [28] and cigarette consumption. It has been postulated that patients consume tobacco as a form of auto-medication to decrease the secondary effects of antipsychotics and, in addition, these substances lessen the capacity to give up smoking. In contrast, other antipsychotics such as clozapine could promote the cessation of smoking and have been associated with a lower consumption of tobacco.

In our study there was a greater prevalence of stroke amongst treated patients than non-treated ones, irrespective of the type of antipsychotics prescribed. Although our study design cannot draw causal relationships, the odds ratio observed of stroke (1.5-2.0) is similar to that of recently published meta-analysis (1.3-2.0) [29].

Whilst it was first thought that the AAD presented a greater risk of suffering a stroke [30] more recent data have contradicted this affirmation [31].

No significant differences were observed for CHD between TP and NTP or between different kinds of antipsychotics. A recent meta-analysis did not find any association between the use of antipsychotics and an increased risk of acute CHD [32]. More than ischemia, prolongation of the QT interval has been associated with the predisposition of patients to arrhythmias and sudden death.

Whilst our results are valuable, the study has some limitations. The first is that there is a possibility of incorrect patient assignation. In spite of the fact that a large number of the population receive primary healthcare, and that the drugs studied must have a medical prescription, it is possible that the medical records did not include a number of patients receiving antipsychotic drugs given that a considerable number of mental health centers in Barcelona do not use the same information technology as PHC. Nevertheless, as one of the principal functions of EHR is to give patients access to the funding of their medication, it appears to be unlikely that health workers would have omitted these treatments in their clinical records. Neither have data referring to treatment and patient compliance been analyzed. Consequently there exists the possibility that some individuals assigned to the TP group were not actually receiving treatment. Nevertheless, errors in patient assignment would have minimally affected the estimation of association observed in the present study.

Treatment with antipsychotics tends to be long-term. Although the study period was limited to three years it did not prevent us from ascertaining the duration of prior exposure of the individuals participating and the type of drugs they had previously taken.

As the data came from clinical care some of the variables of interest, particularly NTP aged less than 65 years, were not registered in the participants' clinical records during the study period and could not be analyzed.

Table VI. Percentage of patients presenting clinical or metabolic alterations according to age group and type of antipsychotic they are receiving.

	18-64 years			≥ 65 years		
	Atypical	Typical	*Odds ratio* [a] (95% CI)	Atypical	Typical	*Odds ratio* [a] (95% CI)
Glycaemia ≥ 6.99 mmol/L	3,501 (6.5%)	1,168 (10.0%)	0.84 (0.66-1.07)	2,360 (17.3%)	1,501 (16.7%)	1.08 (0.90-1.28)
Triglycerides ≥ 1.71 mmol/L	2,995 (38.3%)	1,046 (37.3%)	1.07 (0.92-1.24)	2,138 (27.6%)	1,407 (27.9%)	1.04 (0.89-1.21)
Total cholesterol > 6.22 mmol/L	3,470 (19.3%)	1,174 (23.3%)	0.99 (0.82-1.14)	2,342 (14.7%)	1,505 (17.0%)	0.96 (0.80-1.15)
LDL cholesterol > 4.14 mmol/L	2,711 (18.1%)	970 (21.9%)	0.89 (0.73-1.07)	2,025 (12.1%)	1,341 (14.0%)	0.93 (0.76-1.14)
HDL cholesterol < 1.27 mmol/L (F) < 1.01 mmol/L (M)	1,259 (36.5%)	554 (37.2%)	0.89 (0.72-1.10)	1,290 (38.5%)	959 (31.0%)	1.30 (1.09-1.56)
Body mass index > 30	1,984 (43.8%)	679 (49.6%)	0.92 (0.77-1.10)	1,265 (40.1%)	930 (47.6%)	0.85 (0.72-1.02)
Blood pressure > 140/90 mmHg	3,226 (14.1%)	1,150 (16.5%)	0.96 (0.79-1.16)	2,558 (21.8%)	1,653 (28.1%)	0.74 (0.64-0.86)

Percentages are calculated from the total of the column of each parameter (category of reference: typical antipsychotics). F: females; M: males; 95% CI: 95% confidence interval; HDL: high density lipoprotein; LDL: low density lipoprotein. [a] Adjusted for age and gender.

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Factores de riesgo cardiovascular en el tratamiento crónico con antipsicóticos en atención primaria

Objetivo. Comparar la prevalencia de factores de riesgo cardiovascular (FRCV) y eventos vasculares en pacientes tratados con antipsicóticos, comparándolos con los no tratados.

Sujetos y métodos. Estudio descriptivo transversal de pacientes atendidos en atención primaria de la ciudad de Barcelona y tratados con antipsicóticos entre el 2008 y el 2010, comparándolos con una población no tratada. Se registraron las variables antropométricas y clínicas y los FRCV. Se estudió por separado a pacientes adultos y ancianos, y a los tratados con antipsicóticos típicos y atípicos.

Resultados. Un total de 14.087 pacientes habían sido tratados con antipsicóticos (63,4% atípicos). El más prescrito fue la risperidona. Se aparejaron 13.724 pacientes de la misma edad y género, pero no tratados (*n* total = 27.811). Los tratados con antipsicóticos presentaron una prevalencia superior de obesidad (16,9% frente a 10,6%), tabaquismo (22,2% frente a 11,1%), diabetes mellitus (16% frente a 11,9%) y dislipemia (32,8% frente a 25,8%) ($p < 0,001$). La prevalencia de accidente vascular cerebral fue significativamente superior entre los tratados, tanto en los adultos (*odds ratio* = 2,33) como en los ancianos (*odds ratio* = 1,64). La prevalencia de cardiopatía isquémica fue similar en ambos grupos (*odds ratio* = 0,97). No se observaron diferencias significativas entre los tratados con un antipsicótico típico o atípico.

Conclusiones. Los pacientes tratados con antipsicóticos presentaron una mayor prevalencia de FRCV (diabetes, obesidad y tabaquismo). La presencia de ictus fue superior entre los tratados con antipsicóticos. No se detectaron diferencias importantes entre los pacientes tratados con antipsicóticos típicos y atípicos.

Palabras clave. Antipsicóticos. Atención primaria. Efecto antipsicótico. Enfermedad cardiovascular. Postratamiento. Trastorno cerebrovascular.