


Prevalence of the Use of Aspirin and Statins for Preventing Cardiovascular Events in the Colombian Population with Type 2 Diabetes Mellitus: Comparison of 2008 and 2018

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Abstract

Background: Type 2 diabetes mellitus (T2DM) greatly increases cardiovascular risk. Primary and secondary cardiovascular prevention lead to lower cardiovascular events, improved quality of life and lower costs related to complications. **Objective:** To estimate the proportion of patients with T2DM undergoing drug therapy for cardiovascular prevention (aspirin and statins) in Colombia and to describe the change in patterns of use between 2008 and 2018. **Methods:** This was a cross-sectional study comparing prescriptions for aspirin and statins in 2008 and in 2018 in outpatients diagnosed with T2DM. Records were obtained from a national drug claim database. The proportion of use of cardiovascular prevention drugs and antidiabetic drugs, medications for comorbidities and sociodemographic variables were analyzed for both periods. **Results:** In total, 26 742 patients in 2008 and 188 321 in 2018 with a diagnosis of T2DM treated with antidiabetic drugs were identified, among whom 57.5% and 44.2% received aspirin and 44.9% and 60.2% received statins, respectively. The use of high-intensity statins increased from 1.1% in 2008 to 95.2% in 2018. The probabilities of receiving drugs in 2008 and in 2018 were higher for men (OR: 1.12, 95% CI: 1.06–1.17 and OR: 1.26, 95% CI: 1.23–1.28, respectively), for those persons over 75 years of age (OR: 6.5, 95% CI: 5.3–7.9 and OR: 5.8, 95% CI: 5.4–6.2) and for those who also received clopidogrel (OR: 5.8, 95% CI: 4.4–7.6 and OR: 2.2, 95% CI: 2.1–2.4). **Conclusions:** The use of high-intensity statins in patients with T2DM has increased significantly in the last decade, which should reduce cardiovascular events, morbidity and mortality.

Keywords

Type 2 diabetes mellitus, cardiovascular diseases, aspirin, hydroxymethylglutaryl-CoA reductase inhibitors, hypolipidemic agents, pharmacoepidemiology

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Introduction

Chronic noncommunicable diseases are currently considered an epidemic.^{1–3} Among the leading causes of death globally are pathologies of cardiovascular origin, which are strongly linked to type 2 diabetes mellitus (T2DM), dyslipidemia, and high blood pressure (HBP). According to various reports, cardiovascular disease is the leading cause of death worldwide, including Latin America and Colombia.^{2–4}

T2DM greatly increases cardiovascular risk.^{5,6} Globally, the population with T2DM numbers 476 million, and when standardized by age, the global prevalence of T2DM is

5.8%. In Colombia, the estimated prevalence is between 4% and 8%.⁷ In the absence of adequate control and preventive measures, the pathology of T2DM entails a higher incidence of acute myocardial infarction and other

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cardiovascular conditions.⁵ Recommendations for cardiovascular prevention in this population include healthy lifestyle habits and pharmacological therapies for controlling blood sugar, blood pressure, dyslipidemia, and platelet aggregation. These last 2 therapies have also been used in primary cardiovascular prevention.^{8,9}

Primary and secondary cardiovascular prevention result in decreased cardiovascular events, improved quality of life and lower costs related to complications.¹⁰ However, despite guidelines and evidence supporting the efficacy and safety of lipid-lowering therapies, between 4% and 79% of patients with high cardiovascular risk and diabetes adhere to treatment, with a smaller percentage achieving glycemic control and serum cholesterol treatment goals.^{9,11-13} In the United States, less than half of patients receive the recommended therapies (aspirin, statins, blood pressure, and diabetes medications) for cardiovascular prevention.¹⁴ In Colombia, only 38.6% of high-risk cardiovascular patients achieve cholesterol low density lipoprotein (LDL) goals,¹⁵ and 32.2% of patients who routinely receive aspirin have concomitant T2DM.¹⁶

There is no current published data from Colombia regarding the prevalence of use of medications such as aspirin or statins among individuals with T2DM. From a pharmacoepidemiological perspective, understanding the changes in the patterns of medications over time is important for evaluating the national public health interventions. The purpose of this study was to estimate the proportion of people with T2DM receiving drug therapy for cardiovascular prevention (aspirin and statins for this study) in Colombia, to describe the changes from 2008 to 2018 and to identify possible variables associated with the use of these medications.

Methods

Study Design

A cross-sectional study was conducted. Data were obtained from a national drug claim database containing the records of approximately 6.5 million people, which represents 13.5% of the country's total population. The dispensing information was from 5 different healthcare insurance companies (EPS) of the contributory regime (social health insurance for workers and families), which is present in all regions of Colombia.

The information in its entirety was obtained from the dispensing database of Audifarma SA, which has been used in multiple pharmacoepidemiological studies.^{5,15-17}

Participants and Setting

The study included all ambulatory patients over 18 years of age, of either sex, diagnosed with and treated for T2DM through the Health System of Colombia at 5 healthcare

insurers and who had drug claims registered in the database; a patient was defined as having T2DM if he/she had a registered diagnosis (International Classification of Diseases-ICD10 codes: E110-E149) and received medications for T2DM continuously during the last quarters of 2008 and 2018 (dispensed each month). Exclusion criteria were not considered for this study.

Data Collection

After identification of the included patients, the following variables were determined:

1. Sociodemographic: age (according to groups: young adult: 18-44 years; middle adult: 45-64 years; older adult: 65-74 years; and elderly: over 75 years),¹⁸ sex and city of residence.
2. Diabetes control medications: (a) metformin; (b) sulfonylureas; (c) thiazolidinediones; (d) dipeptidyl peptidase 4 (DPP-4) inhibitors; (e) glucagon-like peptide-1 (GLP-1) receptor agonists; (f) sodium-glucose cotransporter-2 (SGLT-2) inhibitors; and (g) insulins.
3. Cardiovascular prevention medications: (a) prescription of any statin (high-intensity statins were categorized as atorvastatin doses \geq 40 mg/day and rosuvastatin doses \geq 20 mg/day); (b) antiplatelet drugs: use of aspirin and use of P2Y12 inhibitors.
4. Other comedications: antihypertensive, antiulcer, antidepressant, antianginal and anticoagulant medications, nonsteroidal anti-inflammatory drugs (NSAIDs), fibrates, levothyroxine, beta 2-adrenergic agonists and inhaled anticholinergics.

Statistical Analysis

A database was created in Microsoft Excel 2016 with the identified variables. The analyses were performed in SPSS v24.0 (IBM, USA). Frequencies and proportions of the categorical variables were established in order to determine the prevalence of medication use for cardiovascular prevention in patients with T2DM. Bivariate analyses were performed to establish possible associations with cardiovascular prevention drug prescriptions (aspirin and statins together) among the included T2DM patients, and the subsequent multivariate analysis was designed to adjust the associated variables (comparing those T2DM patients with prescriptions for these medications to those without prescriptions). *P* values less than .05 indicated statistical significance.

Bioethical Considerations

The study was approved by the Bioethics Committee of the Universidad Tecnológica de Pereira (Colombia, South

America) in the category of “risk-free research” following the principles established by the Declaration of Helsinki. Access to dispensing data was obtained with the permission of Audifarma S.A.

Results

A total of 26 741 participants were identified from the last quarter of 2008, mostly from the Bogotá-Cundinamarca, Central and Caribbean regions, and 188 321 patients with a diagnosis of T2DM and receiving pharmacological treatment were identified from the last quarter of 2018, mainly from the Bogotá-Cundinamarca, Pacific, and Central regions. At both timepoints, there was a slightly more women than men, and the average patient age was lower in 2018 than in 2008. Among comedications, antihypertensives were predominant (mainly angiotensin II receptor blockers [ARB-II] and angiotensin-converting enzyme inhibitor [ACEI]), followed by antiulcer drugs such as proton pump inhibitors. Table 1 provides the sociodemographic characteristics with comedications for the 2 groups of patients.

Antidiabetic Drugs

The most-prescribed antidiabetic drugs for 2008 were metformin (n: 20 545; 76.8%), sulfonylureas (n: 12 795; 47.5%) and insulins (n: 9065; 34.0%) and for of 2018 were metformin (n: 167 415; 87.7%), insulins (n: 79 857; 42.4%) and DPP-4 inhibitors (n: 32 596; 17.2%). Prescription data for antidiabetic drugs are provided in Table 2. A change in the pattern of use of human insulins was observed: the share of patients receiving these drugs decreased from 31.5% in 2008 to 3.5% in 2018, while the use of insulin analogs increased from 2.5% in 2008 to 38.9% in 2018. Table 3 provides the patterns of use of antidiabetic drugs by group and in combinations.

Use of Aspirin and Statins (Prevention of Cardiovascular Risk)

Among lipid-lowering drugs, the most-prescribed statin in 2008 was lovastatin (98.7% of cases); while atorvastatin was the most-prescribed in 2018 (85.3%) (proportions based on the total number of patients prescribed statins). The drugs used to reduce cardiovascular risk and the prescription frequencies of aspirin and statins are provided in Table 4. Aspirin use decreased from 57.5% in 2008 to 44.2% in 2018, and the use of all statins increased from 44.9% in 2008 to 60.2% in 2018. Notably, the high-intensity statins increased from 1.1% in 2008 to 95.2% in 2018, while the combined use of aspirin + statin continued at about 32% at both times.

Multivariate Analysis

Binary logistic regression revealed statistically significant positive associations of using aspirin and statins in combination in 2008 with male gender (OR: 1.116; 95% CI: 1.056-1.179), age older than 75 years (OR: 6.484; 95% CI: 5.296-7.938) and treatment with clopidogrel (OR: 5.854; 95% CI: 4.463-7.678). In 2018, male patients (OR: 1.262; 95% CI: 1.235-1.289), those older than 75 years of age (OR: 5.819; 95% CI: 5.410-6.258) and those receiving antihypertensive treatment had greater probabilities of receiving prescriptions for aspirin and statins. On the other hand, people receiving fibrates (OR: 0.232; 95% CI: 0.218-0.246) or anticoagulant drugs had a lower probability of receiving the medications for the prevention of cardiovascular risk (see Table 5).

Discussion

General Findings

In 2008 and 2018, one third of patients with T2DM received drugs for the prevention of cardiovascular risk (the combination of aspirin and statins). Between these 2 time points, the proportion of patients receiving antiplatelet prescriptions decreased, whereas there was an increase in prescriptions for lipid-lowering agents. Cardiovascular secondary prevention through the use of aspirin and statins benefits patients by reducing cardiovascular events, and different clinical practice guidelines support the prescription of this combination to reduce morbidity and mortality from cardiovascular-related causes.^{8,19}

Most T2DM patients in 2008 and 2018 were women, in accordance with previous epidemiological analyses in Colombia,⁷ but men were more likely to receive aspirin or statins, which is consistent with a report by Alfredsson J et al²⁰ where men had a higher probability of being prescribed aspirin (81.0% vs 72.5%) or a statin (82.7% vs 73.0%). Notably, in a number of different age groups, epidemiological studies indicate that the cardiovascular risk of women with T2DM is at least 25% greater than that of men.²¹ This can be explained by differences in the perceived risk of patients and the need for therapy, representing a current gap in pharmacological management, especially in women with T2DM.^{22,23} The lower mean age of patients with T2DM in 2018 could indicate an earlier diagnosis from screening programs and better care of noncommunicable chronic diseases such as T2DM, dyslipidemia and HBP.²⁴ In addition, patients older than 75 years were more likely to receive drugs for secondary prevention, possibly due to evidence that age is one of the most important nonmodifiable cardiovascular risk factors. Ramos et al showed that the use of statins reduced atherosclerotic cardiovascular events and mortality from all causes in the population between 75 and

Table 1. Sociodemographic Characteristics and Comedications of Patients with Type 2 Diabetes Mellitus in the Last Trimesters of 2008 and 2018.

Sociodemographic characteristics and comedication		Last quarter 2008		Last quarter 2018	
		n = 26 741	%	n = 188 231	%
Sex	Female	15 096	56.5	108 789	57.8
Age (years)	Mean/SD ^a	69.4/13.6		63.8/13.5	
Regions (Colombia)	Amazonia-Orinoquia	43	0.2	640	0.3
	Bogota-Cundinamarca	13 546	50.7	66 879	35.5
	Caribbean	4000	15.0	32 895	17.5
	Central	6155	23.0	40 314	21.4
	West region	1509	5.6	6438	3.4
	Pacific	1488	5.6	41 155	21.9
Comedications					
Analgesics	NSAID ^b	3798	14.2	16 321	8.7
Antianginal gents	Nitrates	357	1.3	1370	0.7
Anticoagulants	Apixaban	—	—	781	0.4
	Dabigatran	—	—	451	0.2
	LMWFH ^c	240	0.9	2393	1.3
	UFH ^d	20	0.1	617	0.3
	Rivaroxaban	—	—	1378	0.7
	Warfarin	339	1.3	1250	0.7
	Antidepressants	Serotonin uptake inhibitor	1077	4.00	11 335
Serotonin and noradrenaline uptake inhibitor		6	0	545	0.3
Tricyclic		179	0.7	2206	1.2
Antihypertensives		19 838	74.1	135 610	72.0
	ARB-II ^e	8418	31.5	97 253	51.6
	β-blockers	5338	20	41 864	22.2
	Alpha-1 antagonist	884	3.3	7418	3.9
	Clonidine	687	2.6	4791	2.5
	Calcium Channel Blockers	7109	26.6	50 353	26.7
	ACEI ^f	10 716	40.1	28 054	14.9
Antiulcer	Antacids	1181	4.4	10 288	5.5
	Bismuth subsalicylate	—	—	6	0
	PPI ^g	7662	28.7	48 169	25.6
	Ranitidine	621	2.3	6912	3.7
	Sucralfate	182	0.7	2743	1.5
Levothyroxine	Levothyroxine	—	—	458	0.2
Bronchodilators	Anticholinergic	1027	3.8	7845	4.2
	β2 adrenergic agonist	1095	4.1	7188	3.8
Fibrates		4048	15.1	12 272	6.5

^aStandard deviation. ^bNonsteroidal anti-inflammatory drugs. ^cLow-molecular-weight fragment of heparin. ^dUnfractionated heparin. ^eAngiotensin II receptor blockers. ^fAngiotensin-converting enzyme inhibitor. ^gProton Pump Inhibitors.

84 years of age; however, in patients older than 85 years, the findings were not significant. In addition, in the PURE study in Latin America, a low prevalence of statin use was found (4% of joint use of cardiovascular prevention drugs), but among those evaluated, patients older than 65 years had a greater probability of receiving them, similar to the present findings.²⁵ This group of patients constitutes a challenge in the clinical setting, and more studies are needed to help focus cardiovascular prevention, especially in those who continue in a good vital state.²⁶

Use of Aspirin and Statins in the T2DM Population

There was also a marked increase in the prescription of high-intensity statins by 2018, which could be related to accumulating evidence on the benefits of these drugs for reducing mortality²⁷ and major cardiovascular events (acute coronary syndrome, cardiac revascularization, and death of cardiovascular origin) compared with statins of moderate or low intensity.²⁸ The increased prescription of

Table 2. Prescription of Antidiabetic Drugs for Patients with Type 2 Diabetes Mellitus in the Last Trimesters of 2008 and 2018.

Antidiabetic drugs	Pharmaceutical form	Last quarter 2008		Last quarter 2018	
		n=26 741	%	n=188 231	%
Biguanides					
Metformin	500 mg	2	0	14 388	7.6
	850 mg	20 533	76.8	119 781	63.6
	1000 mg	1	0	7266	3.9
Sulfonylureas					
Glyburide	5 mg	12 754	47.4	14 812	7.9
	60 mg	—	—	95	0.1
Gliclazide	80 mg	4	0	—	—
	2 mg	11	0	962	0.5
Glimepiride	4 mg	26	0.1	469	0.2
	—	—	—	—	—
DPP-4 Inhibitors^a					
Linagliptin	5 mg	—	—	4221	2.2
	2.5/500 mg	—	—	401	0.2
Linagliptin/Metformin	2.5/850 mg	—	—	796	0.4
	2.5/1000 mg	—	—	2200	1.2
Saxagliptin	2.5 mg	—	—	38	0
	5 mg	—	—	163	0.1
Saxagliptin/Metformin	2.5/1000 mg	—	—	1493	0.8
	5/1000 mg	—	—	442	0.2
Sitagliptin	25 mg	—	—	51	0
	50 mg	4	0	1474	0.8
	100 mg	36	0.1	944	0.5
Sitagliptin/Metformin	50/500 mg	6	0	503	0.3
	50/850 mg	—	—	1781	0.9
	50/1000 mg	3	0	10 272	5.4
	100/1000 mg	—	—	421	0.2
Vildagliptin	50 mg	—	—	925	0.5
	50/500 mg	—	—	339	0.2
Vildagliptin/Metformin	50/850 mg	—	—	1230	0.7
	50/1000 mg	—	—	4902	2.6
GLP-1 agonist^b					
Liraglutide	Pen 6 mg/mL/3 mL	—	—	2646	1.4
SGLT-2 Inhibitors^c					
Canagliflozin	300 mg	—	—	20	0
	10 mg	—	—	979	0.5
Dapagliflozin	5/1000 mg	—	—	772	0.4
	10/1000 mg	—	—	428	0.2
Empagliflozin	10 mg	—	—	652	0.3
	25 mg	—	—	1344	0.7
Human insulin					
Regular	Vial 100 UI/mL/10 mL	2223	8.3	1382	0.7
NPH	Vial 100 UI/mL/10 mL	6191	23.2	5248	2.8
Insulin analogs					
Aspartat	Pen 100 UI/mL/3 mL	18	0.1	5798	3.1
	Glulisine	Pen 100 UI/mL/3 mL	1	0	16 483
Lispro	Vial 100 UI/mL/10 mL	57	0.2	1499	0.8
	Cartridge 100 UI/mL/3 mL	52	0.2	62	0
Degludec	Vial 100 UI/mL/10 mL	182	0.7	408	0.2
	Pen 100 UI/mL/3 mL	—	—	5127	2.7
Detemir	Pen 100 UI/mL/3 mL	—	—	4090	2.2
Glargine	Pen 100 UI/mL/3 mL	4	0	35 722	19
	Vial 100 UI/mL/10 mL	337	1.3	4038	2.1

^aDipeptidyl-Peptidase 4 Inhibitor, ^bGlucagon-like peptide-1 receptor agonists, ^cSodium-glucose transport protein 2 Inhibitors.

Table 3. Prescription of Antidiabetic Drugs by Group and in Combination with Metformin for Patients with Type 2 Diabetes Mellitus in the Last Trimesters of 2008 and 2018.

Antidiabetic drugs		Last quarter 2008		Last quarter 2018	
		n=26 741	%	n=188 231	%
Metformin	All	20 545	76.8	159 965	84.9
	Metformin (monotherapy)	20 545	76.8	134 977	71.7
	Combined	—	—	24 988	13.3
	DPP-4 inhibitor ^a	—	—	23 866	12.7
	SGLT-2 Inhibitor ^b	—	—	1 181	0.6
Other oral antidiabetic drugs	Sulfonylureas	12 790	47.8	16 250	8.6
	DPP-4 Inhibitors	48	0.2	31 308	16.6
	GLP-1 agonist ^c	—	—	2 646	1.4
	SGLT-2 Inhibitor	—	—	4 098	2.2
Insulin	Total	6 627	24.8	55 191	29.3
	Regular	2 223	8.3	1 382	0.7
	NPH	6 191	23.2	52 48	2.8
	Short acting analog	300	1.1	23 846	12.7
	Long acting analog	340	1.3	47 824	25.4

^aDipeptidyl-Peptidase 4 Inhibitor, ^bSodium-glucose transport protein 2 Inhibitors, ^cGlucagon-like peptide-1 receptor agonists.

high-intensity statins may also be due to their inclusion on the list of medications in the benefit plan of the Colombian health system,²⁹ as well as their recommendation by the clinical practice guidelines of the Ministry of Health of Colombia in 2014. Previously, no such guidelines existed, and there were no specific recommendations for the country.³⁰ However, despite their favorable cardiovascular effects, high-intensity statins are associated with increases of up to 0.4% ($P = .0002$) in the levels of glycosylated hemoglobin (HbA1c) in patients with T2DM as well as an increased risk of de novo diabetes compared with low-intensity statins.³¹ Therefore, patients risk factors should be reviewed to establish the risk/benefit ratio, and guide the therapy to achieve adequate metabolic control.^{32,33}

Approximately half of the patients received aspirin; however, only 2% were jointly prescribed clopidogrel, which would indicate that most of the population was receiving aspirin for primary prevention of cardiovascular risk. However, the use of aspirin after the year of presentation of acute coronary syndrome cannot be ruled out, and dual antiplatelet therapy would not be indicated in this case.³⁴ A study in Japan found no evidence that the use of aspirin in low doses for primary prevention in patients with T2DM prevents any cardiovascular event at 10 years, but a significant increase in the risk of gastrointestinal bleeding was observed.^{35,36} In addition, although the ASCEND study demonstrated the efficacy of aspirin for the primary prevention of serious vascular events, it also found a 29% higher risk of major bleeding in Caucasian patients³⁷; therefore, the risk/benefit ratio of antiplatelet drugs in primary prevention in patients with

high cardiovascular risk, especially those with T2DM, requires further study. The large number of patients receiving aspirin in 2008 could be a medical behavior supported by the recommendations of the 2007 guidelines of the *American Heart Association* (AHA) and the *American Diabetes Association* (ADA) for primary prevention in patients with T2DM and high cardiovascular risk.³⁸ However, the clinical practice guideline of the Ministry of Health of Colombia in 2015 advises against the use of aspirin for primary prevention in T2DM patients.³⁹

Diabetes Treatment

With respect to T2DM treatment, the prescription of sulfonylureas decreased markedly in 2018 compared with 2008 (8.6% vs 47.8%). In Colombia, a decrease in the prescription of glyburide has been observed (from 64.9% in 2005 to 21.8% in 2015),^{17,18} which is probably related to its association with cardiovascular events, its frequent undesirable effects and the emergence of new antidiabetic drugs such as SGLT-2 inhibitors, GLP-1 receptor agonists and DPP-4 inhibitors. These latter drugs have shown cardiovascular benefits or at least do not increase the risk of cardiovascular events; they are also associated with fewer hypoglycemic events.⁴⁰

The prescription of DPP-4 inhibitors increased significantly between 2008 and 2018 because these drugs are now the second line of treatment according to the recommendations of the clinical practice guidelines for Colombia.⁴ In addition, the proportion of new antidiabetic drugs, such as GLP-1 receptor agonists and SGLT-2

Table 4. Prescription of Drugs for Cardiovascular Prevention in Patients with Type 2 Diabetes Mellitus in the Last Trimesters of 2008 and 2018.

Cardiovascular prevention drugs*		Last quarter 2008		Last quarter 2018	
		n	%	n	%
Platelet aggregation inhibitors	Pharmaceutical form				
Aspirin	100mg	15 379	57.5	83 280	44.2
Clopidogrel	75 mg	259	1.1	4270	2.3
Clopidogrel/Aspirin	75/100mg	—	—	4	0.0
Prasugrel	10 mg	—	—	56	0.0
Ticagrelor	90 mg	—	—	300	0.2
Anticholesteremic agents					
Atorvastatin	10 mg	7	0.0	2619	1.4
	20 mg	57	0.2	40 669	21.6
	40 mg	53	0.2	53 426	28.4
	80 mg	2	0.0	1457	0.8
Atorvastatin/Ezetimibe	10/10 mg	—	—	13	0.0
	20/10 mg	1	0.0	43	0.0
	40/10 mg	1	0.0	101	0.1
Atorvastatine/Omega 3	80/840 mg capsule	—	—	6	0.0
Lovastatin	20 mg	11 864	44.4	5799	3.1
Pravastatin	20 mg	1	0.0	7	0.0
	40 mg	4	0.0	—	—
Rosuvastatin	10 mg	7	0.0	671	0.4
	20 mg	9	0.0	4626	2.5
	40 mg	—	—	8640	4.6
Rosuvastatin/Ezetimibe	10/10 mg	—	—	22	0.0
	20/10 mg	—	—	123	0.1
	40/10 mg	—	—	399	0.2
Rosuvastatin/Fenofibrate	5/135 mg	—	—	42	0.0
	10/135 mg	—	—	520	0.3
	20/135 mg	—	—	1326	0.7
Simvastatin	10 mg	1	0.0	—	—
	20 mg	—	—	65	0.0
	40 mg	5	0.0	91	0.0
	80 mg	—	—	7	0.0
Simvastatin/Ezetimibe	10/10 mg	1	0.0	10	0.0
	20/10 mg	23	0.1	66	0.0
	40/10 mg	20	0.1	87	0.0
	80/10 mg	—	—	27	0.0
Aspirin and statins prescription					
Aspirin	100mg	15 379	57.5	83 280	44.2
P2Y12 antagonist		259	1.1	4597	2.4
Statin	All	12 010	44.9	11 3315	60.2
	High Intensity ^a	132	1.12	107 838	95.22
	Ezetimibe	—	—	870	0.5
Combination therapy	Aspirin + Statin	8569	32.0	61 768	32.8

^aTotal number of patients with high intensity statins/total number of patients with statins.

*Tablets, unless otherwise indicated.

inhibitors, increased. These drugs have a significant impact on major cardiovascular events in high-risk patients⁴¹⁻⁴³ and are part of the second line of management based on the recommendations of the ADA for patients with T2DM and atherosclerotic cardiovascular

disease or chronic kidney disease.⁴⁴ Their use should augment the effect of statins and aspirin on cardiovascular risk in patients who are receiving drugs for primary or secondary prevention because of the potential benefits for reducing cardiovascular events.^{45,46}

Table 5. Multivariate Analysis of the Variables Associated with Joint Prescription of Acetylsalicylic Acid and Statins for Patients with Type 2 Diabetes Mellitus in the Last Trimesters of 2008 and 2018.

Multivariate analysis	Last quarter 2008				Last quarter 2018			
	P	OR	95% CI ^a		P	OR	95% CI	
			Lower	Upper			Lower	Upper
Sex (Male)	<.001	1.116	1.056	1.179	<.001	1.262	1.235	1.289
Age								
18-44 years	Ref	1	Ref	Ref	Ref	1	Ref	Ref
45-59 years	<.001	2.579	2.087	3.186	<.001	3.776	3.514	4.057
60-74 years	<.001	5.113	4.18	6.255	<.001	5.939	5.534	6.373
≥75 years	<.001	6.484	5.296	7.938	<.001	5.819	5.41	6.258
Metformin	<.001	1.56	1.453	1.675	<.001	1.499	1.449	1.55
DPP-4 inhibitors ^b	—	—	—	—	<.001	1.123	1.093	1.155
Sulfonylureas	—	—	—	—	<.001	1.226	1.181	1.272
SGLT-2 inhibitors ^c	—	—	—	—	<.001	1.429	1.333	1.533
GLP-1 agonist ^d	—	—	—	—	<.001	1.378	1.258	1.509
Insulin	<.001	1.809	1.695	1.93	<.001	1.623	1.582	1.666
Clopidogrel	<.001	5.854	4.463	7.678	<.001	2.238	2.086	2.401
NSAID ^e	.001	1.132	1.049	1.223	—	—	—	—
Direct oral anticoagulant	—	—	—	—	<.001	0.149	0.133	0.167
Anticholinergics	.078	0.87	0.745	1.016	.02	1.07	1.011	1.133
ARB-If ^f	<.001	1.246	1.172	1.326	<.001	2.027	1.975	2.081
β-blockers	—	—	—	—	<.001	2.098	2.046	2.151
β-2 adrenergics	.007	1.226	1.057	1.422	.002	0.91	0.857	0.966
Fibrates	.078	1.069	0.992	1.152	<.001	0.232	0.218	0.246
Heparins	—	—	—	—	<.001	0.789	0.722	0.862
PPI ^g	<.001	1.14	1.074	1.21	<.001	1.197	1.169	1.226
ACEI ^h	<.001	1.16	1.094	1.23	<.001	2.308	2.235	2.384
Nitrates	—	—	—	—	<.001	2.609	2.287	2.975
Other antihypertensive drug	.086	0.949	0.894	1.008	<.001	1.233	1.205	1.262
Warfarine	—	—	—	—	<.001	0.158	0.133	0.188

An analysis was performed by adjusting associations in 2008 and another in 2018.

^aConfidence interval, ^bDipeptidyl-Peptidase 4 Inhibitor, ^cSodium-glucose cotransporter-2 inhibitors, ^dGlucagon-like peptide-1 receptor agonists,

^eNonsteroidal anti-inflammatory drugs, ^fAngiotensin II receptor blockers, ^gProton Pump Inhibitor, ^hAngiotensin-converting enzyme inhibitor.

Limitations

This research is limited by the cross-sectional design which compares 2 points in time without analysis of the trends between years. We were unable to access the clinical records of patients; this limited the ability to define the difference between primary and secondary prevention strategies. The findings of this study should be applied to populations with similar insurance characteristics and access to medications. Finally, the strength of this study is the evaluation of the entire population with T2DM affiliated with these insurers to report the changes in national pharmacoepidemiological patterns. The data represents more than 13% of the Colombian population.

Conclusions

With the introduction of national clinical guidelines in Colombia, the management of cardiovascular risk in patients

with T2DM seems to be more consistent with international recommendations. The use of aspirin as a prevention measure for cardiovascular risk in patients with T2DM is decreasing, while the use of statins, especially high-intensity statins, has increased over the last decade. The probability of receiving medication for prevention was higher among men, those older than 75 years and patients diagnosed with hypertension. In addition, new antidiabetic drugs that have shown neutral or positive effects on cardiovascular risk are being used more frequently. The changes in drug prescriptions observed in this study suggest that the clinical practice guidelines for the management of patients with T2DM have been adequately implemented. Further research is necessary to understand the findings from this study in relationship to patient and health system outcomes.

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Author Contributions

Jorge Enrique Machado-Alba participated in Conceptualization, investigation, methodology, project administration, resources, supervision, validation, writing review and editing. Manuel Enrique Machado-Duque participated in data curation, formal analysis, investigation, methodology, validation, writing original and review and editing. Andres Gaviria-Mendoza participated in formal analysis, methodology, validation, visualization, writing original draft and editing. Diego Arturo Garcia participated in formal analysis, methodology, validation, visualization, writing original draft and editing. Melissa Hiromi Emura-Vélez participated in formal analysis, methodology, validation, visualization, writing original draft and editing.

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