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Risk stratification and lipid evaluation in mexican patients, evidence of lipid and cardiovascular analysis in REMECAR. The mexican registry of cardiovascular diseases (REMECAR group)

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ABSTRACT

Background and aims: Dyslipidaemia is a significant risk factor for cardiovascular disease in the Mexican population. This analysis aimed to describe the baseline LDL-c levels of patients presenting to cardiovascular clinics and evaluate the proportion who achieved their risk-based LDL-c goals as recommended by 2021 ESC prevention guidelines.
Methods: The REMECAR registry is an observational study of patients attending a specialized cardiovascular clinic for their first visit. The cardiovascular risk was retrospectively determined using the 2021 ESC guideline stratification and the SCORE2 and SCORE-OP.
Results: A total of 5443 patients were included in the analysis. Within this population, 55.96% presented as very high, 39.98% as high and 4.06% as moderate to low risk. 63% of the participants were not on any lipid-lowering treatment at entry, while 12.4% were receiving high-intensity statin therapy. Patients presenting with established atherosclerotic cardiovascular disease had a mean LDL-c of 90.9 ± 40.7 mg/dL. Of these, 14.1% were achieving LDL-c levels of 70–55 mg/dL and 19.3% were achieving LDL-c levels <55 mg/dL. In diabetic patients at very high risk, only 25.7% achieved their LDL-c goal. Finally, in patients without another risk factor and very high-risk evaluated by SCORE2 & SCORE-OP, only 14% of patients achieved their LDL-c goals.
Conclusions: An important number of patients were not receiving any lipid-lowering therapy. Furthermore, in those who were, a significant portion did not achieve LDL-c recommended thresholds. Our results underline the urgent need to improve the prescription and optimization of lipid-lowering therapy

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as the current management appears to be insufficient for achieving optimal recommended goals. Identifying key barriers in lipid management is fundamental to establishing better strategies and health system policies to reduce cardiovascular risk.

Introduction

Despite the continuous efforts of healthcare professionals in reducing cardiovascular disease (CVD) burden and improving the clinical outcomes of such patients, cardiovascular disease remains a major cause of mortality worldwide [1,2]. Risk factors such as hypertension, diabetes, and dyslipidaemia are major contributors to the development and progression of CVD. There is overwhelming evidence demonstrating that improving cardiovascular risk factors reduces cardiovascular morbidity and mortality. Identifying high risk patients is crucial to initiate early therapy and impact people in both primary and secondary prevention. Several international guidelines recommend patient stratification according to risk categories and 10-year risk estimation [2–5]. Reduction in low-density lipoprotein cholesterol (LDL-c) has been shown to significantly reduce the development and progression of CVD. In patients with established CVD, intensive treatment to achieve LDL-c <55 mg/dL has been shown to be beneficial. Additional LDL-c goals are defined according to the risk category to achieve the best risk/benefit ratio [2–6]. Despite the compelling evidence around LDL-c reduction there is still a gap between guideline recommendations and real-world practice. This is especially the case where socioeconomic factors can influence the access and adherence to more potent lipid-lowering therapies. Real-world data is crucial to determine country-specific barriers that adversely impact clinical management and most importantly identify strategies to improve dyslipidaemia management.

While international datasets and national registries across the globe have contributed to the development of the current guidelines [2–5], little is known about cardiovascular disease and management in Latin-American countries. We present an interim analysis from the Mexican Registry of Cardiovascular Diseases (REMECAR). REMECAR is a national multi-center registry created to describe cardiovascular disease and treatment strategies, in real-world clinical practice across Mexico. This analysis aims to describe the baseline LDL-c levels, and evaluate the proportion of patients achieving their risk-based LDL-c goals recommended by the most recently published 2021 ESC guidelines on cardiovascular disease prevention in clinical practice [2]. Additionally, we assessed the baseline lipid lowering therapy (LLT) prior to the study visit and the LLT strategy used in the specialized cardiovascular clinic.

Material and methods

The REMECAR registry included patients attending for their first visit to a specialized outpatient cardiovascular clinic for diagnostic, and clinical management of cardiometabolic diseases. The referrals included patients with any cardiovascular diagnosis (e.g. coronary artery disease, arrhythmias, valve disease, etc) as well as patients with cardiovascular risk factors such as hypertension, diabetes, and dyslipidaemia, among others. Patients were approached for participation at their first clinic visit. The study was carried out in adherence to local regulatory recommendations. Written informed consent for confidential data management was obtained from each patient before they were included in the study. Clinical baseline data was collected during the visit including medical history, medication use, serum pathology and physical examination details. All patients were treated as per standard clinical practice at the discretion of the attending physician. The data used in this report corresponds to the patient status at the time of inclusion in the study and reflects the baseline lipid levels prior to attending specialized cardiovascular clinics.

A total of 5443 patients were included between January 2016 and November 2021. Analysis of the cohort included a >5 year period, during which several updates to American and European lipid management guidelines and risk stratification have been published. We performed a retrospective analysis of the cohort using the most recently published 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. The patients were classified according to the updated risk stratification and 10-year estimated CV risk (SCORE-2 and SCORE-OP). We applied a multi-factor, hierarchical, end-member classification to provide their relative risk category. In summary, patients with established atherosclerotic cardiovascular disease (ASCVD), patients with type 2 diabetes mellitus (DM) with target organ damage (TOD) and severe chronic kidney disease (CKD) were classified as very high risk. ASCVD was defined as a history of acute myocardial infarction, acute coronary syndrome, any arterial revascularization, stroke, transient ischaemic attack (TIA), peripheral artery disease, or documented atherosclerotic disease. Patients with moderate CKD and patients with long-standing diabetes or uncontrolled diabetes without TOD were classified as high risk. Patients presenting with office blood pressure values > 180 were also classified as high risk. In people without ASCVD, DM, CKD, or familiar hypercholesterolemia the 10-year risk of fatal and non-fatal cardiovascular events was calculated according to the Systematic Coronary Risk Estimation 2 (SCORE2), and Systematic Coronary Risk Estimation for older persons (SCORE-OP) and categorized according to risk thresholds for age (Supplementary Material Table S1) As the SCORE2 has not been validated for young people, apparently healthy patients <40 years were excluded from the present analysis. The risk chart for medium-risk countries was used for the calculation. Medium-risk charts were chosen based on similar rates of disability-adjusted life years due to high LDL previously reported in those regions [1]. The statin intensity was defined according to the average LDL-c percent reduction achieved with each medication and dose as reported previously [4]. Strict quality controls with data processing algorithms were applied to cross-check and ensure the quality of the data. Cases that failed the quality controls were excluded from the analysis.

In accordance with the new stepwise approach, the lipid goals were defined according to four different categories (apparently healthy people, patients with established ASCVD, patients with DM, and patients with another risk factor). For ASCVD patients we analysed the first step LDL-goal (<70 mg/dL) and the ultimate LDL-goal (<55 mg/dL). As the intensified goal in step 2 is mandatory, whether for primary prevention, we used the LDL-c levels recommended in the first step approach. The lipid goals definition for each category are summarized in Supplementary Material Fig. S2. It is worth noting that for otherwise healthy participants at low-moderate risk there is no ultimate LDL-c goal defined and we only describe the general characteristics of this population in the overall results.

Statistical analysis

All analyses were descriptive. For baseline characteristics, categorical variables were expressed as frequencies and percentages. Continuous variables were reported as mean and standard deviation for normally distributed data and as median and 25th - 75th percentiles (Q1 and Q3, respectively) for triglyceride levels due to skewed distribution.

Results

A total of 5443 patients were retrospectively categorized into their corresponding risk categories. Within the cohort, 3046 (55.96%) were classified as very high-risk, 2176 (39.98%) as high-risk and 221 (4.06%) as moderate to low risk. Baseline characteristics of the cohort according to risk categories are summarized in Table 1.

Overall, the mean age of the cohort was 62.8 ± 12.2 years. Within the whole cohort, 46.7% were male, 73.2% of patients presented hypertension and 28.4% Type 2 Diabetes Mellitus. Mean LDL-c levels were 110 ± 41.9 mg/dL in the very high-risk group, 128 ± 29.6 mg/dL in high-risk group, and 129 ± 25.7 mg/dL in the low to moderate risk group. Interestingly, 17.9% of the population (977 patients) had high triglyceride levels and low HDL-c levels with normal or slightly elevated levels of LDL-c (<160 mg/dL).

Within the total population, 63% were not on any LLT at the time of their first visit. Only 17.2% were receiving treatment with moderate statin therapy and 12.4% were on high intensity statin (monotherapy or in combination with ezetimibe 10 mg). In addition, 1.7% (91 patients) self-reported being following dietary management for lipid control regardless the use of LLT (e.g. diet, herbal products, supplements). However, these did not include specific programs or referrals to other health professionals such as dietitians, nutritionists, or exercise physiologists as part of the management in the cardiovascular clinics. Within patients receiving treatment, we evaluated the proportion of usage of different LLT from 2016 to 2021. (Fig. 1). Within this group, moderate intensity statins (monotherapy or in combination with ezetimibe) were the most common therapy utilized (41.3–55.4%), followed by high intensity statins (29.2–39.7%), and this was sustained over the 5 year period. Of note, we observed a meaningful increase in the use of moderate-intensity statins in 2019 (from 41.3% to 54%), which corresponded with a 9% decrease in the use of other LLT (eg: fibrates, niacin, omega-3 fatty acids). Only a small portion of patients (1.5%) were using PCSK9 inhibitors, with maximum use observed in 2018.

Clinically established ASCVD

Approximately one-quarter (26.3%) of the population had clinically established ASCVD at the time of presentation. Average total cholesterol within this group was 162 ± 50 mg/dL, LDL-c 90.9 ± 40.7 mg/dL, HDL-c 43.9 ± 12.5 mg/dL and triglycerides 130

Table 1
Baseline characteristics.

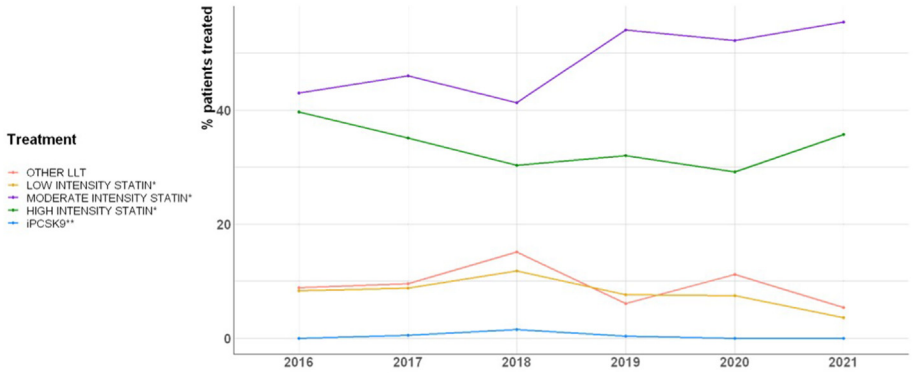
	Low to moderate risk (N = 221)	High risk (N = 2176)	Very high risk (N = 3046)	Overall (N = 5443)
Male gender, n (%)	9 (4.1%)	843 (38.7%)	1692 (55.5%)	2544 (46.7%)
Age, mean ± SD	49.6 ± 4.61	55.4 ± 8.75	69.1 ± 11.0	62.8 ± 12.2
BMI, mean ± SD	28.8 ± 5.12	29.9 ± 5.27	28.8 ± 4.86	29.2 ± 5.06
SBP, mean ± SD	113 ± 9.16	126 ± 16.0	133 ± 20.3	129 ± 19.0
DBP, mean ± SD	74.6 ± 7.89	79.0 ± 10.1	76.9 ± 11.1	77.6 ± 10.7
Cardiovascular risk factor, n (%)				
Hypertension	102 (46.2%)	1446 (66.5%)	2438 (80.0%)	3986 (73.2%)
Diabetes	0 (0%)	509 (23.4%)	1037 (34.0%)	1546 (28.4%)
Smoking	15 (6.8%)	238 (10.9%)	295 (9.7%)	548 (10.1%)
Chronic kidney disease <60 ml/min/1.73 m2	0 (0%)	20 (0.9%)	109 (3.6%)	129 (2.4%)
Chronic kidney disease <30 ml/min/1.73 m2	0 (0%)	0 (0%)	93 (3.1%)	93 (1.7%)
Familial Hypercholesterolemia	0 (0%)	1 (0.0%)	12 (0.4%)	13 (0.2%)
Established atherosclerotic cardiovascular disease, n (%)				
Previous MI	–	–	725 (23.8%)	725 (13.3%)
Ischemic heart disease	–	–	433 (14.2%)	433 (8.0%)
Previous PCI	–	–	617 (20.3%)	617 (11.3%)
Previous CABG	–	–	157 (5.2%)	157 (2.9%)
Peripheral artery disease	–	–	158 (5.2%)	158 (2.9%)
Stroke	–	–	235 (7.7%)	235 (4.3%)
Baseline labs, mean ± SD				
Glucose(mg/dL)	94.7 ± 12.1	111 ± 43.3	114 ± 46.5	112 ± 44.5
Total Cholesterol(mg/dL)	205 ± 27.1	205 ± 32.4	185 ± 50.8	194 ± 44.6
HDL-c(mg/dL)	49.6 ± 12.6	47.1 ± 12.7	45.6 ± 12.8	46.3 ± 12.8
LDL-c(mg/dL)	129 ± 25.7	128 ± 29.6	110 ± 41.9	118 ± 37.9
Triglycerides(mg/dL)	129[103–181]	149[112–203]	143[106–197]	145[108–198]
eGFR (ml/min/1.73 m2)	93.6 ± 15.5	88.2 ± 20.6	70.5 ± 23.4	78.9 ± 23.8
Lipid lowering therapy				
No LLT	192 (86.9%)	1669 (76.7%)	1570 (51.5%)	3431 (63.0%)
Other LLT[a]	3 (1.4%)	97 (4.5%)	109 (3.6%)	209 (3.8%)
Low intensity statin[b]	1 (0.5%)	56 (2.6%)	123 (4.0%)	180 (3.3%)
Moderate intensity statin[b]	23 (10.4%)	266 (12.2%)	645 (21.2%)	934 (17.2%)
High intensity statin[b]	2 (0.9%)	88 (4.0%)	587 (19.3%)	677 (12.4%)
PCSK9 inhibitors[c]	0 (0%)	0 (0%)	12 (0.4%)	12 (0.2%)
Self-reported diet management	4 (1.8%)	29 (1.3%)	58 (1.9%)	91 (1.7%)

Data is shown as mean and standard deviation for continuous variables and frequencies and percentages for categorical variables. ¤ Data reported in median [1st-3rd quartile]. SBP: systolic blood pressure, DBP: diastolic blood pressure, MI: myocardial, PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft, LLT:lipid lowering therapy, PCSK9:proprotein convertase subtilisin/kexin type 9.

[a] Fibrates, niacin, Omega-3 fatty acids.

[b] Monotherapy or in combination with Ezetimibe.

[c] Monotherapy or in combination with other LLT, BMI: Body mass index.



	2016	2017	2018	2019	2020	2021
Other LLT	8.9%	9.6%	15.1%	6.1%	11.2%	5.4%
Low Intensity statin*	8.3%	8.8%	11.8%	7.6%	7.5%	3.6%
Moderate Intensity statin*	43.0%	46.0%	41.3%	54.0%	52.2%	55.4%
High Intensity statin*	39.7%	35.1%	30.3%	32.0%	29.2%	35.7%
iPCSK9**	0.0%	0.5%	1.5%	0.4%	0.0%	0.0%

Fig. 1. Use of different LLT from 2016 to 2021 in treated patients. *Monotherapy or in combination with ezetimibe, ** Monotherapy or in combination with other LLT.

[96–180] mg/dL. Overall, 33.4% of the patients with ASCVD achieved at least one of the LDL-c treatment goals (14.1% achieved the first step goal (LDL-c 70-55 mg/dL) and 19.3% achieved the ultimate goal (LDL-c <55 mg/dL). While the majority of patients (62.5%) were treated with moderate or high intensity statins, 29.9% were not on any LLT at the time of inclusion. As expected, lipid parameters decreased with more potent LLT therapy (Table 2). However, less than one third of the patients using moderate or high intensity statins achieved their ultimate LDL-c goal (Fig. 2). The average LDL-c for patients in the moderate intensity statin group was 82.6 ± 34.8 mg/dL and for high intensity statins 78.0 ± 37.1 mg/dL. Although, the use of PCSK9 inhibitors was low (12 patients), 75% achieved LDL-c goals with an average LDL-c of 38.5 ± 22.8 mg/dL.

Primary prevention

In primary prevention patients, 982 (18%) had a previous diagnosis of type 2 diabetes mellitus. The average total cholesterol level was 199 ± 43.9 mg/dL, LDL-c 120 ± 33.1 mg/dL, HDL-c 44.6 ± 11.9 mg/dL and triglycerides 168[125–235] mg/dL mg/dL. DM patients were then categorized according to their individual risk. As our cohort is derived from specialized cardiovascular clinics, none of the patients with DM were classified as moderate risk (well controlled, short-standing DM without additional risk factors). In contrast, 85% were classified as high risk and 15% as very high risk according to the presence of TOD. In DM patients at very high risk, 25.7% achieved the recommended LDL-c goal (<70 mg/dL). In DM patients at high risk, those with LDL-c <100 mg/dL were even lower at 20.4% (Fig. 3).

For otherwise apparently healthy patients, 1141 (37.7%) were classified as very high risk, 1667 (55%) as high risk and 221 (7.3%) as low-moderate risk according to SCORE2 and SCORE-OP. As mentioned previously, for the low to moderate group we did not apply additional prevention goals. The proportion of high and very high-risk primary prevention patients who achieved their first step LDL-c goals (<100 mg/dL) were 13.3% and 14%, respectively (Fig. 3).

Management after the visit at specialized cardiovascular clinic

Finally, we evaluated the LLT intensification after attending the specialized cardiovascular clinics (Table 3). Overall, we observed a ~50% increase in the number of patients receiving LLT. The increase in the number of treated patients was similar across all risk categories, with the exception of the low to moderate risk category, which had a smaller increase (35.8%). A substantial increase in the use of moderate and high-intensity statin therapy (from 29.6% to 62.7%) was observed. Importantly, the use of high intensity statins in ASCVD patients increased to 50.1%. There was a small increase observed in the use of PCSK9 inhibitors, however, it was still less than 1% of the population. Interestingly, the use of other LLT (niacin, fibrates, omega-3 fatty acids) in diabetic patients, low to moderate, and high risk patients was ~5%.

Discussion

In recent years, multiple efforts have been made to evaluate the lipid profile and the rate of achievement of lipid targets across different populations [7–12]. A previous large population-based study on lipid profiles in Latin-American, including 197 different studies, reported mean levels of total cholesterol of 193.39 mg/dL, LDL-c of 119.98 mg/dL, HDL-c of 46.55 mg/dL and triglycerides of 139.27 mg/dL [7]. Our findings are consistent with these results.

Table 2
Lipid profile parameters in patients with stablished ASCVD according to the lipid lowering therapy.

	NO LLT	OTHER LLT[a]	LOW INTENSITY STATIN[b]	MODERATE INTENSITY STATIN[b]	HIGH INTENSITY STATIN[b]	iPCSK9[c]	Overall
	(N = 428)	(N = 36)	(N = 61)	(N = 394)	(N = 501)	(N = 12)	(N = 1432)
Total cholesterol(mg/dL)	185 ± 51.3	199 ± 48.2	185 ± 43.0	154 ± 41.7	145 ± 45.7	103 ± 28.6	162 ± 50.0
LDL(mg/dL)	110 ± 41.0	120 ± 47.4	106 ± 31.4	82.6 ± 34.8	78.0 ± 37.1	38.5 ± 22.8	90.9 ± 40.7
HDL(mg/dL)	45.8 ± 13.8	43.6 ± 11.6	42.2 ± 12.7	44.8 ± 12.6	41.8 ± 11.1	48.0 ± 9.65	43.9 ± 12.5
Triglycerides(mg/dL)[¤]	135[99–189]	166[125–199]	168[126–220]	126[94–172]	122[91–169]	98[84–113]	130[96–180]

Data is shown as mean and standard deviation for continuous variables and frequencies and percentages for categorical variables.[¤] Data reported in median and 25th - 75th percentiles (Q1 and Q3, respectively).
[a] Fibrates, niacin, omega-3 fatty acids.
[b] Monotherapy or in combination with ezetimibe.
[c] Monotherapy or in combination with other LLT.

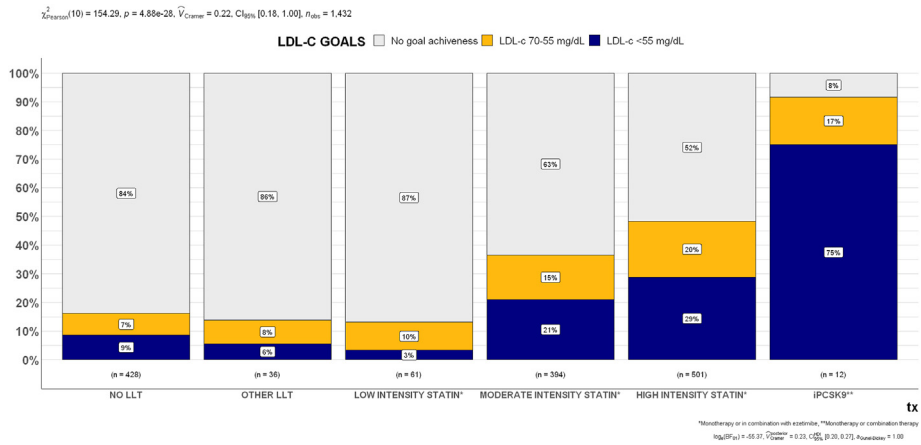


Fig. 2. Proportion of patients with established ASCVD achieving LDL-goals according to the lipid lowering therapy used. Yellow colour corresponds to patients achieving the first step of LDL goal for ASCVD patients (LDL-c 70-55 mg/dL). Blue colour corresponds to patients achieving the ultimate LDL goal for ASCVD patients (LDL-c <55 mg/dL). Grey colour corresponds to the proportion of patients out of LDL-goals., *Monotherapy or in combination with Ezetimibe, ** Monotherapy or in combination with other LLT. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

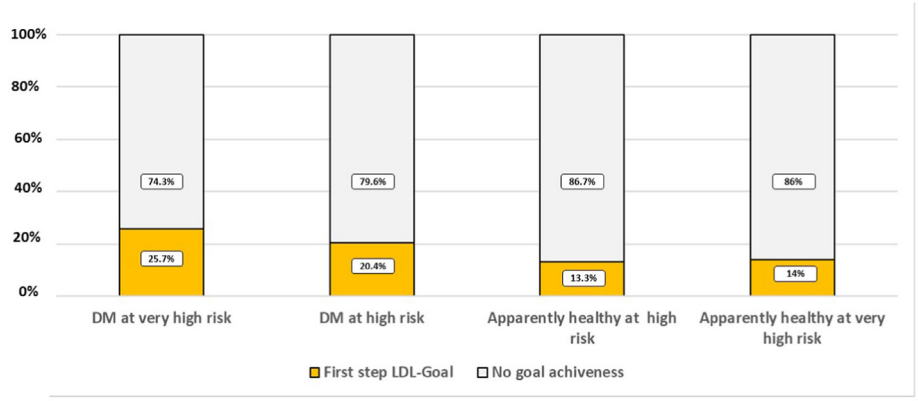


Fig. 3. Proportion of patients achieving individual risk LDL-goal. Yellow colour corresponds to patients achieving the first step LDL goal (<70 mg/dL for DM at very high risk and <100 mg/dL for the rest of the categories). Grey colour corresponds to the proportion of patients out of LDL-goals. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 3
Use of lipid lowering therapies before and after the visit at specialized cardiovascular clinic.

	Healthy participants and other risk factor					
	ASCVD	DM	MOD-LOW RISK	HIGH RISK	VERY HIGH RISK	Overall
	(N = 1432)	(N = 982)	(N = 221)	(N = 1667)	(N = 1141)	(N = 5443)
Treatment **before** visit at specialized cardiovascular clinic						
No LLT	428 (29.9%)	622 (63.3%)	192 (86.9%)	1319 (79.1%)	870 (76.2%)	3431 (63.0%)
Other LLT[a]	36 (2.5%)	58 (5.9%)	3 (1.4%)	67 (4.0%)	45 (3.9%)	209 (3.8%)
Low intensity statin[b]	61 (4.3%)	49 (5.0%)	1 (0.5%)	38 (2.3%)	31 (2.7%)	180 (3.3%)
Moderate intensity statin[b]	394 (27.5%)	184 (18.7%)	23 (10.4%)	183 (11.0%)	150 (13.1%)	934 (17.2%)
High intensity statin[b]	501 (35.0%)	69 (7.0%)	2 (0.9%)	60 (3.6%)	45 (3.9%)	677 (12.4%)
iPCSK9[c]	12 (0.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	12 (0.2%)
Treatment **after** visit at specialized cardiovascular clinic						
No LLT	216 (15.1%)	300 (30.5%)	113 (51.1%)	677 (40.6%)	429 (37.6%)	1735 (31.9%)
Other LLT[a]	19 (1.3%)	50 (5.1%)	11 (5.0%)	84 (5.0%)	28 (2.5%)	192 (3.5%)
Low intensity statin[b]	21 (1.5%)	13 (1.3%)	1 (0.5%)	25 (1.5%)	13 (1.1%)	73 (1.3%)
Moderate intensity statin[b]	439 (30.7%)	344 (35.0%)	65 (29.4%)	552 (33.1%)	398 (34.9%)	1798 (33.0%)
High intensity statin[b]	718 (50.1%)	273 (27.8%)	31 (14.0%)	324 (19.4%)	272 (23.8%)	1618 (29.7%)
iPCSK9[c]	18 (1.3%)	1 (0.1%)	0 (0%)	5 (0.3%)	1 (0.1%)	25 (0.5%)

Data is shown as mean and standard deviation for continuous variables and frequencies and percentages for categorical variables.
Two patients missing due to incomplete recording of treatment administrated at the visit.
[a] Fibrates, niacin, Omega-3 fatty acids.
[b] Monotherapy or in combination with Ezetimibe.
[c] Monotherapy or in combination with other LLT.

In the present analysis, a significant number of patients attending a specialized cardiovascular clinic for the first time had suboptimal LDL-c levels based on their risk category. This finding was further exacerbated by the low number of patients on LLT at the time of presentation achieving their LDL-c goals, even in those treated with moderate and high intensity statins. While these results may be influenced by different risk estimations at the time of presentation, a significant number of patients were not on LLT at the time of consultation, despite having concomitant risk factors placing them in a higher risk category. This was particularly prevalent in patients with established ASCVD in which only a third were achieving the first LDL-c goal (<70 mg/dL), a goal that has been recommended since 2016 ESC/EAS guidelines [3]. Consistent with our results, other studies have also demonstrated showed high levels of undertreatment and failure to achieve LDL-c goals. The EUROASPIRE IV study conducted in 24 European countries revealed that only 21% of patients receiving LLT achieved an LDL-c <70 mg/dL. Furthermore, in patients with coronary heart disease, only 37.6% were prescribed high intensity statins at the moment of discharge and this decreased to 32.7% during follow up [11,13]. The EUROASPIRE V survey showed that in treated dyslipidaemic patients, only 46.9% achieved LDL-c <100 mg/dL [14]. Klimchak et al. reported 72.4% of patients with ASCVD in the United States have LDL-c values > 70 mg/dL and 54% of these were not receiving statins nor ezetimibe [12]. The DA VINCI study evaluated the achievement of LDL-c goal across 18 European countries [15] and found only 54% achieved LDL-c goal based on 2016 ESC guidelines [3], while 33% the achieved LDL-c goals when using the 2019 ESC guideline [5]. A sub-study analysis in Central and Eastern Europe populations showed a lower attainment of LDL-c goals (44% for 2016 and 24% for 2019 guidelines), despite 32% receiving high intensity statins. These findings highlight both the regional differences in lipid management and the discrepancies between guidelines.

There is now overwhelming evidence that statins [16–20], other lipid lowering agents such as ezetimibe and omega-3 fatty acids [21,22] and more recently PCSK9 inhibitors [23,24] can significantly reduce LDL-c levels, which translates to a reduced risk of major vascular events (statins: RR 0.79, 95% CI 0.77–0.81, per 1.0 mmol/L reduction) [25,26]. Consequently, LDL-c reduction is now recommended by all international guidelines as a cornerstone in the treatment of CVD, with more intense treatment goals recommended for those at higher risk [2,3,5]. While lifestyle changes and LDL-c reduction (≥50%) in patients with established ASCVD are consistent, the thresholds for lipid goals vary across guidelines. The 2018 ACC/AHA guidelines recommend <70 mg/dL as a goal for ASCVD patients [4], while the 2019 ESC guidelines recommend <55 mg/dL [5]. Further discrepancies between guidelines include different risk estimators and criteria used to define the risk categories [2,4,5]. Additionally, the ACC/AHA guidelines do not include a specific target goal for primary prevention, and the LLT recommendation is dependent on concomitant ASCVD risk enhancers [3–5]. In this context, the recently published 2021 ESC Guidelines on CVD prevention in clinical practice have proposed new recommendations. This includes a stepwise treatment intensification, focusing on achievement of a first step goal based on the individual risk category, and subsequent intensification of therapy based on individual characteristics. Additionally, the new guideline introduced the concept of “apparently healthy persons” and uses the SCORE2 and SCORE-OP with cardiovascular disease risk thresholds according to age, which were re-calibrated to estimate both fatal and non-fatal CV risk [2]. It is important to recognize that most clinical trials include selected populations, and thus the impact in different conditions, including in low risk patients, are not well established. This highlights the importance of analysing real-world data and identifying the gaps between guideline recommendations and real-world clinical practice. It is fundamental to understand the barriers across different regions that impact the implementation of guidelines according to the country-specific settings.

Latin-Americans have a higher CVD mortality compared with North American and European populations. In recent years Mexico has put in place national projects to increase awareness and improve treatment of CVD, which still remains the leading cause of death and second highest cause of outpatient visits in Mexico [27,28]. As such, the results from this study have important implications, including the significant undertreatment of dyslipidaemia at presentation. Multiple factors may have contributed to this. Lifestyle changes are recommended as first line therapy for CVD risk factor management [2–5], supported by studies demonstrating the beneficial impact of physical activity and diet on cardiovascular risk. [29–36] Many physicians will initially recommend lifestyle changes before implementing lipid lowering medication, however, in most cases, patients have poor adherence and lipid goals are not achieved. There is also the possibility of reluctance to use LLT due to the risk or perceived risk of side effects (eg: statin-associated muscle symptoms, new-onset type 2 diabetes mellitus, hepatotoxicity) [26]. Although these side effects have been well described in the literature, in most cases, they are rare and the benefits of treatment far outweigh the risk [37]. In our setting this nocebo effect has particular importance, as it has caused a trend in using naturopathic approaches that lack scientific evidence. An appropriate awareness and education are essential to achieve the therapeutic compliance of the patients. Recently, a study conducted by Morales-Villegas and demonstrate the impact of moderate and high intensity statins in LDL-c reduction. In this study 43.9% LDL-c reduction was achieved with atorvastatin 10 or 20 mg/day and 56.5% LDL-c reduction with the 40 or 80 mg/day dose, with very low incidence of side effects.[38]These results illustrate the efficacy of LLT on achieving lipid goals when an appropriate therapeutic program is implemented. Other contributing factors in developing countries are the use of generic medications as they are more economically accessible, however the long term comparations in hard outcomes between these products are not frequently evaluated and this must be considered when making clinical decisions.

Of note, our population also exhibited high triglycerides levels. This is of special interest in the context of CVD as previous reports have described high triglycerides, low HDL-c and normal or mildly elevated LDL-c as a frequent lipid abnormality in CVD and one which may contribute to residual CVD risk [39–41]. Several small reports have suggested that Latin-American countries have a higher prevalence of this dyslipidaemic profile, observed in 12.9–24.7% of the population [41]. Of note, is that this residual risk profile is frequently overlooked and most of the guidelines do not include specific recommendations to address this profile, which has led to a need for expert consensus about this topic [39–44]. Clinicians must be aware of the contribution of elevated triglycerides levels in CV risk and should consider them in treatment goals [42–44]. While our results highlight the importance of this particular lipid abnormality, a thorough revision of atherogenic dyslipidaemia in Mexican population is beyond the scope of this manuscript.

Our analysis revealed an important increase in the use of moderate and high intensity statins in 2019, (corresponding to the updated 2019 ESC guidelines). This behaviour reflects the impact of international recommendations on improving lipid management. Importantly, we observed a significant intensification of therapy in the high-risk groups with further consideration of CVD risk enhancers such as DM and TOD, while a more conservative approached was implemented in the low to moderate risk group. This demonstrates the importance of specialized training, particularly when new guidelines are released. Unfortunately, primary health care is frequently plagued by restricted consultation time,

resulting in inappropriate CV risk stratification and a lack of personalized approach. Primary care education and training is fundamental to avoid clinical inertia, in addition to health policies to improve the access to specialized lipid clinics.

Additionally, the choice of the LLT in our cohort may have contributed to our results. Prescription of such therapies is constrained by limited access to more potent therapies such as PCSK9 inhibitors. As demonstrated in the present study, there were a number of high-risk patients who did not achieve LDL-c goals and would benefit from additional medications, including PCSK9 inhibitors. In Mexico however, only limited medications are covered by the public health system, thus the use of newer therapies represents significant out of pocket expense for patients, which is a notable barrier for implementing these therapies in primary care.

The study has several inherent limitations that need to be acknowledged. For patients referred and previously treated by other physicians, we used their status at the time of inclusion in the study. The time-to-diagnosis and treatment, type of previous treatments, discontinuation of therapy or periods out of control goals are not included in the study. Consequently, our results are limited to reflect the clinical progression of long-standing disease, which is highly influenced by all the aforementioned factors. Secondly, given the registry-based nature of the study, the method used to report LDL (directly measured or calculated) was determined by the availability at the participating sites. Finally, of the total number of patients enrolled, a proportion of patients had insufficient data available for evaluation. A strict quality control was applied to exclude cases with insufficient data resulting in a reduction in the sample size. Nevertheless, this study included 53 different practices across thirteen regions. To our knowledge this is the largest multicenter analysis of lipid management within the Mexican population.

In conclusion, using the most recent risk estimator and lipid management guidelines, we evaluated the number of patients presenting to specialized cardiovascular clinics across Mexico who were achieving LDL-c goals. Our results demonstrate the gap between the clinical guideline recommendations and real-world data within the Mexican population. The high proportion of patients not achieving LDL-c goals identifies an urgent need for clinicians and health systems to improve CV prevention. Establishing patient education programs, specialized training in primary care and early effective clinical management are essential to improve lipid control and decrease CV risk in Mexico.

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Author contributions

MODLRI. conceived the study and supervised this work. LMLG contributed to the conceptualization, performed data analysis, validation, visualization, and wrote the manuscript with input from all authors. All authors performed sample and data collection, discussed the results and contributed to the final manuscript.

Declaration of competing interest

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The complete list of investigators and collaborators are listed in Supplementary material, Appendix S3.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.athplu.2022.08.002.

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