ESC European Society of Cardiology

European Journal of Preventive Cardiology (2025) **00**, 1–3
https://doi.org/10.1093/eurjpc/zwaf425

RAPID COMMUNICATIONS
Lipids & atherosclerosis

Evaluation of lipid levels and lipid-lowering therapy by age and sex in dyslipidaemic Mexican population

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Received 12 November 2024; revised 12 February 2025; accepted 27 June 2025; online publish-ahead-of-print 12 July 2025

Introduction

Global national trends have shown a decrease in lipid levels across high-income countries; this is not the case in low- and middle-income countries where the health systems are limited by socio-economic resources.[1] In addition, developing countries also present elevated rates of high cardiovascular (CV) risk with CV events presenting at younger ages.[2,3] Mexico in particular has shown one of the highest proportions of high-risk population (16% for men and 11% for women) compared with wealthier countries.[2]

Current CV risk scores and guidelines have been derived from international datasets and national registries/surveys across the globe.[4–8] However, Latin America is one of the regions with the largest proportion of insufficient data.[1,2] This limits our understanding of contributing factors.

This manuscript aimed to compare age and sex differences in lipid levels and lipid-lowering treatment (LLT) in Mexican patients with a known diagnosis of dyslipidaemia at their initial presentation to specialized cardiometabolic care. Additionally, we assessed the potential lifetime CV benefit of improving LDLc levels using the LIFE-CVD model.[7]

A total of 7058 patients from the REMECAR registry[9] were included in the analysis. Patients were categorized according to sex and age. Women showed higher LDLc levels as compared with men (119 ± 43.1 vs. 108 ± 43.4 mg/dL). Men showed a consistent gradual reduction in LDLc with older ages; in contrast, women showed an increase in LDLc levels in the younger groups with the highest levels (129.7 ± 42.9 mg/dL) in female patients between 50 and 59 years with a significant reduction after 60 years (117.7 ± 43.9 mg/dL) (*Figure 1B*). An adjusted general linear model showed that age between 50 and 59 years was a significant predictor of LDLc increment in women.

As the use of LLT is the major determinant of LDLc levels, we performed a detailed examination of the use of different therapies. Within the whole cohort, 47.5% (3350) were not on any established LLT at the time of their visit. Lipid-lowering treatment was ∼10% more frequently used in men compared with women. While the proportion of LLT usage increased with older age (*Figure 1C*), high-intensity statins were used in less than 20% of all age groups despite the increasing prevalence of atherosclerotic cardiovascular disease (ASCVD). Only 20.6% of patients with clinical ASCVD reached the recommended LDLc target of ≤55 mg/dL. In patients without ASCVD, only one-third (33.7%) achieve the primary prevention goal (≤100 mg/dL). There was a target goal achievement of 14.3% for high-risk (≤70 mg/dL) and 13.8% for very high-risk patients (≤55 mg/dL). Finally, we calculated the potential CV benefit of LDLc reduction using the LIFE-CVD model expressed in years free of CVD. The model was applied for patients > 40 years without ASCVD and/or other comorbidities (e.g. diabetes mellitus, heart failure, atrial fibrillation) (*n* for the model = 3982). According to the model, if our population achieved 1 mmol/L LDLc reduction (38.6 mg/dL), it would translate into an average 1.04 ± 0.33 years of CVD-free lifetime gain. The lifetime benefit was greater in women compared with men (1.17 ± 0.3 years vs. 0.825 ± 0.33 $P < 0.001$), especially

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	Female (N=3679)	Male (N=3379)	Overall (N=7058)
Age	64.1±12.4	59.9±13.8	61.9±13.3
Smoker	169(4.6%)	347(10.3%)	516(7.3%)
Diabetes mellitus	1114(30.3%)	1026(30.4%)	2140(30.3%)
Hypertension	2897(78.7%)	2442(72.3%)	5339(75.6%)
Cardiovascular Risk*			
Very high risk	1314(35.7%)	1712(50.7%)	3026(42.9%)
High risk	1490(40.5%)	1214(35.9)	2704(38.3%)
Moderate risk	35(1.0%)	15(0.4%)	50(0.7%)
Low-moderate risk	707(192%)	171(5.1%)	878(12.4%)
Atherosclerotic Disease	440(12.0%)	890(26.3%)	1330(18.8%)
Previous MI	173(4.7%)	518(15.3%)	691(9.8%)
Previous Stroke	104(2.8%)	105(3.1%)	209(3.0%)

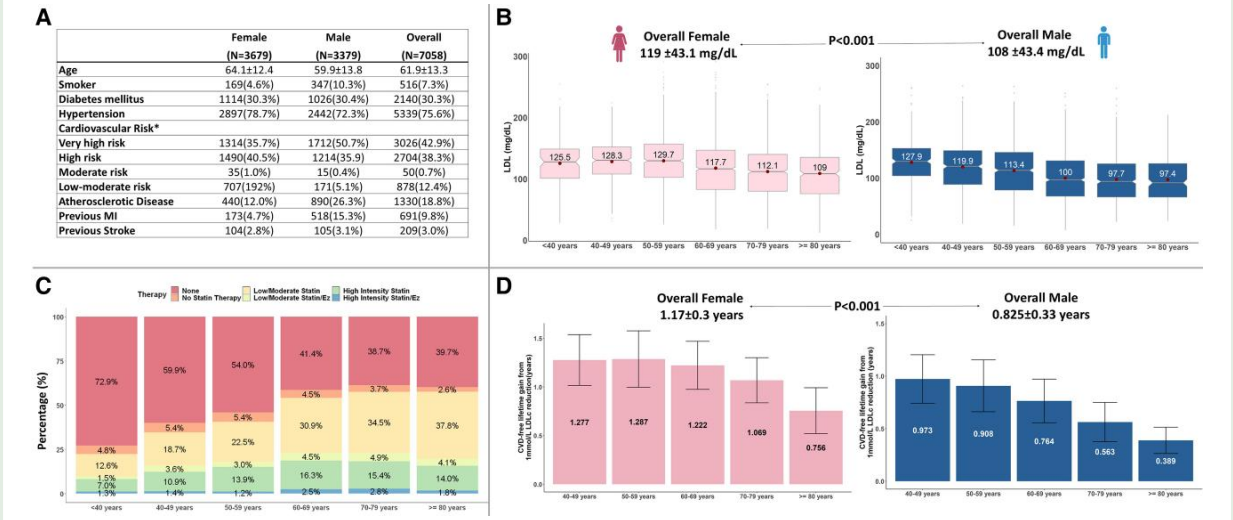

Figure 1 (*A*) Baseline characteristics. *Calculation of risk profile was performed based on 2021 prevention guidelines (missing % correspond to apparently healthy patients < 40 years or >90 as algorithms are not calibrated for this population). (*B*) Boxplot of LDLc levels. Boxes show the Q1 to Q3 quartile values of the data, with a line at the median (Q2), and mean represented as a red dot. The position of the whiskers was set to Q1 − (1.5 * IQR) for the lower whisker and Q3 + (1.5 * IQR) for the upper whisker (interquartile range: IQR = Q3 − Q1) from the edges of the box. Outlier points were added for values that extend past the end of the whiskers. (*C*) Proportions of lipid-lowering therapy usage. No statin therapy included the use of fibrates, niacin, and omega-3 fatty acids. More potent lipid-lowering treatment such as PCSK9 inhibitors were used <1% and hence are not included in the graph. (*D*) Barplot of lifetime benefit of lipid. Cardiovascular disease–free lifetime gain from 1 mmol/L LDLc reduction expressed as years. Values presented are mean ± SE. Sex-stratified results are displayed with data for women on the left and men on the right of each panel.

at younger ages. Women between 50 and 59 years old achieved the highest benefit (1.13 ± 0.33 years) (*Figure 1D*).

Age is a major determinant of CV risk. Younger people are more likely to have lower CV risk, reflecting a lower short- or mid-term CV risk; therefore, the need to achieve optimal LDLc levels is perceived as less urgent, and consequently, these patients are often less treated. However, lipid abnormalities in younger people may also represent considerably higher lifelong CV risk. This has led to recommending earlier screening at younger ages as a preventive measure.

Significantly lower LDLc levels were identified after the age of 60, which was also the group with the highest proportion of MI occurrence. This is likely a contributing factor for the significant reduction in LDLc levels, as LLT is routinely initiated or intensified once a CV event has already occurred.

In our population, >50% of younger patients were not on any established LLT and there was a lower use of LLT in females across all age groups resulting in significantly higher LDLc levels. Several factors can explain this pattern, including that the female sex has historically been attributed with lower CV risk due to biological and hormonal protection.[7] In addition, women generally present with lower modifiable risk factors. All these aspects can affect the disease perception and the therapy decision-making. It is important to highlight that younger women had the highest benefit (extra CVD-free life-years) from improving their LDLc levels, which underlines the importance of lipid management in this population, especially at younger ages when the impact of appropriate interventions can be greater.[7,10]

Recent studies have suggested that early modest and consistent reductions in LDLc could have greater benefits in reducing CV event risk than intense reductions later in life.[3,11] Long-term exposure to LDLc translates into plaque development and progression, and even with treatment, there are limitations to reducing the overall plaque burden. In our population, there was an improvement in achieving primary prevention LDLc goals with older age; however, in ASCVD patients, less than one-third of the patients achieved the recommended goals despite LLT.

Unfortunately, a large proportion of patients with mild lipid elevations may consider it unimportant and continue without any major lifestyle change, following up only if symptoms become apparent when the disease has already been established. In that context, the lifetime gain benefit is a useful tool to help patients understand the chronicity and the implications of the disease.

The results from this study have important implications, as we demonstrated that younger women have higher lipid levels and a lower proportion of LLT use, but also younger women showed the greatest predicted benefit from lipid improvement. Implementing lifestyle changes can be challenging, and a strict follow-up is required to determine if the actions are sufficient to improve lipid control or if initiation of LLT is required. Unfortunately, systematic follow-up is not routinely performed in primary care, leading to a delay in appropriate treatments. Individualized strategies to improve lipid control in primary prevention are essential to minimize the long-term exposure, development, and progression of atherosclerosis, especially in regions where socio-economic factors can influence access and adherence to more potent LLTs.[12]

Acknowledgements

The authors would like to acknowledge the contributions of REMECAR investigators in data collection.

Author contribution

M.O.D.I.R.I. conceived the study and supervised this work. L.M.L.-G. contributed to the conceptualization; performed data analysis, validation, and 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.

Funding

This research received an academic grant from Novartis.

Conflict of interest: M.O.D.I.R.I. has received travel and/or research support from Novartis, AstraZeneca, Boehringer Ingelheim, Novo Nordisk, Bayer, Amgen, Bristol Myers, Janssen, and Sanofi. M.A.A.G. has received travel and/or research support from Amgen, Novartis, and Ferrer. A.R.A. has received travel and/or research support from Amgen, Novartis, MSD, Asofarma, and Servier. P.C. has received support from Amgen, Novartis, MSD, and PTC. L.M.L.-G. has received research support from the National Council on Science and Technology, Mexico (CONACYT). All other authors have no conflict of interest to declare.

Data availability

The data of this study are available upon reasonable request by contacting the corresponding author.

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