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Abstract

Background and Aims: As a result of the current demographics, increased projections of atherosclerotic cardiovascular disease (ASCVD) and prevalence of the disease in Latin America (LA), a panel of multidisciplinary experts developed a review of ASCVD in this Region considering the available and appropriate diagnostic methods, classifying the disease and initiating appropriate treatment. The panel expects to increase the awareness of this prevalent disease, decrease consequences of ASCVD with corresponding cost savings and, ultimately, decrease the overall burden of ASCVD in LA. *Methods:* A selected panel of Latin American experts in fields related to ASCVD were provided with a series of relevant questions to address prior to the multi-day conference. Within this conference, each narrative was discussed and edited by the entire group, through numerous drafts and rounds of discussion until a consensus was achieved. *Results:* The authors propose specific and realistic recommendations for increasing the awareness of ASCVD in LA and in other countries in a similar situation. Moreover, in creating these recommendations, the authors strived to address all barriers and impediments mentioned previously within this review. *Conclusion:* This manuscript provides a review of the current state of ASCVD in LA. Additionally, the panel proposes practical recommendations that should be implemented throughout the Region in order to decrease the burden of ASCVD and effectively preventing the consequences in future generations. These recommendations can serve as a framework for LA and other countries in similar situations.

Strengths and Limitations:

The main strength of our study is the deeply revision of the role of the LDLc in the genesis of the atherosclerosis process and the point of view of different the Latin American experts in this field.

The knowledge of the different situation of the Latin American countries and how they assess the cardiovascular risk and implement the strategies in order to control this risk factor is another important strength.

- Both a strength and a weakness are the size of our author group. While a larger group may have had slightly more robust discussions, it would have been difficult to manage and produce a paper with the following methodology. Therefore, five authors were enough to execute the creation of the document quickly and concisely.
- Another strength of our study are the endorsements found at the end of the document. We have gone through great lengths to successfully discuss the importance of this LDL in Latin America with our peers.
- A weakness of our study could be that only Brazil, Colombia, Mexico, and Argentina are represented in the panel. However, we have included data from countries across Latin America, not just our own.

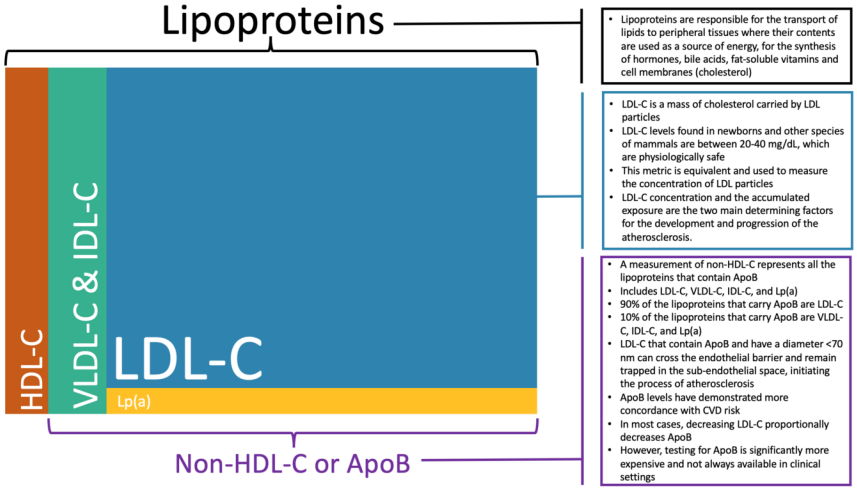
ASCVD in LATAM: A Call for Action on LDL-C Reduction

Introduction

In line with global trends, atherosclerotic cardiovascular disease (ASCVD) is the leading cause of death in Latin America (LA) (1). The evidence derived from different lines of research is concordant, consistent, and irrefutable regarding the direct relationship between low density lipoprotein-cholesterol (LDL-C) levels, apolipoprotein B (ApoB) levels, and ASCVD (2). Risk factors associated with the disease are highly prevalent in the Region, however, the pattern and level of these risk factors varies by country and within countries. Primary and secondary prevention for ASCVD have been demonstrated to be effective in decreasing mortality. Regardless of prevention being vastly encouraged at all levels of care, lack of capacity to identify the right patient, lack of knowledge of pharmacotherapy indications and misunderstanding of basic concepts are hindering the possibility to impact ASCVD outcomes in the region (3).

LDL-C is the essential, causal agent for the atherosclerosis genesis and progression. ASCVD risk factors, such as high blood pressure, smoking, and diabetes favor and enhance the atherosclerosis process initiated by endothelial dysfunction and the deposition of ApoB (Figure 1). This article will assess the reality in LA regarding atherosclerosis, highlight and summarize new evidence available to prevent and treat ASCVD in the region (4).

Figure 1. Total Cholesterol Distribution and Lipoprotein Biology



Materials and Methods

To address the above issues, the Americas Health Foundation (AHF) identified clinicians and scientists with an academic or hospital affiliation who are experts in the field and who have published in the CVD arena since 2013. As a result of this effort, AHF convened a five-member panel of clinical and scientific experts from LA. Great attention was paid to ensure a diverse group representing various disciplines related to CVD.

To better focus on the discussion, AHF staff independently developed specific questions, addressing the salient issues on the subject, for the Panel to address. A written response to each question was initially drafted by a different member of the Panel. During the multi-day meeting of the Panel, each narrative was discussed and edited by the entire group, through numerous drafts and rounds of discussion until complete consensus was obtained. The objective of this article is to create a practical document with standardized guidelines for screening and diagnosing ASCVD in LA.

Supporting evidence

In 1913, Anitschow demonstrated the relationship between cholesterol consumption and the formation of atheroma plaques by feeding mice a high cholesterol diet, reproducing the disease in an experimental model and evidencing the causal role of cholesterol in the pathogenesis of the atherosclerotic phenomenon (5). Later in 1939, Müller described the association between high levels of circulating cholesterol in families and the increased risk of ASCVD (6). The presence of cholesterol in experimentally induced atherosclerotic plaques in herbivores supports and reinforces the biological-experimental evidence of the cholesterol-atherosclerosis relationship (7). Furthermore, the description of populations with extremely high levels of LDL-C such as cases of Familial Hypercholesterolemia (FH), both heterozygous and homozygous, and its high prevalence of ASCVD provides clear pathophysiological evidence of this causal relationship (8).

The evidence derived from prospective epidemiological studies demonstrates a linear relationship between LDL-C levels and the risk of ASCVD. Two large meta-analyses summarize this evidence; the Collaboration Prospective Study and the Emerging Risk Factor Collaborations. The former reported data from 892,337 participants without evidence of ASCVD from 61 prospective cohort studies with a follow-up of 12 million individual-years; as a result, a direct association between plasma cholesterol levels and the risk of mortality from ischemic heart disease (IHD) was demonstrated. The latter collected data from 302,430 people without baseline ASCVD from 68 prospective studies, with a follow-up of 2.7 million individuals-years; as a result, a linear association was described between the levels of LDL-C and fatal and nonfatal myocardial infarction (MI) (9-10).

Mendelian randomization (MR) studies demonstrate evidence of causality, avoiding confounding factors, biases and reverse causation, potential characteristics of epidemiologic studies. MR studies also allow observational anticipation of the results of randomized and controlled studies. These genetic studies have unequivocally determined the association of more than 50 genes related to low levels of LDL-C and decreased risk of ASCVD. Randomized studies (average 5 years of follow up) with statins have shown a relative risk reduction (RRR) of 22% per 38.67 mg/dL (1mmol/L) of decrease in LDL-C (11). MR studies (lifetime effect) showed that with the same LDL-C decrease levels, an RRR of 55% is achieved. This evidences the deleterious cumulative effect of the deposit of LDL-C, emphasizing the need for early treatment strategies (12-13). On the other hand, MR studies have shown that the beneficial effect of the decrease in LDL-C is independent of the mechanism that produces this effect; these types of studies have also provided important information regarding the safety of low levels of LDL-C as well as potential pharmacological targets for the development of new therapeutic strategies (14).

Evidence derived from RCTs provides an unequivocal causality relationship between LDL-C levels and the atherosclerotic phenomenon. Studies using cholestyramine (15), and one study performing partial ileal bypass (16), have shown that decreasing LDL-C levels result in reduced risk of cardiovascular events. The Cholesterol Treatment Trialists' (CTT) Collaboration analyzed 26 studies with statins that included almost 170,000 patients, demonstrating an RRR of cardiovascular events greater than 22% for every 38.6 mg/dL (1 mm/L) of decrease in LDL-C. This effect was independent from the baseline value of LDL-C and from the existence of previous ASCVD, evidenced in the different subgroups analyzed (11, 17).

The IMPROVE-IT trial demonstrated that adding ezetimibe to statins resulted in a reduction of major cardiovascular events through a different mechanism than the inhibition of cholesterol synthesis. The magnitude of the risk reduction in cardiovascular events was consistent with the decrease in levels of LDL-C, agreeing with the evidence in the studies with statins (18).

The use of proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibition in the trials Further Cardiovascular Outcomes Research with PCSK9 Inhibition in study participants with Elevated Risk (FOURIER -27,564 patients-) (19) and (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab) (ODYSSEY Outcomes -18,924 patients-) (20) achieve low levels of LDL-C never seen before, evidencing a reduction in the risk of cardiovascular events proportional to the decrease in circulating levels of LDL-C. It should be noted that there were no safety concerns when reaching such low levels of LDL-C (15-20 mg/dL). In addition, the benefit was continuous as the LDL-C values decreased, implying that there is no J-curve effect with a lower limit for LDL-C (21-22). Finally, GLAGOV

trial with evolocumab, showed statistically significant regression of the atherosclerotic plaque measured by intravascular ultrasound when reaching an average level of 37 mg/dL of LDL-C (22).

Dyslipidemia Prevalence

LATAM is characterized by its high racial diversity, especially in Brazil, which along with other socioeconomic factors have an impact on measured levels of LDL-C. The variation in the different lipoprotein levels among the countries in the region makes it very difficult to compare prevalence and type of dyslipidemia by country (1). Dyslipidemia control in the region is inefficient and awareness of the disease differs by demographics and socioeconomic status. In Brazil, the prevalence of self-reported high cholesterol levels was 12.5%, however, the measured prevalence of dyslipidemia was estimated to be 46.6% (23-24).

The established prevalence of high cholesterol levels > 200 mg/dL in adults older than 25 years of age in LATAM countries ranges from 30-60% of the population (1). A 2019 report by World Health Organization (WHO), comparing total cholesterol levels by region showed that LATAM has higher values compared to most other regions in the world (1). The established prevalence of high LDL-C for the region has been reviewed and is very difficult to establish due to scarce information. However, data on prevalence of hypercholesterolemia in different countries can be seen in Table 1 (25). In the INTERHEART study, alterations of the lipid profile were most frequent in controls from LATAM than the other regions studied (26).

Table 1. Prevalence of Dyslipidemia in different countries of LATAM

Country	Year	Prevalence	Threshold of Total Cholesterol (mg/dl)
Argentina (27)	2018	28.9%	200
Brazil	2011	22%	190
Chile	2013	39%	200
Colombia	2013	8%	240
México	2013	43.6%	200

Adapted from Fernando Lanas, Pamela Serón, Alejandra Lanas. Coronary Heart Disease and Risk Factors in Latin America. Global Heart 2013; 8 (4): 341-348

Familiar Hypercholesterolemia (FH)

In LATAM, FH is largely underdiagnosed and undertreated as a result of the lack of general awareness of the disease. Considering a prevalence of 1/300-500 for the heterozygous and 1/300,000-1,000,000 for the homozygous, it is estimated that there are at least 1,250,000 to 2.5 million people with FH in the region (28). Despite high LDL-C and even after an atherosclerotic event, a large proportion of individuals with FH remain unidentified and untreated. FH is a clear example of high-risk patients, with very high levels of LDL-C in which it is necessary to have an accurate and timely diagnosis and an aggressive treatment approach (29-30).

Treatment of LDL-C

The most important groups of hypolipidemic drugs available for the treatment of LDL-C supported by scientific evidence are statins, ezetimibe, and PCSK9 inhibitors (PCSK9i).

Statins

3-hydroxy-3-methyl-glutaryl-CoA (HMG-CoA) reductase inhibitors, known as statins, constitute the most commonly, useful and effective lipid-lowering group for primary and secondary cardiovascular prevention. HMG-CoA reductase is a key enzyme in cholesterol biosynthesis and its inhibition increases the expression of LDL receptor (LDLr) on the surface of hepatocytes, with greater hepatic uptake of LDL-C, leading to a reduction of the concentration of this lipoprotein in plasma.

There is compelling evidence to support the use of statins in cardiovascular prevention. Statin use reduces LDL-C by 20-50% depending on potency and dose (31) and have shown an overall benefit with a 22% risk reduction in major cardiovascular events (11).

In primary and secondary prevention, the benefit of the use of statins is proportional to the baseline risk (32). The benefit of ASCVD risk reduction includes patients in low and moderate cardiovascular risk categories (11, 33-34). Furthermore, patients with diabetes mellitus (DM), given their higher risk of ASCVD, have improved benefits in terms of the reduction of major events (35).

In patients 75 years or older, statin therapy is recommended with half of the standard dose and has shown benefit, particularly in patients with previous ASCVD or with established disease (36). Discontinuation of treatment in this patient population has demonstrated an increased mortality risk, hence, interruption is not an option (37).

Statins are safe. Adverse events associated with statins are not related with major disease or complications. The most common adverse event of these drugs is statin-associated muscle symptoms and recommendations to manage this clinical condition have been published (38). An increased risk of incident diabetes with statin use (39) has been seen with a low risk in absolute terms and when compared with benefits. The risk is higher with intensive statin treatment (40).

Ezetimibe

Ezetimibe is a selective inhibitor of intestinal biliary and dietary absorption of cholesterol due to interaction with Niemann-Pick C1-like 1 (NPC1L1) transporter protein located in the brush border of enterocytes (41). The reduction in cholesterol content of chylomicrons and remnants produces an increase of LDLr expression, thus reducing circulating LDL-C concentration. Ezetimibe in monotherapy reduces LDL-C by 15-22% (42). The overall impact of adding ezetimibe compared with statin monotherapy was a 23% lower LDL-C (43). The IMPROVE-IT study showed that ezetimibe, when added to a statin, reduced major cardiovascular events in patients after suffering an acute coronary syndrome. In addition to proving its safety, there was no increased risk of muscle or liver toxicity, gallbladder lithiasis or cancer (19).

PCSK9i

PCSK9 is expressed primarily in the liver and small intestine and plays a very important role in cholesterol metabolism (44). PCSK9 is secreted by liver cells, circulates in plasma, binds to LDLr, and is subsequently internalized together with the LDLr, thereby promoting the cellular degradation of the receptor. This reduction in the amount of LDLr at the surface of hepatocytes is responsible for the increase of LDL-C concentration in plasma. PCSK9 and LDLr binding may be interrupted by different mechanisms (45). The use of human monoclonal antibodies against PCSK9 has proven to be effective as monotherapy leading to a 57% reduction in LDL-C, a 46% reduction in ApoB, and a 24% reduction in Lp(a) (46).

The FOURIER was a trial performed with evolocumab (PCSK9i) that showed cardiovascular benefit (22) with RRR of 50% in patients with ASCVD and elevated LDL-C levels treated with moderate or high intensity statins. The addition of evolocumab showed unprecedented LDL-C average levels of 30 mg/dL and 42% of patients reached LDL-C levels < 25 mg/dL (47).

The ODYSSEY OUTCOMES study (48) evaluated the effect of alirocumab (PCSK9i) on residual risk reduction in patients with a recent acute coronary syndrome. The results further demonstrated the utility of PCSK9i in significantly reducing major cardiovascular events and safely reaching very low LDL-C levels.

Most guidelines recommend goals for LDL-C reduction that have been clinically useful as a measure of therapeutic success. In clinical practice, however, not all patients achieve their LDL-C goal with statins alone and increasing awareness of this treatment gap has led to the need to consider the routine use of combination lipid lowering therapy (LLT) (Table 2).

Table 2. Intensity of lipid lowering treatment.

Treatment	Average LDL-C Reduction
Moderate intensity statin (other than rosuvastatin 20-40 mg or atorvastatin 40-80 mg)	[?] 30%
High intensity statin (rosuvastatin 20-40 mg or atorvastatin 40-80 mg)	[?] 50%
High intensity statin + ezetimibe	[?] 65%
PCSK9i as monotherapy	[?] 60%
PCSK9i + high intensity statin	[?] 75%
PCSK9i + high intensity statin + ezetimibe	[?] 85%

Current Guidelines for Management of ASCVD Risk

National and international evidence-based guidelines for primary and secondary prevention of ASCVD are available (49-52). These guidelines are all moving toward the same direction in order to tackle ASCVD with strong emphasis on secondary prevention and LDL-C reduction. Although international guidelines are based on trials of a predominantly white population, the LATAM population is represented.

Several international guidelines, including those for LATAM, were updated in 2018 and 2019 as a result of new evidence from RCTs and genetic studies that support the causal relationship between LDL-C and ApoB in relation to ASCVD. Currently, these guidelines recognize that treatment decision making is based on risk stratification, which is divided into low, moderate, high, and very high. Some subgroups of patients with very high risk should be recognized in order to identify those who need an aggressive treatment approach (Table 3).

Table 3. Risk Stratification of Very High Risk ASCVD Patients

Very high-risk patients
Secondary Prevention + FH
Secondary Prevention + DM
Secondary Prevention + Chronic kidney disease
Secondary Prevention + Polyvascular disease
Secondary Prevention + Recurrent events
Acute Coronary Syndrome during 1 year + LDL-C > 100 mg/dL

All these guidelines recommend lifestyle changes and an appropriate control of all risk factors associated with ASCVD (Table 4). The guidelines recognize that LDL-C is directly related with ASCVD and highlight the importance of statins and other therapies in order to reduce LDL-C levels. Risk stratification in a multivariant analysis includes LDL-C levels and other risk factors to determine the treatment objective. Furthermore, guidelines emphasize that high-risk and very high-risk patients will largely benefit from reduction in LDL-C levels through combination of new pharmacologic interventions. Finally, most agree that achieving lower levels of LDL-C is safe.

In concordance with international guidelines, several countries in LATAM have created their own national guidelines sharing these same basic concepts. Local guidelines reflect epidemiological data, socioeconomic factors, group experiences, pharmacoeconomic analysis and drug availability. Thus, it is critical that local guidelines are utilized in order to determine treatment objectives for patients within each country (53). Furthermore, national guidelines should assess the risk stratification based on population demographics and recommend associated LDL-C goals (49-50, 54-56).

Despite scientific evidence recommendations in clinical practice regarding the benefit of the use of lipid-lowering therapy (LLT), worldwide use of these medications is low even in patients who have suffered a cardiovascular event (3). The Prospective Urban Rural Epidemiology (PURE) study included 5,650 participants with a history of ischemic heart disease (IHD) and 2,292 with a history of stroke from 17 countries with

different income levels. The overall use of cardiovascular proven effective secondary preventive drugs was low, especially for statins where the use was 14.6%. These percentages were higher in high-income countries where statins use was 66.5%, with the lowest use in low-income countries reported to be 3.3%. Importantly, country-level factors (e.g., economic status, income) affect rates of drug use more than individual-level factors (e.g., age, gender, level of schooling, smoking status, body-mass index, hypertension and diabetes) supporting socioeconomic status as a major determinant of these drugs (3).

A sub-study of PURE analyzed statin use in South America and showed that usage in post-IHD patients was only 18% and in previous stroke 9.8% (57). Multivariate analyses revealed markers of wealth had the largest impact in the use of these medications. Thus, socioeconomic status affects the use of secondary prevention medication increasing inequalities for low- and middle-income countries (LMICs) (58).

In cardiovascular primary prevention, the EPICO study found that statins in patients with high cholesterol were used in low rates (40.4%) and in lower doses than those recommended by guidelines (simvastatin 20mg), thus leading to inefficient control of LDL-C (59). The preliminary results of PINNACLE-Brazil show that, despite the relatively high prescription rate of statin therapy (81%), LDL-C targeted level for ASCVD secondary prevention was not achieved in the majority of patients (60). As an example of this situation, in Mexico, only 20% of the hypercholesterolemic patients are being treated adequately (28).

There are many therapeutic interventions that require efforts from the public health perspective in order to prevent ASCVD risk. These interventions have proven to decrease cardiovascular risk and have to be accompanied by lipid lowering drugs to ensure LDL-C levels are at the lowest possible (SOURCE). The general objectives of these complementary interventions are listed on Table 4.

Table 4. Therapeutic Objectives in ASCVD Prevention

Diet Food should be low in saturated fat, with whole grains,

vegetables, fruit and fish

Physical Activity Physical exercise for 2.5-5 hours per week (30-60

minutes for 5 days per week)

Body Weight Maintain a BMI between 20 and 25 kg/m2; and

abdominal girth of <94 cm in men and <80 in women

Blood Pressure Maintaining <140/90 in the general population and

<130/80 in those with diabetes

Smoking cessation Avoid smoking and exposure to tobacco smoke

HbA1c <7.0%

Health Systems in LATAM and ASCVD

Considering LATAM's vast geography and population sizes, there is an unsurprising variability in the demographics and disease indicators within the countries. Across the region, access to healthcare is considered a basic right for every individual. However, LATAM faces the challenge of rising healthcare costs, resource inefficiencies, income disparities and the epidemiological transition from infectious to chronic diseases (61). New health care delivery models have promoted universal health insurance coverage and introduced new financing mechanisms that have shifted health care funding from health care supply to health care demand (62). Additionally, most systems are dependent on out-of-pocket payments, specifically for medications, creating an additional barrier for access (63). For example, statins are not universally covered by systems in the region and studies show that 78% of these medications are paid out-of-pocket (28).

After the Declaration of Alma-Ata, many countries in LATAM introduced reforms to improve access to health, financial protection, and increased efficiency in health services (64). Colombia, Chile, Mexico, Peru,

and Uruguay were the first to implement these health reforms (61). Analysis of a longitudinal community based primary health care program with family health physician strategy in Brazil, acting through ASCVD prevention care and follow-up contributed to decreased cardiovascular and cerebral disease morbidity and mortality (65).

Most health systems in the region are composed of a public and supplementary health systems, which vary vastly, cover different services, and pay differently for medications and technologies increasing inequalities within the population. Most public systems are complex, composed of many agencies, and cover the vast majority of the population with a few exceptions. The private sector includes the insurance companies and health administrators and covers a small portion of the population (66). These inequalities within countries further gaps to prevention, access and adequate treatment in populations across the region.

Accessibility to LDL-C Lowering Treatments

Access to medication in LMICs is limited (67). If LDL-C lowering treatments are not included in the basic medication plans, the population requiring treatment will not have access due to financial barriers. The availability of medication for chronic diseases (including ASCVD) was reported to be less than 30% in public facilities across six LMICs, with a wide variation in affordability of one month of IHD treatment, ranging from 1.5 to 18.4 days of a minimum wage (68). Affordability of combination therapy for secondary prevention of ASCVD (aspirin, beta-blockers, ACE inhibitors, and statin) using a threshold of 20% of per household capacity to pay was evaluated. In low income countries, the use of the four drugs was not affordable for 60% of participants, and 33% of those in lower-middle income countries (68).

Access to pharmacological treatment for LDL-C is uneven within the countries in the region. Costs of these treatments may be more relevant in some instances. For example, in Brazil, the median cost of the recommended statin for ASCVD was only affordable for 3% of Brazilian households (67, 69). High-intensity statins are available in various public health systems across the region. However, in some countries these medications are not covered, making them unaffordable for the majority of the population (70). In other scenarios, high intensity statins, although approved, are not available at local pharmacies. The alternative to access medication through judicialization is a reality in several LATAM countries; this strategy demonstrates the need to implement effective measures for the correct access to medication (71).

Decreasing drug prices achieved with the introduction of generics have a strong impact on the incremental cost-effectiveness ratio for statin therapy and may prove to be appropriate treatment even for very low-risk patients. From a cost perspective, treatment decisions should not be made strictly based on financial criteria, but through an evaluation of each patient's risk level as well as the current drug availability. It should be noted that treating patients based purely on an evaluation of cost-effectiveness would mean statin therapy should be expanded beyond current treatment guidelines to include lower risk patients (72). The programs that follow the clinical practice guidelines based on statin reduction of LDL-C are cost-effective across the spectrum of cardiovascular risk. The addition of ezetimibe and PCSK9i for high risk patients and patients with high-risk FH is also cost effective. These economic analyses are needed to allow health systems to recognize the population that will benefit from such therapies (73).

Several access barriers to management of ASCVD have been identified across the region. Medical inertia to implement preventive medicine has been reported in LATAM countries (74) because physicians treat the disease and not the cardiovascular risk.

Some of the programs implemented in LATAM are aimed at reducing NCDs and focus on reducing ASCVD, however, LDL-C profiles are not measured and treatment awareness in both the primary and secondary settings is lacking (74). Throughout the years, LATAM has strengthened the generic medication policy by encouraging uptake in treatment by patients, aiming to reduce the number of deaths and hospitalizations due to NCDs (75-77). ASCVD is the leading cause of death in LATAM and despite a consistent decrease in mortality trends it continues to account for over 5 years of life lost in most countries (78).

Recommendations

This panel has addressed the particular issues related to the irrefutable need for adequate treatment of elevated LDL-C levels in LATAM. ASCVD is the leading cause of death in the region and the relationship between elevated LDL-C and the risk and progression of this disease has been thoroughly demonstrated (79). Despite vast recommendations for primary and secondary prevention at all levels of care, the possibility to impact cardiovascular outcomes across the region is hindered by several issues. A number of recommendations are proposed in order to achieve a comprehensive approach to the management of LDL-C are listed below and organized by stakeholder:

For Governments

- Address local barriers to ensure appropriate access to treatment for lowering LDL-C, especially for high and very high-risk patients
- Systemically measure treatment to goal as a management metric to better drive diagnosis and treatment
- Initiate dialogs with various stakeholders to approach innovative purchasing mechanisms including managed entry agreements, pooled procurement, and risk sharing schemes, among others
- Include Medical-Scientific Societies in the decision-making process related to the appropriate use of lipid-lowering therapy and ASCVD prevention

- Inform the public regarding the importance of ASCVD prevention to control severe risk with widely broadcasted primary preventive programs

For Scientific Societies

- Ensure continuous education about ASCVD risk among all healthcare professionals involved in CVD prevention
- Develop and update dyslipidemia and atherosclerosis guidelines
- Advise the government in the decision-making process regarding health policies impacting cardiovascular disease
- Implement outreach and education programs for communities on the importance of understanding ASCVD risk factors, specifically measuring and tracking LDL-C

For Physicians

- Recognize the importance of LDL-C in the genesis and progression of atherosclerosis
- Improve cardiovascular outcomes by appropriately stratifying the high risk and very high-risk population
- Avoid delay in therapy initiation for primary and secondary prevention
- Avoid discontinuation of ASCVD medication for all patients
- Highlight the gaps in medical education regarding ASCVD
- Identify patients with high LDL-C and perform appropriate treatment and follow up, reinforcing the proper use of hypolipidemic agents in ASCVD at risk populations
- Dispel myths associated with dangers of very low LDL-C levels and lipid lowering therapy
- Recognize which patients need to be referred to specialists

For Patients

- Follow medical indications to reduce risk of ASCVD
- Understand the major risks of discontinuing LDL-C lowering medication
- Know personal LDL numbers and seek regular wellness physicals with standard lab tests in order to strive for optimal health
- Promote awareness of cardiovascular risk and high LDL-C levels

Endorsements

The panel believes that as a result of implementing the above recommendations all adults will be better informed about ASCVD, factors that may lead to ASCVD, current recommendations and the fact that

ASCVD is, in fact, a major chronic disease affecting many adults in LA. For the official seals of the below societies, please see Appendix A.

These Recommendations have been endorsed by:

- Sociedad Mexicana de Cardiologia (Mexican Society of Cardiology)
- Sociedade Brasileira de Cardiologia (Brazilian Society of Cardiology)
- Sociedad Argentina de Lípidos (Argentine Lipid Society)
- Sociedad Argentina de Cardiología (Argentine Society of Cardiology)
- Sociedad Colombiana de Cardiologia y Cirugía Cardiovascular (Colombian Society of Cardiology and Cardiovascular Surgery)

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Conflicts of Interest

The co-authors declare no conflicts of interest. The organization and implementation of the consensus conference was carried out by the Americas Health Foundation (AHF), a 501(c)3 nonprofit organization dedicated to improving healthcare throughout the Latin American Region and was supported by unrestricted grants from Amgen.

Author Contributions

All authors participated and made significant contributions to the data search, drafting, and discussion of the topic and all subtopics provided in this manuscript.

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Appendix A:

Figure 1: This is a caption