

Beyond LDL Cholesterol

Más allá del colesterol LDL

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If we had to succinctly summarize the key reasons why LDL cholesterol (LDL-C) became the central focus in the management of atherosclerotic dyslipidemia, three core arguments would stand out beyond dispute. The first is the compelling clinical benefit derived from therapeutic interventions—across various drug classes and their combinations—that consistently reduce major adverse cardiovascular events (MACE). These outcomes clearly illustrate the significance of targeting LDL-C.⁽¹⁻³⁾ The second pillar lies in the well-established linear relationship demonstrating that each 1 mmol/L reduction in LDL-C corresponds to a 22% decrease in MACE risk, a figure that is both intuitive and impactful.⁽⁴⁾ Finally, and no less importantly, the absence of a J-shaped curve—together with the broad scientific consensus on the causal relationship between LDL-C and atherosclerosis—reinforces the safety and efficacy of aggressive lipid lowering. This understanding has been crucial in recognizing that intensive treatment prolongs life by directly addressing a core mechanism of the disease.⁽⁵⁾ Thus, LDL-C control has become deeply embedded in all clinical practice guidelines and continues to serve as the foundation for setting precise therapeutic targets based on individual cardiovascular risk profiles.

However, the story does not end there—and that is precisely where the work of Pacce O et al., published in this issue of the *Revista Argentina de Cardiología* (RAC), becomes relevant: it intellectually invites us to look beyond the LDL-C value.⁽⁶⁾ The central value of this publication lies in its contribution—based on local evidence—to highlight the importance of not overlooking the broad universe of pro-atherogenic particles that exist beyond LDL-C, even when LDL-C levels are adequately controlled. This is, in essence, an exploration into the world of residual risk and its clinical relevance, with non-HDL cholesterol (non-HDL-

C) serving as the vehicle for that journey. Much has already been written about the descriptive capacity of lipid-related residual risk attributed to both non-HDL-C and apolipoprotein B (ApoB) when considering MACE or vascular events.

Although ApoB appears to offer greater discriminatory power for overall atherosclerotic risk⁽⁷⁾ and exhibits lower biological variability,⁽⁸⁻¹⁰⁾ this study reaffirms that non-HDL-C remains a clinically relevant parameter. Indeed, its cost-neutral nature—requiring no additional resources beyond the standard lipid panel—and its reasonable correlation with ApoB⁽¹¹⁾ make it a valuable tool, especially in low- and middle-income countries such as Argentina. Moreover, by the end of the article, the strong association between non-HDL-C and short-term MACE in secondary prevention patients—those we encounter daily in our clinical practice—is once again clearly exposed. In this light, the extensive body of work by authors such as Børge Nordestgaard on the clinical impact of triglyceride-rich lipoproteins and remnant cholesterol seems to come alive once again in our region.⁽¹²⁻¹⁵⁾

In conclusion, the article by Pacce O et al. contextualizes the clinical utility of assessing non-HDL-C in the management of our patients—particularly in a country as diverse as Argentina, where financial and technological resources are not always available to support large-scale implementation of even low-cost strategies. It is yet another call to action: to take the initiative in establishing clinical practice guidelines that incorporate treatment goals beyond LDL-C alone, without diminishing its well-established pathophysiological and therapeutic relevance.

Conflicts of interest

None declared

(See authors conflicts of interest forms on the website).

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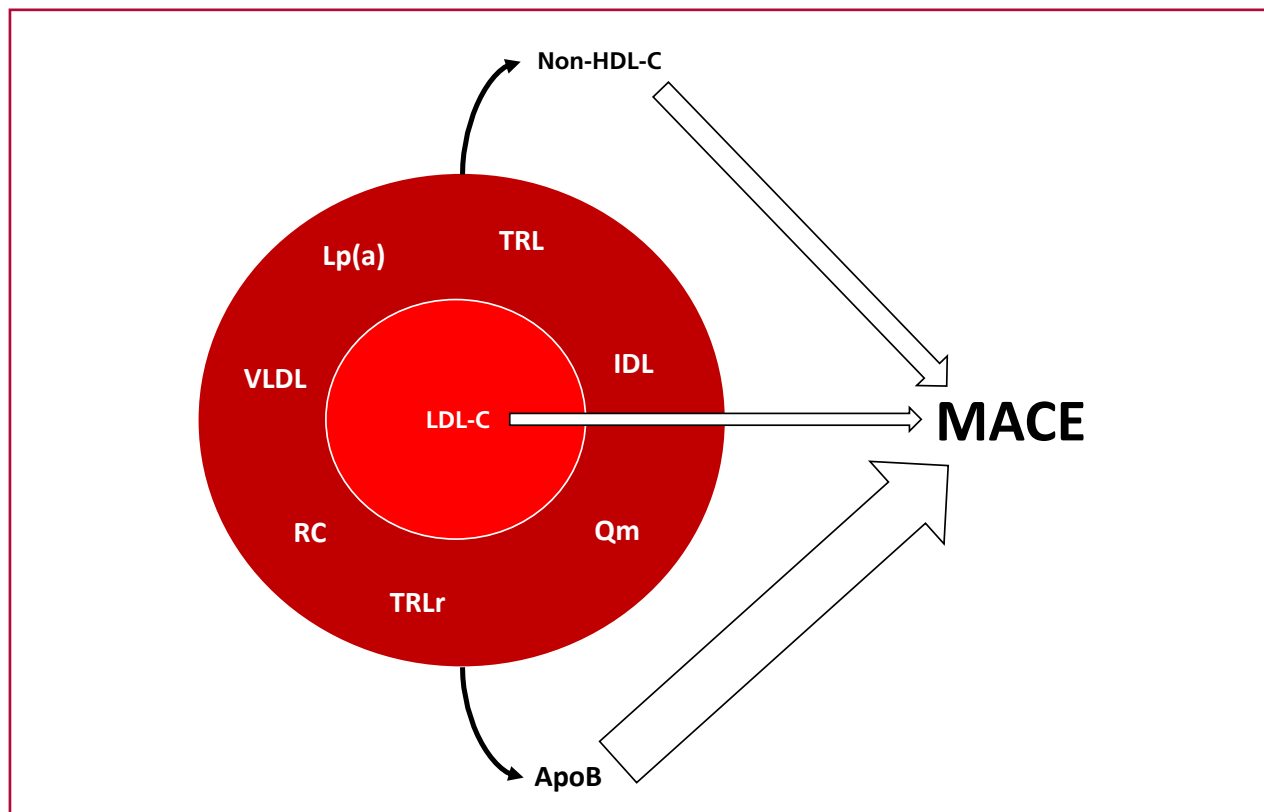


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Fig 1. Lipid species and their impact on MACE

ApoB: apolipoprotein B; IDL: intermediate-density lipoproteins; LDL-C: LDL cholesterol; Lp(a): lipoprotein a; non-HDL-C: non-HDL cholesterol; Qm: chylomicrons; RC: remnant cholesterol; TRL: triglyceride-rich lipoproteins; TRLr: triglyceride-rich lipoprotein remnant; VLDL: very low-density lipoproteins

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