**Summary of the PhD thesis**

# "Algorithm for the Calculation of Cholesterol Fractions Relevant to Atherogenic Risk Assessment"

**PhD Candidate**: Györfi (Ugron) Imola
**PhD Supervisor**: Prof. Dr. Dobreanu Minodora

Over the past two decades, precision medicine has become a central direction in medical research and daily clinical practice, aiming to personalize prevention and treatment to the individual characteristics of each patient [1]. Cardiovascular diseases remain the leading cause of death worldwide, accounting for approximately 18 million deaths annually [2].

The assessment of dyslipidemia in clinical practice involves the determination of the standard lipid profile, which includes total cholesterol, HDL cholesterol, triglycerides, and LDL cholesterol, the latter being considered the main atherogenic risk factor [3,4]. In laboratory practice, LDL cholesterol can be determined either by direct or indirect methods. Direct methods are considered closer to the true value; however, they present certain limitations related to cost and variability between analytical platforms. Therefore, indirect estimation is frequently used in routine practice. To date, more than 20 formulas have been proposed for LDL cholesterol estimation, the most commonly used being the Friedewald formula, which has important limitations in certain clinical situations [5].

The objectives of this study were to evaluate the accuracy of LDL cholesterol determination methods, to analyze the comparability between different analytical platforms, and to identify the most appropriate LDL cholesterol estimation formulas depending on population characteristics and analytical methods. Furthermore, the study aimed to develop and validate calculation models adapted to the Romanian population, allowing for a more precise estimation of LDL cholesterol and a more accurate classification of patients according to cardiovascular risk. The results of the research were materialized in the publication of three scientific articles [6–8].

The first retrospective observational study provided a comprehensive analysis by comparing 24 LDL cholesterol estimation equations applied to two large patient cohorts and referenced against direct measurement methods [6]. Although commonly used formulas such as Friedewald, Martin-Hopkins, and Sampson showed moderate performance, several lesser-known equations proved to be superior, both in value estimation and clinical classification, particularly around the 70 mg/dL threshold. The performance of the equations varied between the two datasets, suggesting that both population characteristics and the reference method influence their accuracy. Overall, the results support the need for an approach adapted to the clinical and population context, especially in patients with low LDL cholesterol values or elevated triglycerides.

The second retrospective observational study evaluated the comparability between different analytical platforms used for measuring lipid parameters and apolipoproteins [7]. The results showed good agreement for total cholesterol and LDL cholesterol, with minimal clinical impact; however, for HDL cholesterol and triglycerides, the differences may become clinically relevant within certain value ranges. Regarding apolipoproteins, the differences between methods were significant and may influence clinical decision-making. These findings support the recommendation that patient monitoring should be performed, whenever possible, using the same analytical platform.

The third methodological study aimed to develop and validate LDL cholesterol estimation equations adapted to the Romanian population [8]. Both developed models demonstrated superior performance compared to the Friedewald formula, in terms of both estimation accuracy and cardiovascular risk classification. The results highlight the clinical value of using population- and platform-specific formulas, although their implementation is currently limited by the lack of clear recommendations in clinical guidelines.

The originality of this work lies in the integrated analysis of LDL cholesterol determination methods, ranging from commonly used calculation formulas to the development of new models adapted to the Romanian population. This represents the first study conducted in Romania to systematically compare a large number of LDL cholesterol estimation equations with directly measured values across two different analytical platforms (Roche Cobas and Abbott Alinity), using a large dataset of over 31.000 lipid profiles. This approach provides a detailed overview of the performance of currently used formulas and highlights population-specific characteristics. Another element of originality is the development and validation of two local LDL cholesterol calculation formulas adapted to the analytical platforms used.

Overall, the thesis contributes to strengthening the role of the clinical laboratory in precision medicine by providing validated tools that can support medical decision-making based on accurate data adapted to the characteristics of the studied population.

## References

1. Schleidgen S, Klingler C, Bertram T, Rogowski WH, Marckmann G. What is personalized medicine: sharpening a vague term based on a systematic literature review. *BMC Med Ethics*. 2013;14(1):55.

2. World Health Organization. Cardiovascular diseases (CVDs). 2025;04–14.

3. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al. 2018 AHA/ACC Guideline on the Management of Blood Cholesterol. *J Am Coll Cardiol*. 2019;73(24):3168–209.

4. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS Guidelines. *Eur Heart J*. 2020;41(1):111–88.

5. Friedewald WT, Levy RI, Fredrickson DS. Estimation of LDL cholesterol. *Clin Chem*. 1972.

6. Györfi I, Oprea OR, Mănescu IB, Curici A, Dobreanu M. Comparative Evaluation of 24 LDL-C Estimation Equations. *Diagnostics*. 2025.

7. Györfi I, Oprea OR, Mănescu IB, Dobreanu M. Variability of lipids and apolipoproteins across platforms. *J Lab Med*. 2026.

8. Györfi I, Mănescu IB, Oprea OR, Curici A, Fotache AM, Dobreanu M. Toward accurate LDL-cholesterol estimation. *Scand J Clin Lab Invest*. 2025.