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Poster #**EE202**

Cost-effectiveness analysis of generalizing reimbursement of Lp(a) testing in secondary prevention in a population of French patients with cardiovascular disease

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KEY FINDINGS & CONCLUSIONS

- The widespread reimbursement of Lp(a) testing is a cost-effective strategy for improving CV risk management as it improves morbidity, mortality, patients' quality of life and generates savings for the healthcare system.
- Today, Lp(a) testing is not reimbursed in France. Reimbursement would facilitate access and broader adoption of the testing, thereby generating even greater savings through more targeted and earlier prevention.
- While Lp(a) testing can enhance cardiovascular risk management, there is still an unmet need to directly reduce Lp(a)-driven cardiovascular risk.

This study is sponsored by Novartis Pharma AG
Poster presented at the ISPOR Europe 2025, held on 10–12 November 2025

INTRODUCTION

- Lipoprotein(a) [Lp(a)] is a unique lipoprotein particle known for its well-established pro-atherogenic and pro-inflammatory effects. Elevated Lp(a), which is genetically determined, represents a lifelong cardiovascular risk factor: With over 90% heritability, Lp(a) levels remain stable throughout life and are minimally influenced by lifestyle [1,2].
- Elevated Lp(a) affects up to 20% of the population yet remains underdiagnosed: Despite its strong association with increased cardiovascular risk, Lp(a) is not routinely measured in clinical practice, leaving most individuals unaware of their elevated levels and missing opportunities for early prevention [2].
- ESC/EAS 2025 Guidelines call for universal Lp(a) screening: The updated recommendations advocate measuring Lp(a) at least once in every adult's lifetime [2].
- Currently, there are no approved therapies specifically targeting Lp(a), although several novel treatments are undergoing clinical development. In the absence of approved Lp(a)-lowering medications, the EAS advises early and intensive management of other cardiovascular risk factors in individuals with elevated Lp(a), based on their overall absolute cardiovascular risk [2].
- In France, Lp(a) testing is not routinely performed, and when it is, it is not specifically reimbursed, resulting in an additional financial burden for the patient or the hospital.

OBJECTIVE

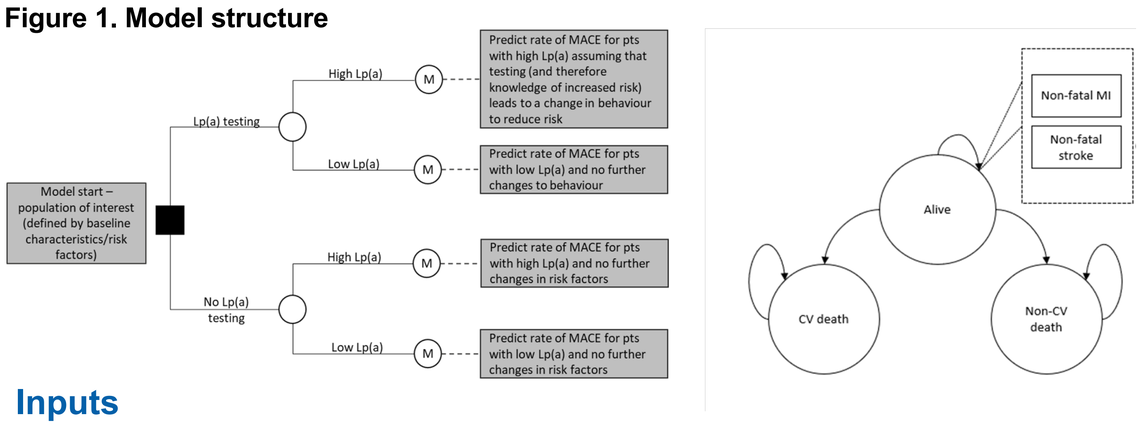
- This study aims to model the impact of risk awareness associated with elevated Lp(a), identified through the testing, on proactive management of other risk factors (RF) to evaluate the cost-effectiveness ratio of generalizing and reimbursing the Lp(a) testing in a French population affected by ASCVD.

METHODS

Structural choices and modeling assumptions

- An economic evaluation was conducted using a decision tree followed by a Markov model (Figure 1), incorporating predictive risk equations derived from regression analyses on UK Biobank data [3, 4]. These equations informed the simulation of cardiovascular outcomes and costs. The model compared scenarios with and without Lp(a) testing, assuming that increased awareness of Lp(a) status could lead to behavioral changes affecting modifiable cardiovascular RF.
- Probabilities of major adverse cardiovascular events (MACE) were calculated from risk equations for each component of MACE (myocardial infarction [MI], stroke, CV death, non-CV death) after incorporating RF from the UK Biobank. Negative binomial competing risk regression models were estimated for each of nonfatal event rates (MACE, MI, and stroke), and Cox regression models were estimated for each fatal event rates (CV death and non-CV death) [4].
- From literature and discussion with experts, modifiable cardiovascular RF to consider were LDL-C (mg/dL), pulse pressure (mmHg), BMI (kg/m²), smoking prevalence (%), and HbA1c (mmol/mol). A comprehensive meta-analysis was retained from a pragmatic literature review to model such behavioral changes and impact on modifiable RF [5].
- The simulated population in the analysis was ASCVD secondary prevention patients, with or without elevated Lp(a). Elevated Lp(a) was defined as >175 nmol/L, aligned with the threshold defined in the inclusion criteria of major ongoing clinical trials investigating Lp(a)-targeted therapies. Based on data from the UK Biobank, 13% of the simulated population would have an elevated Lp(a) following this threshold.
- Following the Haute Autorité de Santé guidelines [6] on the conduct of health-economic analysis, a healthcare system perspective and a lifetime horizon were used for the analysis. Costs and health outcomes were discounted with a 2.5% rate for the first 30 years, which was gradually decreased to 1.5% after 30 years.
- Baseline patient characteristics were taken from the UK Biobank [4] in the absence of available data specific to the French population. Life tables from the French National Statistics Institute were used in the model [7].

Figure 1. Model structure



Inputs

- The utility data are those of the general French population in EQ-5D-5L, adjusted for age and gender [8].The disutilities associated with ASCVD were identified in the HAS opinions for cardiology interventions [9].
- Costs were calculated according to HAS methodological guidelines [6], based on national pricing databases for product acquisition costs, hospitalization costs for ASCVD and HCRU. Cost for Lp(a) testing was estimated at €20 from local feedbacks.
- The impact of increased cardiovascular risk awareness on patient and clinician behavior was estimated from the identified meta-analysis on the impact of CVD risk communication on patient-perceived CVD risk and changes in CVD risk factors [5]. Following a conservative approach, the only change in modifiable RF modeled in the base-case analysis was a 7.1% reduction of LDL-C levels, while other cardiovascular RD remained unchanged.
- In the base case analysis, annualized event rates were reported for three groups: (1) individuals with low Lp(a); (2) individuals with elevated Lp(a) without behavioral changes; and (3) individuals with elevated Lp(a) who adopted behavioral changes. As shown in Table 1, the group aware of their elevated Lp(a) and who modified their behavior experienced a reduction in the incidence of major adverse cardiovascular events (MACE), myocardial infarction (MI), and stroke compared to those with elevated Lp(a) who did not change their behavior.

Table 1. Annualized event rates

Event	Rate – low Lp(a)	Rate – Elevated Lp(a) without behavioral changes	Rate – Elevated Lp(a) with behavioral changes
MACE	18.3%	22.0%	21.2%
MI	14.2%	17.7%	16.8%
Stroke	1.0%	1.1%	1.1%
CV death	1.0%	1.0%	1.0%
Non-CV death	1.0%	0.7%	0.7%

RESULTS

- In our base case analysis, widespread reimbursement of Lp(a) testing was dominant, with an incremental QALY gain of 0.002 and savings of €29.99. For a cohort of 10,000 patients, the testing would prevent 26 MI and 1 stroke, with savings of nearly €300,000.
- Several sensitivity analyses were conducted to assess the results of (1) a different reduction on the LDL-C level or (2) the impact of an isolated reduction on other RF (Table 2). It appears that a slight reduction (>3%) on LDL-C or HbA1c, makes the strategy dominant, whereas a greater reduction (at least 15%) in the other three RFs would be necessary for the testing to become effective, at commonly accepted RDCR levels.
- A combined reduction in two risk factors would make the strategy dominant (LDL-c or HbA1c + another factor) or efficient (combination of two factors other than LDL-C or HbA1c).

Table 2. Sensitivity analysis of minimal change in one modifiable CV risk factor - Results

Change vs baseline	LDL-c	Pulse pressure	BMI	Smoking prevalence	HbA1c
-5%	**Dominant**	87,247 QALY/€	182,546 QALY/€	85,928 QALY/€	6,135 QALY/€
-10%	**Dominant**	30,013 QALY/€	72,290 QALY/€	30,367 QALY/€	**Dominant**
-15%	**Dominant**	10,953 QALY/€	35,867 QALY/€	11,847 QALY/€	**Dominant**

- The analysis has some limitations, notably regarding the representativeness and generalizability of the modelling of clinical outcomes to the French population: use of English data (risk equations and simulated population) and reduction of RF from a meta-analysis with no specific French data, but it is usually accepted that these populations can be considered comparable.

CONCLUSION

- From the literature review, we identified that knowledge of quantifiable CVD risk, such as elevated Lp(a) may improve health outcomes and trigger behavioral change in patients or clinicians, with significant impact on at least LDL-C level or reduction on other RF.
- In this analysis, Lp(a) testing in secondary prevention populations can be a cost-effective strategy. When accounting for a significant reduction in LDL-C following awareness of elevated Lp(a), testing may become the dominant strategy, despite the absence of approved targeted therapies.
- Scenario analyses show that minimal changes (>3%) in LDL-C or HbA1c make Lp(a) testing economically favorable, while greater change on other RF would be needed to reach commonly accepted threshold.
- While Lp(a) testing can enhance cardiovascular risk management, there is still an unmeet need to directly reduce Lp(a)-driven cardiovascular risk.

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Acknowledgements

The authors wish to acknowledge Oliver Burn (Source Health Economics), David Trueman (Source Health Economics), Orfanos Panagiotis (Novartis) and Luiz Causin (Novartis) for the support given throughout the development of this study.

Disclosures

This study was funded by Novartis Pharma SAS France
P-E Saint-Antonin, A-S Moutié and V Vega are employed by Novartis Pharma SAS France
Dr. E Bruckert has received consulting fees/honoraria from Amgen, Genfit, MSD, Sanofi-Regeneron, Aegerion, Novartis, Lilly, Ionis pharmaceuticals, Servier, AstraZeneca and Mylan AKCEA