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Poster# **EE425**

Cost-effectiveness analysis and budget impact model of Lp(a) testing in in Portuguese patients with atherosclerotic cardiovascular disease for secondary prevention

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KEY FINDINGS & CONCLUSIONS

- Testing for Lp(a) in a secondary prevention population can be a cost-effective approach. When considering a significant change in LDL-C after awareness of elevated Lp(a), testing can be cost saving, potentially leading to relevant benefits to the P-NHS, even in the absence of target therapies.
- Although Lp(a) testing may contribute towards an optimization of CV risk management, the unmet need of reducing Lp(a) associated CV risk remains.

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INTRODUCTION/BACKGROUND

- Lipoprotein (a) [Lp(a)] is a distinct lipoprotein, with well-established pro-atherogenic and pro-inflammatory properties [1]. Elevated Lp(a) is a highly prevalent, genetically determined condition that is causally and independently associated with an increased risk for cardiovascular disease (CVD) [2].
- Both the European Atherosclerosis Society (EAS) and the European Society of Cardiology recommend that Lp(a) should be measured at least once in adults [1], which can be performed as routine blood [3].
- Currently there are no approved targeted drugs for Lp(a), however several new therapies for Lp(a) are under clinical development. In the absence of approved specific Lp(a)-lowering drugs, EAS recommends an early, intensive management of other risk factors for individuals with elevated Lp(a) levels, considering their absolute global cardiovascular risk [1].
- Awareness of high levels of Lp(a) and education on its impact on individual's CV risk may help to motivate physicians and patients to adhere to the recommended treatment of other modifiable risk factors [4].
- Despite guidelines recommendation of broad Lp(a) testing and its availability, Lp(a) is not implemented in real-world clinical practice. Absence of targeted therapies and economic concerns have been indicated as barriers on general Lp(a) testing [3].

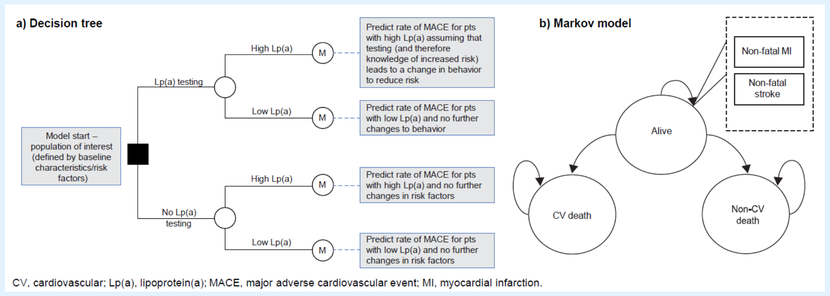
OBJECTIVES

- This study aims to assess the cost-effectiveness and budget impact of implementing Lp(a) testing for secondary prevention in an atherosclerotic cardiovascular disease (ASCVD) population, in absence of targeted therapies, adopting the perspective of the Portuguese National Health Service (P-NHS).

METHODS

- A decision tree economic model followed by a Markov model (model structure in Figure 1) and the UK Biobank's (UKBK) predictive risk equations were used to develop the economic model [5]. The costs and outcomes with and without Lp(a) testing were compared, with the assumption that awareness on Lp(a) might induce a behavioral change which in turn might impact modifiable cardiovascular (CV) risk factors such as: Low Density Lipoprotein Cholesterol (LDL-C) (mg/dL), pulse pressure (mmHg), body mass index (BMI) (kg/m²), smoking (%), and HbA1c (mmol/mol).

Figure 1. Model structure Decision tree and Markov model



CV, cardiovascular; Lp(a), lipoprotein(a); MACE, major adverse cardiovascular event; MI, myocardial infarction.

- The population in the analysis was ASCVD secondary prevention. Elevated Lp(a) was defined as >125 nmol/L [1]. P-NHS perspective and a 30-year time horizon were used for the analysis. Baseline patient characteristics were taken from the UK Biobank [5]. For use of lipid lowering therapies (LLT), data was sourced from the LATINO study in a Portuguese patient population [6].
- 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 risk factors 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) [5].
- Life tables from the Portuguese National Statistics Institute were used in the model [7].
- Utility data was taken from EQ-5D-5L Portuguese population norms [8], and event disutilities were taken from the National Institute for Health and Care Excellence (NICE) TA805 submission [9]. The cost for Lp(a) testing (8.80€) and LLT costs were taken from available public sources [10, 11]. The costs of MI and Stroke were derived from Costa et al. [12] and CV death related costs were taken from NICE TA805 (updated to 2024 and converted to Euros) [9].
- The effects of knowledge of increased CVD risk on patient and/or clinician behaviors were calculated by user input-model after adjusting for risk factor covariates. From a target literature review, we found that an 8.37% reduction in LDL-C has been observed after Lp(a) testing in a retrospective analysis of an ASCVD population LDL-C [13]. This was used as a parameter in the base case model, which considered an 8.37% reduction in LDL-C induced by awareness of high Lp(a), with the rest of the risk factor covariates unchanged.
- In the base case analysis, the annualized event rates in the groups with 1) low Lp(a); 2) high Lp(a) without behavioral changes and 3) high Lp(a) with behavioral changes are presented in Table 1. There is a reduction on the rate of MACE, MI and stroke for the group with awareness of high Lp(a) and consequent behavioral change versus the group with high Lp(a) and no behavioral changes.

Table 1. Annualized event rates

Event	Rate - low Lp(a)	Rate - Elevated Lp(a), no behavioural changes	Rate - Elevated Lp(a), with behavioural
MACE	21,40%	23,80%	23,42%
MI	18,25%	20,80%	20,38%
Stroke	0,76%	0,76%	0,75%
CV death	1,36%	1,37%	1,37%
Non-CV death	1,42%	1,15%	1,15%

- The budget impact of the introduction of Lp(a) testing was calculated using outputs from the cost-effectiveness model over the first 5 years. A 20% testing rate per year of eligible patients until all prevalent and incident patients have been tested by Year 5. Patient numbers included were derived from Costa et al. (estimates for total of prevalent and incident MI or ischemic stroke patients in Portugal) [12] and the rate of elevated Lp(a) was taken from Chora et al. [14].

RESULTS

- In our base case analysis, Lp(a) testing was dominant, with an incremental cost of -42.42€ and an incremental QALY gain of 0.002. Scenario analysis was conduct on the different magnitude of reduction in LDL-C only (from 0.5% to 10%), to test the sensitivity of the model to this parameter. With this, an 1% reduction in mean LDL-C resulted in an ICER of 11 562.37€ below the willingness to pay (WTP) of 20,000€ per QALY and reductions ≥1.5% resulted in dominance of Lp(a) testing.
- Although the sizable reduction of LDL-C (-8.37%) due to a behavioral change induced by awareness of high Lp(a) has been documented in the literature, it may seem arbitrary. Thus, various scenarios were analyzed: Table 2 and Table 3 present the incremental cost effectiveness ratios (ICER), cost per quality adjusted life year, of different the scenarios in which awareness of elevated Lp(a) induces a behavioral change that has a minimal change (< 2%) in only one or in only two modifiable CV risk factors, respectively.
- With a minimal change in only one CV risk factor, Lp(a) testing can be cost-effective at minimal reduction of 0.5% in HbA1c or a reduction of 1% in LDL-C or BMI (Table 2), considering a WTP of 20,000€ per QALY. Greater changes in Pulse Pressure and Proportion of Smokers are required for ICER results of Lp(a) testing to be lower than WTP threshold.
- With a minimal change in two CV risk factors (Table 3), Lp(a) testing was either dominant or cost-effective, in most of the scenarios analysed, considering a WTP of 20,000€ per QALY. This is also true when anchoring the analysis on a change in LDL-C plus another CV risk factor (first three result columns in table 3). The results in the scenario analysis are very sensitive to changes in HbA1c and BMI, while minimal changes in Pulse pressure and Proportion of smoker are less prone to yield a cost-effective result.

Table 2. Scenario Analysis of minimal change in one modifiable CV risk factor – ICER results

Change	LDL-C	Pulse Pressure	BMI	Proportion of smokers	HbA1c
0.5%	53 659.13 €	335 464.58 €	39 096.19 €	161 988.09 €	2 136.88 €
1.0%	11 562.37 €	151 986.37 €	3 893.56 €	65 754.36 €	Dominant
1.5%	Dominant	90 827.35 €	Dominant	33 676.42 €	Dominant
2.0%	Dominant	60 248.13 €	Dominant	17 637.43 €	Dominant

Table 3. Scenario Analysis of minimal change in two modifiable CV risk factors – ICER results

		Change in LDL-C (%)		
		0.5%	1.0%	1.5%
Change in Pulse Pressure (%)	0.5%	37 775.85 €	7 136.06 €	Dominant
	1.0%	26 886.53 €	3 535.05 €	Dominant
	1.5%	18 955.92 €	548.22 €	Dominant
Change in BMI (%)	0.5%	7 364.03 €	Dominant	Dominant
	1.0%	Dominant	Dominant	Dominant
	1.5%	Dominant	Dominant	Dominant
Change in Proportion smoking (%)	0.5%	28 044.79 €	4 010.76 €	Dominant
	1.0%	14 386.29 €	Dominant	Dominant
	1.5%	5 896.74 €	Dominant	Dominant
Change in HbA1c (%)	0.5%	Dominant	Dominant	Dominant
	1.0%	Dominant	Dominant	Dominant
	1.5%	Dominant	Dominant	Dominant

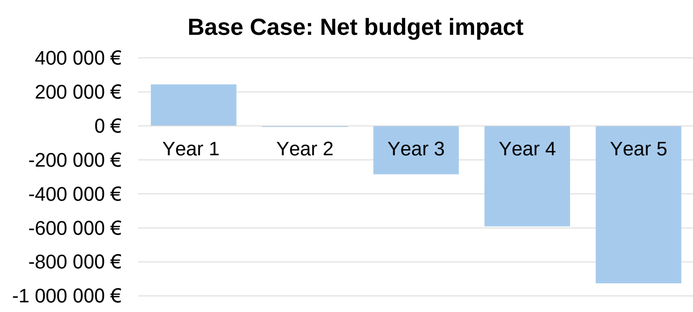
		Change in Pulse Pressure (%)		
		0.5%	1.0%	1.5%
Change in BMI (%)	0.5%	27 719.90 €	19 501.80 €	13 287.10 €
	1.0%	788.51 €	Dominant	Dominant
	1.5%	Dominant	Dominant	Dominant
Change in Proportion smoking (%)	0.5%	95 414.04 €	62 926.23 €	43 682.10 €
	1.0%	45 544.36 €	32 289.38 €	22 926.34 €
	1.5%	23 973.96 €	16 786.34 €	11 248.02 €
Change in HbA1c (%)	0.5%	Dominant	Dominant	Dominant
	1.0%	Dominant	Dominant	Dominant
	1.5%	Dominant	Dominant	Dominant

		Change in BMI (%)		
		0.5%	1.0%	1.5%
Change in Proportion smoking (%)	0.5%	20 462.59 €	Dominant	Dominant
	1.0%	9 701.50 €	Dominant	Dominant
	1.5%	2 693.94 €	Dominant	Dominant
Change in HbA1c (%)	0.5%	Dominant	Dominant	Dominant
	1.0%	Dominant	Dominant	Dominant
	1.5%	Dominant	Dominant	Dominant

		Change in Proportion of Smokers (%)		
		0.5%	1.0%	1.5%
Change in HbA1c (%)	0.5%	Dominant	Dominant	Dominant
	1.0%	Dominant	Dominant	Dominant
	1.5%	Dominant	Dominant	Dominant

- In the BIM analysis, 264,640 prevalent patients and 30,169 incident patients with MI or stroke were included in Year 1. After Year 1, an additional 30,169 incident patients with MI or stroke were included. The annual costs related to Lp(a) testing were off set from year 2 onwards, due to the cost savings yielded by avoided MI and stroke events. The results of the BIM are depicted in Figure 1.

Figure 1. Net budget impact per year over 5 years (base case analysis)



CONCLUSION

- Awareness of high levels of Lp(a) and education on its impact on individual's CV risk may help to motivate physicians and patients to manage earlier and more intensively modifiable CV risk factors.
- Testing for Lp(a) in a secondary prevention population can be a cost-effective approach. When considering a significant change in LDL-C after awareness of elevated Lp(a), testing can be cost saving, potentially leading to relevant benefits to the P-NHS, even in the absence of target therapies. Considering a scenario analysis of a minimal change (<2%) in either just one modifiable CV risk factor or in a combination of two modifiable risk factors, most of the scenarios result in testing for Lp(a) as a cost-effective approach.
- Analyzing the budget impact of introducing Lp(a) test for all MI and stroke patients, the costs related to the test are offset from Year 2 onwards, due to the avoided events, enabled by a behavioral change that the knowledge of Lp(a) could trigger.
- Although Lp(a) testing may contribute towards an optimization of CV risk management, the unmet need of reducing Lp(a) associated CV risk remains.

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Disclosures

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