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The Brussels International Declaration on Lipoprotein(a) Testing and Management

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ABSTRACT

There is striking evidence that a high lipoprotein(a) [Lp(a)] concentration is a strong, independent, and causal cardiovascular risk factor. However, Lp(a) testing rates are very low (1 %–2 %) despite the fact that 1 in 5 individuals have elevated Lp(a) concentrations.

The Brussels International Declaration on Lp(a) Testing and Management was co-created by the Lp(a) International Task Force and global leaders at the Lp(a) Global Summit, held in Brussels, Belgium, on March 24–25, 2025. The event, organized by FH Europe Foundation, brought together scientific experts, people with the lived experience of elevated Lp(a) and policy makers from the European Institutions and World Health Organization. The World Heart Federation, Global Heart Hub, and European Alliance for Cardiovascular Health and scientific organizations such as European Atherosclerosis Society, and International Atherosclerosis Society were formal partners. The Summit was hosted by a Member of the European Parliament, Romana Jerković, and held under the patronage of the Polish presidency of the Council of the European Union.

The Declaration calls for 1) integration of Lp(a) testing and management into Global, European and National Cardiovascular Health Plans; 2) appropriate investment, policy and programmes in targeting Lp(a) testing and management based on a recent study demonstrating the substantial overall cost-saving to health systems across the globe; 3) political commitment to mandate systematic Lp(a) testing at least once during a person's lifetime, ideally at an early age, with full reimbursement; 4) incorporation of Lp(a) test results in the context of a person's cardiovascular risk assessment, with development of personalised cardiovascular health roadmaps as needed, without fear of discrimination; 5) investment in public and healthcare professional education to increase awareness of Lp(a) and its impact on cardiovascular health.

1. Lp(a) in the context of the cardiovascular landscape

Approximately one third of the world's population dies from cardiovascular diseases (CVD) such as myocardial infarctions, strokes and other vascular diseases, many prematurely [1,2]. These diseases are the main cause of death worldwide. The economic and healthcare burden of cardiovascular diseases (CVD) is staggering, with CVD costing the EU alone €282 billion annually [1]. The impact of CVDs is substantially exacerbated by the limited availability of primary and secondary prevention programmes although efforts are made to establish relevant cardiovascular health plans on international and national levels, which should include such programmes.

Well-established cardiovascular risk factors are high LDL cholesterol, high blood pressure, diabetes, obesity, smoking, lack of physical exercise and an unhealthy diet. These so-called "traditional" or modifiable risk factors are major contributors to the global cardiovascular risk of a person and can be influenced by lifestyle interventions and approved medications, thereby reducing the risk of atherogenesis and cardiovascular events. In addition, social and commercial determinants of health, along with profound health inequities existing both within and between countries, play a fundamental role in shaping the global burden of cardiovascular disease [3].

Alongside low-density-lipoprotein (LDL) cholesterol, lipoprotein(a) [Lp(a)] is a further blood lipid particle that contributes significantly to cardiovascular diseases [4]. It has a very characteristic structure consisting of an LDL-like particle with an additional apolipoprotein, called apolipoprotein(a) [apo(a)]. Apo(a) consists of a genetically determined sequence of so-called kringle-IV repeats (up to more than 40 repeats), which thereby determines not only the size of this apolipoprotein resulting in the apo(a) size polymorphism, but essentially also the concentration of Lp(a): the larger the protein, the lower the concentration and vice versa [5]. In addition, Lp(a) contains a large amount of oxidized phospholipids and it is assumed that these are partly responsible for the atherogenic and inflammatory properties of Lp(a) [6,7].

The concentration of Lp(a) is under strong genetic control and about 90 % of the concentration can be explained by genetic variants such as the number of K-IV repeats, some frequent splice site variants (4925G>A or 4733G>A) and other single nucleotide polymorphisms [5,8–13]. These genetic variants are transmitted from one generation to the next. Therefore, a high Lp(a) concentration is the most frequent inherited condition in all disease fields including cardiovascular disease.

First indications for the atherogenic properties of Lp(a) are from the 1970-ies and 1980-ies as reviewed in Refs. [14,15]. In particular, the large and prospective studies from Copenhagen and the UK Biobank underlined the pronounced association between high Lp(a) concentrations and various cardiovascular outcomes [10,16].

It is a common risk factor with a high public health relevance: one in five people has Lp(a) concentrations above 50 mg/dL (equals 105 nmol/L according to a conversion factor of [2.18*Lp(a) in mg/dL – 3.83] as described by Langsted et al. [17]), a concentration associated with an increased atherosclerotic cardiovascular disease (ASCVD) risk [4] (Fig. 1A). Therefore, roughly 1.4 billion individuals worldwide are exposed to elevated Lp(a) [18] and the vast majority of them do not know that they are living with this condition and an increased ASCVD risk. Welsh and colleagues calculated the population attributable risk fraction to be 8.8 % for a composite CVD endpoint and 13–14 % for peripheral vascular disease and aortic stenosis if the entire population would have a very low Lp(a) concentration of 3.8 nmol/L [19]. This is in a similar range as calculated for diabetes (13 %), hypercholesterolemia (10 %) and smoking (10 %) but lower than for hypertension (21 %) as calculated in the ARIC study [20].

Ethnicity has a pronounced influence on the Lp(a) concentrations with the lowest values in East Asians and increasing values in Europeans, Southeast Asians, Latin Americans, Middle Eastern, South Asians and Black individuals (from lowest to highest). Fig. 2 shows the example of a very skewed distribution in White individuals (panel A) compared to an almost Gaussian distribution in Black individuals (panel B). The median values in Black individuals are roughly four times higher than in White individuals (75 versus 19 nmol/L) [4].

There is a dose-response relationship between Lp(a) concentrations and cardiovascular events: the higher the concentration, the higher is the risk [4,16,19] (Fig. 1B). About 70 % of the white population has concentrations below 30 mg/dL (62 nmol/L), a concentration that is not associated with a clinically relevant risk increase. A further 10 % have concentrations between 30 and 50 mg/dL (62–105 nmol/L) associated with a moderate relative risk increase of 30–40 %. The remaining 20 % have concentrations between 50 and more than 200 mg/dL (105 to >430 nmol/L) with relative risk increases ranging from 50 % to >200 % [4,16] (Fig. 1). This continuous relationship between Lp(a) concentration and cardiovascular disease should always be kept in mind when

evaluating the overall risk and should not be rigidly based on thresholds such as 50 mg/dL (105 nmol/L) (Fig. 1). For example, a recent overview from the Copenhagen Studies showed that the 5 % of the population with the highest Lp(a) concentrations (>90 mg/dL or >190 nmol/L) have a three-fold increased risk for myocardial infarctions or aortic valve-stenosis, a two-fold increased risk for peripheral arterial disease, a 1.6-fold increased risk for ischemic stroke and a 1.5-fold increased risk for cardiovascular death [21].

Despite the differences in Lp(a) concentrations between Black and White individuals, the cardiovascular risk increase at a given concentration is very similar in both ethnicities: individuals with an Lp(a) concentration of 300 nmol/L have in both ethnicities a roughly 2.1-fold risk increase as can be seen from Fig. 2C and D of the EAS Lp(a) Consensus Statement using data from the UK Biobank [4].

Mendelian randomization studies have provided strong evidence for a causal relationship in smaller studies in the 1990-ies [22,23] and in large studies a decade later [10,13,24]: on the one hand, genetic variants that are closely linked with lifelong elevated Lp(a) concentrations (e.g. apo(a) isoforms with a low number of K-IV repeats) are more often present in individuals who have had or will experience a cardiovascular event [8]. On the other hand, individuals who carry variants with a large number of K-IV repeats or the two common splice site variants 4925G>A and 4733G>A or rare loss of function variants resulting in low Lp(a) concentrations suffer less often from cardiovascular disease [11,12,25].

Despite the strong evidence that Lp(a) is an independent and causal risk factor for CVD, the testing rate worldwide is estimated to be only 1 %–2 % with a high variability between countries [26,27].

2. The first Lp(a) Global Summit and the Brussels International declaration

The public health impact of testing for elevated Lp(a), as an important risk factor for CVD, and its effective management, would be significant and should be a key pillar of countries' prevention strategies worldwide. The Lp(a) International Task Force organized a Global Summit, held in Brussels, Belgium, on March 24–25, 2025, to convene scientific experts, people with the lived experience of elevated Lp(a) and policymakers from European Institutions and the World Health Organization. The World Heart Federation, Global Heart Hub, and European Alliance for Cardiovascular Health plus scientific organizations such as European Atherosclerosis Society, and International Atherosclerosis Society were formal partners. The Summit was hosted by a Member of the European Parliament, Romana Jerković, and held under the patronage of the Polish presidency of the Council of the European Union.

The Summit reached a powerful consensus among diverse stakeholders that there is an urgent need for systematic Lp(a) testing and personalised, effective cardiovascular risk management. It was highlighted that testing is simple, and cost-saving, even in the primary prevention setting. While specific Lp(a)-lowering therapies are still in the phase 3 trial stage [28–30], significant steps can be taken to empower those with elevated Lp(a) to better manage their condition and prevent or delay development of cardiovascular disease. This should be done in the context of other possible modifiable risk factors to assess the global risk of a given person and to develop personalised preventive measures [4,31].

The Brussels International Declaration serves as a clear roadmap for policymakers to implement practical, life-changing policies and systemic reforms. It aligns with the growing global shift from treating cardiovascular diseases to embracing a more proactive approach to cardiovascular health (Fig. 3). The Declaration is open for endorsement at https://fhef.org/brussels-international-declaration/.

3. The Lp(a) International community calls for

3.1. Call 1 of the declaration

The explicit inclusion of Lp(a) testing and management of elevated Lp(a) in the World Health Organization's Cardiovascular Health/Non-Communicable Disease policy instruments and programmes, in the European Cardiovascular Health Plan and other regional plans, National Cardiovascular Health Plans and national guidelines across the world.

Testing of Lp(a) and management of elevated Lp(a) is inherent to a new narrative and culture towards cardiovascular health, rather than cardiovascular disease, and a personalised approach towards prevention

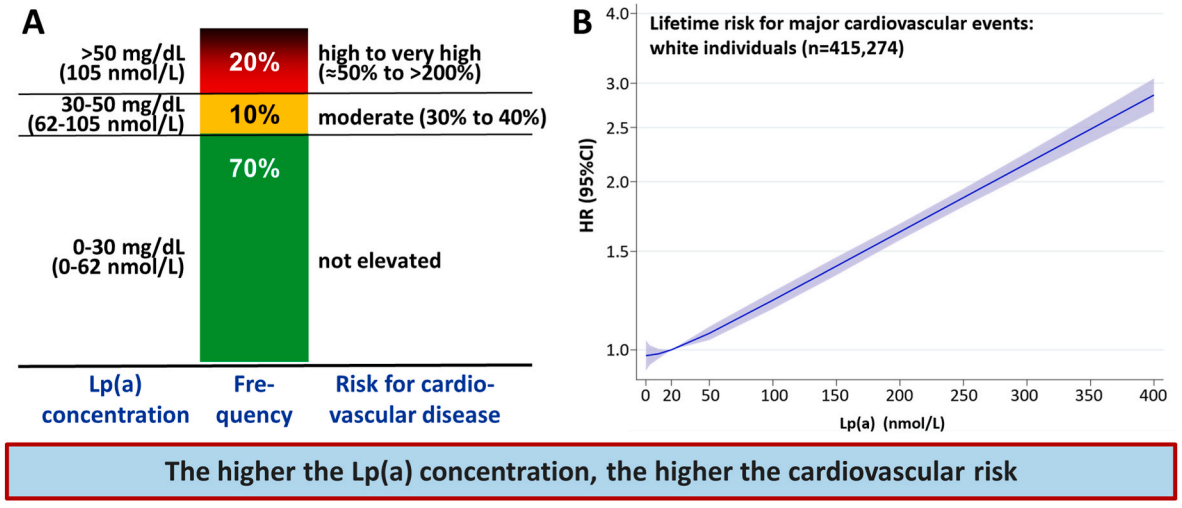

Fig. 1. Panel A: Frequency of Lp(a) concentration ranges and association with cardiovascular disease. We applied a conversion factor of 2.18*Lp(a) in mg/dL–3.83 to convert to nmol/L as described by Langsted et al. [17]). **Panel B** shows the smoothed adjusted hazard ratio (HR) and 95 % confidence interval (95 % CI) for lifetime risk for major cardiovascular events for a given Lp(a) concentration relative to the median Lp(a) in the population (19.7 nmol/L). These data were estimated using a Cox proportional hazards regression model adjusted for age at enrolment, sex, and the first 10 principal components of ancestry and modelled using cubic natural splines. Figure is taken from the recent EAS Lp(a) Consensus statement [4] based on data from the UK Biobank and is here reproduced under the CC BY-NC-ND 4.0 open access license.

and care pathways, reflected in the current progressive policy discourse at international and European level.

Historically, elevated Lp(a) became increasingly visible in the scientific community during recent years, due to growing evidence from epidemiological and genetic studies (for reviews see Refs. [9,14,21,32]). However, it has been entirely invisible in broader public health discussions. Given its prevalence and its profound impact on individuals, society and health systems, Lp(a) testing and management of elevated Lp(a) should be a critical pillar of future global policies, programmes and action plans on cardiovascular health as recommended by several professional societies from around the world [4,31,33–39]. Additional emphasis should be placed on strategies to ensure access to testing in low- and middle-income countries.

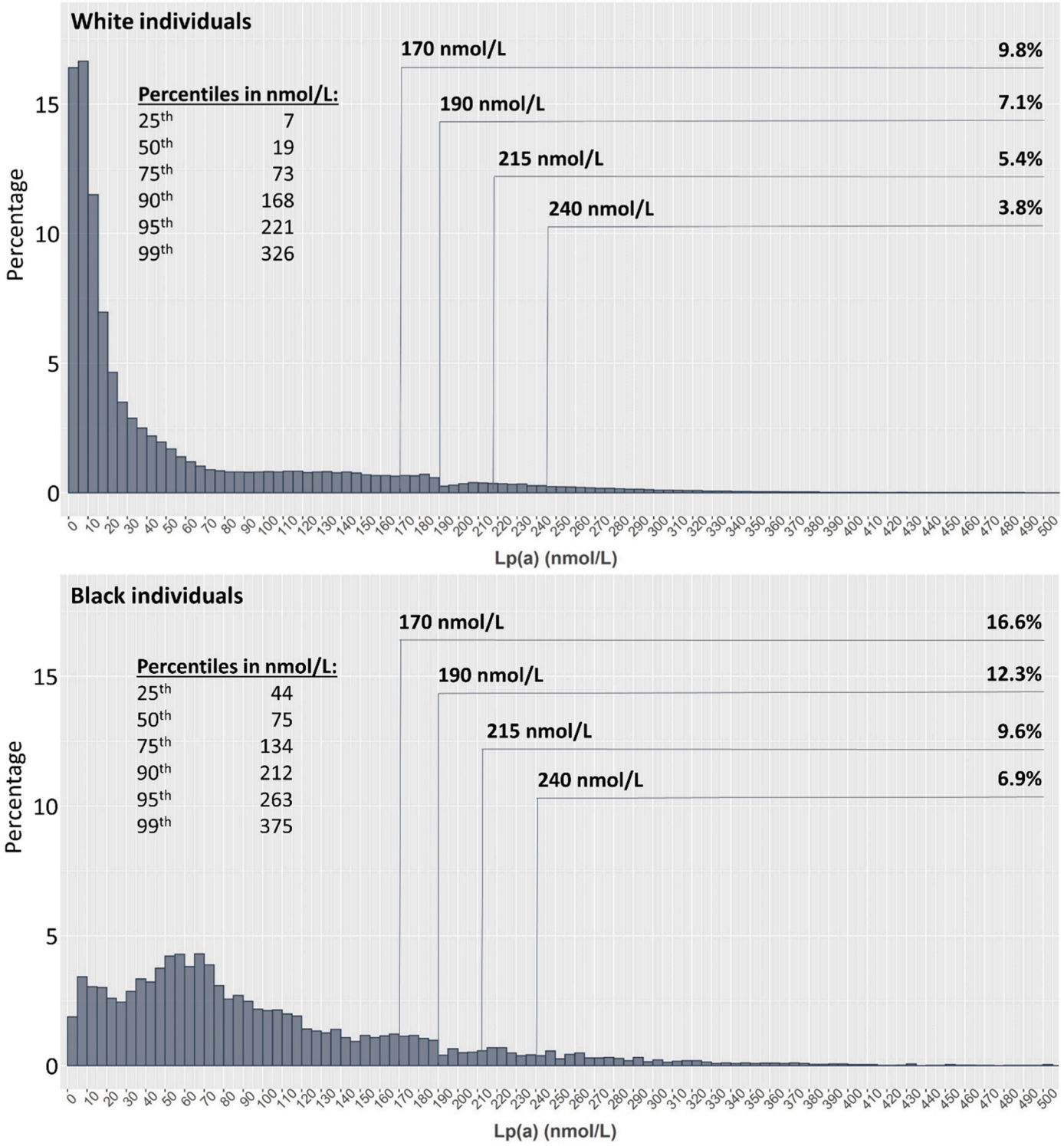

Fig. 2. Distribution of lipoprotein(a) [Lp(a)] concentrations in a general population. Data are from the UK Biobank and show the typical distribution of Lp(a) concentrations in White **(Panel A)** and Black people **(Panel B)**. Percentage of the population with an Lp(a) concentration of 170, 190, 215, and 240 nmol/L or higher are provided. This Figure is taken from the recent EAS Lp(a) Consensus statement [4] and is here reproduced under the CC BY-NC-ND 4.0 open access license.

3.2. Call 2 of the declaration

Appropriate investment, workable and effective policies and programmes in Lp(a) testing and management based on the recent study demonstrating the significant overall cost-saving to health systems across the globe

The recent cost-effectiveness analysis undertaken for high-income countries such as Australia, Austria, Canada, France, Germany, Italy, the Netherlands, Spain, Poland, the United Kingdom and the United States of America reveals that Lp(a) testing to reclassify cardiovascular risk in the primary prevention population is a cost-saving strategy (i.e. saving life and saving costs) for preventing cardiovascular disease (Ademi et al. manuscript under review). This is under the assumption that those with high Lp(a) concentrations are considered in a higher risk category which results ideally in preventive management of e.g. lifestyle optimization as well as lowering LDL cholesterol and blood pressure [4]. For countries aiming to achieve economically sustainable healthcare systems, particularly those with universal healthcare policies, the proven cost-saving outcomes of routine Lp(a) testing presents an opportunity to significantly reduce future expenditure associated with cardiovascular diseases. Early detection via routine testing can reclassify and manage individuals at higher risk effectively, thereby optimizing national health spending and improving population health outcomes. Implementation of Lp(a) testing is not only highly warranted from a clinical perspective but is likely to come with a financial return on investment from both healthcare and societal perspective within a relatively short time. Theses analyses do not only consider direct healthcare costs such as costs for Lp(a) testing, chronic disease treatment and managements cost and direct non-medical costs but also indirect costs such as loss of earnings due to death prior to retirement, workforce dropout due to illness, absenteeism from work and presenteeism at work due to symptoms. These results support the immediate implementation of Lp(a) testing in high-income countries from both a healthcare and societal perspective. With higher testing volume, the cost of testing will decrease, making it more affordable for low- and middle-income countries.

3.3. Call 3 of the declaration

Political commitment and leadership to ensure systematic testing of Lp (a) is actively offered, at least once in a lifetime, initially as early as possible in the life course, with full reimbursement. This is country-specific and should be established in harmony with other testing protocols

Based on current scientific evidence and recommendations from international guidelines and consensus statements [4,31,33–39] and cost-effectiveness analysis, political leaders should commit to ensuring that everyone in their country is actively offered voluntary testing of Lp(a) and LDL cholesterol, free of charge, at least once in a lifetime, initially as early as possible in the life course. This also reflects the perspective of a growing number of advocates living with elevated Lp(a) who are experiencing the serious consequences of inertia in testing policy in their country. Many countries have already established national prevention and screening programmes. Systematically integrating Lp(a) testing into these existing frameworks would allow timely identification of high-risk individuals without significant new administrative burdens.

Unfortunately, for some individuals, the first cardiovascular event may be fatal, underscoring the urgency of early testing. Even if the first incident is survived, the damage to the heart and brain is done and is usually associated with significant future restrictions in functioning and quality of life. This means that many years of prevention were lost, which would otherwise have been avoided, or at least delayed the development of cardiovascular disease [40,41]. Therefore, the earlier a test can be offered, the more the impact of elevated Lp(a) can be mitigated, with due sensitivity and compassion regarding the fear this diagnosis may provoke, for example, in younger individuals.

3.4. Call 4 of the declaration

Testing of Lp(a) undertaken in the context of a global cardiovascular risk assessment to develop a personalised cardiovascular health roadmap

It is important to note that testing for Lp(a) does not necessarily result in the diagnosis of a disease. High Lp(a) is a condition which puts someone at risk for cardiovascular disease, especially when combined

Fig. 3. Key asks of the Brussels International Declaration on Lp(a) Testing and Management derived from the Lp(a) Global Summit, held in Brussels, Belgium, on March 24-25, 2025, organized by the Lp(a) International Task Force.

with other risk factors. Therefore, Lp(a) should never be seen in isolation but always in relation to other (modifiable) risk factors. It would be too narrow a view to focus on a single risk factor in such a multifactorial disease as atherosclerosis. Therefore, to be even more cost-effective, assessment of the global risk of a given person should be done together with the other established risk factors [4,31]. Practically speaking, Lp(a) concentrations must be seen in context of family history of cardiovascular disease, high LDL cholesterol, high blood pressure, diabetes mellitus, smoking, being overweight, and lifestyle factors such as low physical activity and unhealthy diet. Since these risk factors together with Lp(a) concentrations are cumulative or even multiplicative, the global risk of a given person can increase substantially. As Fig. 4 shows, the lifetime risk of cardiovascular diseases increases in the presence of very high Lp(a) values from 25 % to 68 % if someone has a high number of other risk factors at the same time. In case of a medium number of modifiable risk factors, the risk increases from 15 % to 41 %. In these situations, the assessment of an individual risk might be heavily underestimated when the Lp(a) concentration is not considered in the risk assessment. On the other hand, when someone has no or a low number of risk factors, the overall risk only increases from 5 % to 14 %. In this situation and when no family history for cardiovascular disease is present, this person might have a lower risk than the average population. This is all the more important when advising these individuals, in order to avoid anxiety and motivate them to maintain a healthy lifestyle and consistently counteract any risk factors that may arise in the future.

Based on the high prevalence and pronounced effect of high and very high Lp(a) concentrations on cardiovascular risk, future risk calculators should include the Lp(a) concentration to improve risk assessment with the goal to identify possible lifestyle interventions and treatment targets to prolong a healthy life. These should be followed by a lifetime risk calculator, and a personalised cardiovascular health roadmap including psychological and social support.

- **Testing should be undertaken in primary as well as secondary prevention settings.**

Testing should be undertaken in primary as well as secondary prevention settings as an increased Lp(a) concentration is genetically determined in almost all cases. Actionable interventions aimed at decreasing global cardiovascular risk by addressing lifestyle factors and treatment are recommended for both primary and secondary prevention. In parallel appropriate global policies and instruments to address the social and commercial determinants of health should be adopted and implemented effectively.

- **Extended Lp(a) testing should be offered to families of an index person with elevated Lp(a).**

As Lp(a) concentrations are strongly genetically determined [5,8,10,42,43], elevated Lp(a) identifies not only ‘an individual patient at risk’ but ‘families at risk’. It can be expected that approximately 40–50 % (under certain conditions even more) of the first-degree relatives (e.g.

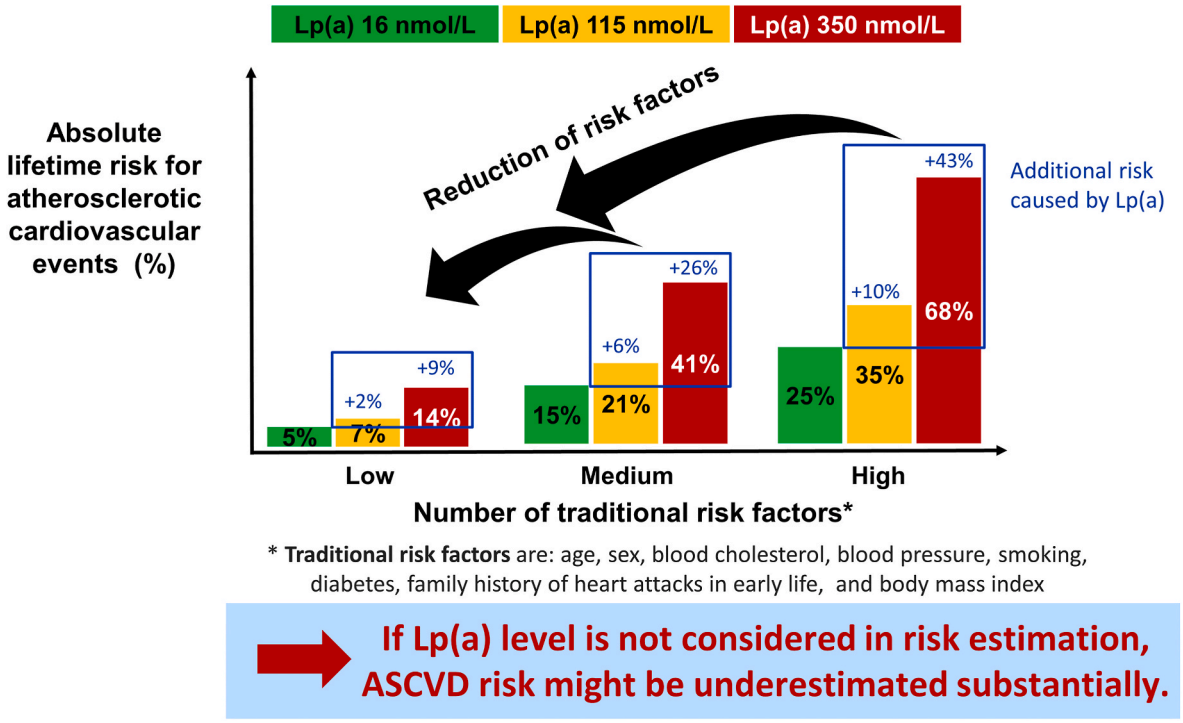

Fig. 4. Association of Lp(a) concentrations with absolute lifetime risk for atherosclerotic cardiovascular disease stratified by the number of traditional (modifiable) risk factors. This Figure is based on calculations for the Lp(a) Consensus statement of the European Atherosclerosis Society (presented as Figure 6 therein [4] and presents the main message in a simplified form. The y-axis shows the estimated absolute lifetime risk for major atherosclerotic cardiovascular events (ASCVD) among 415,274 participants of European ancestry in the UK Biobank. Participants are stratified into categories of baseline estimated lifetime risk of 5 % which equals no or a low number of modifiable risk factors, 15 % (medium number of risk factors), and 25 % (high number of risk factors), respectively calculated using the Joint British Societies (JBS3) Lifetime Risk Estimating algorithm (based on traditional risk factors age, sex, blood cholesterol, blood pressure, smoking, diabetes, family history of heart attacks in early life, and BMI). For each of these three baseline risk categories, the additional risk attributable to increasing Lp(a) concentrations of 115 nmol/L (yellow bars) or 350 nmol/L (red bars) measured at baseline compared to those with the median Lp(a) concentration of 16 nmol/L (green bars) is calculated and added to the baseline risk to provide the global absolute risk. This incremental increase in risk caused by higher Lp(a) concentrations of 115 nmol/L and 350 nmol/L was estimated by adding Lp(a) as an independent exposure to the JBS3 risk estimating algorithm. For example, for a person with a baseline risk of 25 % and an Lp(a) concentration of 115 nmol/L, the absolute risk of a major cardiovascular event increases by 10 % from 25 % to 35 % (versus a person with an Lp(a) of 16 nmol/L). In case of an Lp(a) concentration of 350 nmol/L, the risk increases by 43 % from 25 % to 68 %. The reduction of modifiable traditional risk factors is therefore the ultimate goal in case of elevated Lp(a) concentrations to decrease the global risk of a given person.
Figure is taken and adapted from Ref. [28] and is here reproduced under the CC BY-NC-ND 4.0 open access license.

parents, siblings and children) are also have high Lp(a) concentrations, providing a unique opportunity to mitigate cardiovascular risk in these subjects [9,43].

In the case of a positive family history for ASCVD in particular, family members should be invited for Lp(a) testing and for an extensive examination of other cardiovascular risk factors, followed by appropriate support for their management as recommended e.g. by the European Atherosclerosis Society [4,31] and the National Lipid Association [35].

- **As countries transition towards systematic testing of elevated Lp(a), the testing of high-risk individuals should only be seen as a temporary measure until testing is widely implemented.**

The first Lp(a) EAS consensus statement from 2010 focused the recommendation to measure Lp(a) in individuals with personal or a family history of premature cardiovascular disease, family history of high Lp(a), familial hypercholesterolemia, moderate to high cardiovascular risk or later also in patients with aortic valve stenosis [44]. This was a very important step to put Lp(a) on the map in clinical practice. However, these conditions were only a starting point and had the disadvantage that some of them provide only a post-hoc explanation of an event (for instance, a personal history of an ASCVD event). This might result in lost years of prevention which could have otherwise avoided the event. Furthermore, these groups are already considered at high or very high risk and should in any case undergo intensified treatment to prevent recurrent events. Most importantly, Lp(a) testing comes too late for those in whom the first event was fatal. Meanwhile many guidelines have shifted gear by recommending Lp(a) measurement in all individuals at least once in a lifetime [4,33–39]. Thereby the focus moved to the primary prevention setting. The cost-effectiveness analysis mentioned above further justifies this shift and encourages the implementation of systematic testing as soon as possible.

- **A combination of testing programmes for elevated Lp(a) and familial hypercholesterolemia should be considered depending on the health systems' readiness in individual countries.**

Lp(a) concentrations are low at birth. A prospective study of newborns from Denmark revealed that Lp(a) concentrations almost reach adult levels at 15 months of age [45]. Another large study from Netherlands observed from the age of 8 years onwards until adulthood a mean Lp(a) concentrations increased by 22 % [46]. Therefore, testing of Lp(a) in early childhood (e.g. at the age of 5 years) provides an approximate indication as to whether someone will develop markedly elevated concentrations during adulthood.

Since FH pediatric screening is becoming more widely adopted in some health systems [47], due to the advantages of early intervention, testing for both conditions (FH and Lp(a)) at the same time should be considered in countries where this is available. Knowing about one or the other or both conditions makes it possible to make the prevention of cardiovascular disease a family affair with mutual support between family members. Early knowledge should make it easier to avoid adopting poor lifestyle habits in the family (shared environment) in the first place, as lifestyle changes later in life are much more difficult to implement.

- **Testing for Lp(a) should not discriminate against an individual who is diagnosed with elevated Lp(a)**

As shown for familial hypercholesterolemia, early testing is important to begin effective preventive measures early [48–51]. Those identified with elevated Lp(a) should not experience discrimination in any area of their life on the grounds of their Lp(a) concentration since the Lp(a) concentration is only an indication for risk reclassification and a possibility of increased risk but not the diagnosis of a disease. Insurers should not penalize those who are detected early and are able to take early preventive measures. Knowledge and management of one's own risk factors should be regarded as a greater asset, minimizing the overall risk compared to an individual who chooses not to test and subsequently has a serious cardiovascular event. A relevant parallel can be drawn from the cancer field, where the "Right to Be Forgotten" [52] has been established in several EU countries to protect cancer survivors from discrimination, particularly in accessing financial services such as insurance and loans. This principle recognizes that a prior health condition, if well-managed or no longer active, should not define a person's future opportunities. Similarly, individuals diagnosed with elevated Lp(a) who engage in proactive health management should be empowered, not penalized. As with cancer survivors, legislative safeguards could help ensure that knowledge of genetic or lifelong risk factors like Lp(a) does not result in social or economic disadvantage, thus encouraging early testing and sustained prevention without fear of discrimination.

- **The cardiovascular risk of individuals with high Lp(a) concentrations should be reclassified into a higher risk category with access to appropriate management of these risk factors according to an individualized plan.**

In case of high Lp(a) concentrations combined with modifiable risk factors, it is of utmost importance that all these risk factors are treated accordingly, to reduce the global risk of an individual (Fig. 5). This is even more important in the case of family or personal history of cardiovascular disease. This will remain the case in the future should Lp(*a*)-lowering drugs become available and is supported by cost-effectiveness analysis. Therefore, this is a further reason not to postpone measuring Lp(a).

3.5. *Call 5 of the declaration*

Government investment, as part of wider public health prevention and management campaigns, to enhance public awareness about cardiovascular risk factors including Lp(a)

Governments should invest in raising public awareness and literacy about cardiovascular health and cardiovascular risk factors including elevated Lp(a). Campaigns should draw on sociological and behavioral factors linked to other successful movements such as smoking bans. They should also build on innovation in the field, including personalised communications models, implementation research through "living labs" [53] and social science, digitalization and application of artificial intelligence. Emphasis should be placed on young people in school settings and on general practitioners through medical curricula and continuous professional development, to enable general practices and community health centers be trusted and accessible sources of information and advice on Lp(a).

4. Additional considerations for implementation

To ensure Lp(a) test accessibility to patients and healthcare professionals with no barriers, clinical laboratories and Lp(a) test manufacturers should continue efforts and developments to make sure Lp(a) testing is widely available and meets the quality standards required. Although the standardization of the Lp(a) assays still leaves room for improvement [54], the currently available assays are sufficient to identify those persons who are at low, medium, high and very high risk. This is especially valid when Lp(a) is considered on a continuous scale which is in line with the observation that the CVD risk increases with higher Lp(a) concentrations (Fig. 1B). Ongoing standardization efforts will further improve the situation [55]. In this context, it is interesting that in patients with recent acute coronary syndrome, three Lp(a) tests done in the same samples from the ODYSSEY OUTCOMES trial were similarly prognostic for major adverse cardiovascular events

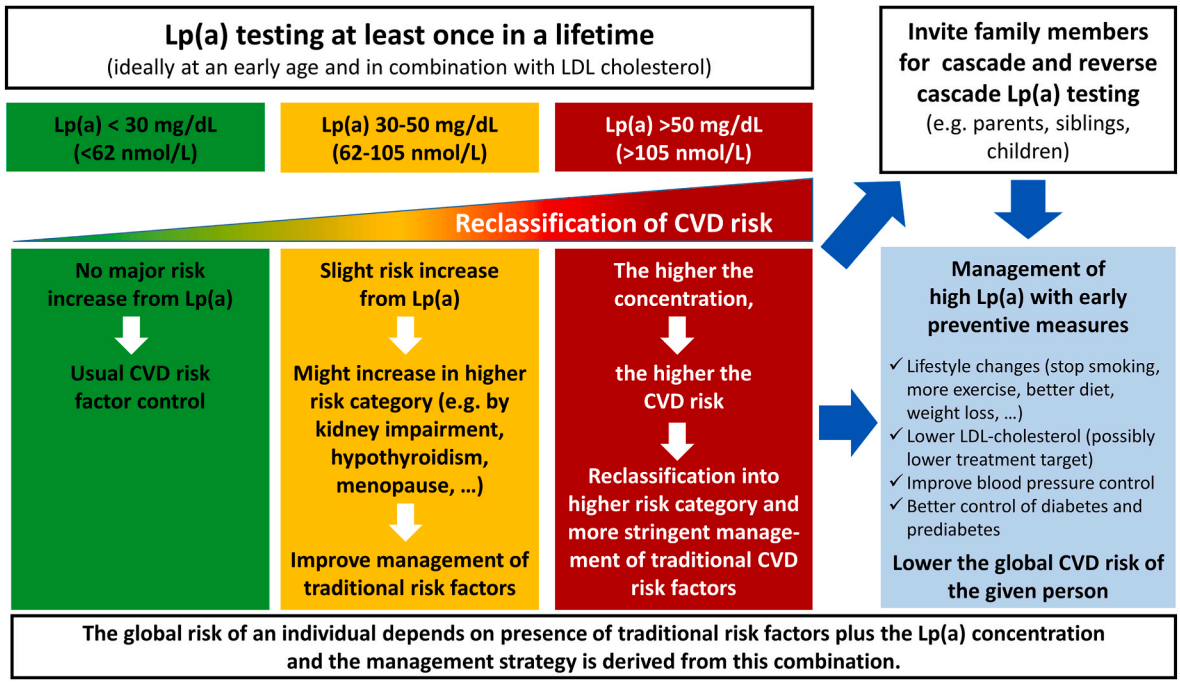

Fig. 5. Flowchart of an Lp(a) testing strategy, risk classification and risk reclassification based on the Lp(a) test result as well as management of high Lp(a) values.

independent whether the measurement was done with a nephelometric mass assay (measurement in mg/dL) or a molar turbidimetric assay or a molar mass-spectrometry-based assay [56]. Furthermore, Lp(a) measurement should occur routinely alongside the measurement of other blood lipids on the laboratories' automated test platforms, with the cost of the test itself fully covered by the health insurance system.

Responsible data sharing, transformational digital tools and ethical artificial intelligence will facilitate the implementation of systematic testing for, and effective personalised management of elevated Lp(a), enhancing efficiency, interoperability and evidence-based decision making.

Additionally, any research gaps identified could be addressed by Research and Innovation funding programmes such as Horizon Europe and the Innovative Health Initiative and successor programmes in Europe, and similar programmes in other regions of the world.

A commitment to shared learning, monitoring and evaluation through exchange and comparisons beyond borders is important to ensure the implementation of this Declaration. Through funding programmes such as EU4Health, and similar schemes in other regions, there could be investment in the transferability and uptake of best practice models in individual's risk assessment including Lp(a) testing from other countries, and country level "score cards" to measure progress according to safety, efficacy, cost-effectiveness, organisational, ethical, legal and social criteria. The experience of Lp(a) testing will be carefully observed and documented for analysis in the context of wider efforts towards better cardiovascular health through collaboration with relevant national, European and Global alliances.

5. Conclusion

The Brussels Declaration marks a pivotal moment in cardiovascular health policy reflecting, for the first time at the EU Council level, the importance of detecting inherited lipid disorders, including elevated Lp(a), as part of the broader strategy to improve cardiovascular outcomes across the European Union [57]. This recognition, embedded in the Council Conclusions of December 3, 2024, signals a paradigm shift in the policy landscape, illustrating the growing consensus on the urgent need to address genetic and often underdiagnosed CVD risk factors. It comes at a time when scientific knowledge, public awareness, emerging clinical guidelines, and health policy momentum are aligning, creating a unique and unprecedented opportunity to "prevent the preventable." By embedding Lp(a) and familial hypercholesterolaemia into strategic discussions on early detection (screening and testing), public awareness, and disease management, the Brussels Declaration paves the way for transformative action in reducing the burden of premature cardiovascular morbidity and mortality while promoting cardiovascular health for all. This development offers a critical window to integrate evidence into policy, drive investment into detection and treatment pathways, and ultimately, reshape the future of cardiovascular prevention.

It is vitally important that international, national and regional policymakers, medical societies, patient and public health organizations, and individual experts across the globe support this Declaration and to help ensure that systematic testing of elevated Lp(a) as early as possible in the life course becomes a reality for all, and those diagnosed with elevated Lp(a) concentrations are supported in managing their condition effectively.

It will also be crucial that model testing and care pathways, to accompany and support the implementation of the Brussels International Declaration on Lp(a), will be developed and shared across the globe in different healthcare and geographic settings.

CRediT authorship contribution statement

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Declaration of competing interest

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