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Lipid clinics worldwide: harmonization and guidance on how to optimally organize and fund. European Atherosclerosis Society consensus statement across 55 countries and more than 500 lipid clinics

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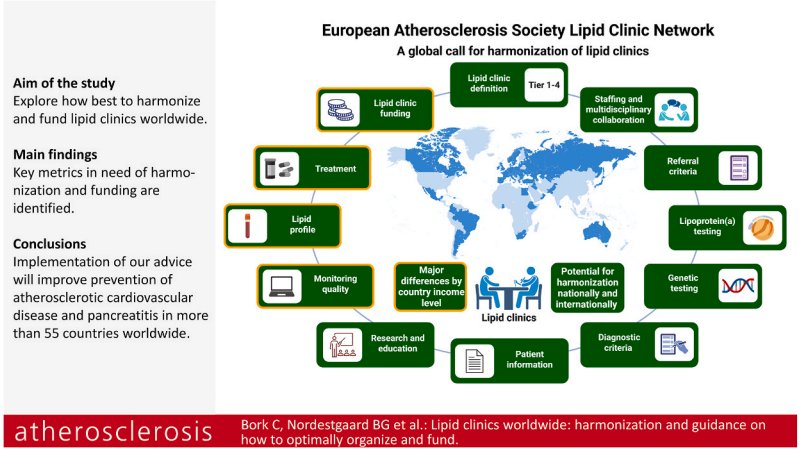
GRAPHICAL ABSTRACT



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ABSTRACT

Because one in three of all individuals die from atherosclerotic cardiovascular disease (ASCVD), prevention of ASCVD is key to public health worldwide. Lipid clinics provide specialized diagnostic assessment, lifestyle management, and evidence-based lipid-lowering treatment to prevent ASCVD and acute pancreatitis in high-risk individuals. This includes individuals with familial hypercholesterolemia and/or markedly increased lipoprotein (a), statin intolerance, refractory or difficult-to-control low-density lipoprotein (LDL) cholesterol, severe hypertriglyceridaemia, and other rare or complex lipid disorders. Such specialized care not only benefits the individual patients and their families but facilitates dissemination of best practices in lipid disorder management to healthcare professionals in individual nations. Despite this, there is a lack of guidance on standards and metrics needed to establish a well-harmonized national lipid clinic network in most countries capable of offering comprehensive care. This consensus paper from the European Atherosclerosis Society Lipid Clinic Network aims to meet this unmet clinical need. We provide recommendations to enhance education and training on lipid disorders and to harmonize lipid clinics at both national and international levels. Furthermore, we provide guidance on optimal staffing structures and development of registries to improve diagnosis and management of lipid disorders. Finally, we offer recommendations to national and regional policymakers on funding of lipid clinics, with the long-term goal of reducing the overall societal burden and costs of cardiovascular and other lipid-related diseases.

Abbreviations:

ApoB	apolipoprotein B
ASCVD	atherosclerotic cardiovascular disease
CAC	coronary artery calcium
CCTA	coronary computed tomography angiography
EAS	European Atherosclerosis Society
HDL	high-density lipoprotein
ICD	International classification of diseases
LDL	low-density lipoprotein
PCSK9	proprotein convertase subtilisin/kexin type 9
SCORE	systematic coronary risk evaluation
WHO	World Health Organization

1. Introduction

Lipid clinics are important in the prevention of atherosclerotic cardiovascular disease (ASCVD) and other lipid-related diseases in all countries. Lipid clinics are often the first to implement the latest lipid testing and therapeutic advances as well as serving as key stakeholders, locally and nationally, for implementation of the latest international and national guidelines on how to optimally diagnose and treat lipid disorders. This specialist care not only benefits individual patients and their families but helps disseminate best practices in lipid management to other physicians and healthcare professionals.

General practitioners/family doctors and hospital-based physicians often refer patients with complex lipid disorders like familial hypercholesterolaemia (FH), chylomicronaemia syndrome, high lipoprotein (a), borderline hyperlipidaemia, common hyperlipidaemia, statin intolerance, and rare lipid disorders including hypolipidaemias to lipid clinics, with the aim of getting specialist care for these complicated cases and their families.

In several European countries, lipid clinics are organized nationwide; however, in many countries only few lipid clinics are in existence and in yet other countries no formal lipid clinics are available. Therefore, there is an unmet medical need for establishment of nationwide networks of well-harmonized lipid clinics in most countries to better implement prevention of ASCVD and other lipid-related diseases through high-quality lipid management.

Based on data from the 2024 European Atherosclerosis Society (EAS) Lipid Clinic Network (Fig. 1) survey, several areas for potential improvement have been identified to enhance future lipid management globally, including i) increased national (in local or regional language)

and international (in English) educational activities on lipid disorders, ii) harmonization of lipid clinic organization and treatment guidelines nationally and internationally, iii) guidance on how to optimally structure staffing at lipid clinics, iv) guidance for how to organize national registries to improve diagnosis and management of lipid disorders, and v) guidance for dialogue with national and local governments on optimal funding of lipid clinics with the long-term aim of reducing national healthcare cost from ASCVD and other lipid-related diseases. The latter is in line with the recently published European Safe Heart plan from the European Union Commission [1].

The practicality of a similar standard of access to lipid clinics and provision of care equally across regions is a challenge. The present consensus statement covers the above-mentioned five topics overall and by region according to the World Bank income groups via their Gross National Income per capita of low, lower-middle, upper-middle, and high income [2]. In addition, within many countries, separate parts of the populations may belong to each of the four income groups. Also, we emphasize the perspective of patients attending lipid clinics. Finally, we also cover other topics necessary for running lipid clinics in different countries. Here we provide a consensus statement based on the available scientific literature combined with expert opinion where such evidence is lacking.

2. 2024 EAS survey of lipid clinics

The 2024 European Atherosclerosis Society Lipid Clinic Network Survey of Lipid Clinics gathered comprehensive, real-world data on lipid clinic operations and clinical practice. The survey targeted leading physicians and senior collaborators from the EAS Lipid Clinic Network, which at that time included over 470 clinics across 55 countries on six continents. The focus was on organization and operation of lipid clinics, risk assessment methods, implementation of guidelines, diagnostic tests, availability and reimbursement of lipid-lowering therapies, follow-up practices, use of registries, coordination of care, staffing models, and training opportunities and challenges. The results of this survey provided inspiration for the content of the present consensus statement. For illustration, a fraction of the results is presented below.

Data was collected from 121 participants across 44 countries. In total, 92% of these lipid clinics followed the EAS/ESC Guidelines on Dyslipidaemia and Cardiovascular Prevention [3,4] or corresponding national guidelines often adapted from the main European Guidelines to local national context (Fig. 2 left). A total of 53% used the European SCORE risk calculators.

Measurement of lipoprotein(a) was available in 44% of the lipid clinics, and genetic tests for molecular phenotyping of lipid disorders in 24%. However, differences were found according to different geographical areas (Fig. 3); the grouping of countries was based on a combination of the number of filled questionnaires from different countries combined with country income levels and worldwide location.

Importantly, all lipid clinics had access to statins and 93% had access to ezetimibe, whereas the availability of more advanced lipid-lowering therapies such as proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor antibodies was more limited (Fig. 2 right), except in Western Europe, North America, Australia, New Zealand and Japan.

Staffing included a minimum of physicians, nurses and dietitians in 69% of the lipid clinics, and multidisciplinary meetings were conducted in 77% of the clinics. However, opportunities for continued medical education among staff were limited. Only 28% of lipid clinics received direct funding from government ministries of health or universities (Fig. 4).

A key limitation of this survey is the likelihood that predominantly the most up-to-date lipid clinics completed the questionnaire. Hence, the values reported in this section should be interpreted as upper estimates, with corresponding figures across all lipid clinics worldwide likely to be lower. A further limitation is the relatively small number of participating clinics, which warrants cautious interpretation of the exact values presented.

Importantly, this bias likely will have minimal impact on the proposed harmonization strategies given in the remainder of this consensus paper, as these recommendations are not based solely on the evidence presented in this survey. Rather, the proposed harmonization strategies are based on the totality of the current evidence in the literature jointly

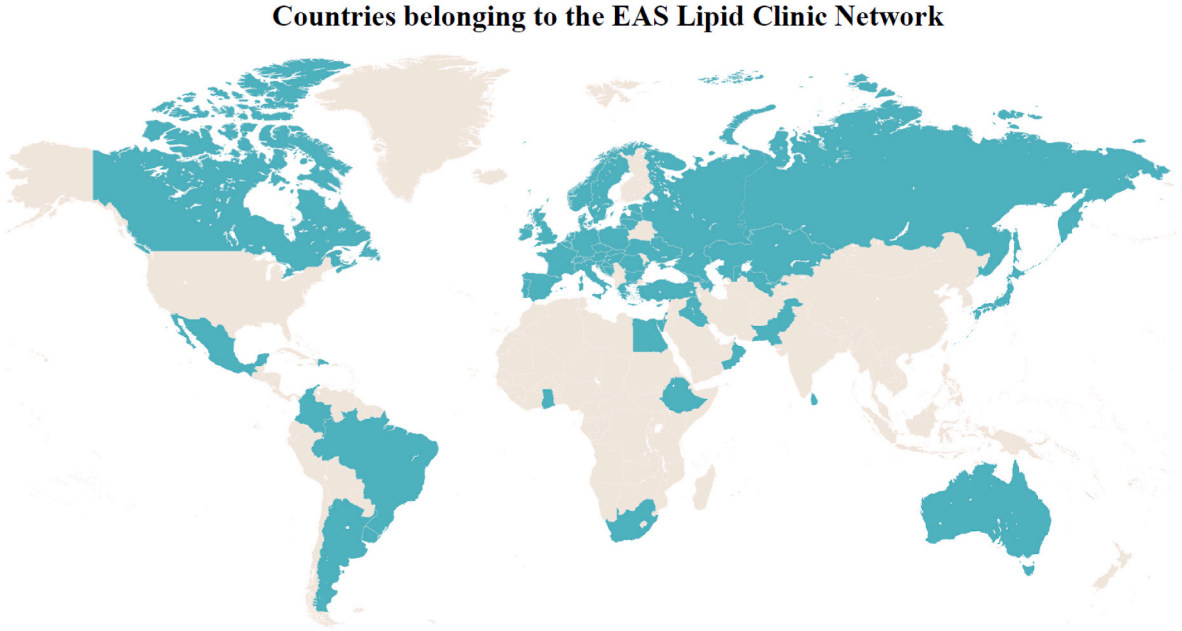

Fig. 1. Illustration of the 55 countries represented in the Lipid Clinic Network by January 2026: Argentina; Asia-Pacific; Australia; Austria; Azerbaijan; Belgium; Bosnia and Herzegovina; Brazil; Bulgaria; Canada; Colombia; Croatia; Cyprus; Czech Republic; Denmark; Dominican Republic; Egypt; Estonia; Ethiopia; France; Georgia; Germany; Ghana; Greece; Hungary; Iraq; Italy, Ireland; Israel; Japan; Kazakhstan; Latvia; Lithuania; Luxembourg; Malta; Mexico; Netherlands; Norway; Oman; Pakistan; Poland; Portugal; Romania; Russian Federation; Slovakia; Slovenia; South Africa; Spain; Sri Lanka; Sweden; Switzerland; Türkiye; Ukraine; United Kingdom; Uruguay; Uzbekistan.

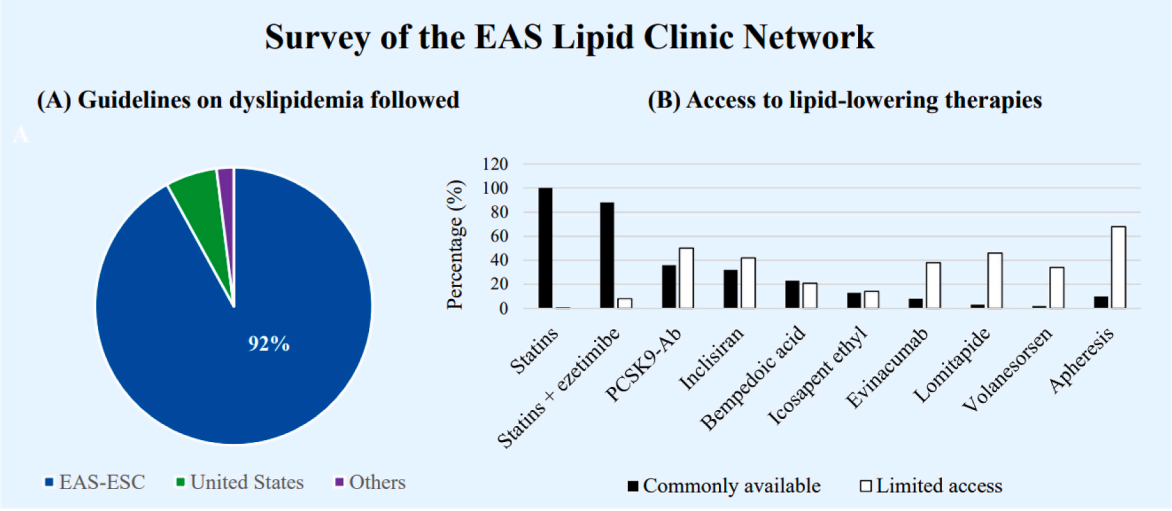

Fig. 2. Examples of overall information generated in the 2024 European Atherosclerosis Society Lipid Clinic Network Survey of Lipid Clinics from 121 participants across 44 countries. Panel A refers to the percentage following specific guidelines on dyslipidaemia, while Panel B refers to percentage with access to specific lipid-lowering therapies. Ab = antibodies; EAS=European Atherosclerosis Society; ESC=European Society of Cardiology; EAS-ESC based guidelines also include corresponding national guidelines often adapted from the European Guidelines.

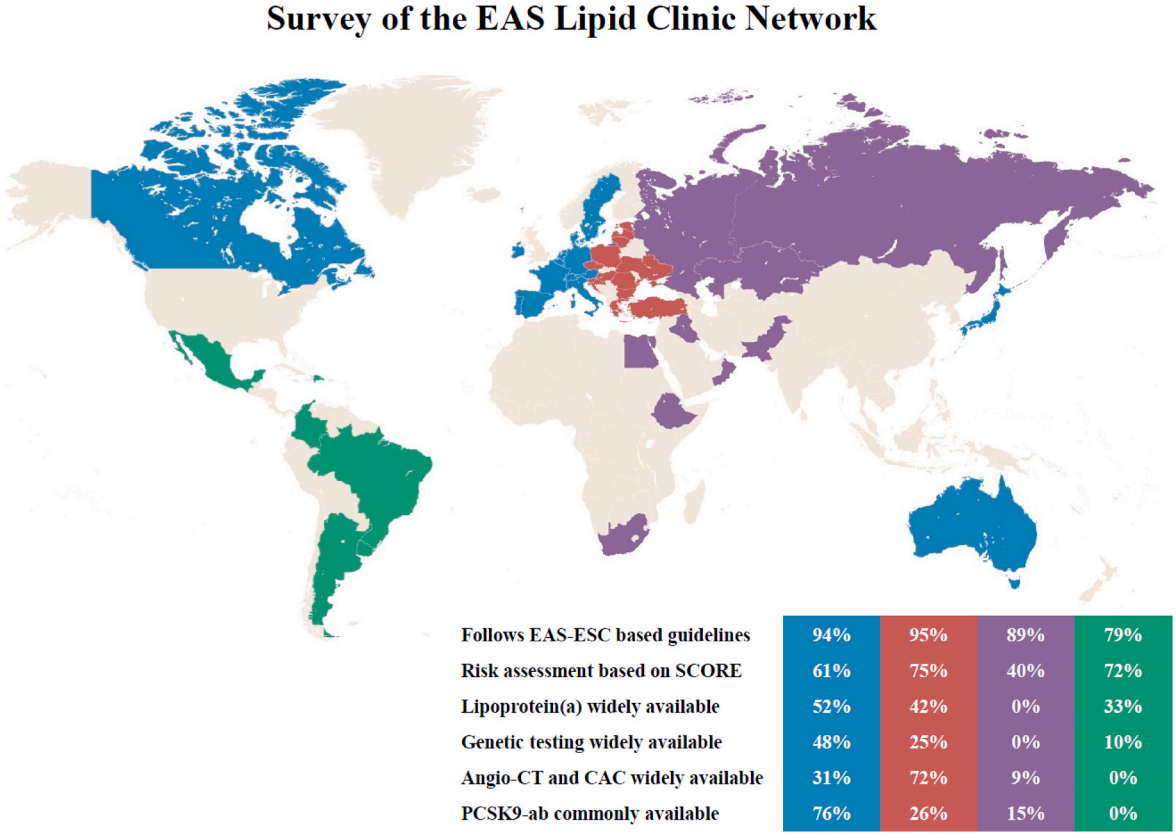

Fig. 3. Examples of information generated in the 2024 European Atherosclerosis Society Lipid Clinic Network Survey of Lipid Clinics by different regions of the world. ab = antibodies; CAC = coronary artery calcium; CT = coronary tomography; EAS=European Atherosclerosis Society; ESC=European Society of Cardiology; PCSK9 = proprotein convertase subtilisin/kexin type 9; SCORE=Systematic Coronary Risk Evaluation developed by the ESC and EAS.

with expert opinions from all authors of this paper.

In summary, major differences exist between lipid clinics worldwide, which leaves a great potential for harmonization of lipid clinics, the focus of the present EAS consensus paper. Priorities for improvements were identified and included, e.g. better post graduate training, higher reimbursement coverage of diagnostics and lipid-lowering therapy, better funding of lipid clinics, increase in staffing levels and better education on hyperlipidaemia overall in practically all countries.

3. Lipid clinic definition

A lipid clinic is a healthcare unit specialized in the diagnosis,

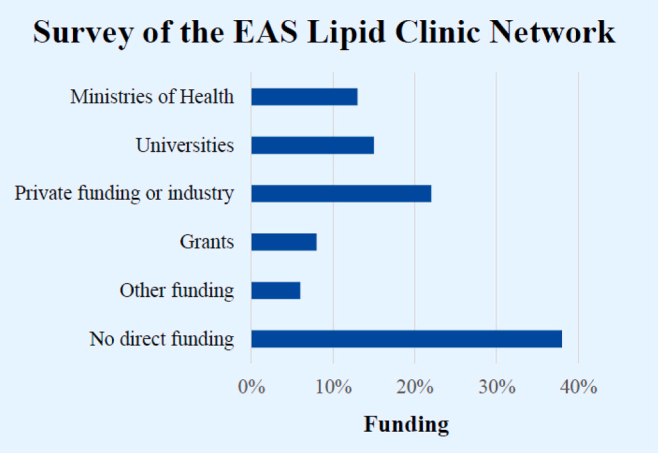

Fig. 4. Funding sources in lipid clinics worldwide based on the 2024 European Atherosclerosis Society Lipid Clinic Network Survey of Lipid Clinics.

treatment and management of patients with lipid disorders that combines patient-centered care, evidence-based medicine and clinical expertise to prevent development of ASCVD, acute pancreatitis and other lipid-related diseases (Fig. 5). We propose to categorise lipid clinics (albeit arbitrarily) into four types of lipid clinics according to increasing specialization and resources allocated (tier 1 through 4). Children with confirmed or suspected inherited lipid disorders should be managed in secondary or tertiary lipid clinics by (or in close collaboration with) specialized paediatricians or in family lipid clinics.

Tier 1 lipid clinics represent satellite healthcare units located in remote geographical areas in low and lower-middle income countries. These lipid clinics should have the capacity to conduct basic lipid testing such as total cholesterol and triglycerides, provide standard diet and lifestyle advices, and to initiate and provide basic lipid-lowering therapies such as statins.

Tier 2 lipid clinics should have the capacity to facilitate standard full lipid profile testing for diagnosis of common lipid disorders, and to perform cardiovascular risk assessment, cascade screening of families, and to give diet and lifestyle counselling. Also, treatment with traditional lipid-lowering therapies like statins and ezetimibe should be carried out in these lipid clinics, while complex lipid disorders can be referred to tier 3 and 4 lipid clinics.

Tier 3 lipid clinics additionally have the capacity to perform comprehensive lipid tests, including access to genetic testing for lipid disorders. They also have resources to provide multidisciplinary management of more complex and inherited lipid disorders, including cascade screening of families and access to more advanced lipid-lowering therapies. Moreover, tier 3 lipid clinics should have access to cardiovascular imaging and other relevant diagnostic tests and resources to participate in research.

Tier 4 lipid clinics represent the highest level of excellence for managing complex, rare, or severe lipid disorders. Further, such clinics in addition have the capacity to contribute to all types of research, education and development on regional, national and/or international levels.

The proposed definition of and categorisation of tier 1 to 4 lipid clinics are based on expert opinion. It can be argued that core multidisciplinary models of tier 2 to 4 lipid clinics are biased towards Western, high-income healthcare infrastructures. Therefore, the guidance provided for low- and lower-middle-income countries may lack the practical adaptations required for constrained healthcare systems, which needs to be developed further in such countries in the future.

4. Harmonization

Key to the success of lipid clinics in individual countries and worldwide is harmonization of what these clinics provide, such that patients and referring physicians know what service to expect. Optimal utilization of resources in lipid clinics relies on ensuring that the right patients are referred for specialized care, and that high quality care in

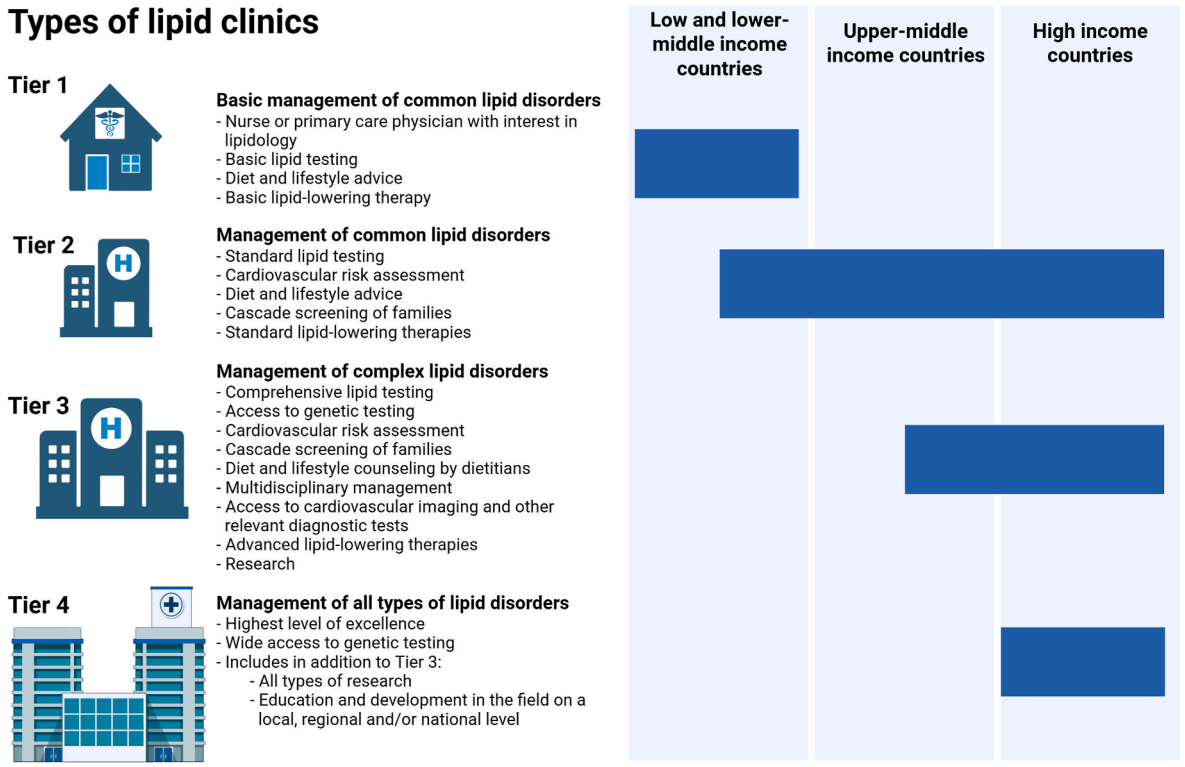

Fig. 5. Type of lipid clinics according to country level income.

the lipid clinics is maintained. This may be facilitated by harmonization of lipid clinic definition, staffing and multidisciplinary care, criteria for referral, lipoprotein(a) testing, genetic testing, diagnostic criteria, patient information, the possibility of involvement in research and education, monitoring quality, lipid profile offered, treatment options and funding of lipid clinics (Graphical abstract). Harmonization should always be possible within any country; however, some of these topics differ markedly by country income level, suggesting that international harmonization in all topics related to lipid clinics may not always be feasible (Graphical Abstract). These different topics are described further above or down in the text. The proposed recommendations for harmonization are based on expert opinions, partly guided by successful local implementation in several European countries.

5. Staff

A multidisciplinary approach within lipid clinics is essential to ensure optimal management based on shared decision making of patients with severe lipid disorders and their relatives. From referral through diagnostics, treatment, and ongoing monitoring, such collaboration promotes adherence to lifestyle modifications and prescribed medications, thereby improving long-term outcomes.

Furthermore, collaboration between lipid clinics nationally is of major importance to improve family cascade screening of relatives and to raise to overall level of knowledge. A multidisciplinary approach should facilitate accurate diagnosis through integrated clinical and genetic assessments, optimize therapeutic strategies by combining pharmacological and lifestyle interventions, and enhancement of patient adherence.

Staffing differs according to the types of lipid clinics. Tier 1 lipid clinics operate in remote geographical areas and may include a nurse or a primary care physician with interest in lipidology, while tier 2 to 4 lipid clinics are operated by specialized physicians trained in lipidology (Fig. 6). Also, tier 2 to 4 lipid clinics have nurses and clinical dietitians/nutritionists trained in lipidology. Administrative staff helps with patient coordination and running of lipid clinics. Finally, tier 3 and particularly tier 4 lipid clinics rely on close collaboration with various collaborators (Fig. 6).

The responsibilities of physicians in lipid clinics include evaluation of referrals, diagnostics, cardiovascular risk stratification, initiation of treatment, and genetic counselling. Moreover, they play a pivotal role in facilitating education and professional sparring with other lipid clinic personnel. Lipid clinic nurses play a key role in collecting information on family history of hyperlipidaemia and cardiovascular diseases as well as family screening and monitoring of patients followed in the lipid clinics. Also, dietitians are considered core staff in lipid clinics providing dietary counselling on healthy diet and lifestyle. Management of children with FH requires specialist knowledge and should be carried out either in specialized paediatric lipid clinics, family lipid clinics or in lipid clinics working in collaboration with paediatricians.

6. Referral criteria

National criteria for referral to lipid clinics are important to identify patients benefitting from specialized care. Optimal use of the resources in lipid clinics requires that common causes of secondary of hyperlipidaemia are evaluated before referral, including hypothyroidism, dysregulated diabetes mellitus, nephrotic syndrome, chronic renal failure, primary biliary cholangitis, drug induced hyperlipidaemia or extreme diets such as ketogenic high-fat diets. Thereafter, the following types of patients should be referred to lipid clinics:

- Suspected familial hypercholesterolemia
  - Adults with LDL cholesterol ≥5.0 mmol/L (≥190 mg/dL) [6]. Total cholesterol ≥7.5 mmol/L (≥290 mg/dL) may be used if LDL cholesterol is not available

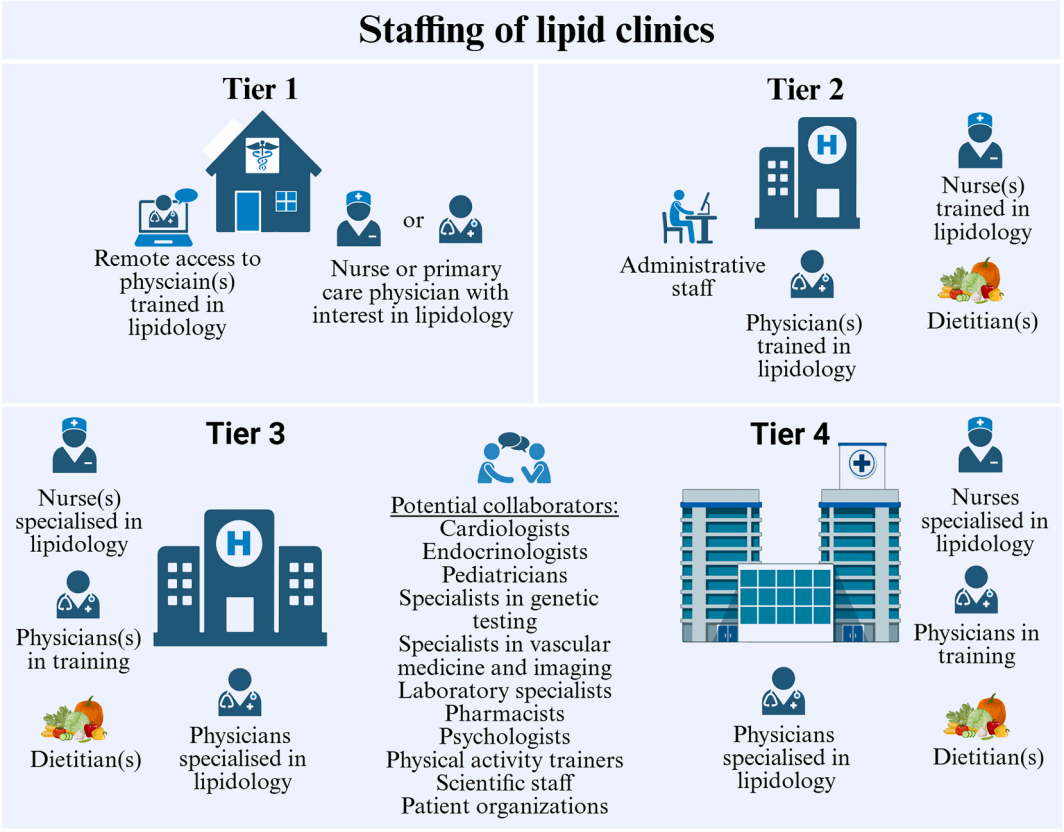

Fig. 6. Staffing according to type of lipid clinics.

- LDL cholesterol ≥4.0 mmol/L (≥155 mg/dL) in patients with early onset ASCVD (men <55 years, women <60 years), tendon xanthomas, or a strong family history of ASCVD [6].
- Children and individuals below 40 years of age with LDL cholesterol ≥4.0 mmol/L (≥155 mg/dL) [6].
- First-degree relatives (biological parent, sibling or child) to patients diagnosed with FH

- Homozygous FH at any age as per EAS diagnostic criteria [7,8].
- Severe hypertriglyceridaemia ≥10 mmol/L (880 mg/dL) or likely hypertriglyceridemia-induced pancreatitis in patients with moderate to severe triglyceride elevations. Persistent triglycerides ≥5.6 mmol/L (500 mg/dL) despite diet and lifestyle intervention and optimal management of secondary causes of hypertriglyceridaemia
- Very high lipoprotein(a) ≥200 nmol/L (95 mg/dL) (recommended as single lifetime test) or progressive or early onset ASCVD in patients with high lipoprotein(a) [9,10].
- Premature or progressive ASCVD despite guideline-directed lipid-lowering therapy, where combination therapy (high-intensity statin + ezetimibe + bempedoic acid) and consideration of advanced lipid lowering therapies (e.g. + PCSK9 inhibitors) is needed or treatment targets remain unmet [11].
- Residual risk in patients with optimized LDL cholesterol and recurrent ASCVD
- Statin intolerance (inability to tolerate ≥2 different statins, including at lowest doses) with unmet LDL cholesterol targets to evaluate alternative lipid-lowering therapy [12].
- Complex or rare hyper- and hypolipidaemias like familial remnant hyperlipidaemia (=dysbetalipoproteinaemia), mixed hyperlipidaemia, sitosterolaemia, chylomicronaemia syndromes, and hypobetalipoproteinaemia [13].
- Pregnancy/pre-conception counselling in patients with FH or familial chylomicronaemia syndrome
- Paediatric hyperlipidaemia, especially suspected FH or severe hypertriglyceridaemia for family-based care and cascade screening in families
- Complicated forms of secondary hyperlipidaemia requiring specialist care such as patients with primary biliary cholangitis, human immunodeficiency virus, systemic lupus erythematosus and some endocrine disorders (e.g. partial lipodystrophy)

Elevated LDL cholesterol and triglycerides that exceeds the specified cut-offs mentioned above should be confirmed by at least two measurements before referral, either in the non-fasting or fasting state. Furthermore, it should be stressed out that the recommended criteria for referral do not constitute a complete list but highlight the most important indications for referral to lipid clinics.

7. Lipid profile

Upon referral to a lipid clinic, the first goal is to make the correct diagnosis for each individual patient. This can only be achieved if the optimal diagnostic tests are available in lipid clinics (Fig. 7).

7.1. Standard lipid profile

All patients shall preferably be referred to the lipid clinic with a standard lipid profile already measured, including concentrations of total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, remnant cholesterol, non-. LDL cholesterol can be calculated by one of the established equations (e.g. Friedewald [14], Martin-Hopkins [15], or Sampson-NIH [16,17]) or measured directly; whether calculated or

Availability of diagnostic tests in lipid clinics

Diagnostic tests \ Countries	Low and lower-middle income	Upper-middle income	High income
Simple screening tests[a]: Total cholesterol (TC), triglycerides (TG)	Available	Standard lipid profile + lipoprotein(a) preferred	Standard lipid profile + lipoprotein(a) preferred
Standard lipid profile TC, HDL-C, TG, LDL-C, remnant-C[b], non-HDL-C[b]	Mostly available	Available	Universally available
Screening for secondary hyperlipidaemia TSH, eGFR, glucose, ALT, AST, GGT, urinary protein (AUCR)	Mostly available	Available	Universally available
Lipoprotein(a)	Limited access	Available[c]	Available[c]
Additional lipid tests ApoB, directly measured LDL-C	Limited access	Available[c]	Available[c]
Genetic testing Screening for FH, diagnosis of rare genetic hyper- and hypolipidaemias	No access	Limited access	Restricted access

Fig. 7. Access to diagnostic tests at lipid clinics differ substantially according to country level income. Colours indicate: Green = available, yellow = mostly available, red = limited to no access. Checkerboard pattern indicates strong heterogeneity within and between countries in that specific combination. ALT = alanine aminotransferase; apoB = apolipoprotein B; AUCR = albumin/creatinine ratio in urine sample; AST = aspartate aminotransferase; eGFR = estimated glomerular filtration rate; FH = familial hypercholesterolemia; GGT = gamma glutamyltransferase; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; Lp(a) = lipoprotein(a); TC = total cholesterol; TG = triglycerides; TSH = thyroid stimulating hormone;
[a] Intended for very inexpensive recognition of serious elevations of cholesterol/triglycerides
[b] Any diagnostic laboratory can calculate and report free of charge these values from the standard lipid profile
[c] Lp(a) measurement might be restricted, direct LDL cholesterol assays can be replaced by e.g. Martin-Hopkins [15] or Sampson-NIH equations [16] and [17]. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

measured LDL cholesterol are superior and less prone to error with high triglyceride levels is unclear [18,19].

Non-HDL-cholesterol and remnant cholesterol levels should be calculated in all patients because non-HDL cholesterol outperforms total and LDL cholesterol in ASCVD risk stratification and better reflects actual ASCVD risk [20], while elevated remnant cholesterol captures the residual risk of ASCVD when triglycerides are elevated after LDL cholesterol therapy [21]. Non-HDL cholesterol is calculated as total cholesterol minus HDL cholesterol while remnant cholesterol is calculated as total cholesterol minus LDL cholesterol minus HDL cholesterol. For screening purposes fasting is not routinely required [22], and most lipid guidelines in the world no longer suggest a follow-up fasting lipid profile even if triglycerides are elevated [23].

7.2. Lipoprotein(a)

Lipoprotein(a) levels should be measured at least once in all individuals [3,11], either at the first lipid profile or the next one if lipid profiles have previously been performed [3,4,9,11,24,25]. Re-measurement of lipoprotein(a) concentrations may be relevant if lipoprotein(a) lowering therapy is administered, after menopause in women, and one month after an acute coronary syndrome or ischemic stroke [11,24].

Plasma lipoprotein(a) levels are >90% genetically determined, and more than 20% of all individuals have levels above 105 nmol/L (50 mg/dL), which is a causal risk factor for ASCVD and aortic stenosis [9,24]. High lipoprotein(a) levels may contribute significantly to plasma levels of LDL cholesterol and high lipoprotein(a) explains up to one quarter of clinical FH diagnoses [26,27]. Measurement of plasma lipoprotein(a) should be available for all lipid clinics when potential underlying causes of hypercholesterolemia are examined, for cardiovascular risk stratification, and for identification of individuals with a significantly increased genetic risk of ASCVD [11,28]. Lipoprotein(a) should be measured on fresh blood samples using assays largely independent of apolipoprotein(a) isoform size [24], and molar concentrations measured in nmol/L is preferred over mass concentrations in mg/dL; however, if only mg/dL is available, it is perfectly fine to measure lipoprotein(a) [24].

7.3. Apolipoprotein B and high-sensitivity C-reactive protein

Because the apolipoprotein B (apoB) concentration is a better predictor of the risk for future ASCVD events than LDL cholesterol, apoB assessment should ideally be offered by laboratories serving lipid clinics [29]. Moreover, contrary to LDL cholesterol levels, apoB and non-HDL cholesterol continue to be predictive of the future risk of ASCVD even in patients treated with statins [30–33]. ApoB has been suggested to be the most reliable proxy for ASCVD risk across LDL cholesterol and non-HDL cholesterol concentrations [34]; however, it is unclear whether non-HDL cholesterol or apoB measurements always is better than the other, and *vice versa*.

Measurement of high-sensitivity C-reactive protein as a marker of low-grade inflammation likewise has additional predictive value, and concentrations persistently >2 mg/L identify patients at increased risk of ASCVD [21].

7.4. Screening for causes of secondary lipid disorders

Initial assessment of hyperlipidaemia must exclude the most common secondary causes of lipid disorders. The biochemical screening shall include evaluation of:

- Thyroid-stimulating hormone (TSH) to exclude hypothyroidism
- Liver function tests (transaminases, gamma glutamyltransferase and alkaline phosphatase) to exclude liver impairment
- HbA1c or fasting glucose to exclude diabetes mellitus
- Estimated glomerular filtration rate (eGFR) to exclude impaired renal function and proteinuria to screen for nephrotic syndrome

Assessment of potential causes of secondary dyslipidaemia or aggravating factors of hyperlipidaemia should also comprise careful pharmacological and personal history and other examinations like body weight, waist circumference and dietary assessment.

8. Genetic testing

Shared decision-making and informed consent between patient and healthcare provider is essential, as patient values and preferences play a strong role [35]. Genetic testing is generally recommended when monogenic hyperlipidaemias (e.g. FH, familial chylomicronaemia syndrome, familial remnant hyperlipidaemia (=dysbetalipoproteinaemia) or rare lipid disorders (e.g. lysosomal acid lipase deficiency, sitosterolemia) are suspected [13]. Other indications for genetic testing include rare lipoprotein phenotypes characterized by decreased lipoprotein levels (e.g. hypo- and abetalipoproteinemia, severe hypo-alphalipoproteinaemia) [13].

Strict adherence to guidelines for genetic test results reporting must be ensured [36,37]. Ana-lysis and interpretation of the results of complex genetic tests might be difficult as often variants of unknown significance (VUS) or novel genetic variants are detected.

9. Subclinical atherosclerosis and imaging

In asymptomatic apparently healthy individuals, identification of subclinical atherosclerosis using imaging can be important. Presence of an unequivocal atherosclerotic lesion in any vascular bed signifies increased ASCVD risk independent of other ASCVD risk factors [3,11]. Although the evidence is less extensive than for CAC, carotid artery or femoral plaques (not intima-media thickness) on ultrasonography probably also reclassifies ASCVD risk and may be considered as a risk modifier in patients at intermediate risk and young adults [20].

Increased coronary artery calcium (CAC) is considered a risk modifier in individuals at moderate risk or among individuals around treatment decision thresholds [11]. Also, ankle-brachial index as the ratio of blood pressures measured on arteries above the ankle over arm arteries can be used as a marker for the presence of peripheral arterial disease, and increased ASCVD risk with an ankle-brachial index <0.9 in individuals without diabetes mellitus [20].

Coronary Computed Tomography Angiography (CCTA) represents another imaging modality to visualize coronary atherosclerosis [38]. Contrary to CAC, the advantage of CCTA includes assessment of non-calcified plaques. However, it is currently unknown whether CCTA performs better than CAC in risk stratification as it has been mostly studied in symptomatic patients. According to recommendations from the Society of Cardiovascular Computed Tomography it may be appropriate to perform CCTA in selected individuals aged <45–50 years who have cardiovascular risk factors such as diabetes, human immunodeficiency virus, smoking, or a strong family history of premature ASCVD [39]. Other high-risk groups include patients with FH and patients with inflammatory conditions like systemic lupus erythematosus, rheumatoid arthritis, or psoriasis.

10. Diagnostic criteria and coding

The diagnostic procedures of the aetiology of hyperlipidaemia should include a detailed medical history and physical examination. The following criteria are recommended for the diagnosis of primary hyperlipidaemias:

Familial hypercholesterolemia: The Dutch Lipid Network (DLCN) diagnostic criteria are one of the most widely used scoring systems for FH in adults [40]. In addition to plasma LDL cholesterol levels, it also includes information on first-degree relatives with premature ASCVD or

elevated LDL cholesterol, clinical history of premature ASCVD, FH stigmata such as tendon xanthomas or arcus cornealis, and detection of pathogenic variants in genes causing FH. According to scores obtained, patients can be divided into those with definite (>8 points), probable (6-8 points), possible (3-5 points) or unlikely (<3 points) FH by the DLCN criteria. However, the DLCN diagnostic criteria are not applicable for children in whom the Simon Broome criteria and/or FH Paediatric Diagnostic Score (FH-PeDS) [41] are options. Genetic testing should be considered in all individuals suspected of having FH. A clinical diagnosis of FH may be established based on a DLCN score ≥6.

Familial remnant hyperlipidaemia (=dysbetalipoproteinaemia): The combination of both increased plasma triglycerides above 5 mmol/L (440 mg/dL) and total cholesterol above 8 mmol/L (300 mg/dL) with a concomitant moderate to low apoB concentration (<1 g/l) is compatible with the diagnosis. Some criteria use cholesterol enrichment of apoB containing lipoproteins [42]; however, these criteria are not standardized. An *APOE* genotype should be requested, where *APOE* E2/E2 genotype and some rare deleterious variants with dominant inheritance makes the diagnosis likely.

Chylomicronaemia: A plasma triglycerides concentration above 10 mmol/L (880 mg/dL) is diagnostic. The criteria proposed by Moulin and coworkers are suggested to distinguish between a monogenic and multifactorial aetiology [43]. Alternatively, the North American Familial Chylomicronaemia Syndrome score may used [44].

Rare lipid disorders like lysosomal acid lipase deficiency, sitosterolaemia, familial chylomicronaemia syndrome and hypo-/abetalipoproteinnaemia should be diagnosed based on genetic testing. ApoB measurement naturally is also necessary for diagnosing hypo- and abetalipoproteinaemia.

Standardization of diagnostic coding should be performed at national levels and validation of disease registries is important to ensure the validity of the registered diagnoses. The World Health Organisation (WHO) International Classification of Diseases (ICD) codes are the recommended option.

11. Treatment

11.1. Treatment optimization according to country income level

Healthy lifestyle counselling and treatment optimization for hyperlipidaemia align with the Sustainable Development Goal no 3 of the United Nations for 2030: to ensure healthy lives and promote well-being. The objective is to reduce mortality from non-communicable diseases by a third by 2030 and to improve environmental health. Below we describe how best to achieve this in different countries, as access to healthy lifestyle counselling and different types of lipid-lowering therapies for ASCVD prevention differ substantially based on country income level (Fig. 8).

11.2. Low and lower-middle income countries

In lower-middle income countries, 50% of the world's population resides but less than 5% of world healthcare spending occurs here [45, 46]. The fraction of world healthcare spending is much less in low-income countries accounting for <10% of the world population. Lower-middle income countries are in South, Central and South-east Asia as well as in Africa and include for example India, Pakistan, Nigeria, Ghana, Cambodia, Kyrgyzstan, and Uzbekistan. Low-income countries are in Africa and Afghanistan, Syria and Yemen.

Lipid clinics must prioritize interventions that provide the best efficiency (cost/effectiveness ratio) while aligning with available resources in the case of common hyperlipidaemia. For rare hyperlipidaemias with a severe prognosis, the challenge is accessing treatments that are otherwise inaccessible without special procedures, such as compassionate access.

11.2.1. Lifestyle improvement

Heart healthy eating, regular physical activity, weight control and smoking cessation counselling should be the cornerstone of all lipid clinic programs for lowering the risk of ASCVD. Furthermore, a healthy diet plays a pivotal role in the treatment of hypertriglyceridemia, whereas the effect of changing dietary habits on LDL cholesterol may be modest. Information on lifestyle factors such as dietary habits, intake of calories, alcohol consumption, and physical activity should be recorded

Availability of treatment possibilities in lipid clinics

Treatment \ Countries	Low and lower-middle income	Upper-middle income	High income
Lifestyle improvement	Available	Mostly available	Universally available
Low-cost treatments Statins, ezetimibe	Limited access for the majority of the eligible population	Difficulties of access	Easily accessible and reimbursed
Middle-cost treatments Bempedoic acid, eicosapent ethyl	Marginal access	Strong restrictions of access	Variable market access delays
High-cost treatments PCSK9-Ab, inclisiran	Marginal / no access	Strong restrictions / no access	Variable limitations of access
Highest-cost treatments Anti apo C3, evinacumab, lomitapide, LDL apheresis	No / compassional access	Ultra-restricted or no access	Strongly restricted access

Fig. 8. Access to healthy lifestyle counselling and different types of lipid-lowering treatments for ASCVD prevention differ substantially based on country income level. Colours indicate: Green = available, yellow = mostly available, orange = strong restrictions, red = limited to no access. Checkerboard pattern indicates strong heterogeneity within and between countries in that specific combination. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

systematically. Dietary counselling must be tailored to the underlying condition. However, for all patients the dietary recommendations should emphasize reducing intake of trans fat, saturated fat, and added sugar while increasing consumption of fruits, vegetables, legumes, and whole grains. This must be achieved using locally available food and cooking styles [47], which can be highly challenging for many patients [48]. Physical activity counselling should integrate community-based initiatives, such as walking groups, active transport, and workplace interventions which require minimal infrastructure [49]. Smoking cessation support must also be systematically offered to counteract the influence of tobacco companies, which face less regulatory pressure in low and lower-middle income countries than in high-income countries [50].

11.2.2. Low-cost drugs

When economically feasible, statins can be offered to all individuals at high and very high risk of ASCVD according to guidelines [3,4]; however, if availability is limited, statin therapy for primary prevention should be restricted to individuals at very high risk of ASCVD such as patients with diabetes mellitus or heterozygous FH [51,52]. This ensures that limited resources are directed toward populations with the greatest expected benefit, consistent with WHO guidelines [53]. The organization of primary health care should allow access to high-intensity statins even in the most remote areas. Statins were added to the WHO Essential Medicines List in 2007. However, in 2022 a study suggested that statins were used by only one in ten eligible individuals for the primary prevention of cardiovascular diseases in low and middle income countries [54].

All patients with established ASCVD should receive statins, ideally at high intensity [51]. However, only one in five eligible people for secondary prevention were reported using statins in 2022 in low and middle income countries [54]. The access to LDL and/or non-HDL cholesterol measurement should be improved to allow a treatment monitoring at least once a year and to improve long-term adherence to statins. When statin intolerance occurs, clinicians should prescribe the maximal tolerated dose of statins. Ezetimibe is the preferred second-line agent and, with increasing generic availability, may be feasible in many low and lower-middle income countries [55,56].

11.2.3. Middle- and high-cost drugs

If affordable, bempedoic acid may be considered for use with statin-intolerant and/or very high-risk patients. PCSK9 inhibitor antibodies should be reserved for selected patients such as those with ASCVD and high residual LDL cholesterol despite optimal combination of statins and ezetimibe, because they may be accessed only under discounted pricing, donor support, or externally funded agreements.

11.2.4. Homozygous FH, familial chylomicronaemia syndrome

Patients with homozygous FH, severe heterozygous FH, and familial chylomicronaemia syndrome should be referred to centralized hubs with specialized expertise. Access to LDL apheresis, highly specialized medication (lomitapide, evinacumab), or liver transplantation (when LDL apheresis is inaccessible) should depend on international partnerships and compassionate-use pathways, due to drastically limited public funding. Familial chylomicronaemia syndrome may be partly controlled by severe fat restriction in the diet.

11.2.5. Conclusions

Due to the scarcity of lipid clinics in low and lower-middle income countries and the challenge of monitoring LDL and/or non-HDL cholesterol in remote areas, a network must be established to connect internists, cardiologists, endocrinologists and biologists to the limited referral centres that exist. Management must balance effectiveness with affordability. Emphasis of lifestyle counselling, weight control, universal use of statins for secondary prevention and targeted primary prevention represents the highest-value interventions. Expensive therapies should be reserved for exceptional cases, ideally through international support mechanisms including scientific advising by international atherosclerosis associations, and support by WHO and pharmaceutical companies. This pragmatic approach provides the most sustainable path for long-term cardiovascular health gains.

11.3. Upper-middle income countries

Upper-middle-income countries represent over 30% of the world's population and account for around 15% of healthcare spending [45,46]. These countries are found in Asia, Southern and Northern Africa, the Middle East, Latin America, and in part of Eastern Europe including for example Kazakhstan, China, Turkey, Iran, Brazil, South Africa, Mexico, Thailand, Ukraine, and Serbia. In most of such countries, the incidence of ASCVD is rising. The problem is further complicated by limited healthcare resources, a high prevalence of risk factors such as smoking, obesity and diabetes mellitus, with insufficient access to the latest preventive therapies [57].

11.3.1. Lifestyle improvement

For upper-middle income countries, lifestyle modification remains a top priority. However, such interventions face many challenges including:

- Lack of awareness in the population about the benefits of lipid and cardiovascular risk factor control
- Implementing comprehensive programs to promote smoking cessation and reduce alcohol consumption
- Setting large-scale campaigns promoting overall healthy lifestyle, particularly healthy eating habits and regular physical activity, whereas a shift of the populations toward the cities is observed [58].
- Ensuring access to primary cardiovascular prevention and healthcare providers (both physicians and nurses) in rural areas, given that rural residence is an established determinant of worse prognosis
- Establishing population-based screening programs adapted to local resources
- Creating strict post-discharge pathways for secondary prevention

While dietary interventions, physical exercise and smoking cessation are the main primary preventive measures, they can be hampered by the lack of availability of certain foods at affordable prices and by the pressure of tobacco advertising, which is less regulated in upper middle-income countries than in high-income countries.

11.3.2. Low-cost drugs

Lipid-lowering therapies are indicated in high-risk subjects and/or in subjects with severe hyperlipidaemia. Statins are the first-line therapy, with generic atorvastatin and rosuvastatin being the most widely used and cost-effective [59,60]; ezetimibe is also available in many of these countries. Primary prevention should target into priority high-risk groups (patients with diabetes mellitus, severe hypertension, heterozygous FH), with emphasis on screening, affordable therapy and risk factor management [61].

11.3.3. Middle- and high-cost drugs

If LDL cholesterol is above goal at maximum tolerated dose of a statin, therapy is escalated to add non-statin therapies with proven cardiovascular benefit, ezetimibe, bempedoic acid and/or a PCSK9 inhibitor monoclonal antibodies, taken alone or in combination; the choice should be based on the magnitude of additional LDL cholesterol lowering needed, cost, patient preference, and treatment availability [3,4]. PCSK9 inhibitors monoclonal antibodies (evolocumab, alirocumab) may be used in very high-risk patients, in case of insufficient control of hypercholesterolemia in secondary prevention [55]. Icosapent ethyl and fibrates could serve as additional options in hypertriglyceridemic patients who are already treated with high-intensity statin [3,11,62].

11.3.4. Highest-cost drugs and apheresis

Accessing these expensive treatments presents several challenges, including establishing referral pathways that direct patients with rare and severe lipid disorders to dedicated national or regional lipid clinics, depending on the specific funding available.

11.3.5. Conclusions

Upper-middle income countries face significant barriers to effective hyperlipidaemia management, including weak reimbursement systems, delayed approvals, and limited infrastructure for lipid monitoring. Pragmatic solutions involve centralized procurement of generics, strengthening local pharmaceutical production, and adopting cost-saving strategies such as fixed-dose polypills. Nurse-led lipid clinics, digital tools, and structured referral pathways can improve access, particularly in rural areas. Ultimately, the most sustainable approach combines strong nationwide prevention campaigns, prioritization of lifestyle interventions, and targeted use of therapies in secondary prevention and very high-risk primary prevention patients. Such strategies will balance affordability, sustainability, and equity in cardiovascular prevention.

11.4. High income countries

High-income countries represent <20% of the world's population and account for >80% of healthcare spending, with the USA alone accounting for 44% of all worldwide healthcare expenditure [45,46]. These countries are found in North America, Western and Central Europe, the Middle East, Asia-Pacific, and in some countries in Latin America including for example Canada, USA, Spain, France, UK, Germany, Scandinavia, Saudi Arabia, Australia, Chile, and Uruguay. In most of these countries, the incidence of ASCVD is declining overall, most pronounced as declining age-standardized cardiovascular mortality rates. That said, the total prevalence of ASCVD remains high even in high-income countries, where the occurrence of ASCVD has been shifted to older age groups.

11.4.1. Lifestyle improvement

Implementation of lifestyle improvement in high-income countries remains a challenge, especially among low-income subpopulations in these countries [63]. Emphasizing the role of physical activity in preventing abdominal obesity, the metabolic syndrome, and type 2 diabetes mellitus is a major challenge, given the clear evidence of low adherence over the long term [58]. Adherence to e.g. a plant-based, Nordic or Mediterranean type diet may also be challenging in countries where vegetables, fruits, and fish are expensive. The fight against smoking is made less difficult in high-income countries thanks to banning of smoking in many public places, high tobacco pricing policies, advertising bans, and the promotion of access to substitute products [64].

11.4.2. Low-cost drugs

In high-income countries, access to general practitioners/family doctors, lipid assessments and generic lipid-lowering drugs is usually not a major issue. The challenges are:

- To optimize screening strategies to improve early access to lipid-lowering treatment and prevent the development of ASCVD
- To improve adherence to lifestyle improvement and lipid-lowering drugs, especially in primary prevention. The revisionism regarding statin prescriptions remains a challenge [65].
- To combat therapeutic inertia by implementing current guidelines
- To confront fake news about statins
- To tailor expensive treatments for the patients with the highest absolute risk, to contain the number needed to treat at a reasonable low level and thus ensure optimal treatment efficiency
- To maintain a high level of clinical research to optimize the treatment options

11.4.3. Middle-cost drugs

Regarding bempedoic acid and icosapent ethyl, price negotiations with health authorities often result in a delay of several years in market access in many countries [66].

11.4.4. High-cost drugs

In most high-income countries, PCSK9 inhibitor drugs are subject to severe prescription restrictions for reimbursement, with a much more limited scope of use than that recommended by EAS/ESC dyslipidaemia guidelines [3,4]. This leaves many heterozygous FH patients without access to these treatments.

11.4.5. Highest cost drugs

Access to these expensive drugs for very rare hyperlipidaemias is possible in several high-income countries under strict conditions, sometimes requiring involvement of the national lipid clinic staff. The limited number of patients makes treatment access possible for familial chylomicronaemia syndrome and homozygous FH, for example. The challenge lies in accessing treatment for patients suffering from the most severe heterozygous FH and multifactorial chylomicronaemia syndrome, who often have no access outside of clinical trials [67,68]. Therefore, the role of a lipid clinics network is important for establishing registers showing the unmet needs for these patients who are at the boundaries of the rare lipid disorders, but often equally in need of such expensive therapies.

11.4.6. Conclusions

Despite the easy access to generic drugs for common hyperlipidaemias, therapeutic inertia creates a gap between guidelines advice and epidemiological surveys of real-world evidence. Consequently, lipid clinic networks have a major role to play through their teaching missions. Even in high income countries, access to new treatments is often delayed and complicated. The role of national registries and patient organizations is crucial in identifying unmet needs and in convincing politicians to make access to expensive drugs affordable.

12. Patient management and follow-up

Effective communication and dissemination of information to patients diagnosed with inherited hyperlipidaemias and other lipid disorders are important because early and lifelong management is needed to prevent adverse outcomes. Providing accurate and tailored information enables patients to understand their condition, ensuring better adherence to preventive lifestyle improvement and treatment.

Therefore, patient information leaflets should be available in all lipid clinics on the most frequently inherited hyperlipidaemias and particularly for patients with FH and high lipoprotein(a), as these conditions are underdiagnosed and undertreated worldwide [9,40]. Also, information to first-degree relatives of patients with inherited hyperlipidaemias is relevant whenever family cascade screening is recommended. Patient material including leaflets and webpages should preferably be developed at national or alternatively regional level to ensure standardization and high quality. Also, messages should be simple and adapted to the characteristics of the target population. Other topics for educational material should include information concerning smoking cessation and healthier dietary habits.

12.1. How can patient education be improved?

Lipid clinics can collaborate with patient organizations and national initiatives to:

- Develop clear and relevant materials that help patients understand their condition and treatment

- Training of referent patients: individuals with severe disease acting as couches for newly diagnosed patients and their families (e.g. patients with homozygous FH)
- Arrange workshops or support groups where patients can ask questions and share experiences with others in similar situations
- Help in raising awareness of lipid-related diseases among the public through national campaigns and information initiatives

Key to lipid management and thus prevention of ASCVD, acute pancreatitis and other lipid-related diseases is patient adherence to optimal lifestyle and prescribed lipid-lowering therapy. Here lipid clinics are centrally placed and in consequence need to follow patients for a period to secure that patients follow the advice given to them (Fig. 9). Only once this has been ensured, can patients be safely referred back to their general practitioner/family doctor.

12.2. Which patients should be followed in lipid clinics?

12.2.1. Familial hypercholesterolemia

Patients with FH should be followed in lipid clinics in partnership with general practitioners/family doctors and specialists in lipidology due to the lifelong condition, including management in childhood, adolescence, pregnancy, adulthood or older age. This condition also includes cascade screening of biological family members and appropriate treatment of affected family members. As medical treatments continue to advance, lipid clinics are uniquely positioned to stay at the forefront of new evidence and clinical guidelines, offering individualized, state-of-the-art treatment tailored to each patient's specific needs.

12.2.2. Extremely elevated lipoprotein(a)

Patients with extremely elevated lipoprotein(a) of ≥400 nmol/L (≈180 mg/dL) should also be followed in lipid clinics due to cascade screening of family members and estimated risk of developing early ASCVD comparable to heterozygous FH [10].

12.2.3. Persistent severe hypertriglyceridaemia

Patients with persistent triglyceride levels >10 mmol/L (880 mg/dL) after exclusion of causes of secondary hyperlipidaemia should be referred to lipid clinics to mitigate the high risk of both acute pancreatitis and ASCVD, via lifestyle modifications and medical treatment. The duration of follow-up in the lipid clinic depends on the complexity of treatment and genetic results.

12.2.4. Insufficient LDL cholesterol reduction

Patients who do not achieve LDL cholesterol, non-HDL cholesterol, and/or apoB goals despite maximally tolerated lipid-lowering therapy should be referred to lipid clinics. Here, treatment like PCSK9 inhibitors may be initiated when patients meet the criteria according to national guidelines and reimbursement criteria.

12.2.5. Statin intolerance

Patients who demonstrate intolerance to multiple statins - or other first-line lipid-lowering agents - should be referred for advanced monitoring and management. Importantly, however, true statin intolerance is very rare [69]. Lipid clinic specialists can guide individualized strategies, including dose adjustment, trial of different statins, intermittent dosing, or non-statin alternatives.

12.2.6. Complex lipid profiles and hypolipidaemia

In case of diagnostic uncertainty, lipid clinics play a critical role in providing comprehensive diagnostic clarity and tailored therapeutic advice.

12.3. Frequency of follow-up

The initial follow-up is typically scheduled within 1–3 months, followed by routine assessments e.g. every 6–12 months. During periods of treatment optimization, follow-up may be conducted via telephone, virtual consultations, or written correspondence. For genetic counselling, face-to-face meetings are recommended to ensure accurate information delivery and to facilitate the initiation of cascade screening in biological family members.

Consultation duration may vary depending on individual requirements, including dietary and lifestyle support, psychological and social considerations, as well as overall cardiovascular risk and the presence of established ASCVD, acute pancreatitis, or other comorbidities.

Shared care involving both the general practitioner/family doctor and the lipid clinic is appropriate for long-term management (Fig. 9). For children up to 18 years of age, annual assessments in lipid clinics are recommended and the transition from pediatric care to adult care should be carefully managed and monitored.

The availability of specialist lipid clinics varies considerably across Europe and the rest of the world, necessitating that follow-up schedules align with both guideline recommendations and local contextual factors. More frequent follow-up is indicated for conditions such as severe

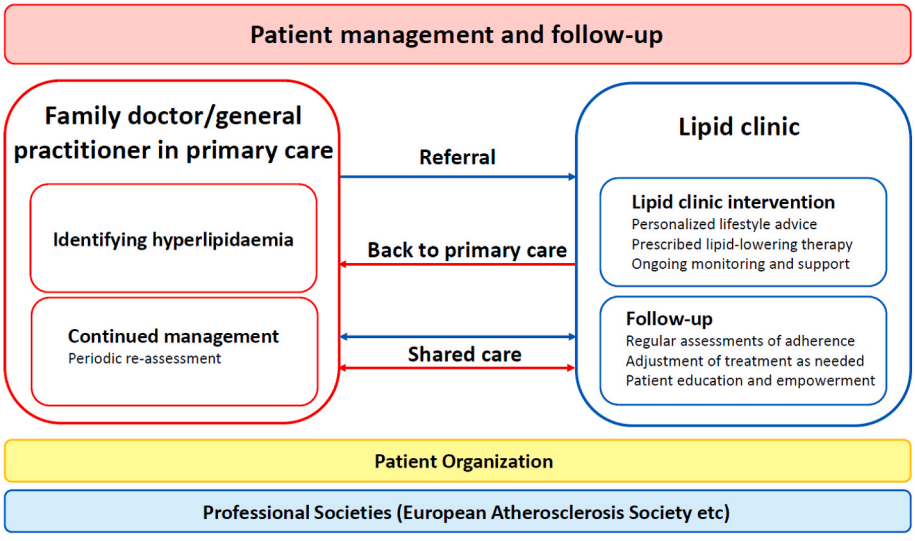

Fig. 9. Patient management and follow-up for severe lipid disorders should be shared between the general practitioner/family doctor in primary care and the lipid clinic.

hypertriglyceridaemia, homozygous FH, severe heterozygous FH, pregnancy, and treatment escalation.

12.4. The patient perspective

Effective management and follow-up in lipid clinics must be personalized, empathetic, and empowering [70]. Care should encompass not only clinical objectives but also the lived experiences of individuals navigating complex conditions such as FH [70,71].

Successfully managing the intricacies of genetic testing and treatment for patients with FH requires clear communication, access to reliable resources, and a comprehensive support structure [70,71]. This process often involves numerous questions, unfamiliar terminology, and decisions that impact both patients and their families.

Professional guidance from trusted healthcare providers, alongside clear and accurate information, and opportunities to connect with others facing similar challenges, significantly enhance patient confidence and understanding [71,72]. Furthermore, collaboration between lipid clinics and patient organizations fosters an environment in which patient perspectives are valued, and individual choices are respected, thereby promoting a collaborative and considerate approach throughout the patient's journey [73].

Patient-centered adaptations are essential, particularly for families affected by FH who require coordinated genetic testing. Barriers such as travel time and associated costs can negatively impact adherence; thus, enhancing clinic accessibility close to where patients live and offering flexible appointment hours are critical. Digital health tools, including appointment reminders, online scheduling platforms, and telemedicine, have been shown to improve follow-up attendance and clinical outcomes, with evidence supporting telemedicine as an effective means to optimize lipid control.

Importantly, the success of follow-up care depends not only on visit frequency but also on the quality of patient-provider interactions, allowing adequate time to address patient concerns and treatment considerations. Workforce shortages and limited clinic time present ongoing challenges; however, prioritizing patient engagement remains fundamental to delivering effective lipid management [74–79].

12.5. Adherence to dietary advice

The term adherence may carry unintended negative connotations for some patients, evoking a sense of surveillance or blame rather than collaboration. Recognizing this can help shift the focus from adherence and compliance to shared decision-making and individualized support [72].

Dietary modification remains a cornerstone of ASCVD prevention yet sustaining long-term changes is challenging. Standardized dietary leaflets are often insufficient; instead, patients require practical, culturally sensitive guidance tailored to individual preferences, family context, age, and gender [72,75].

Access to trained dietitians is particularly important in managing inherited conditions such as FH and familial chylomicronaemia syndrome, where early and sustained lifestyle interventions are essential. Effective counselling should not only provide recommendations but also explain the relevance of dietary changes in relation to genetic risk and pharmacological treatment.

Emerging evidence highlights gender differences in dietary adherence as women are more likely to adopt and maintain changes, while men report greater difficulty despite recognizing dietary importance. This suggests the need for differentiated strategies based on gender, age, and daily routines [80].

To be effective, dietary counselling must go beyond written materials. Integrating dietitians into lipid clinics (Fig. 6) and offering ongoing, adaptive support can improve adherence and align treatment with patients' real-life circumstances.

12.6. Adherence to other lifestyle advice

Lifestyle modification constitutes a fundamental element in the management of hyperlipidaemia, encompassing a heart-healthy diet, regular physical activity, weight optimization, smoking cessation, and moderation of alcohol consumption [3]. While clinical guidelines are well-established, the translation of these recommendations into sustainable daily behaviours remains challenging. Many patients experience feelings of guilt, shame, or discouragement when unable to achieve targets related to diet, exercise, or weight management, which can undermine self-efficacy and reduce engagement with healthcare.

These challenges are further compounded by limited time, energy, and competing responsibilities. For example, caregivers, particularly mothers, often prioritize familial obligations over their own health needs. Additionally, fatigue, demanding work schedules, and socioeconomic constraints act as significant barriers to lifestyle modification.

To address these issues, lipid clinics should integrate psychological and behavioural support within care pathways [11,81] when possible (Fig. 6). Counselling must be empathetic and non-judgmental, reframing lapses as opportunities for learning rather than failure. Practical, incremental strategies such as substituting butter with olive oil, incorporating brief walks into daily routines, or preparing simple, high-fibre meals can facilitate sustainable behavioural change. Engaging interventions, including cooking demonstrations, mobile applications, or group challenges, may further enhance patient motivation.

Group-based approaches offer additional benefits by reducing stigma and fostering mutual support. Peer support groups, family-involved sessions, or community-based programs can enhance accountability and promote culturally tailored strategies, which are particularly important in diverse populations.

Ultimately, lifestyle modification extends beyond a purely biomedical intervention, representing behavioural and psychosocial processes [81]. By combining evidence-based recommendations with personalized support and peer engagement, lipid clinics can improve adherence and optimize long-term cardiovascular outcomes.

12.7. Adherence or persistence to medication

Despite clear benefits of lipid-lowering therapy, adherence remains a major challenge. The SANTORINI study, a large European observational trial, found that only 27% of high- and very high-risk patients achieved LDL cholesterol defined by the 2019 ESC/EAS guidelines [3,81]. Poor adherence compromises individual outcomes and poses public health and economic burdens [81].

Factors contributing to non-adherence include perceived side effects, lack of immediate benefits, and insufficient understanding of cardiovascular risk [73,79]. Treatment regimens must also align with patient lifestyles, for example some patients prefer oral therapies over injectable PCSK9 inhibitors [74], or *vice versa*.

Shared decision-making is crucial to improve adherence by involving patients actively in treatment choices, thus respecting their preferences and concerns. This is especially important during the transition from paediatric to adult care, where adherence often declines. Addressing psychological factors, such as fear of side effects and the nocebo effect, through empathetic communication can further enhance adherence [72,73,81].

Providing information on emerging therapies and clinical trials may also motivate patients by fostering hope and engagement. Overall, improving adherence demands a multifaceted approach that integrates lifestyle alignment, patient involvement, psychological support, and education on future treatment options to optimize lipid management and reduce cardiovascular disease burden.

12.8. Understanding genetic test results

The genetic basis of FH and other inherited lipid disorders, as well as

the significance and potential benefits of genetic testing, may be difficult for patients to understand. Specialized lipid clinics should devote sufficient attention to both pre- and post-test genetic counselling provided either at the lipid clinic or in collaboration with dedicated genetic departments. Providing adequate time and space for discussion helps build trust and improves adherence to medical recommendations. Supplementary printed, digital, or audiovisual materials, as well as referral to patient advocacy groups, can be highly beneficial by enhancing patients' knowledge, supporting their understanding of the consequences of living with the condition, and offering them the opportunity to learn directly from others with the same disorder.

In the context of FH and other inherited lipid disorders, the patient should be informed about the genetic basis of the disease, the associated health risks, and the availability of genetic testing for at-risk relatives. In the era of advanced genetic testing, accurate interpretation of results is essential. Determining whether a detected variant is pathogenic, benign, or of uncertain significance, and establishing its causal relationship to the patient's clinical phenotype, are critical steps in the diagnostic process. This underscores the importance of close collaboration with the laboratory performing molecular analyses, the possible involvement of a clinical geneticist within the multidisciplinary team (Fig. 6), and clear communication with the patient to ensure appropriate understanding of the findings and their implications. Although genetic testing can refine diagnosis as well as clarify individual and familial risk, the clinical phenotype remains central in guiding management decisions. Even in the absence of a confirmed pathogenic variant, clinical findings are decisive for establishing the diagnosis and determining treatment.

Finally, patients need to understand the potential implications for their offspring and receive guidance on family planning, ideally as part of a comprehensive genetic counselling process. Patients should be clearly informed about reproductive risks and supported with empathy and compassion throughout the decision-making process, prenatal planning and during pregnancy.

The proposed recommendations on patient management and follow-up are based on expert opinions, partly guided by successful local implementation in several European countries and through experience in European patient organizations.

13. Research

Research conducted alongside educational activities plays a pivotal role in advancing the understanding, diagnosis and management of lipid disorders. Research should be prioritized in most lipid clinics, and medical time should be dedicated to clinical and translational research particularly in tier 3 and 4 lipid clinics (Fig. 5), which may benefit from coordination at a national level. Furthermore, scientific staff including nurses and sub-investigators are needed to take part in clinical trials investigating new pharmaceutical drugs in lipid clinics. Patient registration in registries for rare lipid disorders must also be prioritized. Integrating research into clinical practice fosters continuous improvement through education and may contribute to the effort to reduce ASCVD and other lipid-related disorders in patients with hyperlipidaemia. The development of new treatments like PCSK9 inhibitors, apo C3 inhibitors, and ANGPTL3 inhibitors have been made possible by translational research on rare lipid disorders in lipid clinics.

14. Education

Continuous education for staff at lipid clinics, other healthcare professionals and patients is essential for achieving optimal patient care. Here, we aim to propose standards for education in lipid clinics and to outline how the EAS, other international organizations, and national or local initiatives can contribute to achieve these standards (Fig. 10). Lipid clinics are encouraged to engage in a strong educational network with healthcare professionals managing patients with hyperlipidaemia. Regular participation in organized continuing education or self-directed learning, such as reading scientific journals on cardiovascular disease prevention and clinical lipidology, represent valuable ways to stay informed about recent developments. Finally, we outline how patient education can be improved ideally involving patient organizations and caregivers.

14.1. Educational standards of lipid clinics

To ensure the best care for patients with lipid disorders, lipid clinics should foster a supportive and educational environment for their staff. A lipid clinic team typically includes several healthcare professional groups, such as nurses, physicians, genetic field workers, dietitians, physical activity specialists and administrative staff, each bringing their own expertise in treating and caring for patients. Educational programs should bring all these professional groups together to promote effective teamwork, potentially in collaboration with patient organizations. Several approaches can be implemented at local, national, and international levels within each lipid clinic.

14.2. Local educational initiatives

- Organize regular meetings, e.g. monthly or every two months, at which staff can receive updates on new research, treatment guidelines, and share practical clinical experiences
- Organize regular case discussions focusing on interesting or challenging patient cases. These discussions help develop clinical judgment, strengthen team collaboration, and facilitate shared learning among staff
- Provide mentorship programmes in which experienced colleagues support and guide those who are less experienced, which can help build confidence and ensure that everyone feels well prepared to manage the varying treatment needs of patients referred to the lipid clinic
- Organize journal clubs, where staff collectively read and discuss current scientific literature. This helps keep everyone updated on the latest research results while promoting a culture of continuous professional development

14.3. National educational initiatives

Participation in national meetings can be beneficial for several reasons as listed here:

- Sharing the latest research results and clinical guidelines
- Creating a national clinical network that can be utilized for example in situations involving cascade screening of families living in different parts of the country
- Fostering the development of common guidelines and patient material, ideally in collaboration with patients or patient organizations

Moreover, the national community of lipid clinics can also be leveraged to support research projects.

14.4. International educational initiatives

Finally, participation in international cardiovascular prevention and lipid meetings and workshops can strengthen knowledge and community worldwide. For rare lipid disorders, sharing experiences and knowledge with international colleagues can be particularly beneficial and enable the establishment of larger research communities.

International organizations such as EAS offer many valuable resources that lipid clinics can use for support, for example:

- Webinars at national (in local or regional language) and international levels make it easy to access expert knowledge and stay updated without traveling. Examples include EAS webinars by

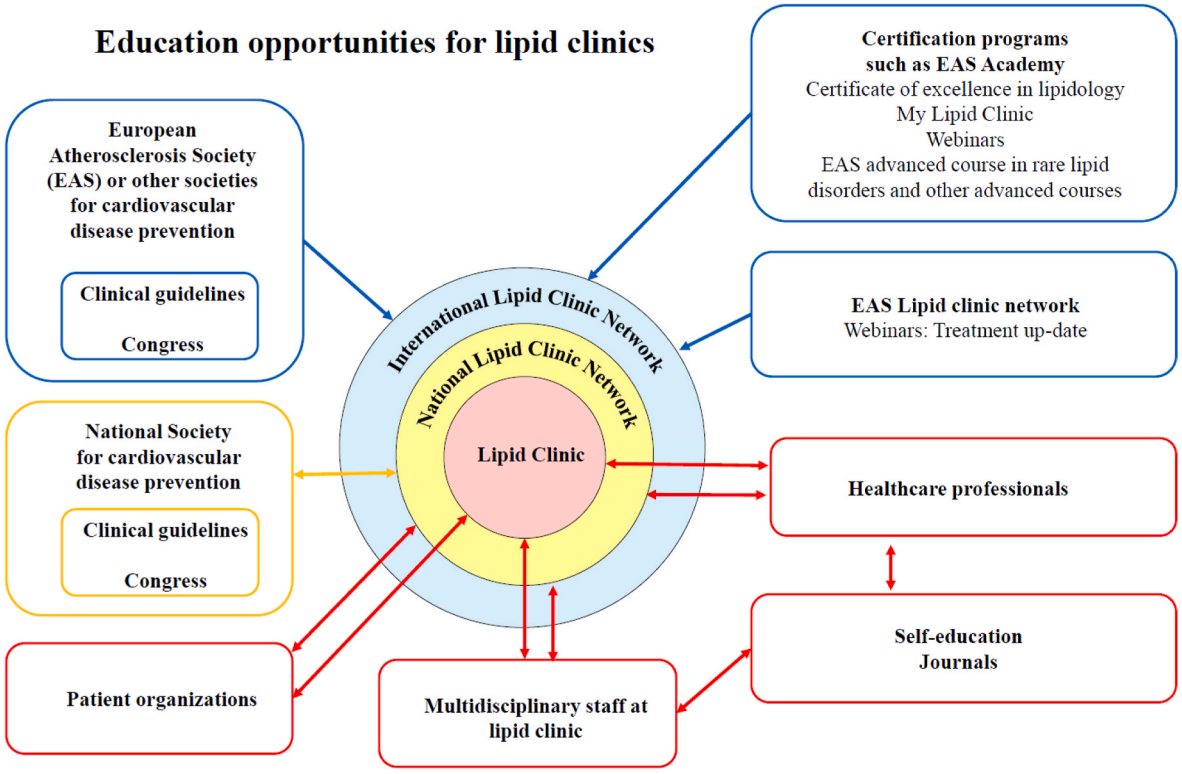

Fig. 10. Education of staff, patients and caregivers at lipid clinics can be achieved through multiple avenues.

country in local language, EAS webinars in English for all, EAS practical clinical cases in "My lipid clinic" (see https://eas-society.org/education/)

- Certification programs through the EAS portal provide opportunities for formal education and documented expertise in lipidology. Examples include the EAS Certificate of Excellence for Clinicians and the EAS Certificate in Lipidology for Health Care Professionals (see https://eas-society.org/education/)
- Support for attending courses and congresses, which provide opportunities to meet other professionals, learn about new research, and find inspiration for clinical practice. Most of the talks presented at the EAS congress are available on the EAS academy website, like EAS Course on Rare Dyslipidaemias and EAS congresses (see https://eas-society.org/academy/)

14.5. Educational network with health care professionals organized by local lipid clinics

Lipid clinics should provide courses and continuing medical education targeted at general practitioners/family doctors, paediatricians, endocrinologists, cardiologists, nurses, dietitians and other relevant specialists in their region or in the whole country jointly with relevant national societies. Here are some examples of educational initiatives that can be very effective:

- The establishment of a dedicated hotline to consult a medical doctor from the lipid clinic regarding any clinical uncertainties
- Regular interdisciplinary meetings with healthcare professionals who refer and manage patients with hyperlipidaemia to foster strong cooperation and improve patient outcomes
- Organizing training sessions on lipidology, treatment guidelines, and referral criteria

The proposed recommendations on education are based on expert opinions, partly guided by successful local implementation in several European countries, through experience in European patient organizations, and through many years of experience within the EAS Lipid Clinic Network educational portfolio.

15. Patient organizations

Patient organizations and ambassador programmes provide vital peer support, advocacy, and education, enabling patients to learn from the lived experiences of others who have encountered similar challenges [82]. Personal narratives are particularly valuable for individuals who may feel apprehensive about treatment or seek to understand the real-world implications of therapy beyond the clinical perspective. Clinics should actively collaborate with patient organizations to enhance patient engagement and extend support beyond conventional clinical settings. The EAS Lipid Clinic Network facilitates collaboration between clinics and patient groups (e.g. FH Europe) to standardize care and amplify patient voices across Europe and elsewhere. Similarly, the European Patients' Forum underscores the critical role of patient organizations in shaping health policy and delivering peer-led guidance, supporting patients in navigating both the practical and psychosocial dimensions of care.

16. Monitoring quality

The quality of the management carried out in lipid clinics on patients with inherited hyperlipidaemias should ideally be monitored continuously for all individuals and for all lipid clinics individually, but also on a national level to identify areas in need of improvement (Fig. 11).

Quality assessment systems can be performed within individual lipid clinics (Fig. 11 top left (A)) or advanced approaches on a national level (Fig. 11 right (B)) and should include indicators of quality that can be used for comparison over time (Fig. 11 bottom left (C)). Important indicators of quality may include indicators of detection and diagnostics, efficacy of cascade screening, initiation and adherence of lipid-lowering therapy, and achievement of lipid target goals. Defining quality

indicators should be done by specialists in collaboration with patient representatives and data collection must comply with national regulations.

Monitoring of quality indicators in lipid clinics should be collected and evaluated according to specified criteria on a national level by a committee including patient representatives and lipid specialists that may provide the local lipid clinics with recommendations for improvement. Key performance indicators for patients with inherited hyperlipidaemia may include the number of patients diagnosed, percentage genetically tested, percentage lipoprotein(a) tested, percentage of first-degree relatives offered diagnostic evaluation, percentage receiving lipid-lowering therapies and the percentage achieving their LDL cholesterol target goal [83].

To ensure implementation, national recommendations to improve management should be forwarded to the hospital managers responsible for the lipid clinics for prioritization of action plans to improve the management.

From a patient's perspective, transparency of data collection is of major importance. Also, individual monitoring is important so patients can be active participants in their own care.

The above recommendations on monitoring quality of lipid clinics nationwide are based on practical experience in Denmark since initiation of the a nationwide quality control database for familial hypercholesterolemia in 2020 [83]. The proposed recommendations on local quality monitoring in individual lipid clinics are based on expert opinions, guided by successful local implementation in several European countries.

17. Lipid clinics funding

To achieve sufficient prevention of ASCVD, acute pancreatitis and other lipid-related diseases at national or regional levels, centralized funding of lipid clinics is of paramount importance. Otherwise, optimal prevention will only occur if single enthusiastic medical specialists happen to be employed at a given centre. Here we delineate the ideal funding framework for tier 1-4 lipid clinics in each country or region (Fig. 12), essential for securing long-term reduction in ASCVD, acute pancreatitis and other lipid-related diseases. That said, the strategy may vary by country's health services structure and complexity. Investment in lipid clinics should be viewed as a cost-effective strategy in the medium and long term.

17.1. Budget

Minimal budget to run well-functioning tier 1-4 lipid clinic (see Figs. 4 and 6) will entail the expenses as shown in Fig. 12. Tier 1-4 lipid clinics can be open from 1 to 5 days weekly, depending on the number of patients referred. Time allowed for duration of consultations for newly referred patients should be 45-60 min and for revisits 30 min.

17.2. Who funds lipid clinics?

Lipid clinics funding must be an integral part of any health care system, as lipid clinics represent an important part of health care and, thus, need to be included in the standards of care. National funding through government, complemented with local funding through regional governments, universities, and/or municipalities, all represent possible models.

Organization of lipid clinics will always be country/region specific and needs to reflect the general structure of the health care systems already in place. Therefore, providing a universal organizational scheme is difficult; however, above we describe essentials that can be taken as the basic principles of lipid clinic funding, elements that already have proven effective in several systems throughout Europe and elsewhere.

The proposed recommendations on budget for lipid clinic funding are based on expert opinions, guided by successful local implementation in several European countries.

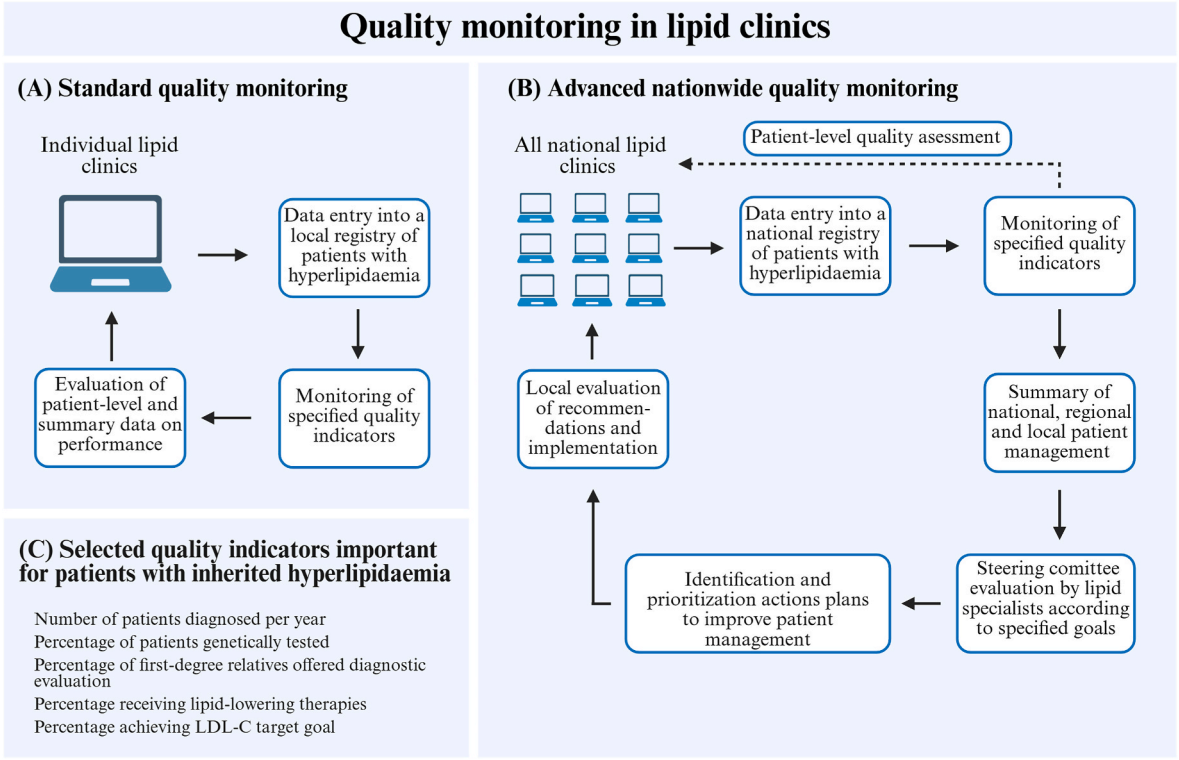

Fig. 11. Standard and advanced approaches for quality monitoring of lipid clinics. LDL-C = low-density lipoprotein cholesterol.

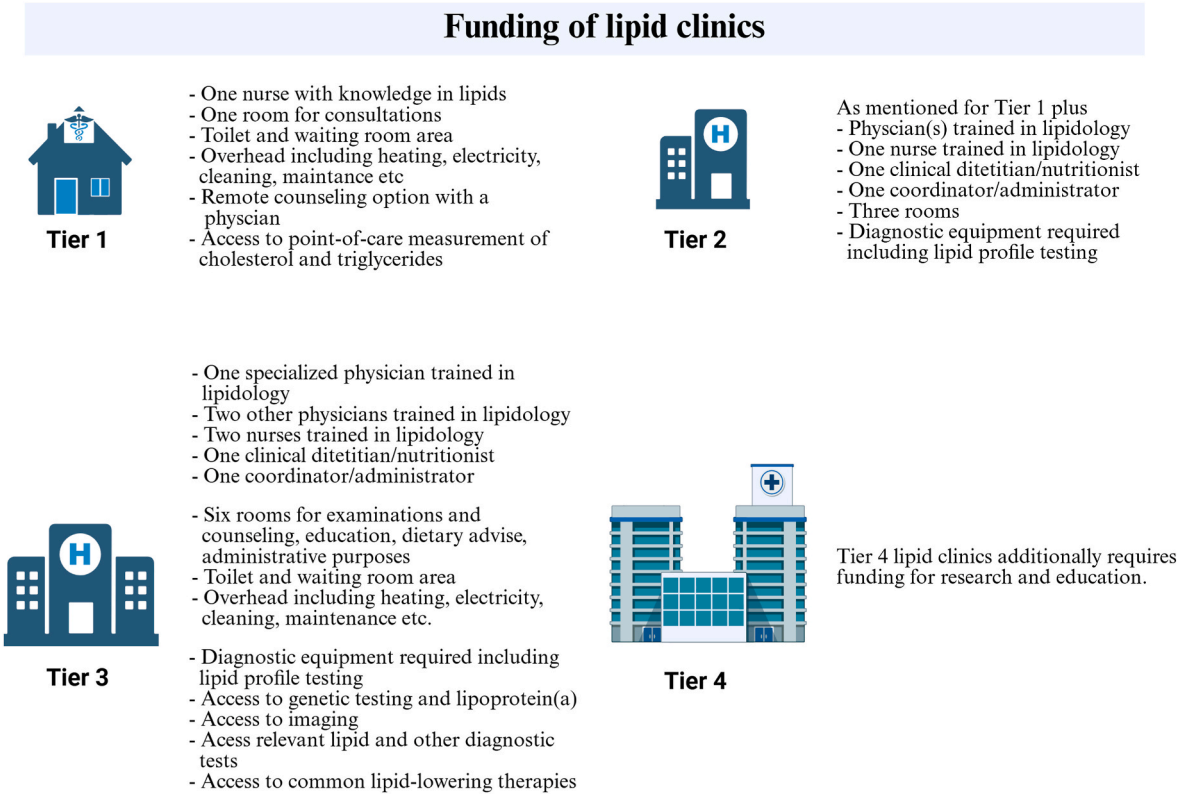

Fig. 12. A realistic scheme for lipid clinic tier 1-4 minimal requirements for funding and organization on a national or regional level.

18. Conclusion

The present EAS consensus paper provides guidance on how to harmonize and organize lipid clinics worldwide, with the long-term aim of preventing atherosclerotic cardiovascular disease, acute pancreatitis and other lipid-related diseases in individual countries. Lipid clinics are not cost drivers but a cost-containing infrastructure for ASCVD prevention. The main unmet need globally is no longer the development of additional guidelines, but rather the implementation of harmonized lipid clinic structures that allow existing guidelines to be effectively applied in clinical practice.

Following publication, a next phase will be to implement the advice given in different countries in Europe and in the rest of the world. The European Atherosclerosis Society will work in the future to secure such implementation. This will include international and national webinars in local language in all countries belonging the EAS Lipid Clinic Network, to disseminate the information given in this consensus paper.

In addition, EAS plans preceptorship courses in selected countries in Europe and beyond, designed to train key opinion leaders involved in running lipid clinics. These courses will focus on strengthening clinical practice and supporting the improvement and harmonization of lipid clinics within individual countries. Preceptorship courses include teaching delivered by physicians and other health care professionals from well-established lipid clinics, alongside structured visits to these lipid clinics and laboratories that provide lipid tests and other diagnostic modalities essential to lipid clinic practice.

Key performance indicators and quality assurance metrics for the success of such teaching initiatives will include increase in number of lipid clinics in individual countries over a five-to-ten-year period. In addition, yearly monitoring in lipid clinics should include number of patients diagnosed, percentage genetically tested, percentage with lipoprotein(a) testing, percentage of first-degree relatives offered diagnostic evaluation, percentage receiving lipid-lowering therapies and the percentage achieving their LDL cholesterol target goal. Such quality assurance metrics has successfully been used nationwide in Denmark since 2020.

Author contributions

EAS Consensus Panel members were nominated by EAS and the Co-chairs Børge G Nordestgaard and Christian Bork, to represent expertise across the EAS Lipid Clinic Network from around the World. The Panel met once in Copenhagen, organised and chaired by Christian Bork and Børge G Nordestgaard. This 2-day meeting critically reviewed the literature, current clinical practice, and a draft manuscript prepared by writing group members prior to the meeting. Following the meeting, a revised manuscript was first circulated for further comments by writing group members and the EAS Executive Committee. Finally, the 2nd revised manuscript was circulated to all national leads of the EAS Lipid Clinic Network for additional comments for further revision of the draft manuscript. All authors agreed to conception and design, contributed to interpretation of available data and clinical practice, agreed to the guidance on how best to harmonize, optimally organize and fund lipid clinics worldwide, all suggested revisions for this consensus document, and all members approved the document before submission.

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Nomenclature

Because hyperlipidaemias due to high levels of (LDL) cholesterol, remnant cholesterol, triglycerides, and lipoprotein(a) are found in most patients referred to lipid clinics, we use the term "hyperlipidaemia" throughout this paper. However, where relevant we directly mention hypolipidaemias and other rare lipid disorders. In contrast, unless we refer to publications using the word "dyslipidaemia" in the title like the EAS/ESC dyslipidaemia guidelines [3,4], we do not use this word. This is because "dyslipidaemia" may be viewed as a historical misnomer from the time when low high-density lipoprotein (HDL) cholesterol was thought to be a direct causal factor for ASCVD, which is no longer supported by current evidence [5].

Declaration of competing interest

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