

WORLD HEART FEDERATION ROADMAP FOR CHOLESTEROL – UPDATE

**Informing health systems approaches to CVD by
prioritizing practical, proven, cost-effective action**



Atherosclerosis is a silent condition, that develops throughout life until it presents suddenly, often with fatal consequences. Despite major advances in our understanding of its causes, its consequences and the development of new preventive therapies, atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of death globally.

The underlying process is well understood, namely cholesterol deposition in walls of blood vessels over time. This update to the World Heart Federation (WHF) Cholesterol Road Map sets out a framework for policymakers, and healthcare professionals to address healthcare systems barriers and implement solutions to prevent undesirable exposure to cholesterol throughout the life-course. Here we move from viewing high cholesterol not as the problem but lowering cholesterol throughout life with different approaches as the solution. This includes screening for genetic causes of elevated cholesterol disorders like familial hypercholesterolaemia and high lipoprotein (a) in the first 20 years of life, a focus on primordial prevention and greater use of combination therapies for those with more advanced atherosclerosis diagnosed later in the life-course. This Roadmap moves from looking at high cholesterol as the problem, to viewing lowering cholesterol as the solution to reduce ASCVD.

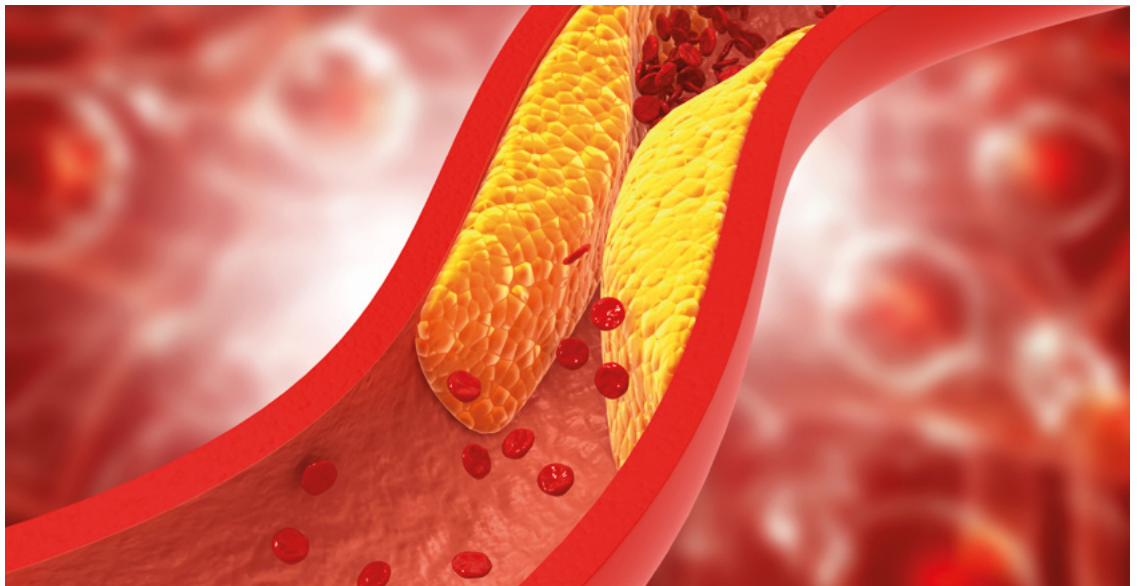
ABOUT CHOLESTEROL

High cholesterol is a risk factor for serious health conditions. If left untreated, it can lead to atherosclerosis, which results from the retention of apolipoprotein B (apoB) containing lipoproteins, mostly in the form of low-density lipoproteins (LDL), in the vessel wall. LDL cholesterol (LDL-C) is not only causal but a cumulative risk factor, over the lifespan, for ASCVD. This, in turn, may lead to heart disease, stroke, and other vascular diseases,¹ which remain major causes of premature death, disability and healthcare expenditure globally.

Preventing the accumulation of cholesterol-containing atherogenic lipoproteins in the vessel wall is therefore central to any healthcare strategy

to prevent ASCVD. Often, individuals have inherited vulnerability to much lower levels of cholesterol, or have additional risk factors which increase the retention/deposition of cholesterol containing particles. These people develop heart disease with only modest elevations of cholesterol.

Advances in current concepts about reducing cumulative exposure to apoB cholesterol-containing lipoproteins and the emergence of novel therapies provide new considerations for how cholesterol lowering strategies can be implemented across the life-course.



INADEQUATELY CONTROLLED CHOLESTEROL AS A RISK FACTOR

MAGNITUDE OF THE PROBLEM

Globally, raised total cholesterol (≥ 5.0 mmol/L) affects **approximately 39% of adults**². In 2019, high non-HDL cholesterol caused an **estimated 4.4 million deaths**³. Even though the death toll has decreased in high-income western countries over the past decades, it has more than doubled in southeast Asia and even tripled in east Asia. This demonstrates a global shift of the disease burden from high-income countries in north western Europe, North America, and Australasia to middle-income countries in east and southeast Asia, as well as some countries in Oceania and central Latin America.⁴ Moreover many people

living with established cardiovascular disease have cholesterol levels inadequately controlled for their level of risk with only **20%** or fewer achieving recommended cholesterol targets.

Familial hypercholesterolemia (FH), a genetic disorder found in people of all races and ethnicities, affects approximately **28 million** people worldwide, i.e., one in 311 people (5). FH remains mostly underdiagnosed and undertreated due to low awareness – only **5-10%** of those affected know about their condition and less than **3%** are adequately treated.

Estimated
4.4 MILLION
Deaths caused by
High non-HDL cholesterol
2019

Globally, raised total cholesterol (≥ 5.0 mmol/L) affects approximately
39%
OF ADULTS²



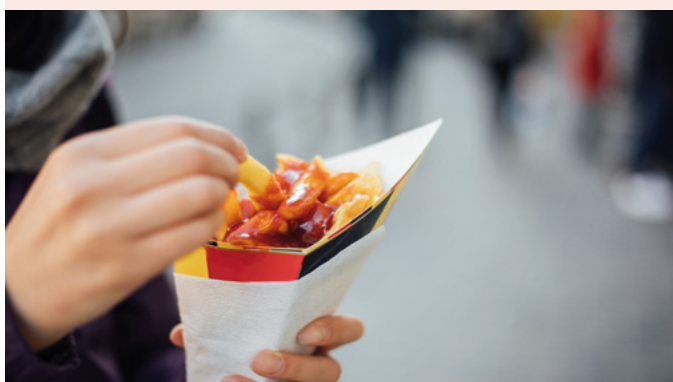
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EFFECTIVE PREVENTION AND DETECTION PRACTICES:

- Change the environment that promotes risk factor development as early as possible to avoid the development of risk factors (Primordial Prevention).
- Roll out population-wide interventions, such as promoting physical activity and access to healthy food, tobacco bans etc.
- Implement large scale screening for elevated cholesterol including FH and Lp(a) in early life (before the age of 18 and ideally in the first decade of life).

EFFECTIVE MANAGEMENT PRACTICES:

- Focus on lifetime risk estimation rather than 10-year risk only to guide therapy.
- Prevent ASCVD events by reducing cumulative exposure to LDL-C, the main cause of atherosclerosis. This can be achieved by maintaining modest long-term reductions in LDL-C beginning earlier in life with diet or through a combination of diet and potent generic LDL-C lowering therapies such as high-intensity statins or combinations of statins plus ezetimibe.
- Prescribe non-pharmacological interventions (weight management, diet, in particular plant-based foods, no smoking, physical activity, moderation in alcohol intake).
- Prescribe pharmacological interventions according to the most recent guidelines, meaning affordable novel therapies for those with genetic causes of high cholesterol or very high-risk requiring combinations of multiple therapies.



FIGURES SURVEY

38
COUNTRIES

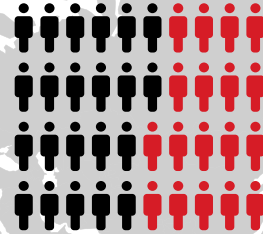


122
RESPONSES

responses from cardiologists, lipid specialists, endocrinologists, nurses, nutritionists, researchers, and health advocates

+370
RESPONSES

from a parallel survey in China



4

Globally,

93.3%

of the respondents report initiating lipid lowering therapy based on ASCVD risk irrespective of the conditions leading to increased ASCVD risk. (About 1 in 10 initiated treatment based only on cholesterol level)



Globally, around

1 IN 4

respondents were uncomfortable with prescribing high potency statins. In LMICs, this figure reaches 60%.



In LICs,

50%

of respondents report that high intensity statins can be freely prescribed.



Only

1 IN 5

respondents report that at least 75% of their patients achieve LDL-C control.



Only

1 IN 4

reports that ezetimibe, fixed dose combinations of statins/ezetimibe and PCSK9 inhibitors can be freely prescribed.



39%

report that less than half of their patients achieve cholesterol control.



ROADBLOCKS IDENTIFIED IN THE SURVEY INCLUDED

- Lack of awareness of Familial Hypercholesterolemia (FH) and FH risk factors among physicians and the general population
- Lack of or suboptimal screening programmes
- Low physician capacity for diagnosing and managing statin treatment among FH patients
- Environmental barriers to lifestyle modification (e.g., food insecurity, few options for physical activity, tobacco marketing)
- Shortage of facilities for large-scale measurement of blood cholesterol levels, especially in rural areas
- Lack of awareness among patients regarding importance of adherence to statin treatment
- Low access to health facilities among poor or remote populations
- Infrequent access to follow-up or support for treatment adherence
- Undue patient fear of side effects of statin treatment
- Lack of awareness among physicians about the importance of CVD risk screening and prevention
- Lack of physician education/training regarding treatment
- Poor physician capacity for monitoring treatment, especially with competing disease priorities
- Multiple, complex (and sometimes contradictory) clinical guidelines
- Statins unaffordable for patients.



FIGURE 1: ACTIONABLE SOLUTIONS TO ADDRESS CHOLESTEROL CONTROL TO REDUCE ASCVD HAVE BEEN IDENTIFIED IN 5 FOCUS AREAS:

A series of actionable solutions to preventing ASCVD events through addressing cholesterol exposure were identified in the Roadmap as highlighted in Figure 1.

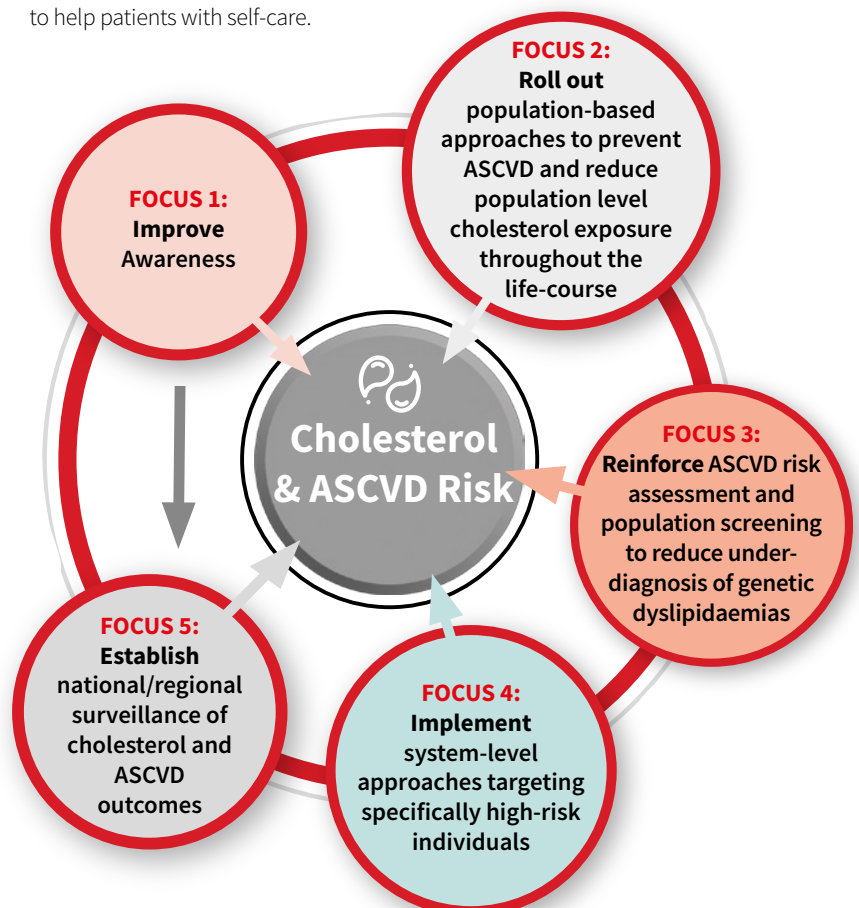
Focus area 1 refers to improving awareness by conducting awareness and education campaigns to ensure that health professionals are aware of the continuous graded association between cholesterol blood levels and ASCVD risk. Better awareness can also be achieved by patients and general populations by promoting advocacy through greater interaction between patient organisations with healthcare professionals and policy makers as well as implementing a more inclusive approach in guidelines development, partnering in advocacy and policy influencing, clinical trials design and involvement in regulatory and the technical assessment process.

Focus 2 aims to deliver population-based approaches to prevent ASCVD such as food reformulation efforts and implementation of the WHO Framework Convention on Tobacco Control (FCTC).

Focus 3 outlines the importance of ASCVD risk assessment and population screening to reduce under-diagnosis of genetic dyslipidaemias. These include simplified locally-adapted guidelines on screening for ASCVD risk based on a total risk approach for general population and Screening for FH and Lp(a).

System-level approaches targeting specifically high-risk individuals (**focus 4**) refers to access and affordability of essential cholesterol lipid lowering medicines (statin and non-statin therapies).

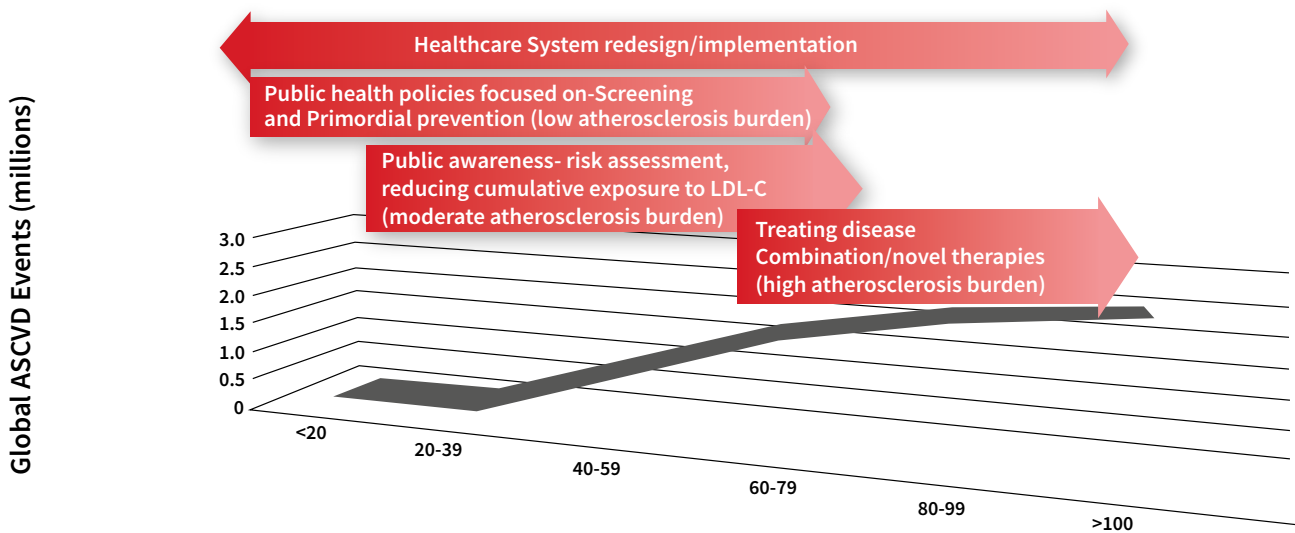
Lastly, **focus 5** defines the need for national/regional surveillance of cholesterol and ASCVD outcomes to monitor whether patients take recommended medications to reduce cholesterol and control other risk factors. This could be in the use of apps and internet-based resources linking patients, pharmacies, and health care professionals or creating health care practitioner monitoring groups (pharmacists; nurses) to help patients with self-care.



Understanding the importance of cumulative exposure to atherogenic lipoproteins and atherosclerosis allows the global community to redesign healthcare systems with different approaches across the life-course, which if implemented across the next decade could significantly reduce long-term healthcare costs through better preventing ASCVD.

Panel A

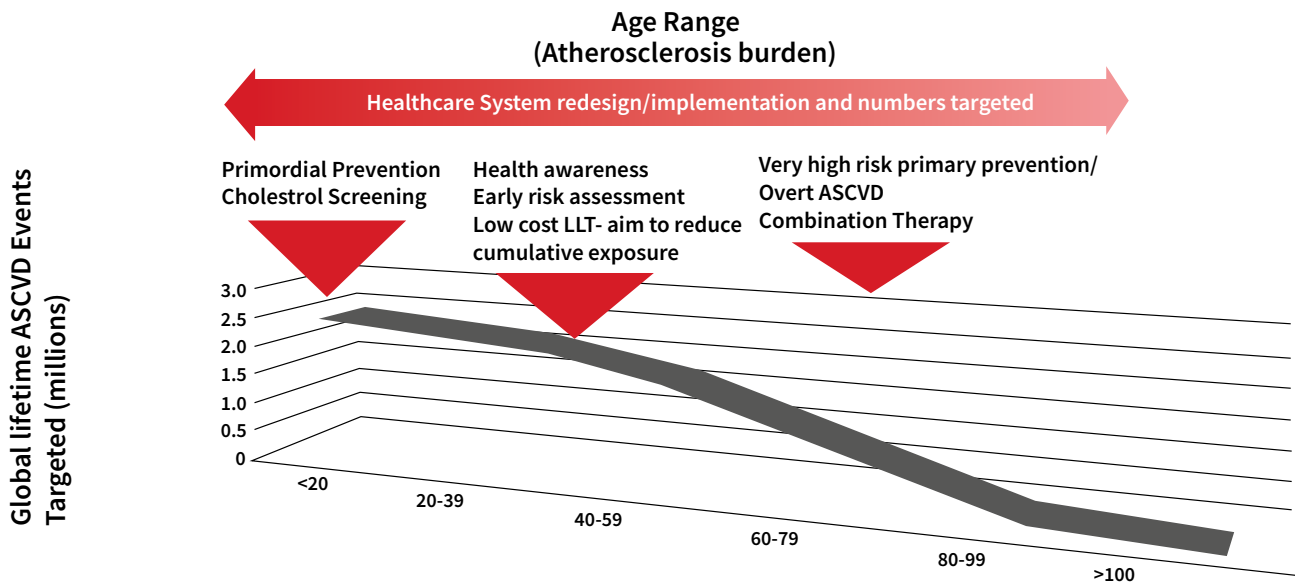
Life-course approach to reducing the ASCVD burden



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Panel B

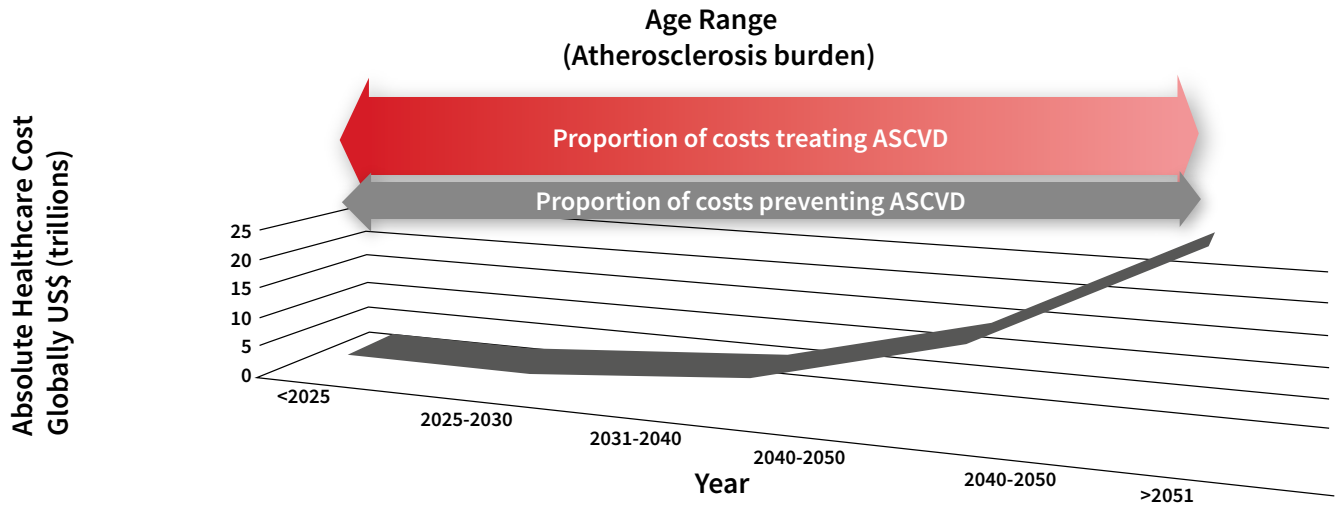
Age adapted interventions to reducing ASCVD burden



Panel B – In 2020 there were 2.6 billion people <20 years of age (33.2%), 2.3 billion people 20-39 years of age (29.9%), 1.8 billion people 40-59 years of age (23.1%), 918 million people 60-79 years of age (11.8%), 147 million people 80-99 years of age (1.9%) and 0.6 million people 100 years of age or older (0.001%).

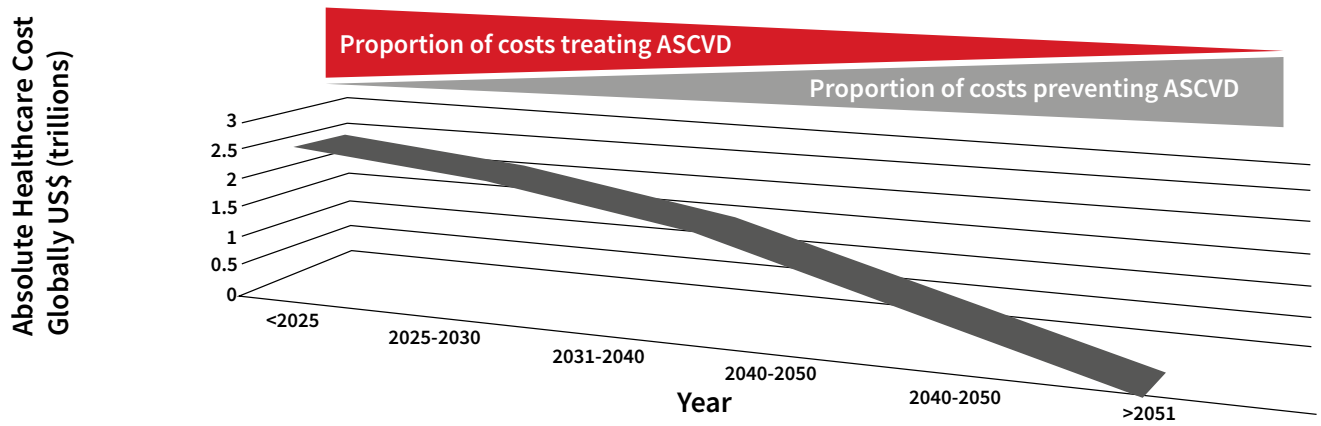
Panel C

Current trajectory of healthcare costs related to ASCVD (escalating overall costs)

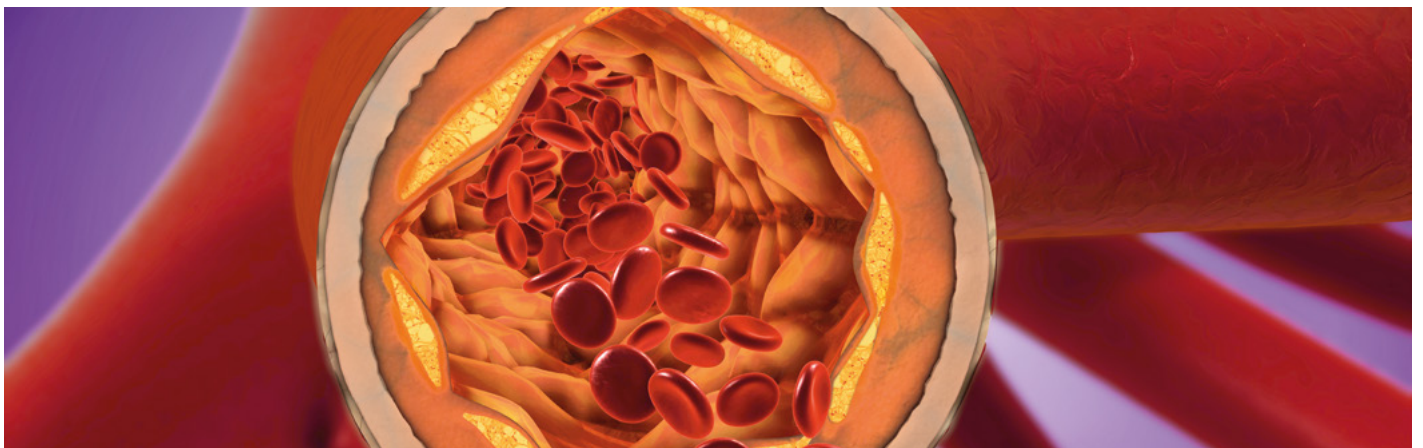


Panel D

Potential future trajectory of healthcare costs related to ASCVD (decrease in overall costs)



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RECOMMENDATIONS FOR POPULATION STRATEGIES, TESTS AND THERAPIES WHICH SHOULD BE AVAILABLE GLOBALLY TO MANAGE LIPIDS AND ASCVD RISK

The table below provides guidance on the essential medications, testing and other approaches that should be implemented in low, middle income countries and high-income countries. This includes policies that are guided through real time data, that are holistic in nature and that build healthcare systems with a focus on preserving health and not just treating disease throughout the human life-course.

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Recommended strategy	LIC	MIC	HIC	Recommended strategy	LIC	MIC	HIC
Awareness and population strategies (e.g. awareness and education campaigns, food labelling/regulation, tobacco legislation, taxation policies on unhealthy commodities)	Y	Y	Y	<i>Statin intolerant patients</i> Ezetimibe Bempedoic acid/ bempedoic acid plus ezetimibe	Y	Y Y	Y Y
Risk assessment and population screening • Population strategy (e.g. all before 10/ reverse cascade) • Individual Lipids (TC, HDL-C, LDL-C, TG, non-HDL-C) • Lp(a) • apoB • Imaging for risk stratification	Y Y	Y Y Y Y Y	Y Y Y Y Y	<i>ASCVD or HeFH</i> PCSK9 Mab Inclisiran		(Based on LDL-C level and/or risk) Y Y	(Based on LDL-C level and/or risk) Y Y
Reshaping Healthcare Systems e.g. Digital Solutions for data generation to inform policy, disease management, decision support tools	Y	Y	Y	<i>Y HoFH-</i> Apheresis Lomitapide Evinacumab	Y Y Y	Y Y Y	Y Y Y
Access to therapies <i>General (primary or secondary prevention including Heterozygous FH (HeFH) and Homozygous FH (HoFH), access through availability and affordability of statins, inclusion of statins into essential medicine packages, inclusion of non-statin therapies, including Low-level laser therapies (LLT).</i>				<i>Icosapent ethyl ester</i>		Y	Y
Generic high-intensity statins (essential medication)	Y	Y	Y	<i>Fibrates</i> (as TG lowering therapies for prevention of pancreatitis)	Y	Y	Y
Generic statin-ezetimibe combination	Y	Y	Y	National/regional surveillance of cholesterol and ASCVD outcomes <i>e.g. monitor patients' medications, attainment of cholesterol goals, stock outages for essential medicines such as statins, collect epidemiological data to provide data driven policies</i>	Y	Y	Y

*These recommendations may not be optimal for implementation in resource-limited LMICs because these countries are unlikely to be able to afford some of the expensive therapies required to achieve very low LDL-C targets. A more effective strategy for LMICs may be to proactively prevent ASCVD events by reducing cumulative exposure to LDL-C, the main cause of atherosclerosis. Lifetime cumulative exposure to LDL-C can be reduced by maintaining modest long-term reductions in LDL-C beginning earlier in life with diet or the combination of diet and low-dose generic LDL-C lowering therapies.

** In LIC industry and governments should reach agreement on significantly discounted costs so that those with inherited lipid disorders are not disenfranchised.

TAKING ACTION

ADAPTING THE CHOLESTEROL ROADMAP TO LOCAL NEEDS ACROSS THE WORLD

A global framework for regional and national action, WHF Roadmaps can be used to convene country-specific Roundtables through WHF and our Members. They allow relevant stakeholders to come together to identify obstacles and potential solutions that are relevant to their settings and produce national plans. Since the original WHF Cholesterol Roadmap was published in 2017, Roundtables have been organised in **10** countries across **5** continents. WHF will continue to convene Cholesterol Roundtables to implement this updated Roadmap

CONCRETE EXAMPLES

A National Roundtable in 2017 in **Colombia** with the Colombian Society of Cardiology and Cardiovascular Surgery, WHF, and the Ministry of Health, Academy and Civil Society resulted in the adoption of the “Colombian Manifesto Against Heart Attacks”, with the ambition to achieve 7000 fewer heart attacks per year in the country by 2025. One of the three priorities included in the Manifesto consists in priority implementation of cholesterol clinical guidelines in all healthcare settings in the country.

2018 / 2021
Mexico (Mexican Society of Cardiology)

2017
Colombia (Colombia Society of Cardiology) and Cardiovascular Surgery)

2017
Brazil (Sao Paulo Society of Cardiology)

In **Belgium**, a National Stakeholder Roundtable was convened in December 2021. Agreed action points include working closely with FH Europe in order to join forces with other EU countries and implement FH screening nationwide.

2021 Belgium (Belgium Heart League)

2017 Spain (Spanish Heart Foundation)

2021 Slovenia (Slovenian Heart Foundation)

2017 Saudi Arabia (Saudi Heart Association)

2021 Russia (Russian Society of Cardiology)

2018 Philippines (Philippine Heart Association)

In the **Philippines**, a National Roundtable organised in 2018 resulted in a plan of action on cholesterol. Priority solutions were strengthening collaborations for patient screening, reinforcing continuing medical education activities, improving access to health facilities among poor or remote populations and updating national dyslipidaemia guidelines.

2022 Australia (Heart Foundation of Australia)

“ National Roundtables, with the participation of scientific societies, foundations, health authorities, policymakers, NGOs, and other institutions, and with the support of WHF, are a fundamental step for the implementation of the health policy changes required to advance in the control of cholesterol in country population. During the Roundtable, the information provided by the Roadmap, together with local information about the magnitude and distribution of the cholesterol control gap, and specific national roadblocks, leads to select the appropriate strategies to overcome barriers and define national policies and goals.

PROFESSOR FERNANDO LANAS
WHF Roadmaps Liaison Officer

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“ As a global community, the destination we want to reach is to reduce the number of deaths from atherosclerotic cardiovascular diseases, the human suffering, societal and fiscal costs. To reach the destination we need to understand the journey which is lifelong accumulation of cholesterol in the walls of our blood vessels. Knowing this the present WHF Cholesterol Roadmap provides pragmatic, scalable solutions, with different solutions for different stages of the life-course which can be applied globally, with the aim of using lifetime cholesterol lowering approach as a tool to reduce the population burden of atherosclerotic cardiovascular disease.

PROFESSOR KAUSIK K RAY

Professor of Public Health Imperial College London, co-chair WHF Cholesterol Roadmap

“ Atherosclerosis is a leading cause of death in the world and blood cholesterol has a pivotal role on its development, the evidence of LDL-C lowering for prevention of cardiovascular disease is one of the more robust available in medicine. Good risk evaluation and early intervention may change the face of disease for good. Now we have potent and inexpensive therapies that if applied adequately will have robust impact on atherosclerosis. The document has identified roadblocks and possible solutions to implement adequate therapies for those at risk. These solutions need to be customized to different models of care and implementation will be essential to success.

PROFESSOR RAUL D. SANTOS

University of Sao Paulo and Hospital Israelita Albert Einstein, co-chair WHF Cholesterol Roadmap



“ Cardiovascular disease continues to be the leading cause of death in the world. Cholesterol, for decades, has been one of the least appreciated and publicly recognized causes of CVD. The WHF Cholesterol Roadmap is a timely and desperately needed public health tool, which has the power to guide global health policies and actions. The implementation of this document will help improve lives of many patients and save lives of many people who have not yet been diagnosed. But the ultimate goal we should aim for is to move from cardiovascular disease towards cardiovascular population health.

MAGDALENA DACCORD

Chief Executive FH Europe, Co-Author WHF Cholesterol Roadmap

¹ World Health Organization. Global Health Risks: Mortality and burden of disease attributable to selected major risks. Geneva, Switzerland; 2009. Report No.: 978 92 4 156387 1.

² World Health Organization. Raised Cholesterol: situation and trends [Available from: https://www.who.int/gho/ncd/risk_factors/cholesterol_text/en/].

³ Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. J Am Coll Cardiol. 2020;76(25):2982-3021.

⁴ NCD Risk Factor Collaboration (NCD-RisC). Repositioning of the global epicentre of non-optimal cholesterol. Nature. 2020;582(7810):73-7.

⁵ Hu P, Dharmayat KI, Stevens CAT, Sharabiani MTA, Jones RS, Watts GF, et al. Prevalence of Familial Hypercholesterolemia Among the General Population and Patients With Atherosclerotic Cardiovascular Disease: A Systematic Review and Meta-Analysis. Circulation. 2020;141(22):1742-59.

⁶ Wilemon KA, Patel J, Aguilar-Salinas C, Ahmed CD, Alkhnefawi M, Almahmeed W, et al. Reducing the Clinical and Public Health Burden of Familial Hypercholesterolemia: A Global Call to Action. JAMA Cardiol. 2020;5(2):217-29.

WORLD HEART FEDERATION ROADMAPS

Already the **world's number one killer**, deaths from cardiovascular disease (CVD) are increasing globally.

CVD and related conditions can often be prevented, but if not, can be detected early

and treated cost-effectively, preventing costly hospitalizations and death. But this requires coordinated national policy and health systems responses built around evidence-based strategies. Health resources are limited and so cost-effective interventions for the prevention, detection and management of CVD must be prioritized in order to plan effective health systems responses.



WHAT ARE ROADMAPS?

WHF Roadmaps are a global framework that can be adapted and used at national or regional level.

THEIR PURPOSE IS TO:

1. Summarize current recommendations to reduce the burden of CVD that are proven, practical and cost effective
2. Highlight obstacles to implementing these recommendations
3. Propose potential solutions for overcoming these obstacles
4. Provide tools and strategies to adapt solutions to local needs.



HOW DO THEY WORK?

WHF Roadmaps offer a global framework, tools and solutions that can then be used and adapted, through stakeholder collaboration, to meet the specific needs of individual regions and nations.

This requires:

- A situation analysis of the current health system based on tools such as WHF CVD Scorecards
- Roundtables with multiple stakeholders to discuss obstacles, solutions and appropriate strategies

- A plan to implement and evaluate the proposed strategies

WHO ARE THEY FOR?

WHF Roadmaps empower our Members, including CVD foundations, societies and patient associations, to lead country specific, action-oriented initiatives, including Roundtables.

These involve diverse stakeholders, such as:

- Governments and policy makers
- NGOs, health activists and advocates

- Healthcare professionals
- Corporate entities
- Academic and research institutions
- Patients and patient groups

WHY ARE THEY IMPORTANT?

To trigger effective action that can measurably reduce premature deaths and the associated global economic burden caused by CVD.

TO DOWNLOAD THE FULL ROADMAP PLEASE VISIT – [CVDROADMAPS.ORG](https://cvdroadmaps.org)

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CHOLESTEROL ROADMAP

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