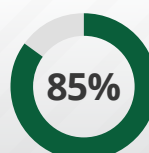


A Framework for the Management and Prevention of Atherosclerotic Cardiovascular Diseases

Atherosclerotic cardiovascular disease (ASCVD) burden



523 million
CVD cases in 2019



85%
Due to
atherosclerosis



ASCVD is a
leading
cause of
death
globally



The early onset of ASCVD
affects the employability,
productivity, and income
potential of individuals
and is detrimental to the
economy



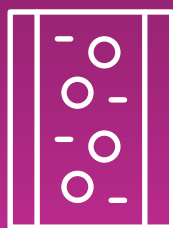
This is concerning especially in low- and
middle-income countries (LMICs), where
much of the global population resides,
and where ASCVDs appear in individuals
almost ten years before they appear in
individuals from higher income countries



ASCVD and its risk
factors also predispose
individuals to other
health problems,
affecting their
caregivers and family

The role of lipids in ASCVD

Among the types of cholesterol,
low density lipoprotein cholesterol
(LDL-C) is known to cause ASCVD



↑ Obesity

↑ Population with a dysfunctional
lipid metabolism

↓ High density lipoprotein
cholesterol (HDL-C)

↑ Non-HDL-C and triglyceride levels

The 8 pillars of scientific information on lipids and ASCVD risk

- 1 Retention of apolipoprotein B (apo B)-containing lipoproteins—mostly LDL lipoproteins—in vessel walls causes atherosclerosis, and LDL-C is an important risk factor for the same
- 2 The retention levels of apo B-containing lipoproteins influences vulnerability to LDL-C exposure; this varies among individuals, so other factors should be considered
- 3 ASCVD can occur without extreme elevations in LDL-C; hence, global risk should be considered
- 4 Genetic LDL-C elevation disorders like familial hypercholesterolaemia (FH) are common and can be monitored through early screening and treatment
- 5 Reducing LDL-C levels is an effective strategy to reduce ASCVD; while this can be done through various means, the amount of reduction in LDL-C and the length of the period for which this reduction is achieved is more important
- 6 Reducing LDL-C levels also promotes a proportional reduction in levels of non-HDL-C and apo B
- 7 Measuring non-HDL-C and apo B levels in blood improves risk assessment in diabetic or obese patients
- 8 An elevation in lipoprotein (a) [Lp(a)] levels is a causal risk factor of ASCVD

How does this information affect healthcare policy and funding?



Time trends in the lipid levels in a population
should be assessed using non-HDL-C or apo B
levels as markers, not total cholesterol levels

Public policy should encourage early initiation
of adequate LDL-C-lowering treatment
regimens

How does this information affect physicians and their prescriptions to patients?



Physicians need to: Identify at-risk patients, which include people with:

- Diabetes, chronic kidney disease, or very high blood pressure
- A genetic disease that results in elevated LDL-C
- High CVD risk
- An increase in any of the ASCVD-causing lipids
- Subclinical atherosclerosis

Start these patients on LDL-C-lowering drugs

Overall approaches for ASCVD prevention

Primary

Focus on decreasing LDL-C levels (and, thereby, non-HDL-C and apo B levels) in at-risk patients to reduce their chances of developing ASCVD



LDL-C lowering approaches

When?

Initiate treatment early and for an adequate amount of time



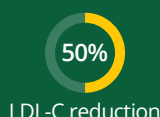
How?

In LMICs, try using equations like the Martin-Hopkins and Sampson equations, which provide a stratified estimation of LDL-C levels from non-fasting profiles and are more economical



What?

Prescribe a daily oral dose of statins such as atorvastatin (40–80 mg) and rosuvastatin (20–40 mg) as first line therapies



Ezetimibe is often used in combination with statins or another drug like bempedoic acid



Prescribe injectable therapeutics like anti-proprotein convertase subtilisin/kexin 9 (anti-PCSK9) monoclonal antibodies, and inclisiran (small interfering RNA) with monthly/yearly dosing intervals



Approaches to reduce triglyceride levels

Lifestyle changes

- Weight loss
- Diabetes control
- Alcohol and carbohydrate reduction



Treatment:

- Treatment with icosapent ethyl is indicated in patients with concomitant cardiovascular disease or diabetes plus additional risk factors



Approaches against Lp(a)

Lp(a) levels should be measured once in the patient's lifetime using isoform independent assays



Apheresis is commonly used to lower Lp(a) levels from the blood



Treatment with anti-PCSK9 monoclonal antibodies also shows some benefit



Genetic influence on primary strategies for ASCVD prevention

FH is an autosomal genetic disorder causing life-long elevations in LDL-C, leading to premature cardiovascular disease



In the absence of FH

Current recommendations

A global region-specific assessment with charts or web-based tools



Integration of estimated risk information and co-morbidities into medical records to improve patient understanding and adherence



Imaging of the coronary arteries also helps in risk assessment and treatment



Future recommendations

Two major strategies to effectively reduce the lifetime risk of ASCVD events:

- Reducing atherosclerotic plaque formation by reducing LDL-C exposure
- Reducing exposure to risk factors like elevated blood pressure, diabetes, and tobacco smoking



Lower LDL-C levels and/or blood pressure



Low lifetime risk of ASCVD

- Artificial intelligence studies link the early pharmacological management of LDL-C with ↓ risk of ASCVD



In Finland, policy level changes to reduce saturated fat exposure resulted in a population level effect



- Mean reduction in cholesterol

1.5 mmol/L

- Mean reduction in blood pressure

8.7 mm of Hg

- 80% reduction in cardiovascular events



In the presence of FH

Two forms of FH:

- Heterozygous (HeFH)
- Homozygous (HoFH)

Early diagnosis through the Dutch Lipid Clinic Network criteria consisting of biochemical measurements, physical examination, and family history

Condition	HeFH	HoFH
Genes affected	Single LDL receptor (LDL-R) gene	Both LDL-R genes
Effective therapeutics	Statins Ezetimibe PCSK9 inhibitors	LDL-R independent therapies like lomitapide and evinacumab

Secondary



In patients with a history of ASCVD, pharmacological treatment should be started without risk intervention



A combination of pharmacological treatment strategies should be employed



Qualitative tools such as SMART (Secondary Manifestations of ARterial disease) and TRS2P (TIMI Risk Score for Secondary Prevention) should be used to determine the absolute ASCVD risk and benefit of treatment

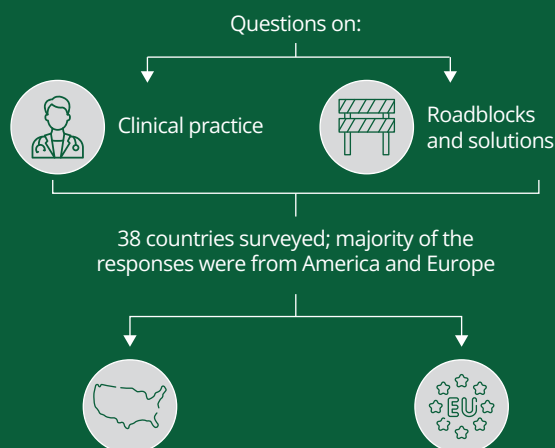
Visit <https://ascvd-lipidology.knowledgehub.wiley.com/> for additional resources

Region-based differences in adherence to ASCVD treatment guidelines

World Heart Federation (WHF) survey



July–August 2021



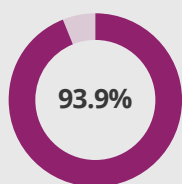
ESC/EAS* ASCVD guidelines are followed in Europe and Africa



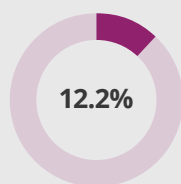
ACC/AHA* guidelines are followed across America and Southeast Asia

*ACC: American College of Cardiology; AHA: American Heart Association; EAS: European Atherosclerosis Society; ESC: European Society of Cardiology

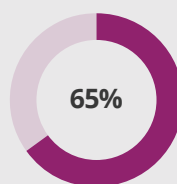
Treatment perceptions



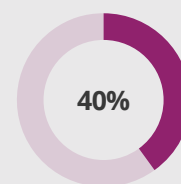
Initiated treatment based on ASCVD risk



Based treatment on cholesterol levels

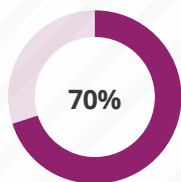


Responders from high income countries were comfortable with statin treatment

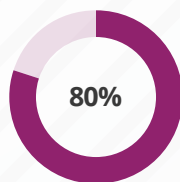


Responders from LMICs were comfortable with statin treatment

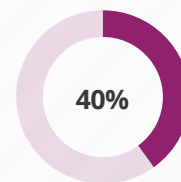
Statistics among LMICs



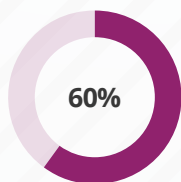
Unsure of the benefits of lowering cholesterol



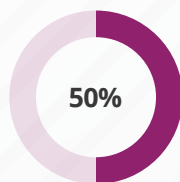
Unaware of the risk of ASCVD



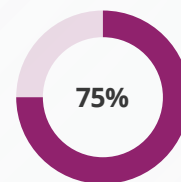
Reported a lack of statin/ezetimibe availability



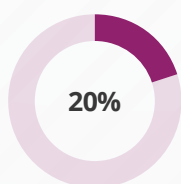
Reported a lack of anti-PCSK9 availability



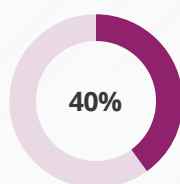
Reported a lack of free statin prescription



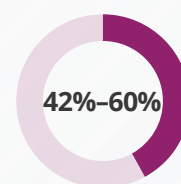
Reported a lack of free ezetimibe and/or anti-PCSK9 prescription



Reported significant (51%–75%) control of LDL-C levels among patients



Reported low (25%) control of LDL-C levels among patients



Reported that less than half of the patients adhere to the treatment strategy

Visit <https://ascvd-lipidology.knowledgehub.wiley.com/> for additional resources

Barriers to ASCVD risk management



Actionable solutions

1. Increase awareness

a. Among health professionals via:

- Education
- Access to qualitative tools
- Guidelines and recommendations for clinical treatment



b. Among patients by encouraging:

- Healthcare personnel-patient interaction for proper spread of information
- Patient inputs while designing policies, guidelines, and assessments
- Educational campaigns



2. Population-based approaches to prevent ASCVD

- Follow World Health Organization (WHO) guidelines and recommendations to:
 - Reformulate food to eliminate trans-fat
 - Control tobacco use
- Provide education on healthy dietary patterns
- Incorporate national level policy changes including taxation on unhealthy items



3. Reinforce ASCVD risk assessment and population screening by developing:

- Local guidelines for the same
- Easy access
- Simple technologies for point-of-care testing
- Policies, funds, and a framework for the efficient screening of genetic disorders



4. Implement system-level approaches targeting high-risk individuals

- Improve the accessibility, availability, and affordability of important therapeutics
- Promote the use of combinatorial treatment strategies
- Promote private-public sector collaborations to ensure progress in therapeutic research and development



5. Establish national/regional surveillance of cholesterol and ASCVD outcomes:

- Monitor:
 - Patient adherence to treatment
 - Extent to which patients meet cholesterol lowering goals
 - Stocks of therapeutics to ensure adequate supply
 - Risk factors and mortality rates among patients
- Implement the WHO monitoring framework
- Collect epidemiological and clinical data and make the required changes to improve upon healthcare policies



The WHF Cholesterol Roadmap presents a scientifically sound foundation for policymakers to implement changes that can lead to a reduction in the burden of ASCVD

Understanding the key role of LDL-C as a risk factor for ASCVD and the existing barriers in LMICs will greatly promote effective implementation of strategies influencing healthcare policy, lifestyle, and pharmacological treatment methods to ensure a shift towards effective management of ASCVD



Reference

Ray, K.K., Ference, B.A., Séverin, T., Blom, D., Nicholls, S.J., Shiba, M.H., ... & Santos, R.D. (2022). World Heart Federation Cholesterol Roadmap 2022. *Global Heart*, 17(1): 75.