

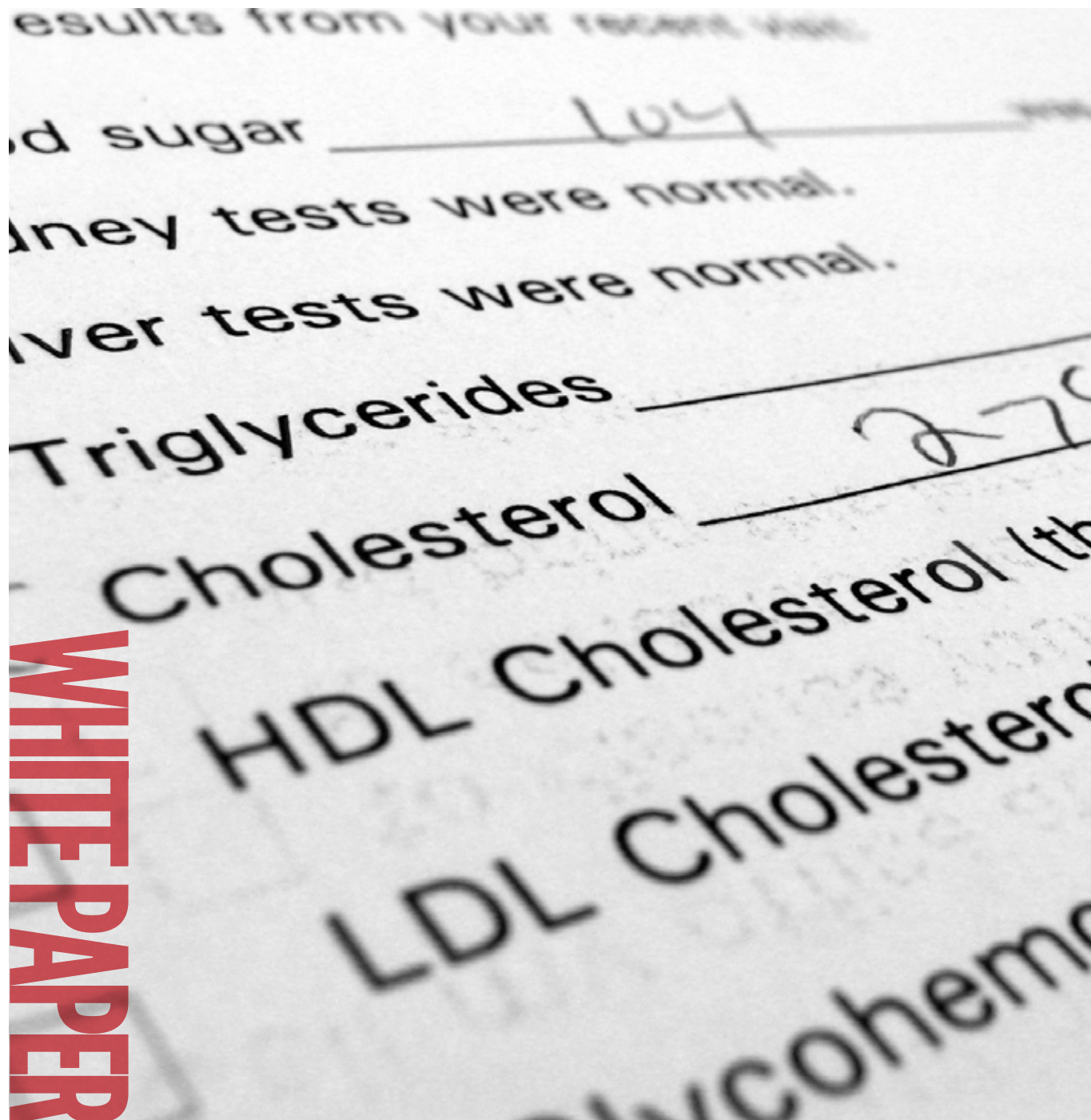


**WORLD
HEART
FEDERATION**

IMPROVING PREVENTION AND CONTROL OF RAISED CHOLESTEROL

A CALL TO ACTION

**A WORLD
HEART FEDERATION
WHITE PAPER**



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WHITE PAPER

ACKNOWLEDGEMENTS

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EXECUTIVE SUMMARY

The Covid-19 crisis which hit us early 2020 has forced most health systems to re-allocate most of their resources to fight this pandemic. However, Covid-19 has also revealed the vulnerability of people affected by Non-communicable diseases (NCD), who are more at risk to develop severe forms of the illness. Tackling NCDs and underlying risk factors, such as high cholesterol, must therefore be considered as fundamental to health security⁽¹⁾.

In this context, this White Paper aims to inform a coherent policy approach to preventing, detecting, treating, and controlling high cholesterol. In a brief introductory chapter, it describes the condition and its

consequences and depicts the global epidemiological situation. Accounting for the burden chronic conditions place on individuals affected, it also provides a space for community voices. Reflecting our conviction that all problems come with a solution, the third chapter of this White Paper presents several success stories in various settings. Chapter four of the White Paper introduces the **OPERATE** change framework (infOrM, PreVent, dEtect, tReAT, mEasure). Based on previous work⁽²⁻⁴⁾ by the WHF and other partners, this framework features a series of recommendations to drive action and progress towards achieving better awareness, prevention, detection, treatment, and control of raised blood cholesterol. Considering that all health systems have limited resources and competing demands, this White Paper emphasizes the importance of cross-sectoral actions and collaborations.

CALL TO ACTION

The Call to Action included in this report:

- Is grounded in evidence
- Has a global relevance, taking into account that regional or national differences may exist
- Echoes and reinforces recommendations included in *2017 WHF Cholesterol Roadmap* and in the *2018 Global Call to Action on Familial Hypercholesterolemia*
- Represents a contribution towards achieving target 3.4 of the United Nations' Sustainable Development Goals (SDGs) "reducing by one-third premature mortality from non-communicable diseases through prevention and treatment and promoting mental health and well-being by 2030".

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OPERATE CHANGE NOW!

STEP 1: INFORM

Hypercholesterolemia and Familial Hypercholesterolemia (FH) are largely silent diseases; they cause no symptoms. As a result, they too often remain unnoticed. When diagnosed, treatment is not systematic, and patients have poorly controlled cholesterol levels. Awareness among both the public and health professionals is still insufficient.

WHF therefore strongly supports:

- Campaigns to raise awareness of the importance of severe hypercholesterolemia and FH as a public health issue
- Campaigns to raise awareness among health professionals and the public of the importance of screening for raised cholesterol and possible FH
- Campaigns to provide balanced information to the public and to health professionals on the safety and efficacy of cholesterol treatment
- The use of novel technologies such as Apps or text messaging to remind and support patients toward treatment adherence.



inform

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STEP 2: PREVENT

Eight modifiable risk factors – high blood pressure, high **cholesterol**, tobacco, high blood glucose, low fruit and vegetable intake, lack of physical activity, high body mass index, and alcohol – account for 61% of cardiovascular deaths. Shaping policies that ensure an environment that is conducive to healthy living can lead to substantial improvements in all settings.

Therefore, WHF strongly supports public health policies that help implement these objectives including:

- Food reformulation efforts, in particular with regard to eliminating artificial trans-fat
- Taxation on unhealthy products such as unhealthy foods and beverages
- Full implementation of the WHO Framework Convention on Tobacco Control (FCTC)
- Sufficient resource mobilisation at national levels, in particular through adequate taxation policies and selected public-private collaborations.



Prevent

STEP 3: DETECT

Because of its silent nature, high cholesterol often remains undiagnosed. For FH, the situation is particularly dramatic, as it is estimated that fewer than 10% of individuals affected are diagnosed. Clear screening policies and adequate facilities to measure cholesterol can make substantial differences through early detection.

WHF therefore strongly supports:

- Simplified national guidelines for whom and how to screen for CVD risk using cholesterol measurement, based on a Total Risk Approach
- The adaptation of risk score charts to ensure appropriateness for specific populations
- Point-of-care testing with inexpensive and easy-to-use technologies (e.g., cholesterol test strips)
- **Universal child-parent screening and cascade testing of first- and second-degree relatives to detect FH.**



detect



STEP 4: TREAT

Recent guidelines recommend treating LDL-C > 190 mg/dl (49 mmol/L) with a high intensity statin beginning at age 8-10 years and at lower levels based on age and risk factor status^(5,6). Although high cholesterol can be easily reduced or treated with inexpensive and cost-effective medications, these treatments remain inaccessible to broad segments of the world's population⁽⁷⁾. Statins are included on the WHO List of Essential Medicines but their availability and affordability remain a hurdle in certain settings. Other barriers – costs, misconceptions about medication, forgetfulness, also lead to treatment discontinuation.

WHF therefore strongly supports:

- Continuing medical education for general practitioners and non-lipid specialists to improve skills and confidence in prescribing statin treatment, including for FH
- The definition of LDL-cholesterol above 190 mg/dl as a high risk threshold
- Greater clarification on statin regimens to use to avoid misconceptions surrounding dose and cholesterol-lowering efficacy
- Free or subsidized drug provision, eliminating duties and taxes on medicines to ensure the affordability of statin and non-statin therapies including new treatments when required and available
- The availability of cholesterol medications in pharmacies and health facilities through local generic drug manufacture
- The use of polypills and statin-non-statin drug combinations in a single pill where available
- The enrollment of pharmacists and nonphysician health workers in patient support and counselling for adherence to drug therapy
- **The availability of specialized centers to guarantee the care of severe and homozygous FH.**



tReAT

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STEP 5: MEASURE

Measuring and tracking progress are key elements to define priorities, adapt strategies, programmes and projects, control progress towards desired outcomes, identify what works and what doesn't, justify the allocation of resources, among others.

WHF therefore strongly supports:

- The collection of epidemiological data to provide a locally relevant, solid basis to use CVD risk calculators (WHO/ISH, SCORE, Framingham etc.)
- The development of reliable health information systems to monitor health behaviours, risk factors, and morbidity and mortality
- The implementation of the WHO Global Monitoring Framework
- A global agreement among governments and intergovernmental agencies upon international standards
- The monitoring of stock outages for essential medicines such as statins
- Financial support for the development of FH registries.



mEasure

SUCCESS WILL ONLY OCCUR IF ALL STAKEHOLDERS JOIN FORCES. IN SUPPORT OF ITS CALL TO ACTION, **WHF COMMITS TO:**



INFORM

- Contribute to raising awareness through international disease days (eg. World Heart Day, FH Awareness Day) and other impactful events.
- Produce, disseminate and regularly update WHF Roadmaps to identify potential roadblocks on the pathway to effective prevention, detection and management of CVD, as well as evidence-based solutions to overcome them and support local/national implementation by organising country-specific, action-oriented Roundtables to meet the specific needs of individual regions and nations in fighting cardiovascular diseases.
- Collect and disseminate educational materials, best practices and success stories across disciplines and regions.



PREVENT

- Advocate for the taxation of unhealthy products (unhealthy processed foods, tobacco, alcohol, sugar) at global, regional and national levels through its network of members and partners.
- Advocate for a global implementation of the WHO REPLACE package and for the inclusion of TFA elimination in a broader, coordinated approach
- Collect and disseminate examples of best practices and success stories on taxation policies and innovative financing mechanisms.



DETECT

- Support staff education and training through its wide network of members and partners.



TREAT

- Support the education and training of healthcare workers to foster optimal prescription of essential medicines and adherence to treatment.
- Action our networks of members and partners to advocate for the improved availability and affordability of essential CVD medicines at global, regional and national levels.



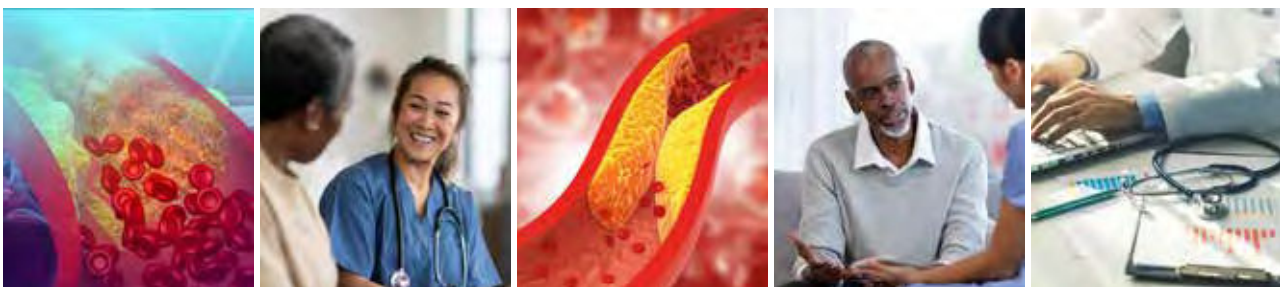
MEASURE

- Advocate for the use of evidence-based approaches whenever data is collected, analysed and disseminated.
- Help collect, monitor and disseminate data to track progress through our wide networks of members and partners.
- Actively support a Countdown to 2030 for NCDs and contribute as deemed fit and advocate for the inclusion of cholesterol management in UHC and other WHO tools.



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CONTEXT AND BACKGROUND

PURPOSE OF THIS WHITE PAPER



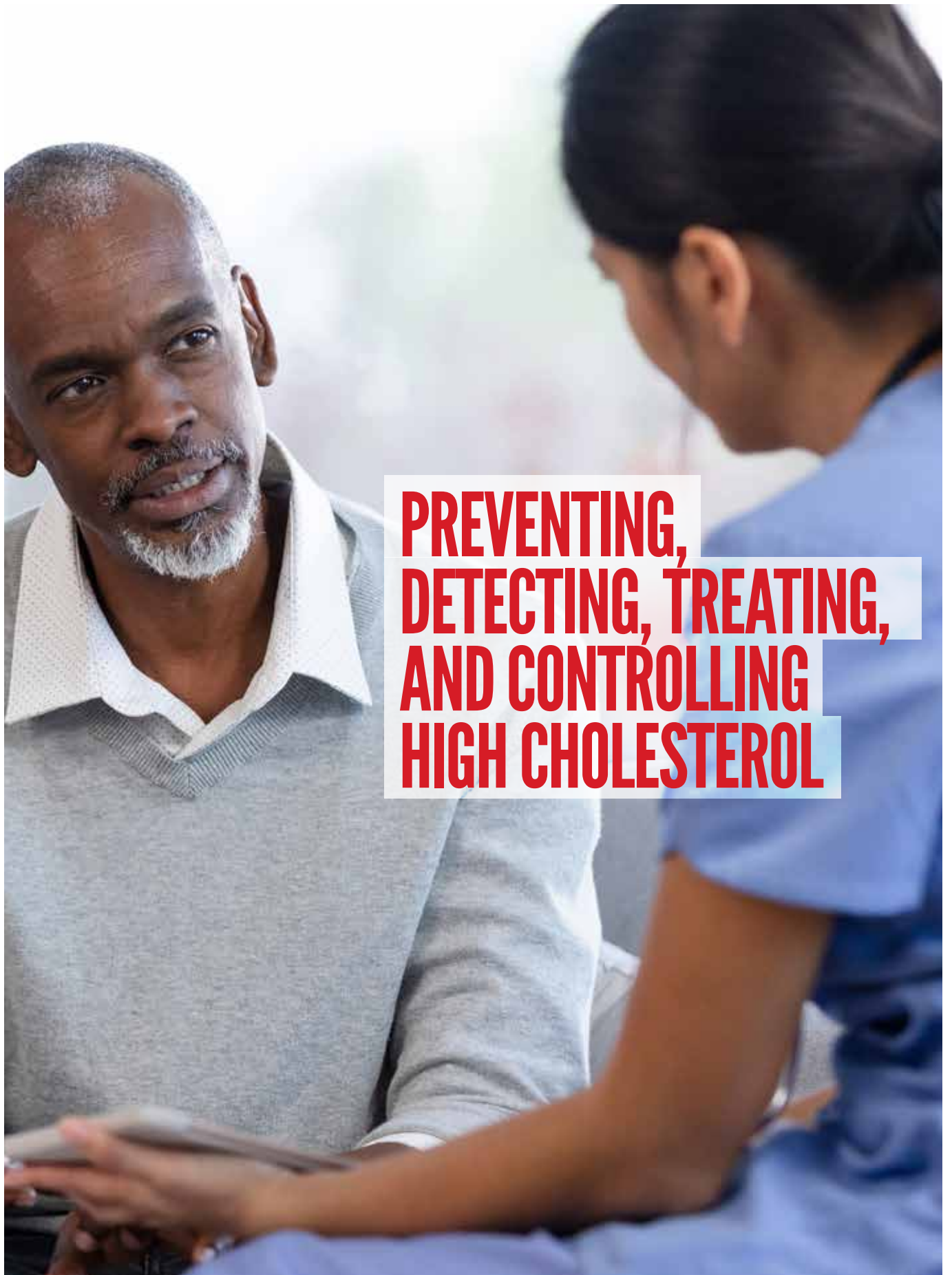
This White Paper aims to inform a coherent policy approach to preventing, detecting, treating, and controlling high cholesterol. It provides policymakers with key information and recommendations. The first part of this White Paper provides a situation analysis. It describes the nature and magnitude of the problem in epidemiological terms. Paying tribute to the fact that there is a human being behind each number and figure, it also gives patients a voice. These individuals shed light on the actual impact high cholesterol/Familial Hypercholesterolemia (FH) has on their day-to-day routine by sharing their stories.

The second part of this White Paper focuses on problem-solving. It presents several success stories in various settings and introduces the OPERATE change framework (infOrm, Prevent, dETect, tReAT, mEasure). This framework includes a series of recommendations to drive action and progress towards achieving better awareness, prevention, detection, treatment, and control of raised blood cholesterol.

This White Paper is to be read in the context of the United Nations' Sustainable Development Goals (SDGs) and in particular of SDG Target 3.4, of reducing by one-third premature mortality from non-communicable diseases (NCDs) through prevention and treatment and promoting mental health and well-being by 2030.

Considering that all health systems have limited resources and competing demands, it advocates for implementing policies that do not focus on a single disease or risk factor, but that do cover a broader spectrum. It therefore emphasizes the importance of cross-sectoral actions and collaborations.

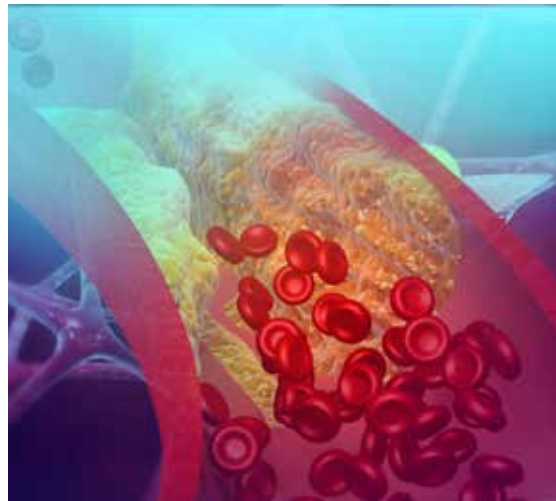
In particular, the Covid-19 crisis, which stretched all health systems worldwide, has once again put infectious diseases in the spotlight. However, this pandemic has also revealed the vulnerability of people affected by NCDs, who were found to be more likely to develop severe forms of the illness, leading to excess mortality. This pandemic has exposed the existing connections between NCDs, infectious diseases, and health emergencies, and the need to stop addressing health issues in siloes. Prevention strategies for NCDs, through management and control of underlying risk factors such as high cholesterol must, therefore, be considered as fundamental to health security.⁽¹⁾



**PREVENTING,
DETECTING, TREATING,
AND CONTROLLING
HIGH CHOLESTEROL**

FACTS AND FIGURES ON CHOLESTEROL

NATURE OF THE PROBLEM



WHAT IS CHOLESTEROL?

Cholesterol is a soft, waxy substance found among the lipids in the bloodstream and in all the body's cells. It is crucial to the healthy functioning of the body. The liver either makes cholesterol or uses cholesterol obtained from other sources: dietary cholesterol and saturated fat, cholesterol carried in the blood, or by reabsorbing bile from the GI tract.

TRIGLYCERIDES are a type of fat found in food and are also stored in the body's fat cells. Being overweight, eating a lot of fatty and sugary foods or drinking too much alcohol may lead to raised blood triglyceride levels. Triglyceride levels may be high despite relatively normal levels of good cholesterol (HDL-C) and non-HDL cholesterol. Triglyceride levels predict future diabetes.

HIGH-DENSITY LIPOPROTEINS (HDL), sometimes referred to as "good cholesterol," are particles which contain cholesterol and are responsible for taking unnecessary cholesterol back to the liver so that it can be eliminated from the body. High HDL cholesterol may be a biomarker for protection against heart disease, but there is a threshold above which

extremely high levels offer no more protection than more modest readings.

NON-HIGH DENSITY LIPOPROTEINS (Non-HDL) are sometimes referred to as "bad cholesterol" and are particles responsible for carrying the cholesterol cargo that can accumulate in blood vessels, a process known as atherosclerosis. This narrowing of the blood vessels limits oxygen-rich blood flow and can ultimately lead to a heart attack or stroke.

Cholesterol and triglycerides are carried in the blood by lipoprotein particles, a combination of fat (cholesterol and triglyceride) and protein. The lipoproteins with the most cholesterol are low density lipoprotein (LDL) and high density lipoprotein (HDL). The lipoproteins with the most triglyceride are very low density lipoprotein (VLDL) and chylomicrons (made to take the food from the gut to the liver). High levels of LDL cholesterol, or alternately non HDL cholesterol, are risk factors for heart attacks and stroke.

Heart disease risk from lipids is assessed by measuring LDL cholesterol, as that is the primary lipoprotein causing atherosclerosis. Non-HDL cholesterol includes LDL cholesterol and other lipoproteins associated with heart risk including lipoprotein (a) and remnant cholesterol.

	Total Cholesterol (mmol/1)	HDL Cholesterol (mmol/1) Men/Women	Non-HDL Cholesterol (mmol/1)	Triglycerides (mmol/1)
High	6.2	1.0/1.2	4.1	2.25
Borderline	5.2	1.24/1.44	3.3	1.69
Desirable				



WHAT IS DYSLIPIDAEMIA?

Dyslipidaemia is an all encompassing term which refers to the presence of non-optimal levels of blood lipids. In clinical practice guidelines, it is typically characterized by raised total cholesterol (TC) and/or low-density lipoprotein cholesterol (LDL-C). The definition is also often extended to include non-optimal levels of high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), apolipoprotein B and apolipoprotein A1⁽⁸⁾.

WHAT IS FAMILIAL HYPERCHOLESTEROLEMIA (FH)?

Familial hypercholesterolemia (FH) is a genetic condition that causes high cholesterol. If left untreated, FH leads to early heart attacks and heart disease. Individuals with FH have a high amount of LDL cholesterol or 'bad cholesterol' due to a mutation in one

of several genes that control how the liver uses cholesterol. As a result, cholesterol accumulates in the bloodstream and can ultimately build up in the arteries' walls. Patients may develop fatty skin deposits, known as xanthomas, on their body or cholesterol deposits may also be visible on the eyelids, a condition called xanthelasmas.

FH is inherited. The number of mutations that are inherited determine the type of FH an individual has.

One inherited mutation – called Heterozygous Familial Hypercholesterolemia (HeFH) – means that one abnormal mutation is passed down to a child, typically from one parent.

Two inherited mutations – called Homozygous Familial Hypercholesterolemia (HoFH) – happen when a mutation for HeFH is passed on from each parent to their child. This results in the more rare and severe form of FH⁽⁹⁾.

THE CAUSES / RISK FACTORS OF DYSLIPIDAEMIA:

Various factors, such as a diet high in saturated fat and trans-fats, different metabolic conditions such as Type II diabetes, and heredity, influence an individual's cholesterol and triglyceride levels. Over three-quarters of ischaemic heart disease, the leading cause of death worldwide are attributable to these combined risk factors. Reducing exposure to major risk factors could increase global life expectancy by almost five years⁽¹³⁾. A diet high in excess calories and sugar worsens high triglycerides.



People with FH may get wart-like bumps on their eyelids

BEHAVIOURAL RISK FACTORS



UNHEALTHY DIET. A diet high in saturated fat (found, for example, in animal products) and trans-fats (found in various industrially processed foods) can lead to an increase in cholesterol levels. Excess sugar and starch intake contributes to high triglycerides.



LACK OF PHYSICAL ACTIVITY. Being physically inactive can have a detrimental effect on non-HDL cholesterol levels. regular physical activity as been shown to have a beneficial impact by reducing non-HDL cholesterol concentrations⁽¹⁴⁾.



SMOKING. Cigarette smoking damages the walls of the blood vessels, making them more likely to accumulate fatty deposits. Smokers are 2–4 times more likely to develop heart disease than non-smokers. Conversely, smoking cessation typically leads to an increase in HDL cholesterol levels⁽¹⁵⁾.

ASSOCIATED CONDITIONS



OBESITY. The typical dyslipidaemia of obesity consists of increased triglycerides, decreased HDL cholesterol with HDL dysfunction, and normal or slightly increased non-HDL cholesterol⁽¹⁶⁾.



DIABETES. High blood sugar reflects in part greater insulin insensitivity which contributes to higher levels of very low-density lipoprotein (VLDL) production by the liver and in turn lower HDL cholesterol. High blood sugar may also directly damage the lining of the blood vessels⁽¹³⁾.

NON-MODIFIABLE RISK FACTORS



HEREDITY. The quantity of cholesterol produced by the body is partly genetically determined. Familial hypercholesterolemia (FH) leads to high cholesterol and, if untreated, to early heart attacks and heart disease. Each child of an individual with FH has a 50% chance of inheriting the disorder. There are many genes that impact cholesterol levels by small increments; having a lot of these genes that raise cholesterol is also not healthy. Therefore, screening parents, siblings, and children of a person diagnosed with FH to find others who may have inherited the genes is essential.




ADVANCING AGE. Growing older constitutes a risk factor, as metabolism changes as with advancing age and may predispose individuals to dyslipidemia. For instance, with advancing age, the liver becomes less able to remove cholesterol containing lipoproteins. Furthermore age reflects years of exposure to undesirable factors. The earlier one reduces this, the better one is able to age in a healthy fashion.



GENDER. High cholesterol affects both men and women. However, oestrogen, a female hormone, raises HDL cholesterol levels, partially explaining the lower risk of CVD observed in pre-menopausal women. Conversely, LDL-cholesterol rises after menopause, which again increases the risk in post-menopausal women.

Leading risks 1990 vs leading risks 2019



	Leading risks 1990	Leading risks 2019
1	Child wasting	High systolic blood pressure
2	Low birth weight	Smoking
3	Short gestation	High fasting plasma glucose
4	Household air pollution	Low birth weight
5	Smoking	High body-mass index
6	Unsafe water	Short gestation
7	High systolic blood pressure	Ambient particulate matter
8	Child underweight	High LDL cholesterol
9	Unsafe sanitation	Alcohol use
10	Handwashing	Household air pollution
11	.	
12	.	
13	.	
14	High LDL Cholesterol	

Source: GBD study 2019

THE CONSEQUENCES OF DYSLIPIDAEMIA

High cholesterol is also in itself a risk factor for serious health conditions. If left untreated, it can lead to atherosclerosis. This, in turn, may lead to heart disease, stroke, and other vascular diseases⁽¹³⁾. The higher the LDL-c, the higher the risk. Therefore, people who are affected by FH have an even greater risk of developing CVD at an earlier age because of lifelong exposure.

In 2019, the number of DALYs due to high non-HDL cholesterol reached 98.6 million. It also caused an estimated 4.4 million deaths⁽¹⁷⁾. From a regional perspective, the death toll has decreased in high-income western countries. Conversely, it has more than doubled in southeast Asia and even tripled in east Asia. As a result, by 2017, half of the deaths attributable to high non-HDL cholesterol were recorded in east, southeast, and south Asia, compared with a quarter in 1990. This demonstrates a global shift of the disease burden from high-income countries in northwestern 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⁽¹¹⁾.

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MAGNITUDE OF THE PROBLEM

Globally, raised total cholesterol (≥ 5.0 mmol/L) affects approximately 39% of adults (37% for men and 40% for women)⁽¹⁰⁾. Global age-standardized mean total cholesterol and non-HDL cholesterol have changed very little since 1980. Regionally, both total and non-HDL cholesterol have decreased in high-income western regions and in central and eastern Europe. By contrast, non-HDL cholesterol increased in east and southeast Asia, parts of sub-Saharan Africa, and Melanesia⁽¹¹⁾.

Unfortunately, decreases in disease burden attributable to tobacco smoking, including second-hand smoke, high blood pressure, and high total cholesterol control in high-income regions, have been partly offset by the increasing risk burden caused by overweight and obesity⁽¹²⁾.

Familial hypercholesterolemia (FH) affects approximately 34 million people worldwide, i.e., one in 200-250 people⁽⁹⁾. This genetic disorder is found in people of all races and ethnicities. FH remains mostly underdiagnosed and undertreated due to low awareness – only 10% of those affected know about their condition and are adequately treated.

Globally, raised total cholesterol
(≥ 5.0 mmol/L)
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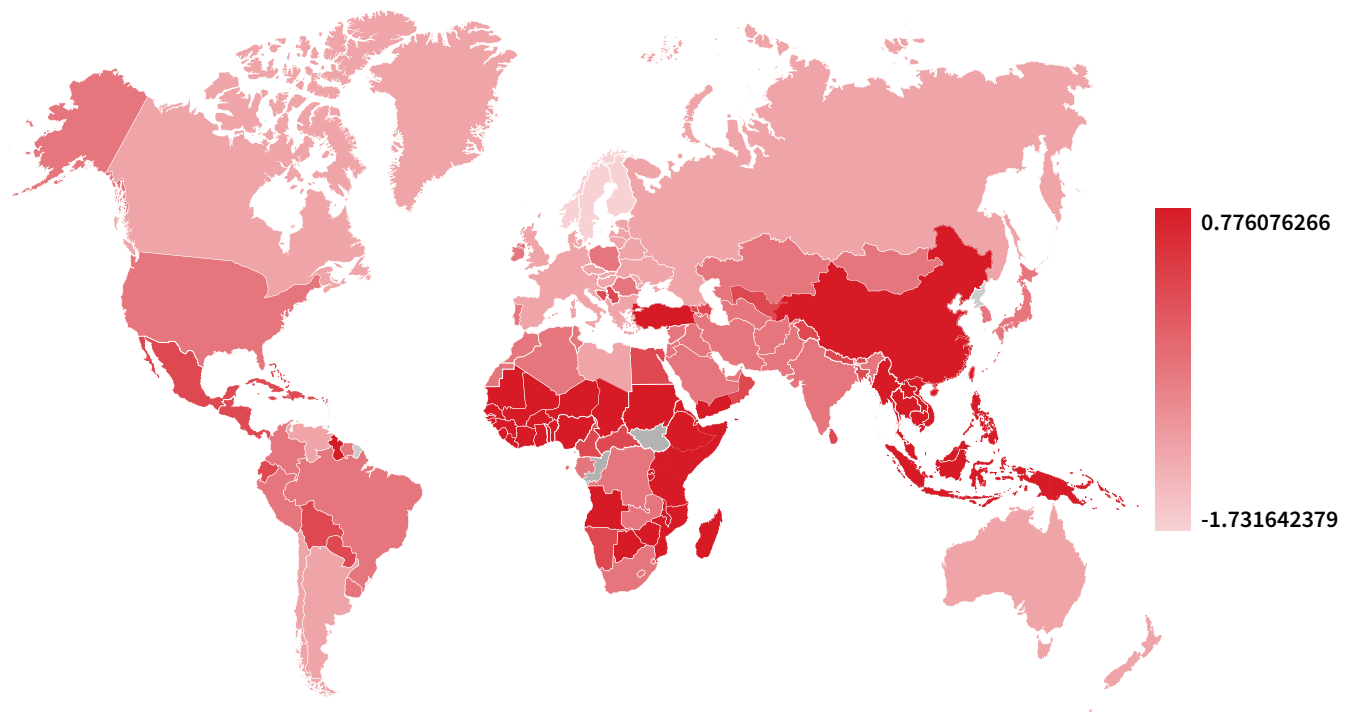


OF ADULTS

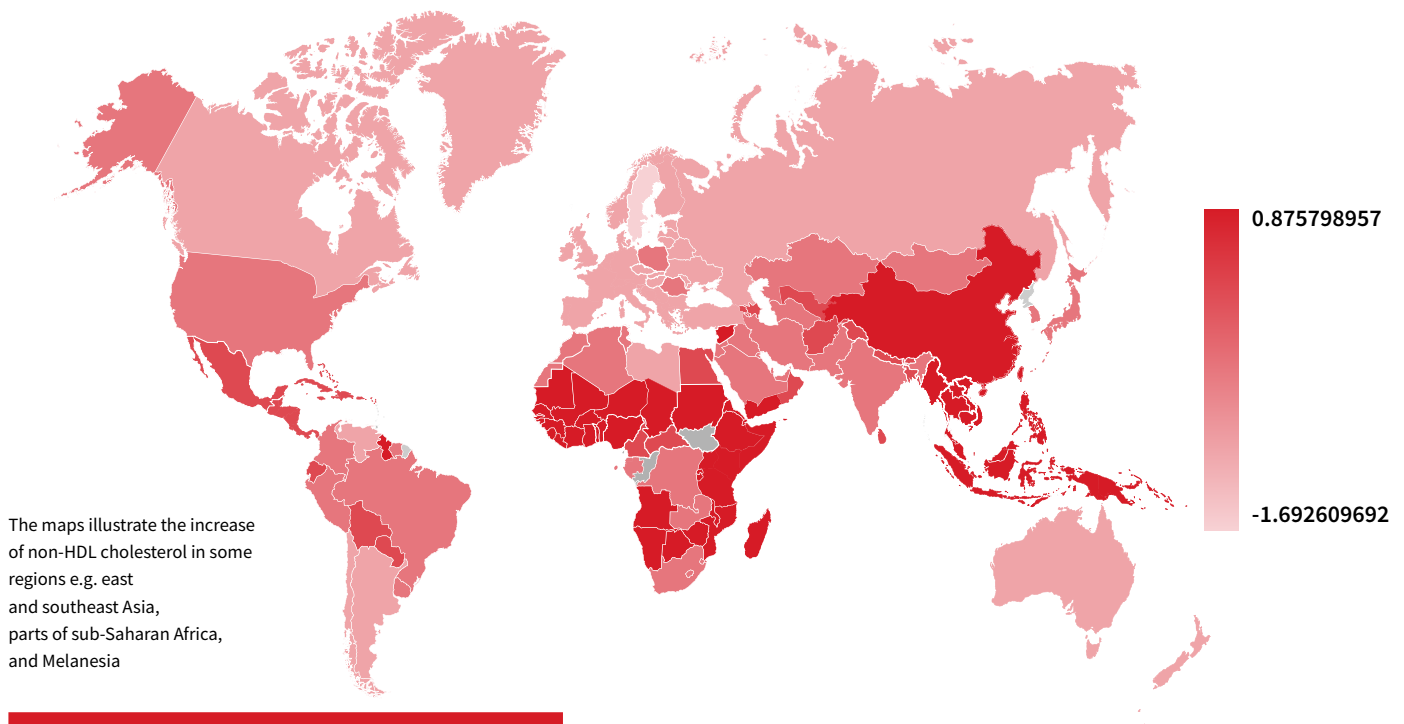
(37% for men and 40% for women)



Mean non-HDL cholesterol (mmol/L) – Difference 1980-2018 (Men) (11)



Mean non-HDL cholesterol (mmol/L) – Difference 1980-2018 (Women) (11)



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THE BURDEN OF FH

Individuals with FH, often untreated, have three times the risk of a heart attack at any given level of LDL cholesterol, because of the lifelong exposure⁽¹⁸⁾. In individuals affected by Heterozygous FH (HeFH), cardiovascular events often develop in men by 30-50 years of age, and in women by 40-60 years of age⁽¹⁹⁾. In individuals affected by Homozygous FH (HoFH), the more severe form of FH, manifestations of coronary or other cardiovascular diseases typically appear in childhood or adolescence⁽²⁰⁾.

Individuals with HoFH are at extremely high risk, and, if untreated, many will die before the age of 30 years⁽¹⁹⁾. FH places a heavy psychological burden on those affected: constraints associated with life-long treatment and feelings of guilt about passing on a disease are some example of the non-physical effects of the condition. It may also come with a personal cost, such as difficulty in obtaining life insurance or other forms of genetic discrimination⁽³⁾.

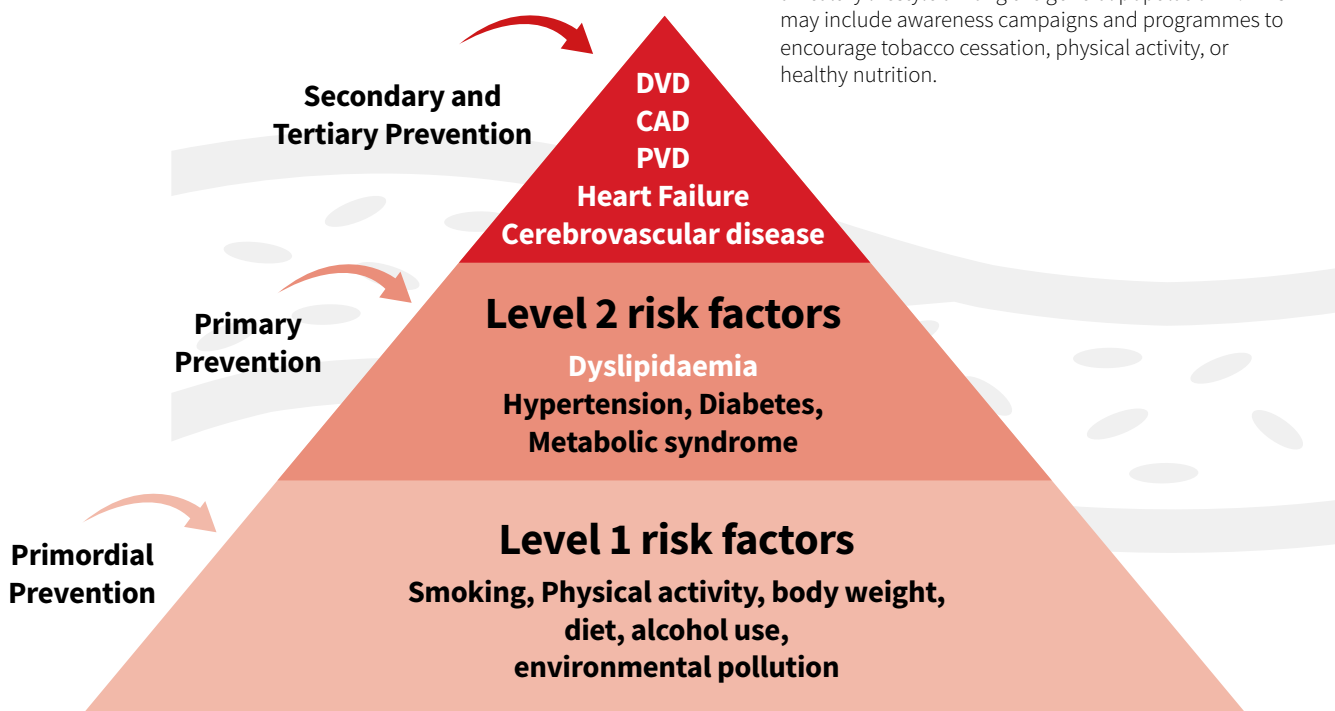
PREVENTING, DETECTING, TREATING, AND CONTROLLING RAISED BLOOD CHOLESTEROL

Healthcare systems which facilitate early detection, and thus offer efficient/early prevention management significantly attenuate the detrimental effects of high cholesterol on CVD. Actions must therefore span across the spectrum of primordial-primary-secondary and tertiary prevention.

PRIMORDIAL PREVENTION

Several lifestyle-related factors affect cholesterol levels. Primordial prevention aims at preventing risk factors for disease from developing⁽²¹⁾. A primary aim of public health interventions for reducing morbidity and mortality due to high non-HDL cholesterol should therefore be to encourage a healthy lifestyle among the general population⁽²⁾. This may include awareness campaigns and programmes to encourage tobacco cessation, physical activity, or healthy nutrition.

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PRIMARY PREVENTION

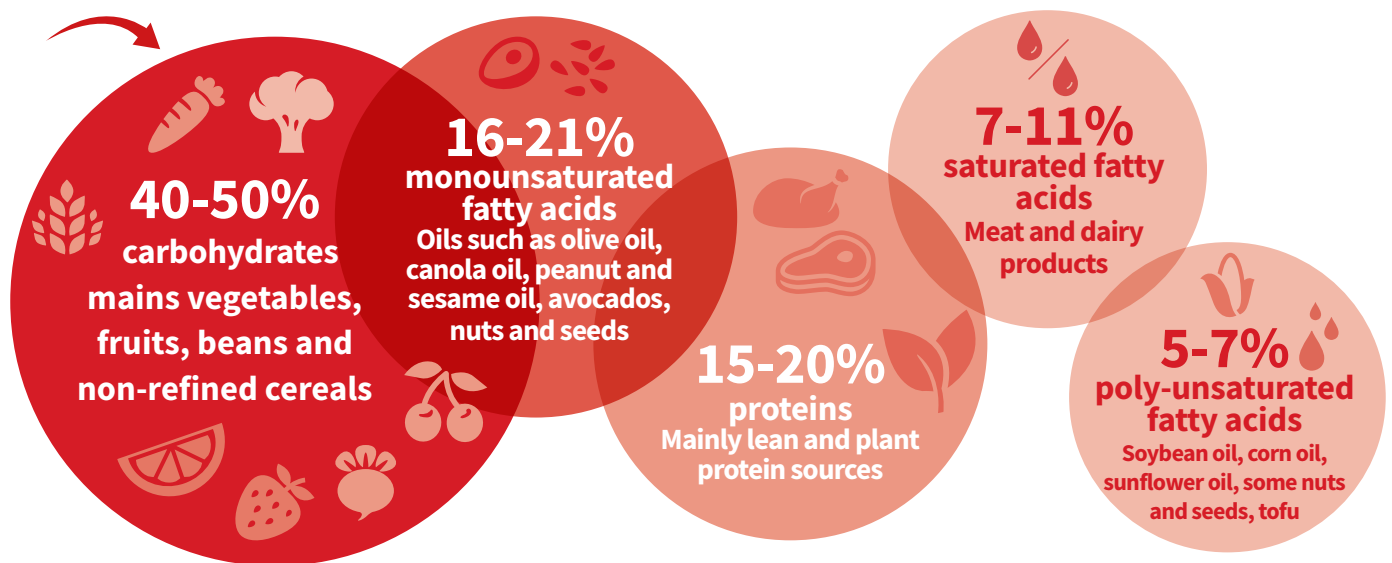
High cholesterol, is a silent condition, which remains undetected unless it is actively sought out. When undetected or when cholesterol is uncontrolled, it leads to an increase in overall CVD risk. This is why the World Health Organization (WHO) has identified the control of cholesterol as part of a Total Risk Approach to preventing CVD as a public health priority. This approach relies on absolute risk of developing CVD over a defined period. The level of absolute risk used to define a ‘high-risk individual’ eligible for primary prevention, including drug therapy, varies between countries.

The Total Risk Approach recognizes that many CVD risk factors may only be moderately raised, but the overall risk is raised because they add up. Therefore, treatment of all risk factors together with healthy lifestyle changes, blood pressure, lipids, and glucose-lowering will produce the greatest reductions in the risk of developing CVD⁽²²⁾. However, FH, because of inherited and lifelong cholesterol levels, is an example of an exception to this rule and should be identified earlier in life.



THE BENEFIT MODEL: The Total Risk Approach is more comprehensive than a single risk approach. However, it is heavily influenced by age and sex (unmodifiable risk factors), and to a much lesser extent, by modifiable risk factors, ie. non-HDL cholesterol, blood pressure, smoking, and diabetes. A new model – the Benefit model – which expands the number of individuals who would be eligible for statin primary prevention therapy by including younger individuals with higher non-HDL cholesterol levels, is currently being developed and tested. ⁽⁴⁰⁾

Promoting healthy nutrition by adapting the traditional Mediterranean-type diet to local customs



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PHARMACOLOGICAL TREATMENT



LDL-cholesterol of > 190 or non HDL-cholesterol > 220 always requires drug treatment after diet intervention⁽⁶⁾. The effectiveness of statin therapy for reducing CVD risk is supported by solid evidence⁽²³⁾. Countries should look to their national or regional guidelines to guide the initiation of statin therapy. These should be informed by the resources available and the effectiveness of treatment in that setting.

Monitoring of patient response to treatment is desirable, especially in cases when non-HDL cholesterol is high to begin with. As cardiovascular risk reduction depends upon absolute lowering for those with high starting cholesterol levels any statin is better than none, with the greatest benefits among those receiving the highest potency treatments. Statins are generally safe and well tolerated and by and large do not require monitoring for side effects. Monitoring cholesterol to assess whether further add-on treatment is needed as well as assessing adherence is desirable.

Other non-statin options including new PCSK9 inhibitors, approaches based on monoclonal antibodies or small-interfering RNA (siRNA) are also available and should be added as needed to achieve the level of cholesterol that is appropriate for the level of risk in the patient. In any case, pharmacological treatment of cholesterol is life-long and must be accompanied by advice and support toward lifestyle modifications.

SECONDARY AND TERTIARY PREVENTION

All patients with a previous CVD event (MI or ischemic stroke) should be considered at risk of recurring CVD events, regardless of non-HDL cholesterol levels, and should be treated with statins. The use of statins as a part of an evidence-based strategy for the secondary prevention of CVD (along with aspirin and other anti-platelet therapies, angiotensin-converting enzyme inhibitors, and beta-blockers) are internationally recognized. In secondary prevention of CVD, treatment with statins should be continued for life.

Sometimes patients, in particular those affected by FH, HoFH Lp(a), do not manage to control their cholesterol levels through traditional pharmacological and non-pharmacological treatments. In such cases, they sometimes undergo lipoprotein apheresis, a non-surgical therapy that removes low-density lipoprotein (LDL) cholesterol and Lipoprotein(a) from the blood. The procedure is similar to dialysis: the plasma portion of the blood, which contains cholesterol, is separated and run through a machine that removes the LDL. The treatment is performed in specialized centres. It is however a complex and costly procedure, which is not available everywhere.

COMMUNITY VOICES



My name is Cristobal von Unger Pinto. I am 22 years old, Chilean and I study medicine at UBA, the University of Buenos Aires. All my life I wanted to study medicine, and Argentina opened the doors for me to fulfill my dream.

Even if studying is something that takes me a great part of the day, I am a soccer fan and I try not to miss any game of my team “Universidad de Chile”, or Chile matches.

I am the third generation of my family with known hypercholesterolemia, my grandfather, my father and now me. I knew I had this disease in 2008, after my dad had his first heart surgery. To take precautions, my brothers and I took the respective tests to see how our blood cholesterol levels were, which, in my case, were abnormal. I had more tests done to see if I suffered from the same disease my father has, and unfortunately that was positive.

It was difficult at first. For a 10-year-old, it is hard to understand why he should no longer eat certain things or why “from one second to the next” there were things he could no longer eat. I couldn’t forget about the new way of eating. I was 10 years old, all birthdays, had hot dogs, pizzas, fries... The first years were the most difficult, I was kind of ashamed. I did not want to explain and did not want to be impolite. But as time goes by, you understand, you learn new things and I realize how lucky I was to have the possibility of receiving treatment since so young, luck that not everyone had.

My life changed in many ways. On the one hand, leave all foods with fat and cholesterol. I was shocked when, starting my new diet, I learned how much food we eat daily without realizing how harmful it can be. That on the one hand is motivating.

Another change was the increase of the number of hours of physical exercise, a fundamental factor to be able to lead a healthy life. As I said, at 10 years of age it is difficult to understand, but with the help of my family, friends and obviously my great doctor,

I was ‘catching the rhythm’ and also learning why I was making this big change.

Today, hypercholesterolemia is a disease that people overlook, in my opinion due to a great misinformation that leads people not to give the problem the proper importance. It is basic that people know about this disease, know its risks and also how to avoid them. As I said before, this is a disease that has been in my family and that I began to treat myself when I was very young, so I, during the past 12 years as a patient, have learned and informed myself as well as the people around me, but it’s not enough.

I believe that we patients, as well as health personnel and all the persons who know about the subject, have the task of transmitting the information to people and, in this way, help to prevent or reduce the giant number of annual deaths due to heart attacks. It is incredible, but overweight and obesity seems more to be an issue of aesthetics than a real problem that affects a big part of our population today. Learning to lead a healthy life is not an easy task, but it is a worthwhile one.

“

I was shocked when, starting my new diet, I learned how much food we eat daily without realizing how harmful it can be

”



Get checked now, know FH, and take control of your health.



My name is Chyrel, I was born in Bekaa, Lebanon in 1990. I'm the middle child of three kids, I have two brothers the oldest Charles 34, and the youngest Richard 28. My mother is a teacher in a public high school, and my father who had worked his entire life in Saudi Arabia passed away due to a cardiac arrest at the age of 57, in 2007.

I've lived my entire life here in Lebanon aspiring to be a strong, independent, and successful woman in life and my career. I've studied Advertising and Marketing and have been working in the field since 2013. You can say that I've led a pretty normal life studying, traveling, living, and loving, except I had an extra little baggage to carry with me through life which is FH.

At the age of nine months old, whilst bathing me, my mother noticed yellowish little xanthelasma on my knees, elbows, and wrists. Not knowing what it was or if it is anything serious, she contacted my paediatrician back then, after running several blood tests the doctor couldn't believe the results that a baby could have such raised cholesterol levels and repeated the tests three times. So, after referral to an endocrinologist,

we got the diagnosis that it's FH, HoFH. The Journey began. Dietary changes and adaptations, switching to light powdered milk, medication in baby bottles, never-ending blood tests, and medical research, not even knowing what Kinder Surprise tasted like.

Everything had to be altered. I even had to carry my own personalized homemade bag of snacks on playdates.

Two years later my little brother was born, following doctors' orders, they got him checked out immediately to find out that he as well has HoFH, I had a companion you might say.

In 1998, we first found out about a possible LDL apheresis treatment, I was eight years old when I had my first experience with the apheresis, and it was horrible. I was somehow traumatized by it, I had no idea what they were doing, I didn't understand, and no one really knew how to prepare me mentally for such a thing, so I refused to go back.

Then a year later with the support of my mother and my family, and my little brother being there with me experiencing the same thing, I went back, and we haven't missed a session since then. It changed our lives for the better, it gave us a ray of hope that we can lead a normal life, our cholesterol levels are under control and we get checked regularly.

Early diagnosis is extremely important, it allows us to live with FH the same way we live life and to understand what we have better and explore our options before it's too late. Same as in Life, living with FH can impose some obstacles that hold back a patient from living a free life.

I've been through a lot physically and mentally; I was diagnosed with anxiety at the age of 24 and had my 1st panic attack during my LDL apheresis session. My brother had an Open-heart surgery when he was 26, he had a lot of complications afterward as well.

All that we have been through has affected our life and our view on things. What I really want to focus on is not only the physical

impact FH has on a person's health, but also on the mental and emotional struggles an FH patient could experience.

I want to share my current situation and what I am facing that is somehow affected by FH.

So, as I said before, I live in Lebanon and most of the people probably know what is happening here now, an ongoing economic crisis and the explosion we've experienced took a toll on all the Lebanese people. A lot of us have lost our jobs and still are unemployed whilst the others are still getting paid the minimum wage. As an ambitious young adult, my brother and I decided to take action regarding our future and decided to apply to various jobs abroad. Several factors had to be considered before taking any step and are related to us having FH and needing the apheresis treatment since our life depends on it. We can only consider selective countries, we had to research the ways we can cover the treatment's expenses, are we going to be dealing with all this alone? If we stayed in our country would we be able to continue with our treatment in the future?

A lot goes through our minds, and it is burdensome and yes it causes us a lot of worry and uncertainty, but what we are certain of is that living with FH is not the end of the world, it is manageable, it does make you consider certain life choices but it doesn't stop you from living your life the way you want it.

Get checked now, know FH, and take control of your health.

POEM BY ÁKOS GESZTES FROM HUNGARY, 2018

*I had FH I was aware,
but in the past I didn't care.
I stopped all my medication
and developed resignation...*

*Later turned thirty, forty,
had no diet, wasn't sporty.
I was stupid, wasn't clever.
I thought I would live forever.*

*But at the age of forty-two
I had to face the deadly truth
FH without the proper drug
Russian roulette, play with luck.*

*Suddenly stopped my
heart to beat,
I fell into coma for a week.*

*There were plenty open issues,
Survived enough active tissue
In my heart and brain to live,
Or is it the time to quit?*

*Does my heart need
transplantation?
Did I reach the final station?
When will I be conscious again?
Will I regain fully my brain?*

*All relatives and my good friends,
Wife, daughter and both parents
Till the limits of their faith
Brought me back with their pray.
I really don't know how and why,
But at the end I've survived.
Out of body circulation
Saved my life and meant salvation.*

*Thanks to God and to my treaters
I am back and fully eager
To share my story with the people.
FH patients! Take your statins
to prevent Heart attacks and
CV events.*

*My ribs were broken many places,
And the fear showed ugly faces.*

*Whatever I felt in the chest,
I was afraid it was the next
Heart attack, the one that kills.
That's why we should take our pills.*



Gesztes Akos

18



My name is Conrado G. Manalad Jr, I am a 64 year-old paediatrician from the Philippines.

I have strong family history of hypercholesterolemia on both paternal and maternal side. We are nine brothers and sisters. My eldest brother died at the age of 56 due to Myocardial Infarction. One of my brothers underwent angioplasty when he was 72 years old. He passed away last April 4, 2020 because of Covid-19 Infection. My eldest sister, also a Doctor of Medicine in the US, underwent CABG surgery and Angioplasty post CABG. One of my brothers

suffered from Stroke, but recovered. All of my siblings have hypercholesterolemia. Many other members of my family, both on my father's and mother's side, have similar health issues.

When I was about to enter medical school, I discovered that I was hypertensive. I was 21 years old then. I had my blood chemistry done for the first time and I discovered that my blood cholesterol level was a little higher than normal. I consulted a Cardiologist and I was given a beta blocker as anti-hypertensive. I was not given any anti-cholesterol medication then. The slightly increased cholesterol did not bother me at all. I was not mindful of what this could do to my body. I was a medical student then and I had no dietary restriction. I ate whatever was available on the table and, because of my hectic schedule, I seldom exercised. After graduation from medical school, I went into residency training. I was still not concerned then with my increased

blood cholesterol level. After graduation from residency, that was the time when I became conscious and concerned about my cholesterol level. This was triggered by the death of one of my cousins on my father side who at the age of 45 years died of massive MI. This was followed by the death of a nephew also on my father side with MI. He was just 34 years old, also a Doctor of Medicine.

After a long time of not having blood chemistry done, I had myself tested. My cholesterol level was about more than 300 mg %. I consulted Dr. Rody Sy, a cardiologist. He gave me maintenance anti-hypertensive and anti-cholesterol drug. This time, I became more conscious of the food I ate. I also engaged in exercise but not on a regular basis since that was the time when I became busy with my practice. Pharmacological treatment with Atorvastatin allowed me to control cholesterol levels.

Sometime in 2000, I experienced shortness of breath and easy fatigability. I had a Myocardial Perfusion study. Result showed areas of my myocardium with ischemia. I underwent angiogram which showed blocked coronary vessels. I underwent

angioplasty. Two metal stents were inserted in the blocked arteries. The drug-eluting stent was not yet available at that time. After my angioplasty, I avoided eating high cholesterol foods, I exercised regularly and I tried to avoid stress as much as possible.

My cholesterol level was maintained at a normal level with Atorvastatin at 40 mg OD. In 2003, I, again experienced shortness of breath and easy fatigability. Tests showed that the previously stented coronary vessels were again blocked. At least three vessels were significantly occluded. I underwent coronary artery bypass grafting (CABG) operation. It was a quadruple bypass. Four of my coronary vessels were bypass and grafted. In 2018, I experienced easy fatigability again. I underwent an angiogram with possible angioplasty. Result showed that one of my native coronary vessel was significantly occluded. A drug eluting stent was inserted to the occluded portion of the vessel. Luckily, all the grafted vessels are all functioning well with no significant occlusion.

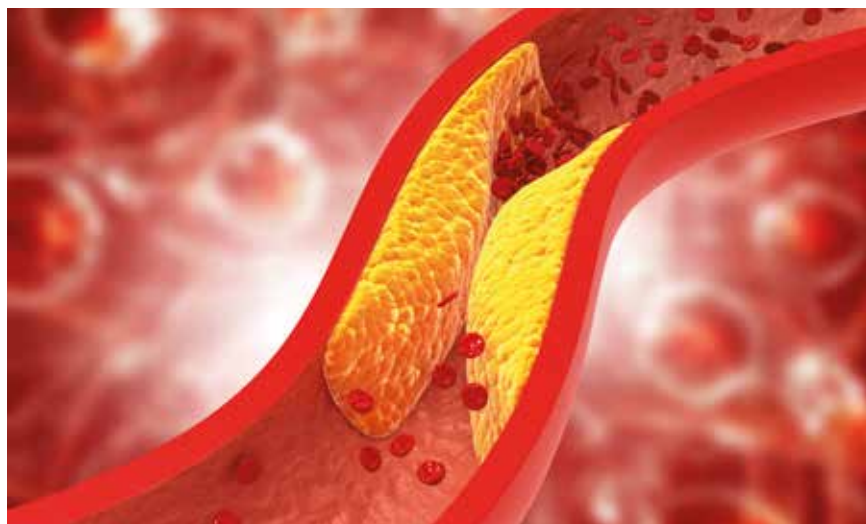
I know that I have familial hypercholesterolemia. All my siblings have it, as well as most of my cousins on both paternal and maternal side. With this knowledge, I know I have to take control of how to manage my FH. My daily life was not affected much by hypercholesterolemia except for the dietary restrictions that I imposed upon myself.

Coping with my disease requires a lot of discipline:

1. I am very religious in taking my anti-cholesterol drugs.
2. Very seldom do I eat food high in cholesterol content. If I cannot avoid eating oily food, I take Orlistat before my meal.
3. I do cardio exercise regularly. Treadmill for one hour most of the time or walking. If I can not do treadmill or walking, I do Zumba with my wife at home with the YouTube videos as our guide.
4. I try to avoid stress as much as possible.
5. I always find time during the day to relax despite my busy schedule.

My personal call to policy-makers:

- 1. A legislation that requires early screening of hypercholesterolemia should be introduced.**
- 2. Education of children on the negative consequences of high blood cholesterol should be taught in school.**
- 3. Paediatricians should take an active role in screening high risk children for hypercholesterolemia. Children who are obese and those with strong family history for Familial Hypercholesterolemia should be monitored and managed accordingly.**
- 4. Public education via mass media, public forum, etc should be done by the Department of Health on a regular basis. The number one cause of mortality in the Philippines is Ischemic Heart Disease. One of the major culprit is the increase in blood cholesterol. Public education on the ill-effects of hypercholesterolemia can help reduce the incidence of death secondary to Ischemic Heart Disease.**



SUCCESS STORIES

INTRODUCTION

The *WHF Cholesterol Roadmap* published in 2017 identified a series of roadblocks which impede detection, treatment, and management of high cholesterol globally. Among these barriers were low awareness among the general population and health professionals – especially in the case of FH -, poor access to laboratory facilities or trained professionals for cholesterol management, unaffordability of statins for patient households, and low awareness of the importance of persistent adherence to lipid-lowering medication⁽²⁾. In order to overcome these roadblocks, public health interventions ranging from taking action at the population level to targeting individuals are necessary. The following case studies introduce a series of interventions in different settings that have positively contributed to the prevention, detection, and control of high cholesterol.

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WHF ROUNDTABLES FACILITATE DISCUSSION AND INFORMATION FLOW

WHF Roundtables provide a national forum for stakeholders in cardiovascular health to identify barriers to and solutions for secondary and primary prevention of CVD and then develop a national plan of action. These Roundtables and their outcomes are an efficient means to inform stakeholders such as Governments and policymakers, Healthcare professionals, Academic and research institutions, NGOs, health activists and advocates and Corporate entities.

In Spain, WHF joined forces with the Spanish Heart Foundation and the Foundation for Familial Hypercholesterolemia to convene a series of Roundtables for a multi-stakeholder group of experts representing different scientific bodies and patient associations, and the Deusto Business School Health (DBS Health), to brainstorm how to address the urgent situation of cholesterol.

The meetings culminated in a press conference in Madrid advocating for the need to improve the approach to hypercholesterolemia by positioning it as a first-level cardiovascular risk factor in Spain and confirming this through a Joint Declaration on the *WHF Cholesterol Roadmap* in Spain.

The press conference had extensive media coverage, with headlines capturing the impact of FH and the need for urgent actions, such as “Cardiologists demand a national plan to combat hypercholesterolemia,” “More than 20% of deaths attributable to cardiovascular diseases are caused by hypercholesterolemia,” and “Experts advice on the gravity of hypercholesterolemia and its neglect in Spain.”



Spain

Similar Roundtables on Cholesterol were organised in Mexico, Colombia, Saudi Arabia, and the Philippines.



Philippines

22



PREVENT

Denmark plays a pioneering role in trans-fat policy



CHALLENGE

Trans-fats are naturally found in dairy and meat products but also generated by industrial processes to produce hard fats from vegetable oils. Consumption of trans-fats is associated with an increase in non-HDL cholesterol levels and a decrease in HDL cholesterol and an increased risk of NCDs, including cardiovascular disease, such as heart disease and stroke, and diabetes⁽²⁴⁾. Replacing industrially produced TFA with healthier oils and fats is cost-effective and feasible, and can be done without changing the taste of food or its cost to the consumer.

RESPONSE

Denmark was the first country worldwide to introduce a policy on trans-fats in 2003⁽²⁵⁾ following the publication of studies which estimated that 50,000 Danes were at high risk for CVD due to their intake of trans-fat. Legislation setting the upper limit for artificial trans-fats at 2g per 100g of fat (2% of total fat) was presented to Parliament in 2003 and approved shortly after. It came into force in 2007 after the Danish government convinced the EU that the measure was justified in the interest of public health⁽²⁵⁾.

OUTCOMES

Limiting the trans-fat content in foods through legislation has been most efficient in reducing or banning trans-fat in the food

supply. It is also the only option effective in reducing all population groups' intake, including high-risk groups such as low-income populations⁽²⁵⁾.

Today, trans-fats are 'virtually eliminated' from Danish food. In quantitative terms, the ban's impacts seem to occur over the long run⁽²⁶⁾. After the ban, Denmark's CVD death rate started to drop slowly but persistently. By 2015, the observed CVD death rate in Denmark was 53 age-standardized deaths per 100,000 inhabitants, compared to 83 in a control population. This implies that the TFA ban is associated with 30 fewer deaths per 100,000 inhabitants⁽²⁶⁾.

Overall, heart disease mortality rates decreased by 70% between 1980 and 2009, likely at least partly due to Denmark's efforts to address multiple CVD risk factors, including TFA intake. This is the largest decrease in the European Union (EU)⁽⁴⁾.

Key success factors included multi-stakeholder support within the Government, support from the wider community (population and media), and manufacturer's readiness for change (in particular the Danish margarine industry).



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THAILAND

Thailand enacted a ban on partially hydrogenated vegetable oils (PHOs) in 2018 to stop the production and importation of Western-style foods high in PHOs due to the negative impact on health of TFAs from PHOs. Thailand used a supply chain approach to policy implementation, working with the small number of PHO producers in the country to adapt their manufacturing processes. Key success factors included accurate data collection on TFAs in the food supply, smooth communication among stakeholders – including the Government, food and oil producers and importers, and academic researchers – and manufacturers' readiness for change⁽⁴⁾.

CHILE

Chile used a two-step policy approach, first enacting a TFA labeling regulation in 2006 followed by a TFA limit in 2009 of two percent of total fat in all foods. Factors that influenced Chile's policy success include its engagement of key external stakeholders throughout the process, such as well-respected academic and industry leaders, multi-stakeholder coordination within Government, situating the TFA policy within a larger healthy eating policy framework, and government capacity to implement the policy⁽⁴⁾.

In 2011, The World Health Organization (WHO) called for eliminating trans-fats from the global food supply in response to the rise in the prevalence of NCDs and identified it as a 'best-buy' public health intervention for low- and middle-income countries. In May 2018, it called for the global elimination of industrially-produced TFA by 2023 and released the REPLACE action framework⁽²⁷⁾.



DETECT

Slovenia introduces universal screening for FH



CHALLENGE

24

Familial Hypercholesterolemia (FH) remains largely undiagnosed due to a general lack of public and health professional awareness ⁽²⁸⁾. Globally, it is estimated that only 10% of individuals affected benefit from a timely diagnosis. As a result, individuals with undiagnosed and/or untreated FH have up to 100-fold increased risk for developing atherosclerosis and CVD in early adulthood ⁽²⁹⁾.

RESPONSE

Various screening strategies to identify children with FH exist – most rely on selective or cascade (within family) screening. These approaches, however, fail to identify patients without a known family history of high cholesterol. This led Slovenia (population two million) to initiate universal screening for hypercholesterolemia in five-year-old children in 1995.

Screening was gradually implemented nationwide.

It consists of a three-step approach:

- (1) universal screening for hypercholesterolaemia in preschool children at the primary care level;
- (2) genetic FH screening in children, referred to the lipid clinic as per clinical guidelines;
- (3) additional cascading screening of family members ⁽³⁰⁾.

OUTCOMES

Screening was gradually implemented nationwide during the programmed visit of all children aged five years at the primary care paediatrician, and as shown by the Slovenian national FH

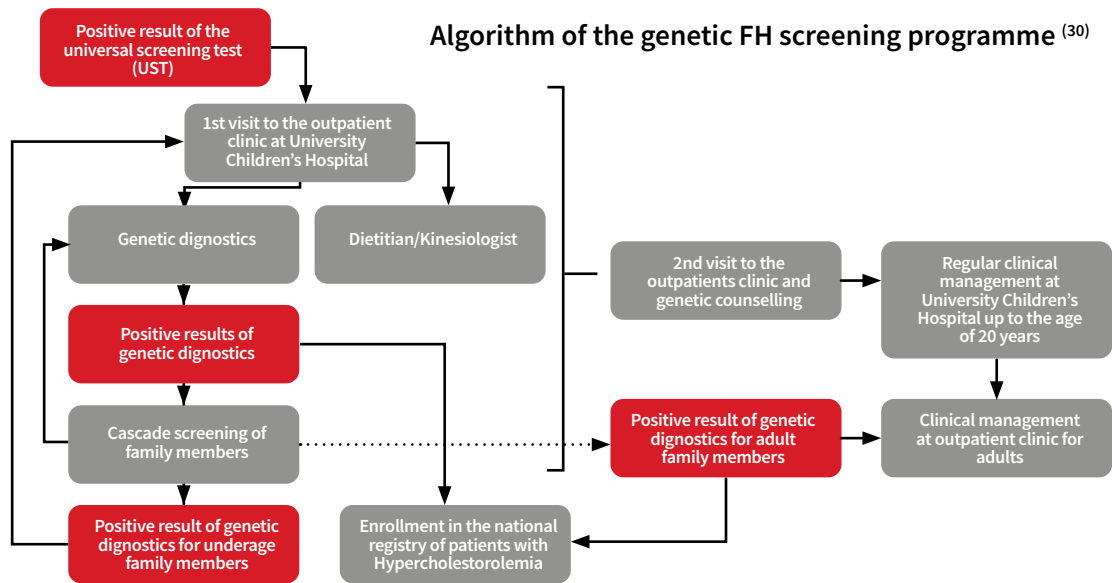
registry, the programme now reaches approximately 91% of the population of around 20,000 children each year.

In recent years, for every 1000 children screened, 2.3 children were identified as having positive screening results for FH and 3.4 children as having possible FH. The prevalence was 1/273 for possible FH, and 1/409 for confirmed FH. The prevalence of homozygous FH was estimated at 1/297,000. Thus, based on recent data, most children with FH are now diagnosed in each generation.

For every child who tests positive, there is now a possibility to provide cascade FH genetic testing to the parent with higher levels of cholesterol (or to both if not clear). According to the Slovenian Heart Foundation, the programme has significantly increased the proportion of diagnosed FH patients from 1% to around 20% in the last 15 years. The direct costs per new genetically confirmed familial hypercholesterolemia case reach approximately \$1,015.

Key success factors included the fact that Slovenia has a solid network of primary care paediatricians and a health insurance system that provides almost universal coverage. Infants and children are entitled to regular preventive examinations, which also include vaccinations and health education ⁽³¹⁾. Substantial efforts were made to increase the awareness of paediatricians to ensure that all children are actually tested. In addition, there is only one centralized referral center for children with hypercholesterolemia, thus enabling a more accurate diagnosis of FH and further improved implementation of universal FH screening programmes. Support from policy-making organisations has also contributed to the success of the programme. Finally, regular education about universal FH screening is part of the medical school curriculum and paediatrics residency and regularly presented to health care professionals at workshops, symposia, and on other occasions.





“Early identification of patients with Familial Hypercholesterolemia is one of the key factors in preventing premature cardiovascular events. Patients in whom Familial Hypercholesterolemia manifests as early as childhood are among the most at risk for such complications. Thus, universal screening of all children at the age of five in the Republic of Slovenia is an extremely useful and effective method to find this population as soon as possible. Last but not least, this program is important because many times after analysis in children, we also find carriers of this disorder among their adult blood relatives who have not yet been identified as patients with familial hypercholesterolemia. Thus, from the very beginning, the Slovenian Heart Foundation supports the program of screening children and finding those who have this form of metabolic disorder.”

DR. MATIJA CEVC
(PRESIDENT OF THE SLOVENIAN HEART FOUNDATION)



“Due to the programme, the detection of individuals with FH in Slovenia has increased significantly. Fifteen years ago, only 1% of individuals with FH were identified, but today we are approaching 20%, which is certainly thanks to this program. The real savings, however, are related to treatment and lifestyle changes. At the Ministry of Health, we continue to follow the program; the key to long-term support will be the assessment of saved healthy life years (HLY) and reduced mortality due to FH.

STATE SECRETARY
MINISTRY OF HEALTH



TREAT

Dutch pharmacists are actively involved in medication adherence ⁽³²⁻³⁴⁾

CHALLENGE

Lipid-lowering medications, including statins, are among the most commonly prescribed treatments. Even though adherence to such medications has been associated with a 25% decrease in CVD risk, treatment discontinuation is quite common ⁽³⁵⁾. 30% to 50% of patients discontinue their statin treatment within one year ⁽³⁵⁾. Improving adherence is therefore key to achieve optimal patient outcomes and to decrease health care costs.

RESPONSE

The Dutch Medication Monitoring and Optimization (MeMO) programme enhances the role of pharmacists in monitoring and supporting patients' adherence to treatment. Participating pharmacies use an information system, which stores the medication history of enlisted patients. When patients redeem their first prescription (eg. statins), the pharmacy team provides verbal and written information about the treatment, the time it will usually take to notice the medications' effects, potential side-effects, and instructions on proper

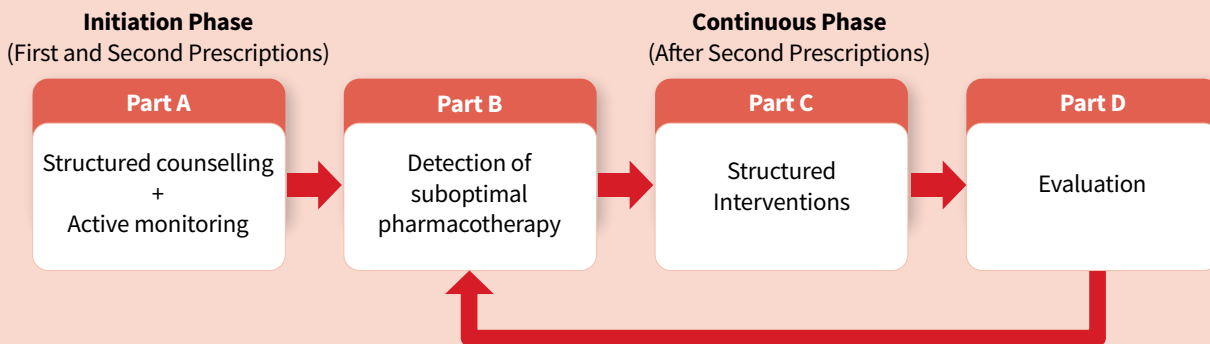
administration. When patients redeem their second prescription, counselling on drug use, side effects, beliefs and expectations, and possible discomforts, is provided.

Patients who do not redeem their second or third prescription are contacted to discuss medication problems or administration difficulties. After their third prescription, patients enter the continuous phase of the programme. Pharmacists perform database searches to detect suboptimal pharmacotherapy and contact patients when an anomaly is detected. The interventions are personalised and look at both medication (discussing side-effects, benefits of adherence etc) and lifestyle (advice on smoking cessation, exercise, diet). Pharmacists may also refer patients to a physiotherapist or dietician.



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MeMo* Initiation, Monitoring, Intervention, and Evaluation Phases ⁽³⁹⁾



*MeMo = Medication Monitoring and Optimization program

OUTCOMES

This pharmacist-led programme significantly improved patient adherence to treatment. After one year, only 13.6% of the patients had stopped their treatment, versus 25.9% in the group which was not in the MeMO programme. After two years, the discontinuation rate in the MeMO group was reduced even further, to less than 5%.

In addition, most patients are highly satisfied with the programme and with the information provided by the pharmacy. The majority

of patients (74%) feel that their knowledge has increased on the medication effectiveness and administration and on the importance of therapy adherence. According to a model using 1,000 primary (40%) and secondary (60%) prevention patients, the MeMO program resulted in a reduction of seven non-fatal strokes, two fatal strokes, 16 non-fatal myocardial infarctions (MI), seven fatal MIs, and 16 revascularizations over patients' lifetimes. Finally, the programme was shown to be cost-effective.



USING TEXT MESSAGING TO SUPPORT LIFESTYLE CHANGES

CHALLENGE

Interventions which modify lifestyle factors are among the most effective, but are poorly adhered to.

RESPONSE

In Australia, 710 patients with documented Coronary Heart Disease (CHD) were enrolled in a text message-based prevention programme. Participants received four messages per week during 24 weeks. Messages were semi-personalized and provided advice, motivation and information which aimed to improve diet, increase physical activity and encourage smoking cessation if relevant.

EXAMPLES:

SMOKING: [NAME], for many it may take several attempts to quit, so keep trying.

NUTRITION: Did you know that 90% of people don't eat the recommended daily intake of vegetables (five serves a day)?

PHYSICAL ACTIVITY: Walking is cheap. It can be done almost anywhere. All you need is comfortable shoes and clothing.

GENERAL INFORMATION: Studies show that stress, worry and loneliness can increase the risk of heart disease. Please talk to a health professional if you need help.

OUTCOMES

This programme showed that a simple, low-cost automated program of semi-personalized mobile phone text messages supporting lifestyle change compared with usual care led to significant differences in non-HDL cholesterol levels, systolic blood pressure, and BMI in patients with CHD. After six months, non-HDL cholesterol levels, systolic blood pressure, and BMI were all significantly lower in the intervention group compared with the control group (difference in LDL-C level, -5mg/dL ; difference in systolic blood pressure, -7.6mmHg ; difference in BMI, -1.3), as were the majority of other measured cardiovascular risk factors. Intervention participants were also substantially more likely to exercise regularly and to stop smoking.

Key success factors included the high degree of acceptability of the intervention. In addition, text messages can be sent quickly, at low cost and can be easily automated. Most people across all income groups own a mobile phone, so a text message-based intervention can have substantial population effects. A feature of e-health or mobile health interventions is the potential for scalability owing to affordability and ability to deliver personalized services.



MEASURE

Turkey builds a nationwide registry for FH

CHALLENGE

In Turkey, the prevalence of FH is unknown; however, extrapolating data from different nations and given the relatively high prevalence of consanguinity (23%), HeFH prevalence is estimated to be 1 in 200 people, which suggests that at least 429,000 people are affected ⁽³⁶⁾. This high ratio may be one of the major reasons for the high prevalence of premature myocardial infarctions in the country. Until recently, Turkey had neither a national FH registry, nor a national screening program to detect FH.

RESPONSE

In line with a call to action by the European Atherosclerosis Society (EAS), the Turkish Society of Cardiology (TSC) endorsed implementing a series of FH registries, called A-HIT1, 2, and 3. A-HIT1 is a nationwide survey of adult HoFH patients undergoing low-density lipoprotein (LDL) apheresis (LA). A-HIT2 documents adult FH patients admitted to outpatient clinics. Finally, a third registry is planned to document patients admitted to coronary care units with a diagnosis of premature myocardial infarction ⁽³⁹⁾.

the lack of a standardized approach to LA and to low awareness of LDL targets among attending physicians in the LA centres. A-HIT1 also showed that adult patients with HoFH undergoing LA experience significant impairment of QoL with an increased risk of depression ⁽³⁷⁾.



The data collected through these two nationwide FH registries was instrumental in assessing the current situation of FH detection and care in Turkey. These results will contribute to a better understanding of FH in Turkish patients and can now be used as a guide to establishing a national policy for the diagnosis and treatment of FH.

Results of A-HIT registries were shared and interpreted with the study sites and presented at cardiology congresses, thus increasing awareness among cardiologists and hematologists who conduct LA in Turkey. In 2019, the Ministry of Health established a new project to standardize primary cardiovascular care and risk factor management all over the country. A screening and follow-up web-based programme and management algorithm including FH were prepared and integrated into e-pulse, the online family physician-patient follow-up programme. And through a trainees training program, all primary care physicians (n=24,671) are now educated for CV risk factors and care including FH in detail. Increased awareness among family practitioners is due to increase the early diagnosis of FH.

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OUTCOMES

A-HIT1 and A-HIT2 were the first two nationwide FH registries implemented in Turkey. They provided critical evidence on the real-life management of Turkish FH patients. Both registries revealed the lack of effectiveness in FH management, even in specialized centers. A-HIT1 shed light on a long delay between diagnosis and initiation of LA in HoFH patients in real clinical practice. It also revealed that most patients experienced ineffective LA and failed to reach LDL targets, perhaps due to

KEY SUCCESS FACTORS

Key success factors in this programme included sharing data with continuous educational meetings among secondary care physicians; implementing FH into the standard of care of primary care physicians; collaboration of TSC with the Ministry of health; enthusiasm of the Lead investigators of the A-HIT studies and the FH project; partnership with patient advocacy groups. The support of physicians in the diagnosis of FH is also a key factor in persuading policy makers and medical societies to take action to increase the awareness of FH.

For instance, an awareness campaign will only show results if screening and treatment are then available, accessible and affordable. Similarly, as shown in Slovenia, implementing universal screening will not work if doctors are not informed/aware that testing should be performed as part of their routine examinations. Conversely, a programme which is aimed at reimbursing a treatment will not succeed if patients are not screened and remain undiagnosed, or if they do not adhere to treatment.

Finally, measuring outcomes is essential to understand what works and what doesn't and to inform programme adaptation and continuation/discontinuation.

OVERALL ASSESSMENT

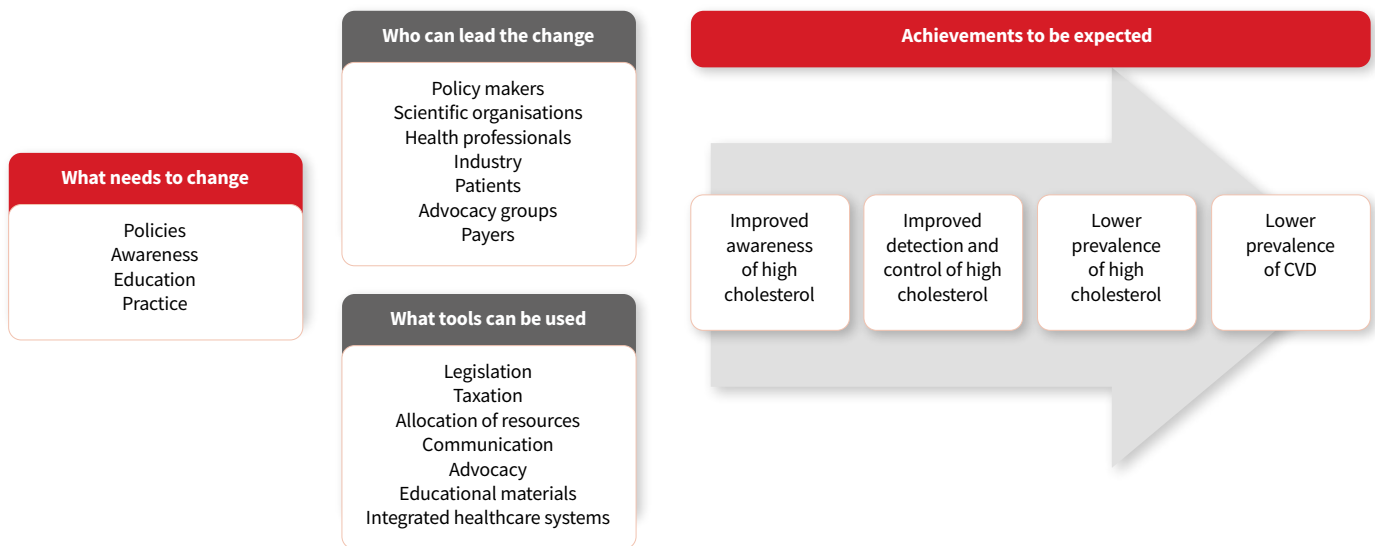
A lesson that can be drawn from these successful programmes from around the world is that even if they focus on one aspect of the OPERATE change framework (inform-prevent-detect-treat-measure), they also consider other dimensions.



CALL TO ACTION

FRAMEWORK OF INTERVENTION

Preventing, detecting, treating and controlling raised blood cholesterol is a multifaceted undertaking. As outlined in the figure below, there is a need to identify the areas where change is needed (box 1), the stakeholders who may be apt to lead the change (box 2) and the most adequate tools to support the change (box 3) to achieve desired outcomes (box 4).



O-P-E-R-A-T-E



inform



Prevent



dEtect



tReAT



mEasure

The OPERATE change framework (inf**Or**m **P**revent **dE**tect **tRe**AT **mE**asure) presents a range of recommendations aimed to drive action and make progress towards achieving better awareness, prevention, detection, treatment and control of raised blood cholesterol. Recommendations echo and reinforce recommendations from the 2017 WHF Cholesterol Roadmap⁽²⁾, from the 2020 Call to Action to reduce the burden of FH⁽³⁾ and the NCD Alliance⁽⁴⁾.

As illustrated in the table on the next page, achieving desired outcomes is a shared responsibility of individuals, healthcare professionals and the community and health system at large.

Recommendations included in this document however focus on possible actions in terms of policy-making rather than those related to individual behaviours or professional practice.

Selected actions to achieved desired outcomes, by stakeholder

	INFORM	PREVENT	DETECT	TREAT	MEASURE
Individuals	Seek trustworthy health information	Healthy eating Limit consumption of foods rich in saturated fats/trans-fats	Attend regular preventive screenings	Adhere to long-term treatment	Monitor individual health parameters
Health professionals	Discuss lifestyle as a standard of care	Prescribe specific diet and exercise recommendations to patients	Assess patient risk (eg. Total Risk Approach) and screen	Follow up-to-date treatment guidelines Adopt a patient-centred approach	Track patient parameters Participate in national registry efforts
Community/health system	Conduct public health education campaigns to raise awareness	Regulate/abolish the use of trans-fats in industrial foods	Stage screening campaigns Provide point-of-care testing	Ensure availability, affordability and accessibility of treatments	Implement reliable, simple, and fit-for-purpose surveillance systems for monitoring disease burden

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Priority interventions should focus on limiting the occurrence of high cholesterol and promoting affordable prevention and treatment of high cholesterol. The interventions supported in this document echo and reinforce recommendations included in 2017 WHF Cholesterol Roadmap and in the 2018 Global Call to Action on Familial Hypercholesterolemia.



High cholesterol is a largely silent disease, which causes no symptoms. As a result, it often remains unnoticed. Even when diagnosed, high cholesterol is not systematically treated, and it is often poorly controlled. This may in part be attributable to a lack of screening, lack of access to care and medications, but it is also due to frequent non-adherence to treatment by patients, due to forgetfulness, lack of awareness of the importance of treatment adherence, concerns about medication safety/quality or fear of side effects. Low physician and healthcare workers awareness is also a reality, in particular with regard to FH.

WE THEREFORE URGE GOVERNMENTS TO:

- Conduct campaigns to raise awareness among health professionals and the public of the importance of screening for raised cholesterol and possible FH.
- Conduct campaigns to provide balanced information to the public and to health professionals on the safety and efficacy of cholesterol treatment with statins.
- Foster the use of novel technologies such as Apps or text messaging to remind and support patients toward treatment adherence.
- Raise awareness of the importance of severe hypercholesterolemia and FH as a public health issue – by targeting the general public, educational institutions, the medical community and healthcare delivery systems.

WHF COMMITMENT

- Contribute to raising awareness through international disease days (eg. World Heart Day, FH Awareness Day) and other impactful events.
- Produce, disseminate and regularly update WHF Roadmaps to identify potential roadblocks on the pathway to effective prevention, detection and management of CVD, as well as evidence-based solutions to overcome them and support local/national implementation by organising country-specific, action-oriented Roundtables to meet the specific needs of individual regions and nations in fighting cardiovascular diseases.
- Collect and disseminate educational materials, best practices and success stories across disciplines and regions.



Prevent

Eight risk factors – high blood pressure, high cholesterol, tobacco, high blood glucose, low fruit and vegetable intake, lack of physical activity, high body mass index, and alcohol – account for 61% of cardiovascular deaths. Combined, these same risk factors account for over three quarters of Ischaemic heart disease. Like many other major NCDs, high cholesterol can be prevented by intersectoral approaches to reduce exposure to these risk factors, leading to a significant increase in global life expectancy ⁽¹³⁾.

The World Heart Federation therefore urges governments to shape policies that ensure an environment that is conducive to healthy living. Governments can do so through legislative action, policies, programmes and campaigns that encompass tobacco, alcohol and unhealthy foods, and an environment which fosters safe physical activity. Such initiatives will not only have a beneficial effect on cholesterol levels, but also on other risk factors such as hypertension and associated conditions such as diabetes and obesity.

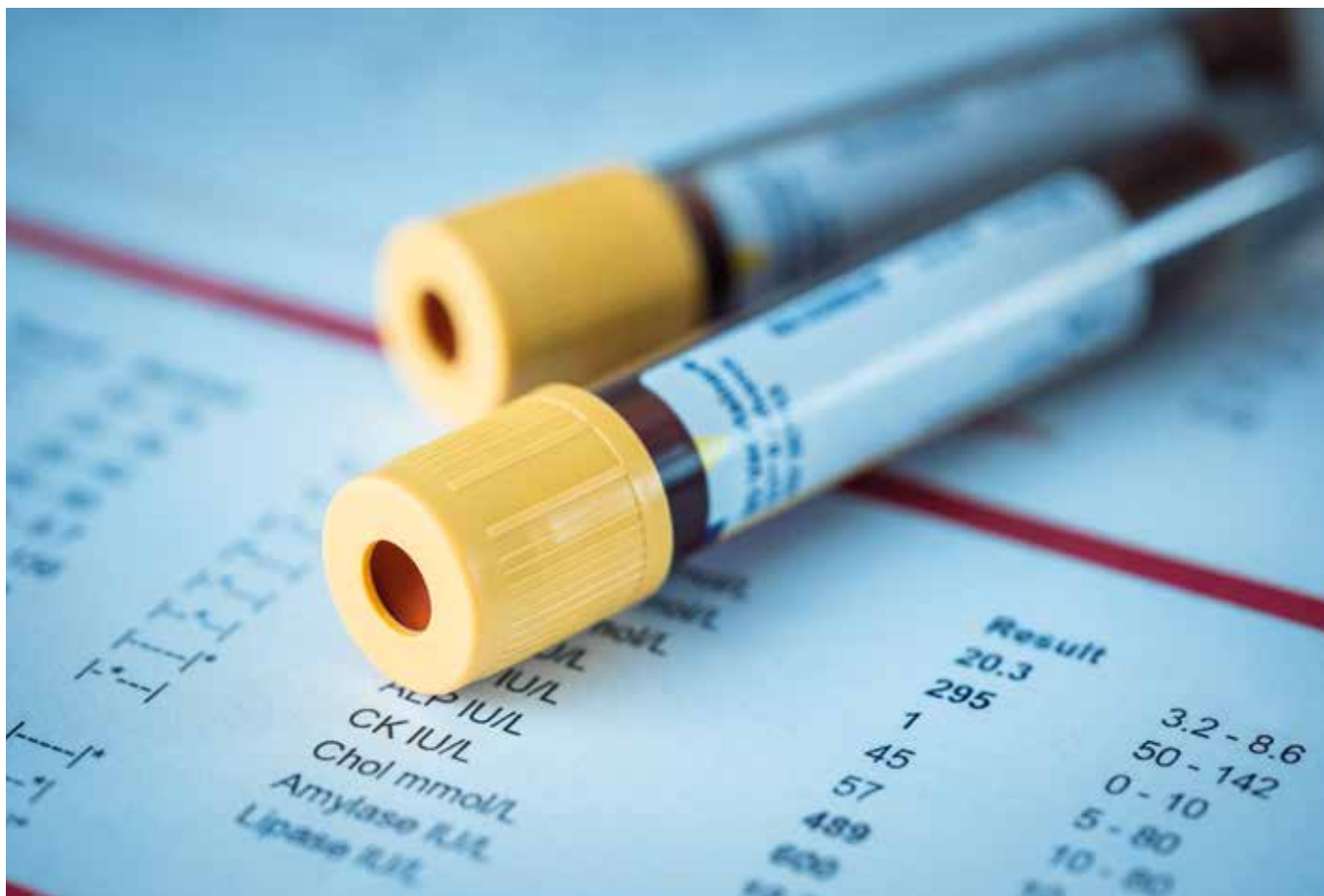
WE THEREFORE ASK GOVERNMENTS TO:

- Support food reformulation efforts, in particular with regard to eliminating artificial trans-fat.
- Follow WHO recommendations to enact a mandatory 2% limit on industrially-produced TFAs in foods or to ban PHOs. The WHO's REPLACE action package and technical support in country should be leveraged by policymakers to protect their populations from the health harms of TFAs.⁽⁴⁾
- Embed TFA elimination in a broader, coordinated approach to improve diet and nutrition and reduce NCDs to maximise the impact of TFA policies on NCDs.
- Introduce taxation on unhealthy products such as unhealthy foods and non-alcoholic beverages (such as sugar-sweetened beverages), tobacco and alcohol, and allocating these revenues for advancing the prevention and control of NCDs.
- Fully implement the WHO Framework Convention on Tobacco Control (FCTC), in particular: raising tobacco taxes, introducing comprehensive bans on tobacco advertising and sponsorship, placing large health warnings on packaging and legislating for smoke-free environments.
- Mobilise sufficient resources at national level, in particular by enforcing adequate taxation policies and by entering into carefully selected public-private collaborations.

WHF COMMITMENT

- Advocate for the taxation of unhealthy products (unhealthy processed foods, tobacco, alcohol, sugar) at global, regional and national levels through its network of members and partners.
- Advocate for a global implementation of the WHO REPLACE package and for the inclusion of TFA elimination in a broader, coordinated approach.
- Collect and disseminate examples of best practices and success stories on taxation policies and innovative financing mechanisms.





detect

Because of its silent nature, high cholesterol often remains undiagnosed. A study, for example, identified levels of undiagnosed high cholesterol in countries at all stages of development, ranging from 16% in the USA to 78% in Thailand⁽³⁸⁾. For FH, the situation is even more dramatic, as it is estimated that only about 10% of individuals affected are diagnosed. The lack of facilities to measure cholesterol is another hurdle to detection as facilities to analyse blood samples are not universally available at primary care level.

WE THEREFORE URGE GOVERNMENTS TO:

- Develop simplified national guidelines for whom and how to screen for CVD risk using cholesterol measurement, based on a Total Risk Approach.
- Adapt risk score charts to ensure appropriateness for specific populations.
- Set up point-of-care testing with inexpensive and easy-to-use technologies (e.g., cholesterol test strips).
- Support screening for FH based on country-specificities and guidelines. Screening may be based on cholesterol levels or positive genetic tests. Governments are encouraged to consider, in particular, universal child-parent screening and cascade testing of first- and second-degree relatives.
- Allocate sufficient resources for screening and diagnosis throughout the life-course, and risk stratification beginning in childhood on a fair basis, in the best interests of the child, similar to other genetic conditions.

WHF COMMITMENT

- Support staff education and training through its wide network of members and partners.
- Collect and disseminate examples of best practices and success stories.





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Although high cholesterol can be easily reduced or treated with inexpensive and cost-effective medications, these treatments remain inaccessible to broad segments of the world's population ⁽⁷⁾. Despite the fact that statins – the most commonly prescribed drug to treat high cholesterol – have been included on the WHO List of Essential Medicines for over a decade, their availability and affordability remains a major hurdle for some populations. In particular, adherence is likely to be negatively affected when co-payments are required ⁽²⁾.

In addition, psychological barriers to long-term treatments are not to be under-estimated: patients lack health literacy, do not realize the importance of treatment adherence or have misconceptions about their medications, and therefore stop taking them. Considering the availability of robust evidence that successful treatment can substantially reduce morbidity and mortality from CVD, for instance, leading to a 30% reduction of heart disease over five years ⁽⁸⁾.

WE ENCOURAGE GOVERNMENTS TO:

- Support continuing medical education for general practitioners and nonlipid specialists to improve skills and confidence in prescribing statin treatment, including for FH.
- Define a threshold of LDL-cholesterol above 190 mg/dl as a high risk threshold.
- Support a greater clarification on statin regimens to use to avoid misconceptions surrounding dose and cholesterol-lowering efficacy.

- Ensure affordability of statin and non-statin therapies through free or subsidized drug provision, eliminating duties and taxes on medicines.
- Ensure availability of cholesterol medications in pharmacies and health facilities through local generic drug manufacture.
- Support the use of polypills (combination pill including aspirin, a beta-blocker, a statin and an ACE inhibitor) among certain high-risk groups (e.g., post-MI, diabetics) and statin- non-statin drug combinations in a single pill where available.
- Support the engagement of pharmacists and nonphysician health workers in patient support and counselling for adherence to drug therapy.
- Acknowledge the importance of integrated management of CVD and associated NCDs to improve access to care and efficiency, as well as the need to reinforce integration with existing communicable disease programmes (e.g. HIV, Tuberculosis).
- Allocate sufficient resources for person-centered, available and affordable treatment of FH to prevent premature ASCVD.
- Guarantee the care of severe and homozygous FH, which necessitates specialized centers for diagnosis and management.

WHF COMMITMENT

- Support the education and training of healthcare workers to foster optimal prescription of essential medicines and adherence to treatment.
- Action our networks of members and partners to advocate for the improved availability and affordability of essential CVD medicines at global, regional and national levels.





mEasure

Measuring and tracking progress are key elements to define priorities, adapt strategies, programmes and projects, control progress towards desired outcomes, identify what works and what doesn't, justify the allocation of resources, among others.

WE THEREFORE CALL UPON GOVERNMENTS TO:

- Collect epidemiological data to provide a locally relevant, solid basis to use risk calculators (WHO/ISH, SCORE, Framingham etc) or adapt existing risk algorithms.
- Develop reliable health information systems to monitor health behaviours, risk factors, and morbidity and mortality.
- Implement the WHO Global Monitoring Framework.
- Reach an agreement among governments and intergovernmental agencies upon international standards.
- Monitor stock outages for essential medicines such as statins.
- Financially support the development of FH registries to quantify current practices, identify knowledge-practice gaps, publish metrics for monitoring and standardizing care, identify areas for future resource deployment, dissemination and defining best practices as well as facilitating FH awareness and screening. Patient-centered approaches including patient platforms for data entry and education should be considered, ensuring optimal privacy and confidentiality.

WHF COMMITMENT

- Advocate for the use of evidence-based approaches whenever data is collected, analysed and disseminated.
- Help collect, monitor and disseminate data to track progress through our wide networks of members and partners.
- Actively support a Countdown to 2030 for NCDs and contribute as deemed fit and advocate for the inclusion of cholesterol in UHC and other WHO tools.



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IMPROVING CHOLESTEROL

IMPROVING PREVENTION AND CONTROL OF RAISED CHOLESTEROL



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