Cardiovascular diseases

A handbook for pharmacists

2022

FIP Development Goals

Cardiovascular diseases

FIP Practice Transformation Programme on NCDs

International Pharmaceutical Federation

Colophon

International Pharmaceutical Federation (FIP)
Andries Bickerweg 5
2517 JP The Hague
The Netherlands
www.fip.org

Authors
Dr Inês Nunes da Cunha, FIP Practice Development and Transformation Projects Manager

Prof. Pedro Amariles, Universidad de Antioquia, Medellín, Colombia; Research Group on Pharmaceutical Promotion and Prevention, Universidad de Antioquia, Medellín, Colombia; Associate, Pharmaceutical Care Research Group, University of Granada, Spain

Dr Genuine A. Desireh, FIP YPG Intern and Associate, inSupply Health, Kenya

Dr Victoria Garcia Cardenas, University of Technology Sydney, Australia

Andi Nurul Annisa, FIP YPG Intern, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand; Centre for Health Economics Studies, Universitas Muhammadiyah Purwokerto, Indonesia

Álvaro Sosa-Liprandi, Cardiology Department, Sanatorio Güemes, Buenos Aires, Argentina; President. Inter American Society of Cardiology, Argentina

Lum Zheng Kang, FIP YPG Intern and CEO, Collabring Consultancy Pte Ltd, Singapore

Editor
Gonçalo Sousa Pinto, FIP Lead for Practice Development and Transformation

Figure design
Daria van Beek, FIP Marketing Coordinator

Recommended citation
International Pharmaceutical Federation (FIP). Cardiovascular diseases: A handbook for pharmacists. The Hague: International Pharmaceutical Federation; 2022.

Cover image
© maica | istockphoto.com

Contents

Cardiovascular diseases

FIP Practice Transformation Programme on NCDs

Executive summary

Cardiovascular diseases (CVDs) are the leading cause of death worldwide, with an estimated 17.9 million lives lost each year, according to the World Health Organization (WHO). The term "CVDs" includes different conditions related to the heart and blood vessels, such as myocardial infarction and stroke. Different behaviours are risk factors for the development of these conditions, among which are poor diet, physical inactivity, use of tobacco, alcohol consumption and stress. Therefore, most people who are smokers, are overweight or obese, or have high blood pressure or blood lipid levels are at risk of developing serious cardiovascular health complications.

The practice element of FIP Development Goal 15 (People-centred care) outlines collaborative interprofessional strategies and people-centred professional services to support the prevention, screening, clinical management and therapeutic optimisation of non-communicable diseases (NCDs) and long-term conditions, including CVDs.

Pharmacists can play a key role in the screening, prevention and modification of risk factors, providing useful advice on how to keep or achieve a healthier lifestyle and reduce the impact of risk factors (e.g., through smoking cessation and weight management services). They also provide excellent medication management for patients on long-term treatments. This can include specific activities such as patient education and counselling, medication review or the identification of risk factors through, for example, the measurement of blood pressure or glycaemia.

As experts in medicines, pharmacists are uniquely positioned to provide evidence-based pharmacotherapeutic recommendations, identify and resolve medicines-related problems, support primary care providers with the development of treatment and monitoring plans, provide comprehensive education to patients, and promote adherence to their prescribed treatment. When developing treatment and monitoring plans, pharmacists are encouraged to work collaboratively with other healthcare professionals to ensure optimal outcomes for their patients.

Pharmacists can also recommend non-pharmacological measures that patients may follow in addition to their prescribed medicines to improve their blood pressure, lipid profile, glycaemic control, weight and health outcomes. Pharmacists have a fundamental role in supporting the adoption of healthy lifestyles with the aim of preventing and reducing the burden of CVDs to both people and health systems. Since pharmacies are easily accessible and widely distributed in the community, a maximal benefit could be expected from interventions provided in this context.

In addition to providing people-centred care services, pharmacists also have an opportunity to be involved in practice-based research to evaluate the impact of CVD services in their practice setting. Pharmacists should also be mindful of ethical considerations, such as respect for the person and safeguarding privacy and confidentiality when providing CVD services. Pharmacists should respect patients' values, beliefs and preferences when developing care plans and goals.

There are many opportunities for pharmacists to engage in CVDs and, with the appropriate knowledge and skills (which are defined in the companion publication "Knowledge and skills reference guide for professional development in cardiovascular diseases"), pharmacists are well-positioned to provide services to people living with CVDs, in collaboration with other members of the healthcare team, ranging from prevention and screening to management and treatment optimisation.

Acknowledgements

FIP thanks the authors and reviewers for their contributions to this publication.

FIP and the authors acknowledge those who contributed to this publication and all the members of the expert advisory group, whose names are listed below, for their valuable comments and suggestions on this handbook.

Prof. Pedro Amariles, Universidad de Antioquia, Medellín, Colombia; Research Group on Pharmaceutical Promotion and Prevention, Universidad de Antioquia, Medellín, Colombia; Associate, Pharmaceutical Care Research Group, University of Granada, Spain

Leticia Caligaris, FIP Community Pharmacy Section observer, Uruguay

Dr Prabhakaran Dorairaj, chair of World Heart Federation Science Committee; vice president (research and policy) and director, Centre for Control of Chronic Conditions, Public Health Foundation of India; executive director, Centre for Chronic Disease Control and head, WHO Collaborating Centre for Surveillance, Capacity Building and Translational Research in Cardio-metabolic Diseases for the South-East Asia Region, India

Jean-Luc Eiselé, CEO, World Heart Federation, Switzerland

Dr Victoria Garcia Cardenas, University of Technology Sydney, Australia

Dr Jorge M. Núñez Córdoba, Research Support Service, Central Clinical Trials Unit, Clínica Universidad de Navarra, Spain

Óscar Penín Álvarez, member of the hypertension and vascular risk group of the Spanish Society of Clinical, Family and Community Pharmacy, Spain

Dr Daniel Sabater-Hernández, CEO, La Unión 32 Community Pharmacy; associate, Pharmaceutical Care Research Group, University of Granada, Spain

Prof. Stephane Steurbaut, Centre for Pharmaceutical Research, Research Group of Clinical Pharmacology and Clinical Pharmacy, Vrije Universiteit Brussel; Department of Hospital Pharmacy, UZ Brussel, Belgium

Lars-Åke Söderlund, FIP vice president and FIP Community Pharmacy Section immediate past president, Sweden

Benigna Villasuso Cores, member of the hypertension and vascular risk group of the Spanish Society of Clinical, Family and Community Pharmacy, Spain

Dr Francesca Wirth, senior lecturer, Department of Pharmacy, Faculty of Medicine and Surgery, University of Malta; member of the European Society of Clinical Pharmacy Research Committee, Malta

The content of this report has been produced independently by the authors and editors.

FIP thanks the World Heart Federation and the European Society of Clinical Pharmacy for their expert contributions to this publication.

WORLD HEART FEDERATION

ESCP European Society of Clinical Pharmacy

Foreword

By the president of the World Heart Federation

Non-communicable diseases (NCDs), including cardiovascular disease (CVD), continue to be a significant and growing problem worldwide. Deaths from CVD, which currently represent 32% of all deaths globally, are projected to increase from 18.9 million in 2020 to 32.3 million by 2030.[1] The number of people developing and living with CVD is also increasing, especially in low- and middle-income countries.[2] As a result, the demand for cardiovascular prevention, care and treatments continues to grow.

While people are needing healthcare more than ever, access to healthcare remains inadequate in many settings, particularly for NCDs.[3] In addition, the highest burden from CVD weighs on lower-resource settings, where access to care is most limited.[1] Adapting health systems to improve access to CVD care will be essential in responding to these challenges. These adaptations should include moving to a more integrated health system, involving the whole health workforce in providing person-centred CVD care.

The pharmaceutical workforce is an essential pillar of the healthcare system and Is ideally positioned to strengthen primary care delivery. It will therefore have an important role to play as healthcare systems evolve to improve access. This is particularly true for cardiovascular disease, which can often be addressed by simple, affordable interventions that can be delivered in the pharmacy setting. For example, up to 80% of secondary events in people with known vascular disease could be prevented through treatment with four proven medicines and tobacco cessation,[4] interventions that can be undertaken or facilitated by pharmacists.

Pharmacists can contribute to CVD risk factor management and prevention through preventive education, medication management and facilitating medication compliance.[5] Pharmacy-based screening and referral programmes, for example, for hypertension, could also help prevent CVD morbidity and mortality through the early detection of people at risk.[6] Pharmacists are clearly a natural ally in the fight against cardiovascular disease. We cannot forget, however, that several enabling factors must be in place for such initiatives to be implemented. Adequate health professional training, strong medication delivery systems providing affordable therapeutics, and adaptation of interventions to local contexts are all required to fully realise the potential contribution of pharmacists to CVD care.

The World Heart Federation (WHF) applauds the important and timely work undertaken by FIP to develop this handbook. In its forthcoming Vision 2030 report, the WHF calls upon all health professionals to strengthen their engagement in preventing and combatting CVDs.[7] This handbook aims to do exactly that within the pharmacy profession, by providing a valuable resource to help pharmacists implement evidence-based interventions for CVD in their practices. We hope it is used widely, not only by practising pharmacists but also by FIP members, advocates and educators who are responsible for creating the contexts that will allow the evidence-based recommendations contained in this handbook to be effectively implemented. The challenge of CVD is sizeable, but in working together towards the goal of ensuring everyone has access to the information, care and treatment they need, we are taking important steps towards tackling it.

Professor Fausto Pinto
WHF president

Foreword

Cardiovascular diseases (CVDs) include a range of conditions such as coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, and deep vein thrombosis and pulmonary embolism.[1]

Together, CVDs are the primary cause of death worldwide. The World Health Organization (WHO) estimates that 17.9 million people die from CVDs each year, representing 32% of all global deaths.[8] Evidence also suggests that the number of people worldwide suffering from CVDs almost doubled from 271 million in 1990 to 523 million in 2019.[9] Out of the 17 million premature deaths (in people under 70 years of age) due to NCDs in 2019, approximately 6.4 million were caused by CVDs,[1, 10] with over 75% of deaths occurring in low- and middle-income countries, where the population has less access to primary health care services for prevention, early detection, management, and treatment of people with cardiovascular risk factors.[1]

CVDs are also responsible for a substantial global health-economic burden in terms of direct, indirect and intangible costs. To the European Union economy alone, CVDs costs around EUR 210 bn annually, of which 53% is due to healthcare costs, 26% to lost productivity, and 21% to informal care of people with CVDs.[11] In the United States, CVDs direct and indirect costs sum up to around USD 378.0 bn annually. The estimated direct costs of CVDs in the USA increased from USD 103.5 bn in 1996–97 to USD 226.2 bn in 2017–18, with hospital inpatient care representing the highest direct cost (USD 99.6 bn).[12]

CVDs develop progressively over time, mainly resulting from an interaction and multiplication of risk factors. Hypertension, dyslipidaemia, diabetes and smoking are the major risks factors for CVDs. In addition to these, other factors such as obesity and overweight, physical inactivity, unhealthy diet, excessive alcohol consumption, stress, and sleep disorders directly contribute to the development of chronic diseases, and particularly to CVDs.[13, 14] These risk factors are considered modifiable because interventions in lifestyle make it possible to obtain gains in health and quality of life for patients suffering from CVDs, by reducing morbidity and mortality, and reducing individual, social and economic costs arising from the treatment of these diseases.[15, 16]

Pharmacists are experts in medicines, health and well-being. Due to their unique role set and accessibility they play an essential role in public health and disease prevention. They promote well-being and healthy lifestyles through their daily contacts with people and support them in achieving positive outcomes at every level of self-care.

Pharmacy-based, people-centred care goes well beyond medicines use and optimising effectiveness and safety. Given their prevalence and the health-economic burden that CVDs can put on patients and health systems, actions are needed to prevent these diseases from developing. Interventions preventing risk factors and better disease management, especially improving access to healthcare and improving adherence to evidence-based therapies, will consistently give better health, well-being and economic outcomes.

Considering the global prevalence and burden of CVDs, it is important that pharmacists are able to provide for needs in this area and that their services and roles are leveraged, expanded and consolidated. In addition, it is essential that pharmacy professional organisations at global, regional and national levels support practitioners in implementing and providing services in this area.

In the framework of FIP's work on NCDs, and particularly as part of FIP's Practice Transformation Programme on NCDs initiated in 2021, FIP has collaborated with an international group of experts, the World Heart Federation and the European Society of Clinical Pharmacy to develop this practice-support handbook and its companion guide on the knowledge and skills required to deliver a range of proposed interventions in the area of CVDs.

These tools highlight the important role of pharmacists in identifying individuals living with CVD, mitigating risk factors, identifying CVD symptoms, helping patients avoid risk factors (e.g., through smoking cessation and nutrition-related services), educating patients and their caregivers about the disease and its management, counselling on healthy lifestyles, promoting adherence to treatments, and providing support to ensure the

safe and effective use of medicines by people living with CVDs, especially in medicines that may require closer monitoring by a healthcare professional.

Overall, through the provision of person-centred pharmaceutical services, pharmacists play a key role in the healthcare system and contribute through a holistic approach to ensure healthy living and well-being, as well as by promoting more effective, rational and economic use of medicines in people suffering from CVDs.

In summary, pharmacists can contribute to the prevention, care and management of CVDs through different roles, including:

- Health promotion and education;
- Early detection;
- Triage and referral;
- Interprofessional collaborative practice;
- Disease management including medication adherence;
- Treatment optimisation;
- Helping to shape public policies; and
- Practice-based research.

This handbook compiles several examples of evidence-based interventions by pharmacists around the world that have led to positive health and economic outcomes for patients living with CVD. We are sure you will find them valuable and inspirational.

FIP looks forward to working together with its member organisations and all individual pharmacists around the world to ensure the optimisation and expansion of pharmacists' scope of practice in CVDs, to better serve patients and health systems, and improve the well-being of our communities.

Dominique Jordan
FIP president

Paul Sinclair
Immediate-past chair of the FIP Board of Pharmaceutical Practice

Daragh Connolly
Chair of the FIP Board of Pharmaceutical Practice

1 Background

1.1 Definition and characteristics of cardiovascular diseases

Cardiovascular diseases (CVDs) are defined as disorders that affect the heart and blood vessels. Thus, CVDs include more than 10 health conditions ranging from acute ischaemic syndromes, such as myocardial infarction, stroke and peripheral arterial disease (atherosclerotic disease), to chronic diseases, such as heart failure, atrial fibrillation and valvular diseases.[1]

Coronary heart disease (CHD), also known as coronary artery disease or ischaemic heart disease, typically occurs due to the accumulation of atherosclerotic plaque in the walls of the arteries and is characterised by angina. CHD can result in myocardial infarction, heart failure and sudden cardiac death. Atherosclerosis underlies the development of CHD, and atherosclerotic plaque can either be obstructive or non-obstructive. Chronic accumulation of atherosclerotic plaque, followed by plaque rupture, can partially or totally block circulatory systems.[17] This process restricts the appropriate supply of oxygen-rich blood to the heart and around the body. Consequently, this may result in myocardial infarction. Myocardial infarction can lead to left ventricular remodelling and eventually progress to heart failure.

Cerebrovascular diseases are pathological conditions that occur when oxygen-rich blood cannot circulate properly to the brain due to blood clot formation in the brain. The clinical manifestations of cerebrovascular disorders include stroke, transient ischaemic attack (TIA), vascular dementia, and cognitive impairment. However, the most frequent cerebrovascular events are stroke and TIA.[18] Stroke can be classified as ischaemic or haemorrhagic.[18]

Haemorrhagic stroke usually presents as sudden onset of severe and diffuse headache, accompanied by vomiting, decreased consciousness and neck pain.[19] Ischaemia occurs when the supply of blood, oxygen and nutrients to the brain is disrupted. This results in brain injury. This therefore leads to small vessel disease, which is called lacunar stroke. Another type that is attributed to ischaemia is non-lacunar stroke, which is classified into four stroke subtypes, namely, cardioembolic, cryptogenic, large artery atherosclerosis and those attributed to other causes.[20]

Peripheral arterial disease (PAD) results from a blockage of blood supply due to a build-up of fatty deposits in the arteries. The infarction may be found in the carotid, vertebral, mesenteric or renal arteries.[21, 22] Not all patients with early PAD present symptoms with intermittent claudication. The clinical manifestations from untreated PAD may lead to increased risk of disability and mortality. It is therefore critical to assess the impairment severity of PAD. The ankle-brachial index is mainly used to rule out a diagnosis of PAD. In addition to this, supplementary diagnostic methods such as the toe-brachial index, exercise treadmill and other imaging tests may be required to objectively assess the degree of functional limitation.[23]

Venous thromboembolism, also known as deep vein thrombosis, and pulmonary embolism are pathological conditions that result from a blood clot in a deep vein of the extremities or lungs. Venous thromboembolism is associated with significant morbidity. It typically presents with swelling, pain, tenderness and warmth.[24] Pulmonary embolism results in dyspnoea, tachypnoea, chest pain and tachycardia.[24]

1.2 Burden of CVDs and their risk factors

1.2.1 Epidemiological and economic burden of CVDs

NCDs are chronic conditions, and mainly include CVDs, cancers, chronic respiratory diseases, diabetes and mental illnesses, which are the leading causes of death worldwide. Obesity, hypertension, hyperlipidaemia, diabetes mellitus, chronic kidney disease, and smoking are common risk factors for all five NCDs. Both modifiable and non-modifiable risks should be accounted for when evaluating and managing patients with NCDs.[25]

Among these chronic conditions, CVDs are a group of highly prevalent NCDs worldwide, and they are responsible for almost a third of all deaths, and almost half of those due to NCDs. Thus, CVDs, and among them ischaemic heart disease and stroke, are the leading causes of death and disability worldwide and have a significant impact on morbidity, mortality and global healthcare expenditure.[25, 26]

The WHO Global Action Plan for the Prevention and Control of NCDs (endorsed by World Health Assembly in 2013) had as a goal "to reduce the preventable and avoidable burden of morbidity, mortality and disability due to NCDs by means of multisectoral collaboration and cooperation at national, regional and global levels, so that populations reach the highest attainable standards of health and productivity at every age and those diseases are no longer a barrier to well-being or socioeconomic development".[26] Thus, the plan defined a roadmap and menu of policy options that would be implemented from 2013 to 2020 oriented to achieve nine objectives in 2025 regarding NCDs.[26] Minimising the influence of cardiovascular risk factors and reducing CVD mortality are key to achieve a 25% relative reduction in premature mortality from NCDs by 2025.[25]

Cardiovascular diseases have a great economic, social and health impact at global level, especially in low- and middle-income countries (LMICs), where health systems have limitations to respond more effectively and equitably to the healthcare needs of people with NCDs. Therefore, CVDs are causing an important reduction in life expectancy at birth in these territories.

Similarly, the 2030 Agenda for Sustainable Development recognises that NCDs are a key obstacle, and emphasises the need to reduce premature deaths due to NCDs by 33% by 2030 through prevention and treatment, with a special focus on CVDs.[27]

The burden of disease (BD) includes the total and cumulative consequences in health, social and economic costs to society of a defined disease, for instance CVDs, with respect to disabilities at a population level. The difference between the situation where everyone lives free of disease and disability, and the cumulated current health status comprise the BD. Premature deaths, expressed as disability-adjusted life years (DALYs), including years of life lost and years with disability, also determine the BD.[28]

The Global Burden of Disease (GBD) study, led by the Institute for Health Metrics and Evaluation, is the principal source of BD data on CVDs and cardiovascular risk factors. For 2019, the key BD calculations with regard to CVDs were:[9]

- Number of persons worldwide with CVDs: doubled from 271 million in 1990 to 523 million in 2019.
- Number of deaths due to CVDs: progressively increased from 12.1 million in 1990 to 18.6 million.
- Years lived with disability due to CVDs: doubled from 17.7 million in 1990 to 34.4 million.
- DALYs and years of life lost related to CVDs: increased significantly from 271 million (1990) to 523 million (2019)

It is estimated that in 2019, 197 million people suffered from ischaemic heart disease (IHD) and there were 101 million cases of stroke.[9] IHD and stroke were the second and third cause of DALYs in 2019, reaching 182 million and 143 million DALYs, respectively.[9, 10]

Similarly, the WHO estimates that 17.9 million people die from CVDs each year, representing 32% of all global deaths.[8] IHD and stroke were the first and the second leading causes of death, responsible for 16% (8.9 million) and 11.2% (6.2 million) of the world's total deaths in 2019, respectively.[11]

In 2019, CVDs were responsible for approximately 9.3 million deaths in men and 8.5 million deaths in women worldwide.[10] Out of the 17 million premature deaths (in people under 70 years of age) due to NCDs in 2019, approximately 6.4 million were caused by CVDs. Over 75% of deaths occurred in LMICs, where populations have limited access to primary healthcare services for prevention, early detection, management and treatment of people with cardiovascular risk factors.[9, 10]

Worldwide, among the 10 leading causes of death in 2019, seven were NCDs, representing 44% of all deaths. However, NCDs accounted for 74% of deaths globally in 2019. Therefore, to meet the targets for United Nations Sustainable Development Goal 3 and attain a 30% reduction in premature mortality due to NCDs, there is an urgent need to apply evidence-based, cost-effective policies and interventions to reduce the burden of CVDs (mainly IHD, stroke and hypertensive heart disease) and their risk factors (mainly hypertension, diabetes, hyperlipidaemia, smoking, obesity, sedentary lifestyles and unhealthy diet) by at least 30%.

In the United States, the prevalence of CVD and cardiovascular risk factors is projected to increase significantly by 2060. The prevalence of hypertension is projected to increase by 27.2%, hyperlipidaemia by 27.5%, stroke by 34.3%, and diabetes by 39.3%. Furthermore, these increases in prevalence are projected to affect racial and ethnic minorities disproportionately.[29]

CVDs are responsible for a substantial global health-economic burden in terms of direct, indirect and intangible costs. To the European Union economy alone, CVDs cost around EUR 210 bn annually, of which 53% is due to healthcare costs, 26% to lost productivity, and 21% to the informal care of people with CVDs.[12] In the United States, CVDs direct and indirect costs sum up to around USD 378 bn annually. The estimated direct costs of CVDs in the USA rose from USD 103.5 bn in 1996–97 to USD 226.2 bn in 2017–18, with hospital inpatient care being the highest direct cost (USD 99.6 bn).[30]

In LMICs, a systematic review report estimated that the financial hardships for CVDs ranged between USD 500 and USD 1,000. In specific cases such as hypertension, treatment accounted for approximately USD 22 per month. For stroke and IHD, estimated treatment costs ranged between USD 300 and USD 1,000 per month.[31] Uncontrolled hypertension is one of the most significant factors that contributes to an increase in the economic burden of CVDs in LMICs compared with high-income countries.[32] Therefore, appropriate interventions should address both the burden of disease and the financial hardships arising from CVDs.

In conclusion, the burden of CVDs, measured in number of DALYs, continues to increase globally. In this context, population growth and ageing demand that countries and health systems prioritise prevention and adequate treatment of CVDs. In 2019, CVDs caused 9.6 million deaths in men and 8.9 million deaths in women, globally, representing 33% of all deaths. Of these, 6.1 million occurred in people between the ages of 30 and 70 years. Thus, CVDs are a common cause of premature death among young and middle-aged adults. For instance, in 2019 there were 1.2 million deaths from CVDs in people younger than 50 years.[33]

1.2.2 Burden of the main modifiable (behavioural) or controllable (metabolic) CV risk factors

Atherosclerosis (atherosclerotic plaque accumulation in the endothelium of blood vessels) is the pathophysiological cause of atherosclerotic CVDs, which include:

- IHD (acute coronary syndrome — unstable angina and myocardial infarction) and chronic coronary syndrome or stable IHD (stable angina);
- Cerebrovascular disease (stroke and transient ischaemic attack); and

- Peripheral arterial disease (PAD; impaired circulation to the lower extremities). Among patients with PAD, critical limb ischaemia is the most severe phase, which increases the risk of atherosclerotic CVD events, amputation and death.[34]

Recent evidence has shown that, primarily in patients with IHD (secondary prevention), the atherosclerotic CVD risk is determined mainly by the extent of atherosclerotic disease burden (plaque burden) and to a lesser extent by the presence of coronary stenosis or inducible ischaemia. Therefore, in patients with obstructive and non-obstructive IHD, evaluation of the plaque burden could be used to identify patients most likely to get maximal benefit from preventive medicinal therapies.[35] Evidence has also shown that, although preventive treatments reduce the relative risk of atherosclerotic CVD events, the absolute risk of subsequent events remains high. As a consequence, for instance, for the USA it is estimated that by 2035 nearly half the population may have some CVD clinical conditions and costs may double to USD 1.1 tn annually. As such, it is essential to improve the effectiveness of preventive treatments to reduce these negative projections.[36]
Modifiable or controllable risk factors are the main cause of the global CVD burden. Therefore, adequate control of risk factors is a critical global challenge that requires innovative and creative health solutions.[33]

The CV risk factors associated with CVDs may be metabolic, behavioural or environmental. Metabolic causes for the development of CVDs include elevated levels of total cholesterol, blood pressure and fasting plasma glucose, while behavioural causes involve smoking, unhealthy diets, physical inactivity and excessive alcohol consumption.

Therefore, the number and intensity of CV risk factors determine severity and progression of atherosclerosis, a process that is inflammatory and systemic (all vessels of the body) and begins in the first decade of life. In addition, in childhood and in adolescence, cardiometabolic alterations (overweight and obesity, hypertension, high fasting plasma glucose and high cholesterol levels) are the most important CV risk factors. Hence, prevention and control of these risk factors are essential to reduce the global burden of CVDs.[37] It is important to note that in 2020, approximately 3% of children and 5% of adolescents had metabolic syndrome, a prevalence that globally highlights an urgent need for intersectoral interventions to reduce the global burden both of this condition and its risk factors, including childhood overweight and obesity.[38]

In 2017, 34.1 million deaths (95% UI 33.3–35.0) and 1.21 billion (1.14–1.28) DALYs were attributable to GBD risk factors. Globally, 61.0% (59.6–62.4) of deaths and 48.3% (46.3–50.2) of DALYs were attributed to GBD risk factors. Ranked by death and DALYs, the six main risk factors were:[39]

1. High systolic blood pressure.
2. Smoking
3. High fasting plasma glucose
4. High body mass index
5. High low-density lipoprotein cholesterol (hyperlipidaemia)
6. Low physical activity (sedentary lifestyle)

It is estimated that dietary risks (diets low in fruits, vegetables, legumes, whole grains, nuts and seeds, fibre, calcium, seafood omega-3 fatty acids, polyunsaturated fatty acids and milk; or diets high in red meat, processed meat, sugar-sweetened beverages, trans fatty acids and sodium) cause 10.90 million deaths and 219 million DALYs.

Similarly, in 2019 the leading GBD risk factors were high systolic blood pressure, smoking, high fasting plasma glucose, low birthweight, and high body mass index. Other notable shifts include the large increase in the percentage of attributable DALYs and rank for ambient particulate matter pollution, high LDL cholesterol, and alcohol use. For 2019, the burden of disease risk factors was ranked by contribution to total of DALYs (percentage), see Table 1.[40]

Table 1. Ranking of 10 global burdens of disease risk factors by disability-adjusted life year (DALYs)[40]

Ranked risk factors	Percentage of DALYs (95% CI)
1. High systolic blood pressure*	9.3 (8.2 to 10.5)
2. Smoking**	7.9 (7.2 to 8.6)
3. High fasting plasma glucose*	6.8 (5.8 to 8.0)
4. Low birthweight	6.3 (5.5 to 7.3)
5. High body-mass index*	6.3 (4.2 to 8.6)
6. Short gestation	5.5 (4.7 to 6.3)
7. Ambient particulate matter (air environmental)	4.7 (3.8 to 5.5)
8. High LDL cholesterol*	3.9 (3.2 to 4.7)
9. Alcohol use**	3.7 (3.3 to 4.1)
10. Household air pollution (indoor pollution)	3.6 (2.7 to 4.6)

*Controllable metabolic risk factors; **Modifiable behavioural risk factors; CI: Confidence interval.

Regarding the risk factors associated with the burden of CVDs, since 1990 the 12 main ones have remained similar. In 2019, the ranking of risk factors was:[9]

1. High systolic blood pressure (metabolic risk)
2. Dietary risk (behavioural risk)
3. High LDL cholesterol (metabolic risk)
4. Air pollution (environmental risk)
5. High body-mass index (metabolic risk)
6. Tobacco (behavioural risk)
7. High fasting plasma glucose (metabolic risk)
8. Kidney dysfunction (metabolic risk)
9. Non-optimal temperature (environmental risk)
10. Other environmental risks (environmental risk)
11. Alcohol use (behavioural risk)
12. Low physical activity (behavioural risk)

Experimental and epidemiological studies have demonstrated a robust association between air pollution and cardiovascular morbidity and mortality.[41] Therefore, there is strong evidence that higher levels of ambient air pollution increase the risk of CVDs, especially all-cause CVD mortality, stroke and IHD.[42] This suggests the need for developing services that aim to minimise the impact of air pollution on health, as recommended in FIP's report "Mitigating the impact of air pollution on health: The role of community pharmacists — Global survey report" and in the publication by FIP and The Clean Breathing Institute, "The global threat of air pollution and its impact on patient care: Supporting pharmacy practice and workforce development".

1.2.3 Specific modifiable (behavioural) or controllable (metabolic) CV risk factors

1.2.3.1 High blood pressure

Hypertension is the largest single contributor to the global burden of disease; estimates suggest that 31.1% of adults (1.39 billion) worldwide had hypertension in 2010. Hypertension accounts for 10.4 million premature deaths and 218 million DALYs per year.[39, 43] Therefore, it is one of the most important risk factors for IHD, stroke and chronic kidney disease.

Worldwide, hypertension is a key preventable cause of CVD mortality and burden of disease.[44] In addition, among patients with hypertension, 10–20% have resistant hypertension, which is related to worse cardiovascular and renal outcomes, and death compared to non-resistant hypertension.[45]

1.2.3.2 Diabetes

Cardiovascular comorbidities in patients with type-2 diabetes mellitus are associated with a significant disease burden both at population and patient levels. At the population level, CVD costs contributed between 20% and 49% of the total direct costs of treating diabetes. The median annual costs per patient for CVD, IHD, heart failure and stroke were, respectively, 112%, 107%, 59% and 322% higher compared with diabetes patients without CVD. On average, treating patients with CVD and diabetes resulted in a cost increase ranging from USD 3,418 to USD 9,705 compared with treating patients with diabetes alone.[46]

Among 1,483 patients with myocardial infarction, 42% of those without known diabetes had elevated plasma glucose levels on admission and a greater risk of cardiovascular events (new myocardial infarction, heart failure, stroke, all-cause death) at 180 days.[47]

The prevalence of overweight, obesity and diabetes is rising rapidly in LMICs. For instance, a dataset analysis from a sample size of 685,616 people living in 57 LMICs showed that the overall prevalence of overweight, obesity and diabetes is 27.2%, 21.0%, and 9.3%, respectively. The pooled analysis indicated a higher risk of diabetes at a BMI of 23 kg/m^2 or higher, with a 43% greater risk of diabetes for men and a 41% greater risk for women compared with a BMI of 18.5–22.9 kg/m^2. Diabetes risk also increased abruptly in people aged 35–44 years and in 25- to 34-year-old men in sub-Saharan Africa. It is noteworthy that optimal BMI thresholds for diabetes screening range from 23.8 kg/m^2 among men in East, South, and South-East Asia to 28.3 kg/m^2 among women in the Middle East and North Africa, and in Latin America and the Caribbean.[48]

1.2.3.3 Hyperlipidaemia

Among metabolic CV risk factors, cholesterol-rich atherogenic lipoproteins play a central role in the pathogenesis of atherosclerosis. In middle-aged adults, the size of the total atherosclerotic plaque burden is influenced by the concentration of circulating atherogenic lipoproteins and the total duration of exposure to these lipoproteins. Thus, there is enough evidence supporting the causal link between lifelong elevations in atherogenic lipoproteins and future risk of atherosclerotic CVD risk.[49]

Lowering cholesterol by about 1.0 mmol/L in men with average cholesterol and no IHD is associated with 8.9 fewer atherosclerotic CVD events and a saving of 56.0 hospital days per 100 persons. In those with IHD this difference gave, depending on starting level, 26.8–36.5 fewer atherosclerotic CVD events and savings of 158.2–247.3 hospital days per 100 persons. Comparison of cumulative events in 45–54 vs 55–64 year-olds shows greater benefit from intervention in the younger age group.[50]

According to the data available, some authors proposed to investigate whether intensively lowering plasma apolipoprotein (apo) B levels in younger and early midlife adults will regress earlier stages of atherosclerosis, thereby eliminating the risk of developing clinical atherosclerotic CVD events later in life.[36]

1.2.3.4 Smoking

Globally, there are approximately 1.1 billion smokers, and over eight million people die each year due to cigarette smoking.[39] Smoking acts as a risk factor for a variety of diseases, including CVDs, chronic obstructive pulmonary disease (COPD) and cancers.[39]

Similarly, there is significant association between smokeless tobacco and mortality due to all cause, all types of cancers, and specific cancers, for instance upper aero-digestive tract, stomach, and cervical cancer; and also, for IHD and stroke. Subgroup analysis showed regional differences: 88% of the 652,494 attributable deaths from all-cause mortality associated with smokeless tobacco was borne by the South-East Asian region.[51]

In addition, CVD patients who are smokers have an increased risk of all-cause, CVD and cancer mortality, and the risk decreases significantly after quitting smoking.[52] For instance, among heavy smokers, smoking cessation is associated with significantly lower risk of CVD within five years relative to current smokers.[53] Therefore, there is strong evidence for the recommendation to quit smoking for the prevention of premature deaths among people with CVD. However, compared with those who never smoked, former smokers' CVD risk remained significantly elevated beyond five years after smoking cessation,[53] and adverse effects of smoking may persist for more than two decades, which is inferior to the time defined in current clinical guidelines for risk assessment of lung cancer and CVDs.[54]

The major NCDs share four modifiable behavioural risk factors: unhealthy diet, sedentary behaviour, smoking, overconsumption of food and alcohol excess. Therefore, adoption of healthy lifestyles, which include no excessive alcohol intake, no smoking, a healthy diet and regular physical activity, represents a crucial and economical strategy to counteract the global burden of NCDs.

From 1990 to 2016, a greater decrease in cardiovascular mortality in developed countries was registered; by contrast in LMICs there are indications of increases in CVD burden. For instance, in Mexico in 2015, a CVD expense equivalent to 4% of total health expenditure was reported. Overall, in LMICs CVDs rank first in health expenditure in almost all these nations and the economic burden will continue to be significant for some more decades.[55]

Similarly, there is an increasing incidence of CVDs in Middle Eastern countries. For instance, the overall prevalence of CVD is 10.1%. In addition, the prevalence of CV risk factors is higher — dyslipidaemia (43.3%), hypertension (26.2%) and diabetes (16%). Therefore, the burden of dyslipidaemia (43.3%) in this region is twice as high as that of hypertension (26.2%) and diabetes mellitus (16%). Also, the prevalence rates of other risk factors, such as smoking (12.4%) and family history of CVD (18.7%), are also high.[56]

2 Pharmacists' integration in CVD care: current and future

2.1 Patient-centred care by pharmacists

CVDs are the leading cause of morbidity and death globally. Thus, it is imperative that all healthcare professionals contribute to the prevention and management of CVDs. Pharmacists' integration in CVD care in outpatient and inpatient settings needs to be improved and strengthened. The care of patients with CVDs must be patient-centred, and have a multidisciplinary team-based approach, with shared health goals, long-term care relationships, evidence-based practice, effective patient access, and effective interprofessional and interinstitutional communication and coordination.[57]

In the context of patient-centred care, pharmacists should develop competencies for patient-centred communication, such as:[58]

- Individualising and respecting each patient as a unique person that has specific problems and requires personalised solutions;
- Focusing more on the patient than on the product, and at all times providing respect and empathy in relationships with patients;
- Establishing mutual understanding and agreement for the pharmacist and patient to participate in two-way communication;
- Sharing control and responsibility with the patient as much as possible, respecting the patient's right of access to complete and correct information;
- Empowering the patient to be self-sufficient;
- Adapting communication style to each patient's needs and preferences; and
- Considering communication as a key element of the pharmacy profession and therefore understanding the need to strengthen competencies in this area.

Overall, in patients with CV risk factors or with CVDs there is a gap between evidence-based recommendations and usual clinical practice.[59] Thus, this group of patients includes a high percentage of individuals for whom evidence-based therapeutic interventions are not used or for whom the therapeutic goals are not achieved; for instance, close to 50% maintain LDL cholesterol levels higher than 100 mg/dL (2.6 mmol/L) or 70 mg/dL (1.8 mmol/L) or blood pressure values higher than 140/90 mmHg.[59]

The Pharmaceutical Care Network Europe (PCNE) has stated that "pharmaceutical care is the pharmacist's contribution to the care of individuals in order to optimise medicines use and improve health outcomes".[60] Pharmacists may achieve contributions to the care of patients with CV risk factors or with CVDs through professional pharmacy services, for instance, medication review (pharmacotherapeutic follow-up), counselling and health education, and dispensing, in the context of pharmaceutical care.[61, 62]

Pharmacists can contribute to improving both the process of care and health outcomes and can contribute to reducing the burden of CVDs and improving quality of care of patients with CVDs through optimisation of pharmacotherapy. Overall, these pharmacy services may be performed at a patient or population level, require the cooperation of patients and other healthcare team members, and are mainly focused on identifying and addressing negative outcomes associated with medication and their preventable causes (medicine-related problems), contributing to effectiveness and safety of the pharmacotherapy and leading to positive health outcomes.[59, 63]

Some studies undertaken in patients with CVD or CV risk factors have shown that pharmacists' integration in designing and implementing professional pharmacy services could:[59, 64, 65]

- Improve the patient's knowledge;
- Facilitate the adoption of and outcomes from healthy lifestyles;

- Optimise the identification of people who most need and would benefit from cardiovascular preventive interventions and contribute to improving the results of primary and secondary prevention interventions;
- Increase the percentage of patients with high CV risk who achieve the goals related to blood pressure, HbA1C, and LDL cholesterol; and
- Improve adherence to prescribed medication for patients with IHD (secondary prevention) or without CVDs (primary prevention).

Similarly, some systematic reviews have documented that pharmacist-led care, or care in collaboration with other health care professionals (mainly physicians or nurses, as part of team-based care), improves health outcomes, reduces healthcare costs and increases patient satisfaction.[66, 67] In addition, pharmacist-led interventions optimise the therapeutic management of major CV risk factors in outpatients and ambulatory clinical settings and can significantly contribute to control of CV risk factors. The results of these systematic reviews support the involvement of pharmacists as integral members of the healthcare team in managing patients with CVDs or with CV risk factors to improve clinical management and outcomes in patients with hypertension, diabetes or dyslipidaemia.[66, 68-72] In addition, a recent umbrella review found conclusive evidence that pharmacist intervention can provide positive effects in therapeutic management of patients with CVDs, which range from risk factor control, improvement of adherence to prescribed medication and, in some settings, reduction of morbidity and mortality.[73] However, there are some limitations regarding the precision and details of the intervention or group and interventions used, which are usually poorly described, multifaceted interventions leading to high heterogeneity.[71]

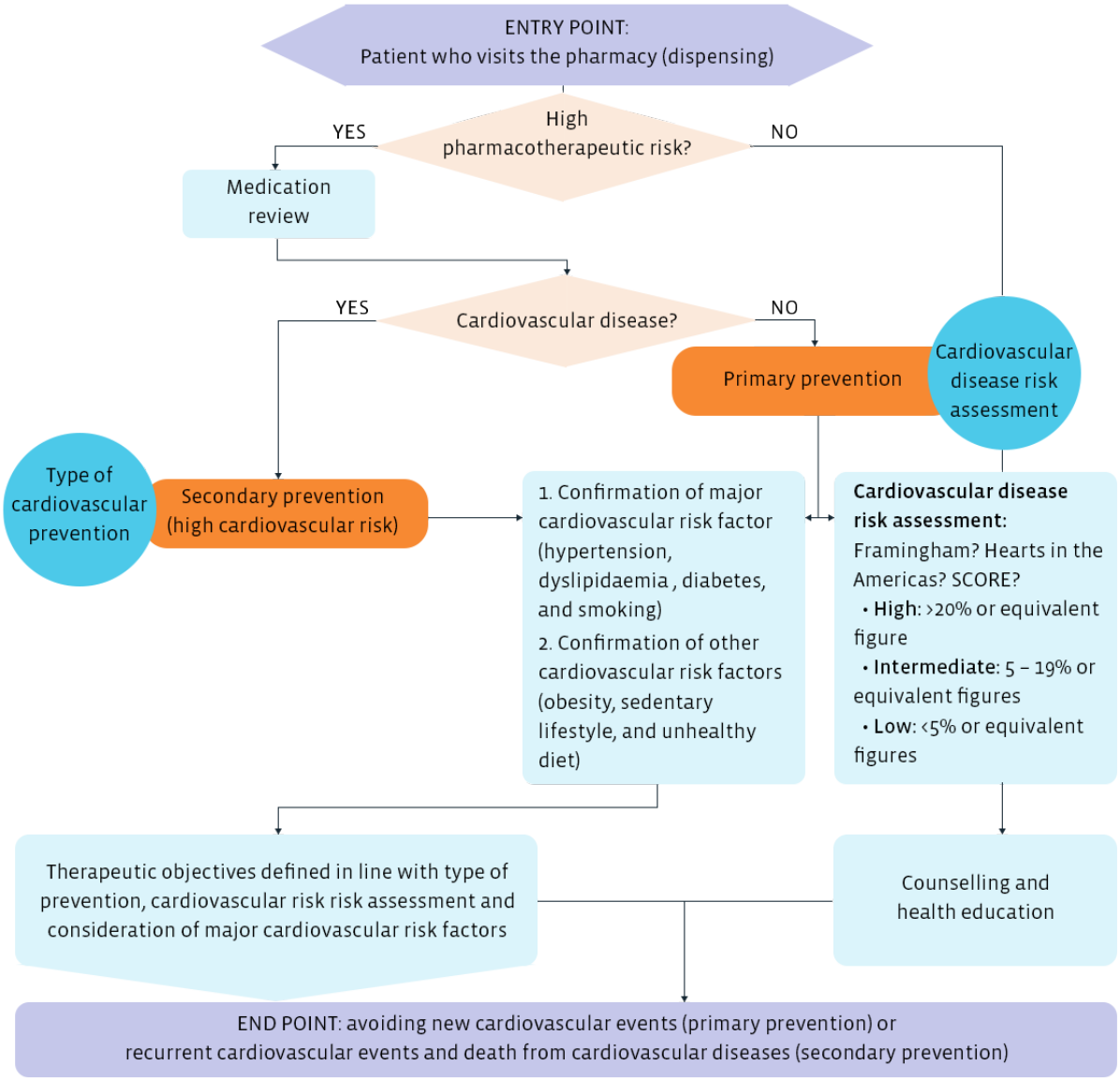
Consequently, relevant clinical guidelines recommend pharmacists' engagement as members of the team-based care of patients with CV risk factors, for instance, guidelines on hypertension management. Thereby both the guideline from North America[74] and Europe[75] include pharmacists as part of the healthcare team for patients with hypertension.[76] The North American guidelines say that the responsibilities of pharmacists include "comprehensive medication management, which involves identification and documentation of medication-related problems, initiating, modifying and discontinuing medication to address identified problems and educating patients on their medication regimen".[74] Therefore, pharmacists' integration as care team members should be the standard of care for patients with hypertension,[76] since the physician-pharmacist collaborative intervention is effective in the therapeutic management of hypertension, for example, in reducing mean systolic blood pressure (BP) and improving BP control in patients with uncontrolled hypertension with diabetes or chronic kidney disease, according to different BP guidelines used.[77]

Notably, patients with one or more major CV risk factors, for instance, hypertension, initiating a new or adjusted pharmacotherapy regimen should have a follow-up assessment of the adherence to, and effectiveness and safety of treatment each month until therapeutic goals are achieved, with follow-up every three to six months.[74]

2.2 Intervention and follow-up of patients with cardiovascular risk factors or with CVD

It is important to present some specific and complementary information[78] to the contents presented in other handbook sections, which is illustrated by Figure 1, showing the main steps of pharmacist intervention in patients with risk factors or with CVDs through pharmacy professional services.

Figure 1. Main steps of pharmacist intervention in patients with risk factors or with CVDs through pharmacy professional services.[78, 79]



Adapted from: Amariles P, González M, Sabater D. Actuación farmacéutica en Prevención Cardiovascular. Granada; 2006. p. 68. [accessed: 6 August 2022]. Available at: https://www.researchgate.net/publication/215898825_Actuacion_Farmaceutica_en_Prevencion_Cardiovascular

Overall, it is important to assess a patient's pharmacotherapeutic risk and if it is high, this is an indicator that the patient needs a medication review to minimise the risk (see above). Thus, the process requires that the pharmacist interviews the patient, measures and assesses vital signs, reviews clinical records, including medication therapy and laboratory tests, and collaborates with other healthcare team members to solve any questions regarding the patient's health conditions or pharmacotherapy. In addition, some details regarding relevant steps of pharmacist intervention in patients with risk factors or with CVD are:

- **Identification and confirmation of major cardiovascular risk factors (hypertension, dyslipidaemia, diabetes and smoking) and of other risk factors (obesity, sedentary lifestyle and unhealthy diet):** It is important to note that both therapeutic management aimed to control or modify CV risk factors and preventive interventions must be guided by the patient's type of prevention and CV risk, beyond the treatment determined by the patient's specific risk factors, for instance hypertension, dyslipidaemia or diabetes.

- **Individualised cardiovascular disease risk assessment:** In patients with CVD or with CV risk factors, personalised CVD risk assessment is a key step to identify patients' needs regarding preventive interventions, for instance, antiplatelet drugs, as well as treatment thresholds and intensity of pharmacotherapeutic regimens (doses or combination of different groups) needed to achieve the therapeutic goals for CV risk factors, for instance in blood pressure, HBA1c, or in LDL cholesterol levels.[14, 80]

Patients with CVDs (secondary prevention) or without CVDs (primary prevention) but with some clinical conditions that are indicators of high risk, for instance, type 2 diabetes, familial hypercholesterolaemia or heart failure, are considered as patients with high cardiovascular risk. Thus, for these patients, use of methods and risk calculators for CV risk estimation would not be necessary. Therefore, patients are assigned to one of the following groups:

- **Secondary prevention patients** for whom the presence of some atherosclerotic CVD conditions (IHD, stroke or peripheral arterial disease) indicates a high CV risk; or
- **Primary prevention patients with risk conditions** to be considered as patients at high-risk for CVDs.

Overall, in patients with major CV risk factors but without both CVDs and high-risk conditions for CVD (primary prevention), it is recommended to estimate the 10-year risk of CVDs. To do this, there are different methods and risk calculators recommended by academic and scientific associations. It is important to identify the most adequate one for a region or country, for instance, Heart of Americas[78] for Central and Latin America, Systematic Coronary Risk Estimation 2 (SCORE-2)[14] for Europe, or ASCVD Risk Estimator Plus[80] for the USA. Once the CV risk is assessed, the patient is assigned to one of the following groups:

- **Primary prevention patients with high CV risk**: CV risk estimation >20% (or equivalent figures with other methods and risk calculators);
- **Primary prevention patients with moderate CV risk**: CV risk estimation 10–19% (or equivalent figures with other methods and risk calculators); or
- **Primary prevention patients with low CV risk**: CV risk estimation <10% (or equivalent figures with other methods and risk calculators).

Pharmacist interventions include patient counselling and health education about metabolic and behavioural CV risk factors, identifying barriers to adherence, identifying and solving negative outcomes associated with medication and medicine-related problems, including adjusting medication regimens, in cooperation with the patient and physician, and regular follow-up every one to three months, according to CV risk and pharmacotherapeutic risk.[14, 77, 79]

2.3 Pharmacists' perspectives in cardiovascular diseases care

It is important to note that, through pharmacy professional services, pharmacists can contribute to ideal cardiovascular health by optimising pharmacological and non-pharmacological therapies, leading to achievement of therapeutic goals. Therefore, in patients with CVDs or CV risk factors, pharmacists have an excellent opportunity to contribute to achieving the best possible health outcomes. In addition to pharmaceutical professional services (dispensing, counselling and health education, and medication review) detailed previously, there are other services that pharmacists can provide to improve the management and control of CVDs and CV risk factors, such as point-of-care testing for major metabolic CV risk factors (blood glucose, cholesterol and blood pressure) and medication reconciliation.[81]

To strengthen their role in healthcare systems, pharmacists may provide additional services.[82] These pharmacy services must be characterised by a humanised pharmaceutical care focused on patient needs and preferences, as well as solidarity, humanism, creativity and innovation.

These additional services include:

Counselling and health education in the context of community pharmacy: This may have a small beneficial effect on health-related behaviour, intermediate clinical outcomes and quality of life of patients.[83] In addition, interventions could be cost-effective on several metabolic and behavioural risk factors. The magnitude of the effects varies, but effectiveness could be increased with greater conceptual support of interventions and mechanisms associated with behavioural changes.[83]

Providing evidence of the effectiveness of pharmaceutical services: Overall, medication review provided by pharmacists, mainly levels 2 (intermediate) and 3 (advanced), is considered effective for the control of major CV risk factors; nevertheless, in some studies, the evidence is contradictory. Systematic reviews show that medication review is associated with better control of blood pressure, cholesterol and type 2 diabetes. However, some reviews have shown that pharmacist interventions had differential effects on the control of these CV risk factors, varying from very large to modest or no effect; thus, continuous clinical outcomes failed to achieve statistical significance, due to their high heterogeneity.[70, 71] Therefore, further research should:

- Utilise a homogenous method for medication review to reduce heterogeneity.[71] In addition, it is needed to identify heterogeneity sources and improve the efficiency and cost-effectiveness;[67]
- Define goals and objectives for evidencing that clinical outcomes have statistical significance;
- Improve the effective access to sources of patient-specific information regarding current health problems and pharmacotherapy (patient, medication therapy and electronic clinical records, other healthcare professionals). It is important to identify preferred communication strategies and create mechanisms for documentation and establishing an evaluation plan;[84] and
- Collect data and define mechanisms to disseminate and achieve appropriate results of pharmacist interventions associated with the achievement of better health outcomes to support the need for pharmacists services.[84]

Contributing to improving the management of CVDs in people with a low socioeconomic status: The management and prevention of CVDs in people with a low socioeconomic status or in LMICs are poor. Greater availability, access and affordability for acute coronary syndrome management and secondary prevention are important. Also, primary prevention should focus on tackling the social determinants of health as well as policy and individual interventions for CV risk factor control, supported by task sharing and use of digital health, including telepharmacy (see section 7.4).[85]

Pharmacist training and continuing education for CVD management and prevention: There is a need to develop and evaluate educational programmes for pharmacists focused on identification and confirmation of major cardiovascular risk factors, individualised CVD risk assessment and achievement of pharmacy professional services, mainly medication review and counselling and health education, in patients with CVDs or with CV risk factors. These programmes should assess the knowledge and skills of pharmacists in assessing and managing these issues before and after enrolling in the educational programme and assessing pharmacists' satisfaction and perceived effectiveness.[86]

Pharmacist prescribing: It is important to design and conduct research focused on assessing clinical and economic effects of pharmacist prescribing programmes for specified medicines and patients, and that it is consensus-based in partnership with physicians. It is an important challenge for the pharmacy profession to provide evidence of effects of pharmacist prescribing for CV risk reduction or control leading to evidence-based clinical practice guidelines in outpatient and clinical settings.[87]

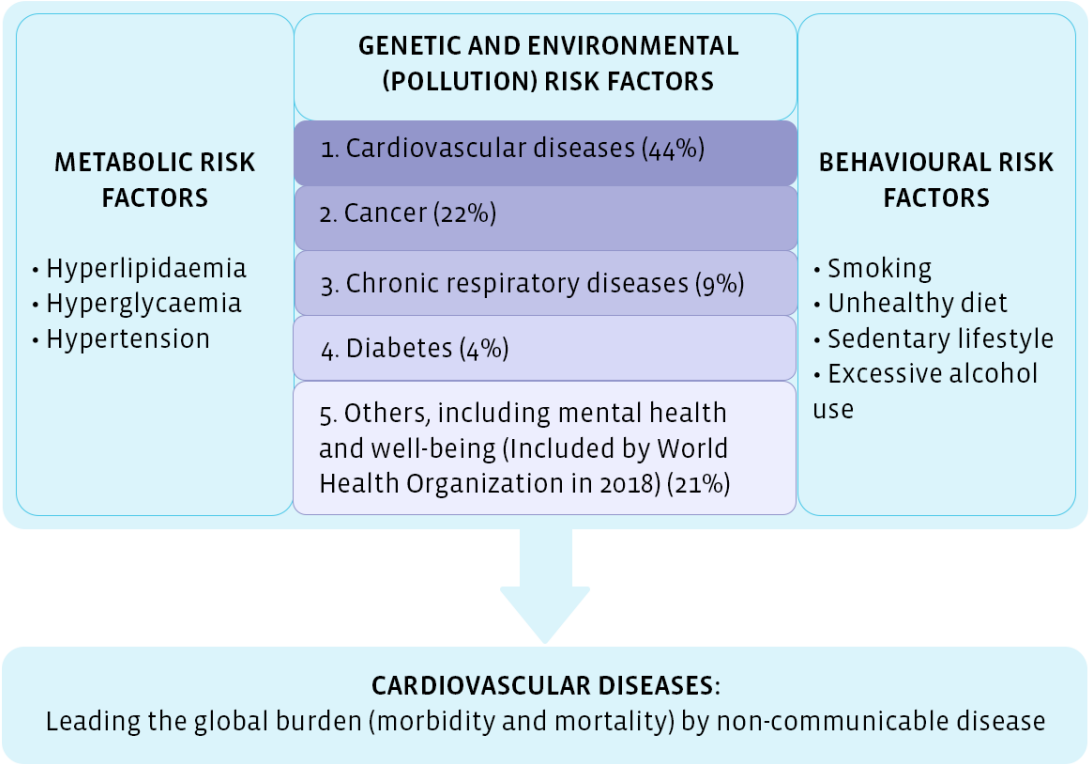
3 Prevention and control of cardiovascular diseases

3.1 Pharmacists' role in promoting cardiovascular well-being and healthy lifestyles

In 2015, the United Nations adopted its 2030 Agenda for Sustainable Development (SD) with 17 goals (SDGs). In the case of health, SDG 3 exists to "ensure healthy lives and promote well-being for all at all ages". It has a target (3.4) to "reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being" by 2030.[78, 88]

NCDs are responsible for the highest burden of global morbidity and mortality resulting in 41 million deaths yearly (71% of all mortality globally). They share genetic, physiological, environmental and behavioural risk factors (see Figure 2). Therefore, promotion and prevention interventions aimed at controlling these factors may contribute to reducing the health burden and negative effect of NCDs, including CVDs.[33, 89]

Figure 2. Risk factors and contribution (percentage) of non-communicable diseases to global mortality.[33, 88]



Adapted from: Amariles P. El paciente con factores de riesgo o con enfermedad cardiovascular en el contexto de la atención farmacéutica y el objetivo de desarrollo sostenible-3. Vitae. Vitae 28(Supl1):23-26. [in Spanish]. [accessed: 6 August 2022]. Available at: https://revistas.udea.edu.co/index.php/vitae/article/view/348083/20806693

The main goal of health promotion and disease prevention programmes and interventions is maintaining people's health for the longest time possible, by reducing exposure to risk factors and improving healthy environments. Health promotion aims to involve and empower people and populations to adopt healthy behaviours and generate changes that reduce the risk of developing either risk factors or NCDs, including CVDs. These interventions and programmes may be oriented to populations (primordial prevention) or to individuals (primary and secondary prevention).[78, 88, 90] These interventions aimed at developing and maintaining good CV health are both cost-effective and value-added health benefits; therefore, their early

implementation (ideally from childhood) may reduce the need for more expensive later treatments or interventions, for instance rehabilitation and palliative care.[33, 89, 91]

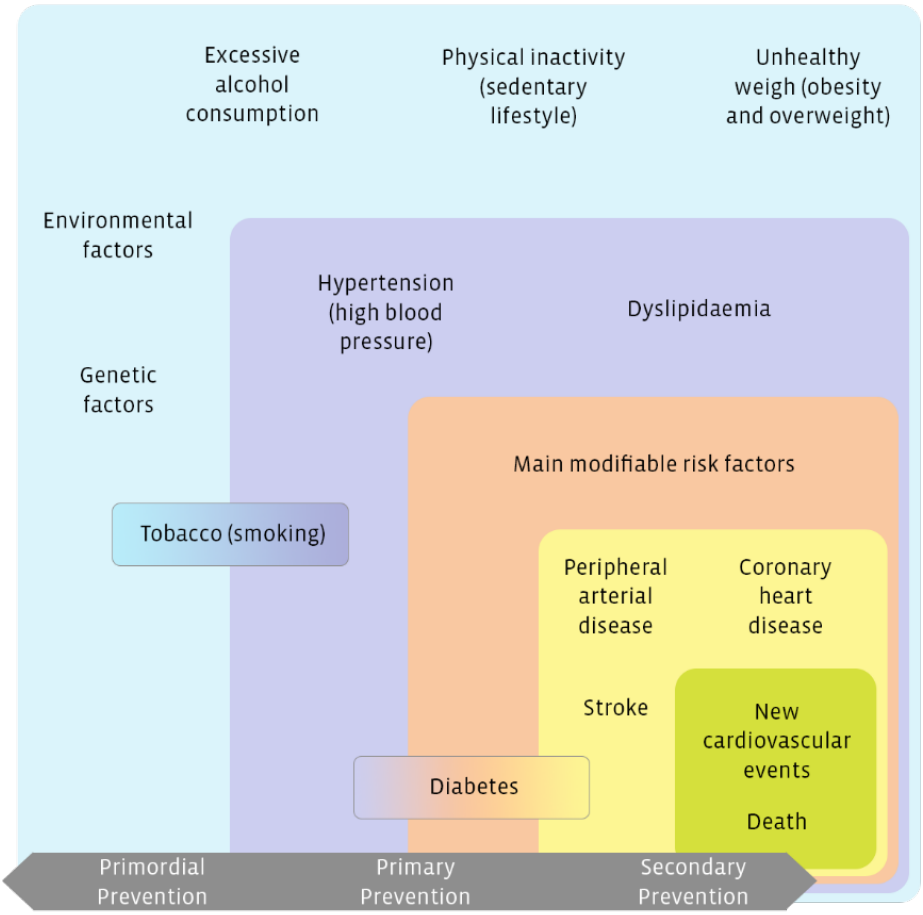
Primordial prevention: Focused on an entire population, aims to reduce both exposure to environmental (pollution) and behavioural (modifiable) risk factors (including smoking that is a major or independent CV risk factor), and avoid development of controllable, major or independent CV risk factors, for instance hypertension, dyslipidaemia and diabetes, considered as indicators of high atherosclerotic CVD risk.

Primary prevention: Focused on the person without atherosclerotic CVD, it aims to avoid its development through modifying or controlling major CV risk factors (including smoking), using pharmacological and non-pharmacological treatments.

Secondary prevention: Focused on the person with atherosclerotic CVD, it aims to avoid death or new CV events by modifying or controlling major CV risk factors (including smoking), using pharmacological and non-pharmacological treatments.

Figure 3 shows the CV risk factors, clinical conditions of atherosclerotic CVD (IHD, stroke, PAD) and types of cardiovascular prevention.[79, 90, 92]

Figure 3. Cardiovascular risk factors, clinical conditions of cardiovascular disease, and types of cardiovascular prevention.[79, 90, 92]



Adapted from: Amariles P, González M, Sabater D. Actuación farmacéutica en Prevención Cardiovascular. Granada; 2006. p. 68. [accessed: 6 August 2022]. Available at: https://www.researchgate.net/publication/215898825_Actuacion_Farmaceutica_en_Prevencion_Cardiovascular

3.1.1 Primordial prevention

Primordial prevention includes population-level interventions aimed at reducing exposure to risk factors, mainly behavioural and environmental risk factors, seeking to avoid the development of controllable or modifiable risk factors. Thus, improving healthy lifestyles or behaviours is a key target in the primordial prevention of CVDs. Behavioural interventions focus on tobacco control (smoking increases CV risk), promotion of healthy foods intake (fruits, vegetables, legumes, nuts, fish rich in omega 3), restriction of unhealthy foods (saturated and trans fats, refined carbohydrates, excessive salt and alcohol consumption), promotion of regular physical activity, and weight control.[93] Control of ambient and indoor pollution is a key environmental intervention.[90, 92]

Promotion and adoption of lifelong healthy lifestyles is the basis of CV health, therefore attaining and conserving healthy behaviours is a key task for all healthcare providers in cooperation with families and carers.[94] Thus, healthcare and education to attain and conserve healthy lifestyles are important elements of an effective preventive healthcare programme.[95]

Regular physical activity, healthy foods consumption, and unhealthy foods reduction can lower blood pressure, improve lipid profiles, and thus reduce the risk of developing hypertension and dyslipidaemia. In addition, healthy diet and physical activity are critical to maintaining healthy weight. Moreover, some behavioural factors, such as stress management, sleep duration and quality, portion control and meal timing,

may contribute towards reaching and maintaining a healthy weight, and therefore are relevant interventions for primordial prevention.[96]

In adults and older adults, dietary patterns including approximately 400g per day of vegetables and fruits, as well as legumes, nuts, whole grains, unsaturated vegetable oils, fish, lean meat or poultry and low-fat dairy products (similar to Dietary Approaches to Stop Hypertension [DASH] or to a Mediterranean diet) reduce the risk of all-cause mortality.[97] Moreover, adherence to the DASH diet reduces the incidence of heart failure, mainly in persons over 75 years old.[98] Similarly, fruit consumption and regular physical activity are positively associated with reduction in all-cause and CVD mortality.[99] For instance, physical activity in a dose-response relationship resulted in a reduction in the risk of CVD mortality, of 20–30%, in healthy individuals. Moreover, physical activity has been associated with mortality risk reduction by 50% and 40%, in men and women, respectively.[100]

Consumption of whole grain foods significantly reduces at least one inflammatory marker, for instance C-reactive protein, interleukin (IL)-6, or tumour necrosis factor; also, a higher intake of shelled fruits may lower levels of IL-6.[101] Red meat consumption and frequent intake of sweets are associated with an inflammatory pattern.[102] More information about nutrition and weight management can be found in the FIP "Nutrition and weight management services: A toolkit for pharmacists".

Overall, weight loss in people who are overweight or obese can significantly lower blood pressure; therefore, weight-loss diets in patients with hypertension can lower blood pressure. As a consequence, substantial weight loss may require downward adjustment of antihypertensive medication, for instance, systolic blood pressure can decrease by 10 mmHg or more after bariatric surgery.[103, 104] In addition, physical activity improves both sensitivity and insulin action in insulin-resistant people, since physical activity contributes to resolution of the molecular abnormalities responsible for insulin resistance and restores physiological insulin sensitivity.[105]

The positive effects of regular physical activity in the CV and respiratory systems are many, for instance, it:[100]

- Increases cardiorespiratory fitness, commonly measured by maximal oxygen uptake;
- Expands skeletal muscle oxygen sensing and angiogenesis;
- Enhances cardiac output, increasing body capacity to transport and diffuse oxygen;
- Improves lipid profile, by increasing the HDL/LDL cholesterol ratio and lowering plasma triglycerides concentrations;
- Reduces blood pressure;
- Contributes to counteract visceral fat accumulation, reducing cardiometabolic risk. Physical activity stimulates reduction in adiposity, due to increase of thermogenesis, and transformation of white into brown adipose tissue, which is the metabolically active form; and
- Reduces heart failure risk. High levels of total physical activity, leisure-time activity, vigorous activity, occupational activity, walking and bicycling combined and cardiorespiratory fitness are associated with reduction in risk of developing heart failure.[106]

There is unquestionable evidence that regular training (regular physical activity), aerobic exercise (continuous walking, jogging, and cycling) or resistance exercise (weights), prevents or delays development of independent CV risk factors. Additionally, there is information regarding the quantitative improvement in these CV risk factors due to physical activity or training:[100, 105]

- **Glycosylated haemoglobin A1C (HbA1C):** Systematic reviews show that exercise training significantly reduced plasma levels of HbA1c, a long-term glycaemic control marker, from 0.37% to 0.66%, an effect that is independent of modifications in body weight.[107, 108]
- **High-density lipoprotein (HDL):** Some meta-analyses show that exercise training significantly increases the plasma levels of HDL-cholesterol levels by 3–9% (equivalent to a mean ranged from 2.5–3.15 mg/dL).[109, 110] In addition, the beneficial effects depend on the amount of physical activity rather than exercise intensity or fitness improvement, and systematic reviews have found improvement in HDL-C levels from 0.27–5.41 mg/dL.[111]

- **Systolic blood pressure (SBP) and diastolic blood pressure (DBP):** Systematic reviews show that all types of physical activities reduce both SBP and DBP.[110] The magnitude of decrease attributable to endurance training in SBP/DBP is significantly higher in hypertensive (– 8.3/– 5.2 mmHg) compared with pre-hypertensive (– 2.1/– 1.1 mmHg) or normotensive subjects (–0.75/–1.1 mmHg). Noticeably, dynamic resistance training is more effective in reducing SBP/DBP in pre-hypertensive subjects than in hypertensive or normotensive subjects (–4.0/–3.8 mmHg).[112] Also, it is known that walking is associated with a lower risk of hypertension.[113]
- **Body weight:** Systematic reviews show the positive effects of exercise on people with unhealthy weight, which induces weight loss of 1–5 kg. High intensity exercise is more effective than moderate or light intensity exercise in increasing weight loss.[105]
- **Waist circumference:** Some studies show that aerobic exercise produces a reduction in waist circumference, an indicator of metabolic risk, by 2.2 cm.[110]

CV health promotion needs polices oriented to population-wide reductions in sodium consumption, increased availability and affordability of healthy foods, and the creation and availability of scenarios for practising physical activity. The formulation and implementation of healthy diet and physical activity policies need to consider the sociocultural, economic and political contexts.[114] Furthermore, policy makers and politicians should prioritise population-wide strategies for CV health promotion and for CVDs prevention, for example:[115]

- **Taxation on tobacco, salt, sugary foods, and alcohol:** These are effective polices to decrease their consumption and contribute to promote healthy lifestyles associated with cardiovascular well-being and to the reduction of the CVD burden. In addition, label regulations for processed foods and baked goods, focused to highlight the amount of unhealthy ingredients like salt, sugar and saturated and trans fats, is another policy that may reduce the risk of developing CVDs and other NCDs.
- **Educational interventions focused on reducing or controlling CV risk factors to the whole population (primordial prevention):** Screening for the presence of behavioural (unhealthy diet, sedentary, unhealthy weight, smoking and alcohol excess consumption) and metabolic (hypertension, dyslipidaemia and high fasting plasma glucose) CV risk factors is key to reinforcing the positive effect of healthy lifestyles in CV health.
- **Reduction of population exposure to ambient and indoor air pollution and improve healthy environments:** It is urgent to improve social and environmental factors to reduce exposure of populations to this risk factor for developing CVDs and others NCDs, mainly respiratory disease and cancer.

Evaluation of the effectiveness of the proposed preventive strategies should include monitoring of the incidence and prevalence of CV risk factors and CVDs.

3.1.2 Primary prevention

Primary prevention seeks to avoid the development of CVDs in people with elevated risk (defined by the presence of one or more CV risk factors). Before primary prevention interventions are initiated, it is important to determine an individual's level of risk of developing cardiovascular complications. At the individual level, aimed at modifying or controlling risk factors, identification of people at high multifactorial risk and guideline-driven management of hypertension, LDL cholesterol and diabetes are required. In health systems, healthcare and patient level strategies to improve adherence to healthy lifestyles and medication therapies are essential, and these could be implemented using education, technologies and personalised approaches.[90, 92]

Primary prevention includes interventions such as smoking cessation, dietary changes, physical activity, reducing alcohol and salt consumption, and weight control. In addition to recommending these interventions

for at-risk individuals, Riegel and colleagues encourage healthcare providers to promote a self-care approach to prevention and management of chronic diseases.[116] Self-care is defined as a process where patients and their families maintain health through health-promoting practices and illness management.[116] Self-care allows for increased autonomy and accountability by patients and their families, resulting in better outcomes aligned with individual health and life goals. A critical first step for self-care primary prevention interventions is patients knowing and understanding their health status and being aware of CV risk factors. Healthcare providers need to develop partnerships with patients to promote self-care practices through explaining all risk factors and providing patients with appropriate access to information on their health status.[116]

Effective lifestyle changes may be sufficient to prevent or delay the initiation of pharmacotherapy in patients with grade 1 hypertension. Lifestyle modification may also enhance the effect of antihypertensive therapy but should not delay the initiation of medication therapy in hypertensive patients with high CV risk. Hence, some guidelines on hypertension management recommend lifestyle modifications, for example, reduction in salt consumption and other unhealthy foods, moderating alcohol consumption, and increased intake of vegetables and fruits. Overall, in patients with hypertension and low CV risk, the reduction in salt consumption and lifestyle modifications continue to be effective therapeutic options.[75] However, in all countries, salt intake levels remain higher than the WHO recommendation, highlighting the need for further worldwide efforts to lower salt consumption and to assess salt reduction strategies.[117]

Some systematic reviews have shown that measurement and surveillance of lipid variability may have important clinical implications for risk assessment of CVDs and all-cause mortality.[118] Furthermore, there is evidence that cardiometabolic risk factors are associated with increased risks of all-cause mortality, CVDs and other health outcomes, for instance:[119]

- High lipids are associated with increased mortality and elevated risks of CVD, diabetes, end-stage renal disease and dementia.
- High blood pressure is associated with increased mortality, myocardial infarction and hospitalisation. In addition, hypotension may cause dementia.
- High glucose is associated with increased mortality, microvascular and macrovascular complications of diabetes, and hypoglycaemic events, leading to hospitalisation.
- Body weight is related to mortality, diabetes, obesity, CVD and cancer.

For key populations, accurate CV health management and health promotion, focusing on monitoring and controlling metabolic risk factors (hypertension, dyslipidaemia, diabetes and unhealthy weight) over time is a key strategy. For instance, people between 50 and 69 years of age are a group that needs effective programmes for prevention of CVD and promotion of CV health.[120] In addition, medicine therapy (for instance statins, antidiabetic and antihypertensive medicines) and changes in lifestyle behaviours improve the control of cardiometabolic risk factors.[90] Thus, the coverage of essential medicines, task distribution and employment of technology contribute to improving the effectiveness of CVD prevention programmes.[85, 121]

3.1.3 Secondary prevention

Secondary prevention aims to avoid deaths or new cardiovascular events in persons with atherosclerotic CVD. Communicating the benefits of a CV strategy increases support for actions across different behaviours and policies. Presenting the multiple benefits of policies enhances public support.[122] Increased clarity in interventions, definitions and assessments of treatment adherence are factors that need attention in future research.[123]

A self-management intervention has an impact on some risk factors. Therefore, it is recommended to use self-management support in myocardial infarction patients during the discharge process to improve their lifestyle.[124] Behaviour change interventions initiated in the ambulatory hospital setting significantly increased physical activity and reduced body weight, body mass index and waist circumference.

Regular screening for cardiovascular complications is important in secondary prevention. Screening helps in identifying probable risk of CVD before permanent damage occurs.[125] Some of the key screening tests include blood pressure, fasting lipoprotein profile, body mass index, and blood glucose tests. Other recommended screening tests include resting electrocardiograms, exercise treadmill tests, stress echocardiography and coronary angiography. Pharmacy based-screening programmes are able to measure most of the key screening

test outcomes, and such programmes have been recognised as ideal sites for detection, education and referral of individuals with a high risk of CVD complications.[126]

Following regular screening, healthcare providers may be required to institute pharmacological interventions in addition to already existing primary prevention interventions. Preventive pharmacological interventions have been shown to be more affordable than major preventive surgical procedures such as bypass surgery.[125] Core medicines required for secondary prevention of CVD complications can be found in Table 2.

Table 2. Core list of therapeutic groups for secondary prevention of cardiovascular disease complications

Therapeutic group	Indication
Antiplatelet medicines	Secondary prevention of ischaemic heart disease and ischaemic stroke
Thiazide diuretic	Hypertension
Calcium channel blockers	Hypertension
Statins	Primary and secondary prevention of ischaemic heart disease and ischaemic stroke
Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers	Hypertension, primary and secondary prevention of ischaemic heart disease and ischaemic stroke, heart failure
Beta blockers	Hypertension, secondary prevention of ischaemic heart disease, heart failure
Loop diuretics	Heart failure
Aldosterone receptor antagonist	Hypertension, heart failure, secondary prevention of ischaemic heart disease
Nitrates (glyceryl trinitrate)	Ischaemic heart disease
Sulphonylureas	Diabetes mellitus
Biguanides	Diabetes mellitus
Insulin	Diabetes mellitus

Adapted from WHO list of essential medicines[127]

The prescription of these medicines must be guided by standard treatment guidelines and they should go hand-in-hand with appropriate and sustainable behavioural interventions.[4] The WHO recommendations expressly state that hormone replacement medicines, vitamins B, C and E, and folic acid supplements are not recommended for the reduction of cardiovascular risk.[128]

To stress further, and in support of self-care, medication adherence is absolutely critical in the success of secondary pharmacological interventions. Pharmacists should be at the forefront of informing patients about their medicines, any potential side effects and potential for drug interactions.[116] Furthermore, pharmacists are best placed to promote the responsible use of cardiovascular medicines to support the prevention of cardiovascular complications.

3.1.4 Technologies for health promotion and disease prevention

There is evidence that supports mHealth-based disease management as a safe programme that may reduce blood pressure in people with multiple lifestyle-related diseases at risk of developing CVD. These findings will help shape the future.[129] In addition, a multicomponent mHealth diet and activity intervention involving connected coaching and modest initial performance incentives holds potential to reduce chronic disease risk.[130]

Mobile health may be an effective means of delivering customised individually directed health promotion interventions for CVD primary prevention. Text messaging interventions on smoking cessation may be useful to disseminate among university students who are at risk of developing a strong dependence.[131] The WHO supports harnessing mobile technologies to improve smoking cessation adherence rates in smoking cessation programmes.[132]

However, evidence on the effectiveness of mobile health-based interventions in reducing the risk for CVD and type 2 diabetes is low, mainly due to the quality of the studies and the small effects measured. Therefore, there is need for further high-quality research to assess the potential of mobile health interventions.[133]

3.1.5 Pharmacists' role in health promotion and disease prevention programmes

There is evidence that pharmacists contribute to prevention and control of CV risk factors and CVDs. Furthermore, community-based CVDs preventive interventions are effective to improve a person's level knowledge related to CVDs and risk factors, which potentially helps to counteract the growing burden of CVDs.[134]

Pharmacist interventions can effectively increase pharmacotherapy optimisation and improve quality of life of patients with atherosclerotic CVD. Moreover, there is evidence supporting that clinical pharmacist interventions successfully achieved reduction in blood glucose, blood pressure and total cholesterol levels, while supporting medication adherence post-myocardial infarction.[135]

Pharmacists can play a role in modifying CV risk factors by supporting or developing programmes focused on unhealthy lifestyle modification. Pharmacists can play a part in encouraging their patients to modify behaviours that put them at risk of developing CV risk factors (primordial prevention) or CVDs (primary or secondary prevention). For instance, some meta-analyses have shown that pharmacists' interventions provided favourable outcomes in controlling blood pressure and total cholesterol. Similarly, some studies show that pharmacists can contribute significantly to improve healthy weight (BMI), systolic blood pressure and lipid management.[136] Moreover, there is evidence of possible benefits from pharmacists' role in patients with heart failure, such as reduction or cessation of smoking, and reduced blood glucose levels and undesirable cardiovascular outcomes.[137]

In the future, pharmacist-led management can improve primary and secondary prevention of CV risk factors as well as healthcare costs, since pharmacists can possibly reduce morbidity and mortality of cardiometabolic events.[137]

Pharmacists' role in heart-healthy lifestyle or cardiovascular health programmes: Pharmacists can play a determinant role in designing, implementing and evaluating strategies focused on getting populations and people to adopt and follow a heart-healthy lifestyle (cardiovascular health) and thus prevent the development of CV risk factors and CVDs. For this goal, several organisations have developed materials with strategies to help people to know the relevance of behavioural risk factors and the actions to take in following a heart-healthy lifestyle and improving cardiovascular health.[138, 139]

Cardiovascular health: Concept and metrics: Seven modifiable or controllable metrics determine ideal CV health: four are modifiable and related to lifestyles and behaviours (physical activity, body mass index, diet plan and smoking) and three are controllable major CV risk factors (blood pressure, total cholesterol and fasting blood glucose).[140] Overall, according to defined levels and values, each metric is classified and assigned a score of 2 (ideal: optimal levels), 1 (intermediate: treated and controlled, or untreated/elevated), or zero (poor: uncontrolled). Therefore, for a specific person, CV health score ranges from zero to 14 points, and it determines the level of CV health as ideal (12 to 14 points), medium (8 to 11 points) or low (zero to 7 points).[90, 140, 141] See Table 3.

Table 3. Cardiovascular health metrics, scores and levels for assessment and classification of cardiovascular health.[90, 140]

Cardiovascular health metrics	Cardiovascular health metric level (points)		
	Ideal (2)	Medium (1)	Low (0)
Diet: servings of fruits and vegetables per day	>4	2–4	0–1
Physical activity: minutes per week of moderate to vigorous intensity	≥150 min/week moderate intensity or ≥75 min/week vigorous intensity or combination	>0 but <150 min/week	0

Cardiovascular health metrics	Cardiovascular health metric level (points)		
	Ideal (2)	Medium (1)	Low (0)
Tobacco/smoking	Never or quit >12 months ago	Previous and quit for ≤12 months ago	Current
Body mass index (kg/m²)	<25	25–29.9	≥30
Blood pressure (mmHg)	<120 and <80	Systolic 120–139 and/or diastolic 80–89 or <130 and <80 with drug treatment	Systolic ≥140 or diastolic ≥90
Total cholesterol (mg/dl)	<200 without drug treatment	200–239 or <200 with drug treatment	≥240
Fasting plasma glucose (mg/dl)	<100 without drug treatment	100–125 or <100 with drug treatment	≥126

Ideal cardiovascular health score (ICHS) is an independent predictor of the presence and progression of subclinical atherosclerosis, thus it is recommended for use in primary prevention. Therefore, the ICHS is inversely associated with all-cause mortality and CV events, supporting the use of CV health metrics as a suitable tool to predict mortality and CVD risk.[142] More relevant, some meta-analyses have evidenced that ideal CV health status, or even a one-point increase in CV health metrics, can result in substantial reduction in the risk of CVD, stroke and mortality. Improving metrics of smoking, diet, physical activity, plasma glucose levels and blood pressure will achieve the highest benefits.[143] Moreover, conserving healthy life-style behaviours could help diminish the development and progression of subclinical atherosclerosis and prevent CV events.[144]

From a practical perspective, there is a simplified and validated method to assess and define the degree of cardiovascular health, known as Fuster-BEWAT, an acronym formed by the initials of the five metrics included, namely, blood, exercise, weight, alimentation and tobacco (see Table 4).[141, 145]

Table 4. Fuster-BEWAT method for assessing CV health — Simplified cardiovascular health metrics

Cardiovascular health metrics	Cardiovascular health metric level (points)			
	Ideal (3)	Medium (2)	Low (1)	Poor (0)
B (blood pressure, mmHg)	<120 and <80	Systolic 120–129 and/or diastolic 80–84	Systolic 130–139 and/or diastolic 85–89	Systolic ≥140 or diastolic ≥90
E (exercise: minutes per week of moderate to vigorous intensity of physical activity)	≥ 150	75–149	74–11	<10
W (weight: body mass index, kg/m²)	<25	—	25–29.9	≥30
A (alimentation, diet: servings of fruits and vegetables per day)	> 4	3-4	1-2	< 1
T (tobacco: smoking packs per day)	Never	-	< 1	> 1

The five metrics of the Fuster-BEWAT method can be adapted to a dichotomous scale (positive or negative) as follows:

1. Scores of 3 (associated with ideal CV health metric level) is positive, while scores of 2, 1 or zero are negative (see Table 4).
2. Positive and negative metrics correspond to 1 and zero points, respectively. Therefore, a final score from zero to 5 points results as a sum of the five metrics.
3. The final score determines a person's CV health level as ideal/optimal (4–5 points), intermediate (2–3 points) or low (0–1 point).

Since it is a practical, simple and validated way of assessing and following CV health, the Fuster-BEWAT method can be easily used. Each person would maintain or perform the necessary changes to achieve a

positive point in each of the five metrics, which is associated with an ideal/optimal cardiovascular health (scores of 4 or 5).[141]

Overall, pharmacists can provide information and education programmes to people about the five CV health metrics with the aim of maintaining or performing the necessary changes to achieve a positive point in each of the five metrics, which is associated with an ideal/optimal cardiovascular health.[92, 139]

Pharmacists can contribute to people achieving and maintaining ideal/optimal cardiovascular health (4 to 5 positive cardiovascular health metrics). In addition, they can contribute to best practices and policies, related to effective interventions to favour behaviours that contribute to good cardiovascular health, including a healthy diet and regular physical activity.

Blood pressure: High blood pressure can damage the heart and blood vessels. To identify this condition, regular screening is important and therapeutic (non-pharmacological and pharmacological) actions are taken to control systolic and diastolic blood pressure levels, which ideally would be lower than 120 and 80 mmHg, respectively, or less than 140 and 90 mmHg, according to individual clinical conditions and type of CV prevention (primordial, primary or secondary).

Nutrition — healthy diet: A healthy diet can help protect the heart, improve blood pressure and cholesterol, and reduce the risk of type 2 diabetes. The Dietary Approaches to Stop Hypertension (DASH) eating plan and the Mediterranean diet are two examples of healthy food plans that include vegetables and fruits (400 g or five servings/day), beans or other legumes, lean meats and fish, low-fat or fat-free dairy foods, whole grains and healthy fats (olive oil).

Overall, intake of salt, sugar, processed carbohydrates, alcohol and saturated fat (found in red meat and full-fat dairy products) and trans-fat (found in fried fast food, chips and baked goods) should be limited. In detail, a healthy diet is characterised by the following:[14]

- The diet should be plant-based and less animal-based;
- Saturated fatty acids should contribute less than 10% of total energy intake, mainly by eating whole grains, which are rich in polyunsaturated fatty acid, monounsaturated fatty acid and carbohydrates;
- Trans unsaturated fatty acids should be limited as far as possible with none from processed foods;
- Total salt intake per day should be <5 g;
- Fibre per day should be 30–45 g, ideally from wholegrains;
- Fruits and vegetables per day should be >400 g (>200 g of fruit per day distributed in two or three servings, and >200 g of vegetables per day distributed in two or three servings);
- Red meat should be reduced to a maximum of 350–500 g per week, and processed meats should be limited;
- Fish, especially fatty fish, should be consumed once or twice per week;
- Unsalted nuts should amount to 30 g per day;
- Alcohol consumption should be limited to a maximum of 100 g per week; and
- Sugar-sweetened beverages (for instance soft drinks and fruit juices) must be discouraged.

Weight — maintain a healthy weight: Unhealthy weight (overweight or obesity) mainly around the middle of the body can lead to CV risk factors, including high blood pressure, high cholesterol and type 2 diabetes, and increases the risk of CVD. Body mass index (BMI) uses height and weight to determine whether a person is overweight or obese. A BMI of 25 or higher indicates unhealthy weight and it is associated with higher cholesterol, higher blood pressure, and an increased risk of CVDs. Thus, reducing weight can help decrease triglycerides, cholesterol, blood sugar (glucose) and the risk of type 2 diabetes.

Exercise — physical activity: Regular, daily physical activity (150 minutes a week of moderate aerobic exercise, such as walking at a brisk pace; 75 minutes a week of vigorous aerobic activity, such as running or two or more strength training sessions a week) can lower the risk of heart disease due to helping to control weight, reducing the probability of developing CV risk factors. Activities such as gardening, housekeeping, taking the stairs and dog-walking count towards total daily physical activity.

Tobacco — smoking: Smoking increases CV risk, therefore being a non-smoker, stopping smoking and avoiding second-hand smoking greatly contribute to CV health. The benefits for cardiovascular health and general health attributed to non-smoking status or smoking cessation are well known.

For control of some CV risk factors, for instance hypertension, hyperlipidaemia or high fasting plasma glucose (diabetes), medicines and lifestyle changes may be needed. Adherence to pharmacotherapy and a healthy-lifestyle plan is critical for control of these CV risk factors.

3.2 Identifying and preventing modifiable CVD risk factors

Identification and prevention of modifiable CVD risk factors are pivotal in addressing the rising prevalence and burden of CVDs globally. Driven by rapid urbanisation and globalisation, the prevalence and burden of CVDs have been increasing across high-income, middle-income and low-income countries.[146] Furthermore, the rate of major cardiovascular events, including heart failure, stroke, myocardial infarction and mortality from cardiovascular causes were highest in low-income countries (6.43 events per 1,000 person-years), followed by middle-income countries (5.38 events per 1,000 person-years), and high-income countries (3.99 events per 1,000 person-years).[146] Pharmacists can play an essential role in identifying and managing CV risk factors, especially in LMICs. An umbrella review of 85 meta-analyses on pharmacist-led interventions in cardiovascular risk assessment and management of cardiovascular risk factors reported significant improvements in lipid control and glycaemic control.[73] The same umbrella review also reported significant increase in smoking cessation rates with pharmacist-led educational interventions.[73] While age, race, gender, and genetic predisposition to CVDs were non-modifiable, there remains numerous modifiable risk factors that should be identified, prevented or managed at the earliest possible opportunity. This handbook will focus on modifiable risk factors as discussed below.

3.2.1 Hypertension

Hypertension is one of the major risk factors for CVDs and mortality. Hypertension is a state of persistently elevated blood pressure. The minimum criteria for a positive diagnosis is a systolic blood pressure (SBP) of ≥140 mmHg, a diastolic blood pressure (DBP) of ≥90 mmHg or both, following two or three visits to a doctor's office at one to four-week intervals.[147, 148] Hypertension can be classified as resistant or secondary. Other types are hypertension in pregnancy and hypertensive crisis.

Resistant hypertension: Resistant hypertension is characterised as seated office blood pressure of ≥140 and/or 90 mmHg for those undergoing treatment with three or more optimal doses of antihypertensive medicines, including a diuretic-based treatment, and excluding pseudo-resistance (BP measurement, white coat hypertension, medication compliance). The common risk factors include age, ethnicity, alcohol intake, obesity, end-stage renal disease, diabetes and heart failure.[149] Evaluation of resistant hypertension should include considerations of individual characteristics, pseudo-resistance, and screening for secondary hypertension.[74, 147]

Secondary hypertension: Secondary hypertension refers to arterial high blood pressure that is due to identifiable causes and can be resolved after removing the underlying cause.[150] The main causes of secondary

hypertension are obstructive sleep apnoea, renovascular hypertension, renal parenchymal disease, primary aldosteronism, and iatrogenic related. Screening for secondary hypertension is recommended, especially in young people who are diagnosed with hypertension.[150] Recommendations on screening and diagnostic tests as well as treatment for secondary hypertension can be found here. Basic laboratory testing is required (physical examination and blood biochemistry, dipstick urine analysis) before starting pharmacological intervention.[74, 147, 151] A summary of interventions to manage secondary hypertension is provided in Table 5.

Table 5. Summary of potential interventions to manage substance-alcohol-medicine-induced secondary hypertension

Agents	Intervention
Alcohol	• Limiting alcohol consumption to ≤1 drink daily for females and ≤2 drinks for males
Amphetamines	• Quitting or lowering dose • Considering behaviour therapies for attention-deficit/hyperactivity disorder
Antidepressants	• Considering alternative agents • Avoiding tyramine-containing foods with monoamine oxidase inhibitorss
Atypical antipsychotics	• Discontinuing or limiting use when possible • Considering behavioural therapy where appropriate • Recommending lifestyle changes • Considering alternative agents associated with lower risk of weight gain, diabetes mellitus and dyslipidaemia
Caffeine	• Limiting caffeine consumption to <300 mg daily • Avoiding use in uncontrolled hypertension patients
Decongestants	• Using for shortest duration • Avoiding in severe or uncontrolled hypertension patients • Considering possible therapies such as nasal, intranasal, antihistamines, etc.
Herbal supplements	• Avoiding use
Immunosuppressants	• Considering for converting to tacrolimus
Oral contraceptives	• Using low-dose such as 20–30 µg ethinylestradiol or a progestin-only contraceptive • Considering other possible forms of birth control • Avoiding use in women with uncontrolled hypertension
NSAIDs	• Avoiding systemic-medicine-delivery when possible • Considering alternative analgesics, including paracetamol, tramadol, topical preparations, etc.
Cocaine, methamphetamine etc.	• Avoiding use
Systemic corticosteroids	• Avoiding or limiting use where possible • Considering alternative medicine-delivery route such as inhaled, topical, etc.
Angiogenesis and tyrosine kinase inhibitors	• Initiating or intensifying antihypertensive medicines

Adapted from: Whelton PK, Carey RM, Aronow WS et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018;71(19):2199-269. [accessed: 4 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29146533

Hypertension in pregnancy: Hypertension in pregnancy is associated with significant maternal and fetal risks, specifically increasing the maternal risks of preeclampsia, eclampsia, stroke, heart failure and renal failure, and fetal risks of congenital malformations, prematurity and stillbirth.[152] Low-dose aspirin may be recommended for prevention of preeclampsia.[152] Since not all medicines are safe to use during pregnancy, collaborations between pharmacists, obstetricians and cardiologists can improve perinatal outcomes.

Hypertensive crisis: Hypertensive crisis is generally defined as a rapid elevated SBP of >180 mmHg and/or DBP of >120 mmHg with signs of end-organ damage (known as hypertensive emergency) or without signs of end-organ damage (known as hypertensive urgency).[153] Hypertensive emergencies are linked to acute hypertension-mediated damage to organs, including retina, brain, heart, large arteries and kidneys. Hypertensive emergencies can result from malignant hypertension, hypertensive encephalopathy and hypertensive thrombotic microangiopathy.

3.2.2 Dyslipidaemia

Dyslipidaemia is a leading risk factor that promotes the build-up of atherosclerotic plaque in arterial walls. It is characterised by higher-than-normal levels of serum triglycerides, LDL cholesteerol, and total cholesterol with lower concentrations of HDL cholesterol. Independent predictors that lead to cardiac sequelae include hypertension, ischaemic stroke, cerebrovascular disease, myocardial infarction, and unstable and stable angina.[154] Lowering of LDL cholesterol is significant in reducing atherosclerotic CVD. A meta-analysis of 26 randomised controlled trials on 22,095 individuals found that pharmacist-led interventions (medication management, health education and lifestyle counselling) resulted in significantly greater reduction in LDL cholesterol than usual physician-centric care.[155] Specific non-pharmacological interventions that pharmacist can adopt to manage dyslipidaemias are detailed in the 2019 ESC/EAS "Guidelines for the management of dyslipidaemias".[156] More information on pharmacological treatment of dyslipidaemia can be found in section 6.3 of this handbook.

3.2.3 Diabetes mellitus

Diabetes mellitus is a life-threatening condition that is classified as an independent risk factor for many types of vascular disorders, including hypertension and dyslipidaemia.[14] People living with diabetes have a higher cardiovascular risk due to hyperglycaemia-related mechanisms that promote atherosclerotic plaque formation by induced oxidative stress (i.e., activation of protein kinase C and lipoxygenase pathway).[157, 158] It is therefore important to maintain lowering of LDL cholesterol status and HbA1c level among people living with diabetes.[14] Pharmacist-led management and intervention for diabetes has been extensively discussed in the FIP 2021 "Diabetes prevention, screening and management: A handbook for pharmacists".[159]

3.2.4 Smoking

Exposure to tobacco, through active smoking or second-hand cigarette smoke, increases the risk of developing CVDs, such as heart failure, hypertension, myocardial infarction, coronary heart disease and stroke.[160, 161] Furthermore, nicotine exposure due to smoking can lead to development of metabolic syndrome and diabetes.[160] Reactive oxygen species in cigarette smoke induce oxidative stress, trigger release of cytokines, lead to vasodilation and inflammation, and hence increase the risk of sudden cardiac death.[162]

Globally, all-cause mortality due to tobacco smoking has increased by 11.3% from 2007 to 2017.[39] In the same period, deaths from ischaemic heart disease attributed to tobacco smoking increased by 7.8%, and deaths from ischaemic stroke attributed to tobacco smoking increased by 13.4%.[39] In addition, DALYs attributed to all-cause mortality from tobacco smoking have increased by 6.8%.[39] Evidently, smoking has brought about a significant health burden. Smoking cessation and tobacco control are therefore pivotal in reducing cardiovascular risk caused by tobacco exposure.

The WHO Framework Convention on Tobacco Control (FCTC), a global public health treaty, was launched in 1992, calling for tobacco control advocates to address the unmet needs for tobacco control.[163] However, implementation of the FCTC over the past 30 years has been weak and slow.[163] One of the key challenges to its successful implementation is tobacco industry interference, especially in LMICs.[164] While system-level and structural changes are required to address most of the challenges posed by tobacco industry interference, pharmacy associations can encourage garner the pharmacy profession to advocate tobacco control and

smoking cessation through some of the WHO MPOWER measures, which are evidence-based and cost-effective.[165] MPOWER is an acronym for:

- Monitor tobacco use and prevention policies — can be lobbied by pharmacists
- Protect people from tobacco use — can be advocated and lobbied by pharmacists
- Offer help to quit tobacco use (cessation) — can be advocated and lobbied by pharmacists
- Warn about the dangers of tobacco — can be advocated and lobbied by pharmacists
- Enforce bans on tobacco advertising, promotion and sponsorship — can be lobbied by pharmacists
- Raise taxes on tobacco — can be lobbied by pharmacists

Pharmacist-led smoking cessation programmes have shown promising clinical and economic outcomes globally. A study conducted in Thailand found that community pharmacist-led smoking cessation services resulted in a significant reduction in the mean number of cigarettes smoked daily (from 15.3 to 1.9, $p<0.001$).[166] A cost effective analysis of a community pharmacist-based smoking cessation programme found a cost saving of USD 500 to the health system and 0.18 life years gained for men and a cost saving of USD 614 to the health system and 0.24 life years gained for women.[167] The WHO has also presented the health and economic benefits of investing in interventions to support smoking cessation (publication can be accessed here). Evidently, pharmacists can play an essential role in addressing the health and economic burdens of smoking on CVDs through the MPOWER measures and facilitating implementation of the FCTC.

3.2.5 Obesity and overweight

Being obese or overweight can be a strong independent predictor of developing cardiometabolic events such as coronary heart disease, stroke, heart failure and type 2 diabetes. Obesity is attributed to an increase in pro-inflammatory cytokines that are produced by the adipose tissue. The adipose tissue normally controls caloric intake, appetite, and individual stamina for physical activity. Thus, adipocyte dysfunctions alter haemodynamic status and body composition. This process promotes the build-up of fatty plaques in the arterial wall.[168, 169] Therefore, maintaining a healthy weight is an effective strategy to prevent cardiometabolic diseases.

Body mass index (BMI) is often used as an initial screening tool due to its simplicity, its low cost and its non-invasive nature. A study in Lebanon showed BMI measurements can support pharmacist-led weight management at the community level.[170] Pharmacists can play an integral role in weight management by educating patients on how to track their body composition using several methods, such as waist circumference, bioelectrical impedance and hydrostatic weighing. As part of collaborative practice along with other healthcare professionals, pharmacists can successfully enhance weight-loss outcomes.[171]

3.2.6 Physical inactivity

Physical inactivity is defined as failure to achieve the recommended levels of physical activity (i.e., at least 150 minutes of moderate-intensity or at least 75 minutes of vigorous-intensity physical activity or an equivalent combination of moderate- and vigorous-intensity physical activity).[172] Physical inactivity can increase the likelihood of cardiometabolic complications and premature mortality.[172] Physical inactivity contributed to approximately 7.6% of all CVDs mortality, while 74% of all cardiovascular deaths in middle-income counties were attributed to physical inactivity.[172]

Insufficient physical activity can be attributed to both intrinsic and extrinsic factors. Intrinsic factors include gender, lack of motivation, lack of knowledge about physical exercise, poor financial status, lack of companionship and lack of exercise skills, while extrinsic factors include inaccessibility to exercise facilities, living in urban areas and unfavourable weather.[173, 174]

The intensity of physical activity is measured in metabolic equivalent of task (MET) and is commonly used to assess lifestyle-related improvements. One MET reflects the amount of oxygen consumed at rest, which is equivalent to approximately 250 ml of oxygen consumed per minute. A person is classified as inactive when they have a low level of energy expenditure or their MET value is ≤1.5.[175] Further description of MET thresholds is presented in Table 6.

Table 6. Classification of physical activity intensity[176]

Intensity	Relative intensity		Absolute intensity		
	VO2max (%), Heart rate reserve (%)	Maximal heart rate (%)	RPE	Intensity	METs
Very light	<25	<30	<9	Sedentary	1–1.5
Light	25–44	30–49	9–10	Light	1.6–2.9
Moderate	45–59	50–69	11–12	Moderate	3.0–5.9
Hard	60–84	70–89	13–16	Vigorous	≥6.0
Very hard	≥85	≥90	>16		
Maximal	100	100	20		

METs: indicates metabolic equivalents;
RPE: rating of perceived exertion;
V02 max: maximal aerobic capacity.
% Heart rate reserve (HRR) formula=Maximal heart rate (HR)–resting HR=HRR;
calculate HRR target by (HRR×%value)+resting HR.

Having moderate- and vigorous-intensity of physical activity helps individuals keep fit and gain favourable body composition. The WHO has called for global collaborative actions across sectors to reduce physical inactivity by 10% by 2025.[177] The Bangkok Declaration on Physical Activity and Health is a consensus statement that provides a foundation to achieve this WHO's goal.[177]

While encouraging people to be physically active based on the MET criteria, outlined in Table 7, pharmacists can also support the WHO's initiatives by conducting sustainable programmes to ensure their communities are regularly active. Promotion of physical activity in the community is an invaluable investment for improving the levels of physical activity of the population.[178]

Table 7. Classification of intensity of physical activity according to METs[179]

Intensity	Light (<3 METs)	Moderate (3–6 METs)	Vigorous (≥6 METs)
Walking	Walking slowly	Walking at brisk pace	Jogging, running
Household or occupation	Washing dishes	Washing window	Shovelling, digging ditches
	Ironing	Sweeping floor	
	Making beds	Vacuuming	
	Working at desk	Mowing lawn	
Leisure or sports	Billiards	Badminton	Basketball
	Croquet	Dancing	Soccer
	Darts	Golf	Skiing
	Fishing	Bicycling (light)	Bicycling (moderate/high)
	Musical instrument	Swimming (light)	Swimming (moderate/high)
		Tennis (double)	Tennis (single)

Adapted from: Nam G-B. Exercise, Heart and Health. Korean Circ J. 2011;41(3):113. [accessed: 24 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3079129/.

3.2.7 Unhealthy diet

Unhealthy diet is a behavioural risk factor for NCDs (including vascular diseases, diabetes and cancer) and other conditions associated with obesity and overweight. Poor dietary habits occur when people consume foods high in saturated- and trans-fats, salt and sugar, or low in fibre intake. This affects the normal body function, altering daily active life. Malnutrition, indigestion and inflammatory process can occur and these lead to atherosclerosis. Hence, healthier eating habits are advisable to prevent the increased risk of morbidity due to cardiometabolic diseases. Individuals can adopt the Dietary Approaches to Stop Hypertension (DASH) diet which is designed to support a heart-healthy eating plan.

The NCD Alliance and the WHO also recommended the consumption of more-nutrient-rich-foods, as follows:[180, 181]

- Low-fat dairy products and limited intake of saturated fats (less than 10% of total energy); trans-fats should not be consumed;
- High consumption of at least 400 g per day of vegetables, fruits, nuts and seeds;
- Reduced sugar-sweetened beverages and sweets intake that is at least no more than 10% of total energy; a total of less than 5% is preferable;
- Reduced salt intake (less than 5 g/day, which is equivalent to one level teaspoonful).

These healthier eating patterns have a significant benefit in cardiometabolic diseases prevention.[182] It is an effective dietary strategy to control blood pressure and increase the effectiveness of antihypertensive medicines.[183] More details on DASH eating plans can be found in the FIP publication on nutrition and weight management services.[184] Pharmacists can also take inspiration from a roadmap for the transition towards trans-fat elimination in 2023 and the NCD Alliance guideline "Trans fat free by 2023: Case studies in trans fat elimination".[185]

3.2.8 Excessive alcohol consumption

The prevalence of alcohol consumption is approximately 67.3% in high-income countries, 47.4% in upper middle-income countries, 30.1% in lower middle-income countries, and 26.8% in low-income countries.[186] Alcohol consumption has a causal relationship with cardiovascular events as well as numerous health and social burdens. It can weaken and enlarge heart muscles, resulting in alcoholic cardiomyopathy. Acute alcohol consumption can disrupt heart rhythm, most commonly manifesting as atrial fibrillation.[187] Heavy or binge drinking contributes to the increase of inflammatory and oxidative damage, which plays a role in the build-up of unhealthy fat deposits.[188, 189]

Avoiding harmful consumption of alcohol is advisable in protecting the heart from any potential alcohol-related damages. The WHO has promoted the "10 target areas of policy options and interventions" to reduce deleterious effects of alcohol consumption, as follows:[190]

- Leadership, awareness and commitment;
- Health services' response;
- Community action;
- Drink-driving countermeasures;
- Regulating availability of alcohol;
- Market restrictions;
- Pricing policies;
- Reducing negative consequences of drinking;
- Addressing informal and illicit production; and
- Monitoring and surveillance.

Since pharmacists can provide a large range of primary healthcare services and interventions, the "Health services' response" strategy is one action that can be adopted in the pharmacy setting.[191] Pharmacists can play essential roles in early identification and in encouraging alcohol use awareness through provision of alcohol-misuse services.[191] The success of these interventions is dependent on having well-trained and skilled pharmacists who are confident in delivering screening and brief interventions and improving alcohol-related

knowledge.[191] Further information related to policy indicators for national action that pharmacists can get involved in are available in WHO publications.[186, 190]

3.2.9 Stress and psychosocial factors

Stress can release high levels of cortisol that can be harmful to well-being and health status. The clinical consequences include elevated blood pressure, blood sugar, triglycerides, cholesterol and suppressed immune system. Therefore, optimum cortisol levels are important to maintain normal body functions. Pharmacists can motivate their patients to reduce stress and anxiety by engaging in exercises regularly, engaging in mindful meditation and obtaining quality sleep.[192] Pharmacists can initiate collaborative interventions by referring their patients to physicians and psychologists for further care. Pharmacists can get involved in medical counselling to prevent adverse medicines reactions and any foods or medicines interactions, and also improve therapy compliance and intervention success rate.[192, 193]

3.2.10 Sleep disorders

Sleep deprivation may contribute to high levels of stress hormone due to the role of glucocorticoids in the sleep-time cycles. Glucocorticoid hormone produces and releases cortisol to control circadian rhythm.[194] Circadian rhythm plays a part in regulating physical and mental function for resting and recuperating.[194] The disruption of circadian rhythm could enhance the activation of the hypothalamic-pituitary-adrenal axis, which may disrupt the regulation of blood pressure by increasing blood volume resulting in secretion of vasopressin and glucocorticoids.[194] A dysfunctional circadian rhythm occurs due to insufficient sleep but also due to later bedtimes. A late onset of sleep, starting 11.00pm or later, may increase the cardiovascular events rate by around 25% compared with those with a sleep-time from 10.00 to 10.59pm.[195] Metabolic impairment such as diabetes, dyslipidaemia and obesity can increase the incidence rate of chronic sleep apnoea through complex pathogenic pathways.[194]

Quality of sleep can be modified by non-pharmacological approaches. Pharmacists can play a role in helping patients to identify predisposing factors (such as smoking, living alone and anxiety), precipitating factors (such as alcoholism, stressful life events and comorbidities) and perpetuating factors (such as excessive time spent in bed, worries and use of certain medicines) to poor sleep quality.[196] Pharmacists can educate patients on sleep hygiene, such as limiting alcohol, nicotine, smoking, caffeine use or consumption of heavy meals near bedtime, reducing blue light levels, sleeping in a quiet and clean bedroom, and exercising regularly but not within four hours of bedtime.[196] Pharmacists can recommend their patients to use stimulus control such as a drink of mixed herbs, a glass of warm milk, a mint infusion and a good sleep environment (reducing light, noise and activity).[197, 198]

3.3 The role of vaccination in the prevention and management of CVDs

Vaccines can prevent approximately two to three million deaths annually, however, vaccine-preventable mortality still remains high at around 1.5 million each year.[199] Vaccine-preventable infections contributed significantly to the development of cardiovascular complications.[200] Furthermore, people living with CVDs are at an increased risk of these infections. Cardiovascular complications such as heart failure, myocardial infarction, arrhythmia and stroke, can also develop during acute viral infection or years after recovering from the infection.[201] A global meta-analysis reported 15.6% overall pooled event rates for cardiac complications among people having pneumonia severity index class IV or V or among people admitted to intensive care unit for pneumonia.[202] A study conducted among the elderly in the United Kingdom also reported significant associations between influenza infection and hospitalisation due to myocardial infarction or stroke.[203] Similarly, influenza infection accounted for excess cardiovascular-related hospitalisations among the elderly in Singapore.[204]

In addition, people living with CVDs are more susceptible to infection by severe acute respiratory syndrome coronavirus 2 (SARS CoV-2), causing the disease known as coronavirus disease 2019 (COVID-19). Diphtheria and pertussis infections, caused by bacteria, can also result in severe cardiovascular complications. Therefore, people living with CVDs are recommended to receive the following vaccinations:

- Influenza vaccination;
- Pneumococcal vaccination;
- Diphtheria, tetanus, acellular pertussis vaccination; and
- COVID-19 vaccination.

Influenza viral infections contribute significantly to morbidity and mortality throughout the world. Numerous deaths and cardiovascular complications take place during influenza epidemics, especially in vulnerable populations.[205] People living with CVDs are particularly at risk and represent a population that could benefit the most from vaccination.[206, 207] In the past 15 years, influenza vaccination in high-risk populations has become an effective strategy to reduce the incidence of respiratory infections and therefore associated cardiovascular complications. A meta-analysis of 63 studies found that influenza vaccination was associated with reduction in risk of developing cardiovascular complications from influenza infection.[208]

In addition, the meta-analysis revealed a reduction in risk of all-cause mortality among people vaccinated against influenza.[208] However, the prescription of influenza vaccination is not a cardiologists' usual practice, and vaccination rates vary widely among high-risk vulnerable populations in different regions of the world.[209]

Influenza vaccination rates varied and are often low in populations with pre-existing CVDs. For example, influenza vaccination rates among people living with heart failure ranged from nearly zero in Asia to approximately 80% in Europe.[210] In particular, most LMICs have not reached the target of 70% vaccination coverage rate set by the WHO for high-risk groups.[210] The reluctance of cardiologists to incorporate immunisation as a routine cardiovascular prevention strategy for their patients has also been observed in Latin American countries.[211-213]

During the past two years, new meta-analyses and guidelines, and two randomised controlled trials (RCTs) were published.[214-216] The Influenza Vaccination After Myocardial Infarction (IAMI) trial contributed evidence to the safety and efficacy of influenza vaccination right after an acute myocardial infarction hospitalisation or after a percutaneous coronary intervention among high risk patients with coronary artery disease.[214] A significant reduction in mortality was observed.[214] More recently the Influenza Vaccine to Prevent Adverse Vascular Events (IVVE) trial, conducted in 10 countries across Asia, the Middle East and Africa, did not meet the primary cardiovascular endpoint among people living with heart failure.[215] However, a significant reduction was observed during the seasonal peaks of influenza circulation.[215]

A recent meta-analysis of four RCTs and 16 observational studies including 237,058 patients, indicated that influenza vaccination was safe and effective in reducing cardiovascular events, and it was included in the most updated guideline.[216] A large retrospective cohort study conducted among adults hospitalised for the treatment of influenza infection in the United States also found significant risk reduction in mortality and development of cardiovascular complications with influenza and pneumococcal vaccinations.[217] Specifically, influenza vaccination was associated with reduced risks of myocardial infarction.[217]

Furthermore, people who received both influenza and pneumococcal vaccinations were at a reduced risks of mortality and cardiac arrest.[217] Despite these benefits and the recommendations for its prescription by scientific societies and health regulatory agencies, the vaccination rate remains lower than expected globally.

Infection by SARS CoV-2 can lead to severe cardiovascular complications and hence the recommendation for COVID-19 vaccination. COVID-19-related cardiac complications include arrhythmia, myocardial injury, heart failure, thrombotic changes and acute coronary syndrome.[19] Furthermore, COVID-19 infection can lead to long term cardiovascular complications, with dyspnoea being most commonly reported and the prevalence of chest pain ranging from 13% to 21%.[19] Therefore, cardiologists and pharmacists should address patients' concerns and beliefs as well as any misinformation regarding COVID-19 vaccination, and recommend COVID-19 vaccination accordingly.

As with other prevention measures, medical knowledge through continuous education, clear regulations and conviction regarding the risk-benefit ratio appear to be the main determinants of implementation of an intervention. The personal experience of the physician, as well as that of other health workers, with influenza vaccination also appears to be a determining factor. When "missed opportunities" were analysed in unvaccinated people, lack of recommendation during medical visits was identified as the main cause.[218] The correct understanding of implementation barriers, which involve doctors, patients and their context, are essential when continuous improvement strategies are planned, in order to improve the vaccination rate

among at-risk individuals. In addition, implementation research should focus on elucidating factors associated with vaccine hesitancy. Clinicians, practitioners, administrators and researchers have to collaborate to develop and implement targeted interventions to enhance vaccination rates among people living with CVDs.

4 Screening and identification of clinical manifestations of CVDs

The prevalence of CVDs is rising in LMICs, and CVDs remain major causes of mortality and morbidity.[219] In addition, many LMICs are also facing challenges in adequately managing the rising burden of infectious diseases due to constraints in health systems.[220] Therefore, screening for cardiovascular risk, identifying CV risk factors, and early management of CVD risks are key to addressing some of the challenges. Community pharmacists, being accessible and often the first port-of-call, can play an integral role in cardiovascular risk assessment. For example, a cross-sectional study conducted in Nigeria reported that community pharmacist-led cardiovascular risk screening resulted in early detection of cardiovascular risk factors.[221]

4.1 Blood pressure measurement

Blood pressure is estimated through non-invasive methods and generally can be classified as office blood pressure and out-of-office blood pressure.

Office blood pressure measurement, defined as the measurement on the arm over the brachial artery taken during a healthcare visit, is generally used for diagnosing hypertension.[222] Hypertension is conventionally classified into the categories outlined in Table 8.

Table 8. Classification of hypertension based on office blood pressure[14, 147]

Category	Systolic (mmHg)		Diastolic (mmHg)	Recommendation
Optimal	<120	and	<80	Reassess within three years when the result is <130/85 mmHg (one year in people with combined risk factors)
Normal	<130	and	<85	
High-normal	130–139	and/or	85–89	If possible, confirm with ambulatory or home BP measurement to detect white coat or masked hypertension. Alternative option is to confirm with repeated clinic visits if the result is 130–159/85–99 mm Hg
Grade 1 hypertension	140–159	and/or	90–99	
Grade 2 hypertension	160–179	and/or	100–109	Confirm within a few days or weeks
Grade 3 hypertension	≥180	and/or	≥110	Confirm within a few days or weeks
Isolated systolic hypertension	≥140	and	<90	Same as for high-normal and grade 1 hypertension

Out-of-office blood pressure can be determined by ambulatory or home blood pressure measurement (ABPM/HBPM).[222] ABPM and HBPM can be used to identify white coat or masked hypertension. ABPM assesses blood pressure during routine daily activities whereas HBPM assesses blood pressure at specific times during the day and night.[223] Out-of-office measurement is often used for monitoring hypertension control and titration of blood pressure-lowering medicines. Both office and out-of-office BP measurements are necessary to classify hypertension, as shown in Table 9.

Table 9. Description of BP measurement based on office and out-of-office BP measurement criteria[147]

	SBP/DBP mmHg
Office BP	≥140 and/or ≥90
Ambulatory BP measurement	
• 24h average	≥130 and/or ≥80
• Day time (or awake) average	≥135 and/or ≥85
• Night time (or asleep) average	≥120 and/or ≥70
Home BP measurement	≥135 and/or ≥85

A hypertension guide has recently been published by SEFAC (the Spanish Society of Clinical, Family and Community Pharmacy) and Spanish medical societies of primary and specialised care in which the values and conditions of the patient for screening, control, monitoring and referral by community pharmacists are made clear.[224, 225] In the SEFAC guide for the approach of hypertension by the community pharmacist and in one systematic review, a threshold value is suggested for the measurement of hypertension in a community pharmacy of SBP/DBP 135/85 mmHg.[226, 227]

Both ABPM and HBPM are required to confirm the diagnosis of elevated blood pressure either in untreated or treated patients with grade 1 hypertension.[148] The classification of hypertension using office and out-of-office blood pressure measurements is summarised in Table 10.

Table 10. Classification of hypertension using office and out-of-office blood pressure measurements

Classification	Office BP	Out-of-office BP
Normotension	Not raised	Not raised
Sustained hypertension	Raised	Raised
White-coat hypertension	Raised	Not raised
Masked hypertension	Not raised	Raised

Early detection of white-coat hypertension and masked hypertension can prevent progression to hypertension-mediated organ damage. Early detection also allows timely pharmacological and non-pharmacological interventions.[74, 147]

Pharmacists can contribute to therapeutic guidance and in ABPM or HBPM measurements. Community pharmacists, being accessible and often the first port-of-call for people living with hypertension, can play a collaborative role with general practitioners to ensure continuity of care and adequate monitoring for BP control.[226, 228, 229] Different studies highlight the usefulness of blood pressure measurement by community pharmacists in the management of hypertension.[230, 231] For example, in Argentina, in May 2019, the Argentinean Pharmaceutical Confederation started a partnership with the Argentinean Society of Hypertension and together they carried out a campaign in order to assess the risk of CVDs in outpatients at community pharmacies. More than 100,000 measurements were taken, 50% of the people showed high blood pressure and 26.8% of them did not previously know about their condition. The campaign is still running and is demonstrating the crucial role of the community pharmacist in prevention, the value of pharmaceutical services and the importance of interprofessional networking for the benefit of patients.

More information related to BP measurement can be accessed through a 2017 Guideline for the prevention, detection, evaluation and management of high blood pressure in adults;[74] the 2020 International Society of Hypertension global hypertension practice guidelines;[147] and the 2021 European Society of Hypertension practice guidelines for office and out-of-office blood pressure measurement.[148]

Table 11 summarises the utility of office and out-of-office BP measurements for low-resource settings.

Table 11. The utility of office and out-of-office BP measurement methods in low-resource settings

Best for	Office BP	Out-of-office BP	
		ABPM	HPBM
	Routine screening of untreated individuals and follow-up treated patients	Preferred method for diagnosis of hypertension if available	Preferred method for long-term follow-up of patients using treatment
Screening	+++	–	+
Initial diagnosis	++	+++	++
Medication dose adjustment	+	+++	++
Follow-up	++	+	+++
Affordability	+++	+	+++
Hypertension diagnosis, mmHg	≥140/90	≥130/80	≥135/85

Adapted from: Schutte AE, Srinivasapura Venkateshmurthy N, Mohan S et al. Hypertension in Low- and Middle-Income Countries. Circ Res. 2021;128(7):808-26. [accessed: 27 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33793340.[32]

4.1.1 Considerations in special populations

People who are obese: Some people may require a cuff that is >50 cm in circumference, known as a thigh cuff. While a thigh cuff can obtain accurate BP measurement, studies on the validity of its use among obese people is limited. An alternative to a thigh cuff is measuring BP on the wrist.[222] Obese people may also have arms that are tronco-conical (truncated cone) in shape, hence a cone-shaped cuff may offer a more accurate estimate of BP.[222]

Pregnant women: Hypertension complicates approximately 10% of all pregnancies and is associated with adverse maternal and fetal outcomes.[222] The accurate measurement of BP in pregnancy is essential to guide medical decision making that affects both mother and fetus. BP should be taken in the seated position. Information on validated BP measurement devices for use in pregnancy can be found here.

The elderly: Coupling impaired baroreceptor sensitivity with increased arterial stiffness means the elderly may be susceptible to orthostatic hypotension.[222] BP should be measured in duplicate in the seated and standing positions (at one minute and three minutes after rising) to detect any potential hypotension.[222]

4.2 Lipid profile

Lipid-lowering therapy, specifically reduction of LDL cholesterol, has been associated with a reduction of cardiovascular risk.[232] While the prevalence of dyslipidaemias is higher in high-income countries, the prevalence in low-income countries is increasing significantly due to socioeconomic developments.[233] Thus, an initial screening test is critical to improving plasma lipid profiles among people living with CVDs. According to the 2021 ESC guidelines on cardiovascular disease prevention in clinical practice, lipid profile assessments are classified into:[156]

- **Fasting vs non-fasting assessments:** In most cases, non-fasting sampling is preferable for general risk screening since it has several practical benefits, including similar prognostic value as fasting samples, has better individual acceptability and outweighs the potential of imprecision. As a result, a number of clinical guidelines recommend non-fasting tests although fasting sampling has slightly different results for lipid parameters.[14, 234]

- **Low-density lipoprotein cholesterol and triglycerides assessments:** An elevated LDL cholesterol level is a dominant cause of atherosclerotic plaque. “Triglycerides” (TG) refers to the concentration of circulating apolipoprotein B-containing TG-rich lipoproteins.[234, 235] As a result, reducing LDL cholesterol and TG is one of the effective measures to lower CVD risk.

- **Non-high-density lipoprotein cholesterol assessment:** Non-HDL cholesterol is a combination of very low-density lipoprotein (VLDL) and LDL cholesterol. Non-HDL cholesterol can be an alternative method to measure lipid profile. It does not depend on the concentration of TG. It can be quantified by: total cholesterol – HDL cholesterol level. This method may be more precise for those with diabetes or hypertriglyceridaemia and in a non-fasting setting.[14, 234]

- **High-density lipoprotein cholesterol assessment:** Elevated HDL cholesterol is associated with reduction in TG or LDL cholesterol, or both. The HDL cholesterol level is inversely associated with risk of atherosclerotic CVD. However, there is no conclusive evidence that the increase in plasma HDL cholesterol level is associated with reduction in risks of major cardiovascular events.

- **Apolipoprotein B:** Apolipoprotein B (ApoB) is the protein that encloses LDL and VLDL cholesterols. ApoB is a stronger indicator of build-up of fatty deposits than LDL cholesterol.[235] Therefore, ApoB provides a better assessment of a patient's exposure to atherogenic lipid particles, specifically for those with high TG, diabetes, obesity or lower LDL cholesterol concentrations.[14, 234]

In conclusion, lipid modification is mandatory to reduce cardiovascular risks. Further information related to lipid profile goals is summarised in Table 12.

Table 12. Lipid profile depends on risk-based categories[234]

Lipid parameters	Risk classification based on lipid profile
LDL cholesterol	Very high risk: <1.4 mmol/l or <55 mg/dl High risk: <1.8 mmol/l or <70 mg/dl Moderate risk: <2.6 mmol/l or <100 mg/dl Low risk: <3.0 mmol/l or <116 mg/dl
Non-HDL cholesterol	Very high risk: <2.2 mmol/l or <85 mg/dl High risk: 2.2–2.6 mmol/l or 85–100 mg/dl Moderate risk: 3.4 mmol/l or 100–130 mg/dl
Apolipoprotein B	Very high risk: <65 mg/dl High risk: 65–80 mg/dl Moderate risk: 80–100 mg/dl
Triglycerides	<1.7 mmol/l (<150 mg/dl) indicates lower risk. Higher levels indicate a need to look for other risk factors.

4.3 Weight and body mass index

Maintaining a healthy body composition is one of the effective prevention strategies to reduce cardiovascular risk. There is a range of body composition measurements that can be used to identify clinical manifestations of being obese and overweight. The most basic method of determining body weight is anthropometry. Anthropometry is classified into indirect methods that include three assessments, namely BMI, waist circumference and skinfold assessment.[236] BMI is more popular and broadly used in clinical practice since it is easy and simple to measure. BMI has a classification that depends on weight status, as outlined in Table 13.

Table 13. The WHO classification of body weight based on body mass index in adults.[237]

Body Mass Index for individuals over 20 years of age (kg/m²)	Weight status
>18.5	Underweight
18.5–24.9	Normal weight
25.0–29.9	Pre-obesity
30.0–34.9	Obesity class I
35.0–39.9	Obesity class II
≥40.0	Obesity class III

Waist circumference can be an indicator of abdominal obesity. There should be no further weight gain when waist circumference is ≥94 cm in men and ≥80 cm in women.[14] Weight reduction is strongly advised when waist circumference is ≥102 cm in men and ≥88 cm in women.

Skinfold assessment measures the areas of subcutaneous fat thickness. Although it has an upper measurement limit of 45 to 55 mm, skinfold testing is useful in assessing body composition in children.[236] Another indirect method is bioelectric impedance analysis, which estimates total body water, fat-free mass and intracellular and extracellular water independently by incorporating multiple frequencies and multiple body segments.

4.4 Diabetes and prediabetes

Diabetes mellitus (type 1 and type 2) and prediabetes are independent predictors of cardiometabolic disorders. Diabetes can increase the risk of developing CVDs such as dyslipidaemia, hypertension and heart failure and may increase the risk of sudden cardiac death.[74] Therefore, risk-based management is important to control blood glucose, lipid profile and blood pressure. Screening should include assessment of HbA1c and fasting or non-fasting blood glucose. Generally, a HbA1c level of <7.0% (53 mmol/mol) should be the target in order to reduce the risks of macrovascular and microvascular complications.[14] In lipid management, people living with diabetes should achieve LDL cholesterol reduction of ≥50% from baseline or LDL cholesterol goal of <1.4 mmol/l (in very-high risk) or <1.8 mmol/l (in high risk).[234] In addition, a blood pressure goal should be set at <130/80 mmHg. The intensive control of blood pressure was found to be more beneficial than standard control of blood pressure, as reported in the SPRINT randomised trial.[238]

4.5 Anticoagulation management

Given the complexity of anticoagulation management, pharmacist-led clinics have been developed and implemented in many countries to ensure effective and safe use of anticoagulation therapies. Specifically, people prescribed vitamin K antagonists, such as warfarin, have to be monitored for under-coagulation (risks of blood clot formation) and over-coagulation (risks of bleeding) through the measure of the international normalised ratio (INR). The gold standard for measuring INR is through venepuncture; however, pharmacist-led clinics have tapped into point-of-care INR testing due to its convenience and fast turnaround of results. The INR is the prothrombin time (time taken for clot formation: measuring the time taken to produce thrombin and conversion of fibrinogen to fibrin by thrombin) ratio, standardised with the international sensitivity index.[239]

Pharmacist-led anticoagulation management services generally include:[240, 241]

- Setting of INR target and initiation of anticoagulant dose
- Monitoring of INR and vitamin K antagonist dose adjustments
- Identification of patient risk factors
- Continuous patient education on vitamin K antagonist use

Community pharmacists can play a vital role in complementing the primary healthcare team in managing anticoagulation therapy. For example, the Community Pharmacist-led Anticoagulation Management Service (CPAMS) in Nova Scotia, Canada, has shown improved time-in-therapeutic range (TTR) outcomes for people whose warfarin therapy was managed by community pharmacists. The effectiveness and safety of CPAMS were also observed in a New Zealand study, with modest change in TTR from 76.4% to 74% despite a large increase in patient numbers from 850 to 4,530. There was also no change in the proportion of people with INR above 4.0, and bleeding was reported in less than 4% of the visits.[242] Therefore, pharmacist-led anticoagulation management, specifically by community pharmacists, can add value to ensuring safe and effective use of vitamin K antagonists.

4.6 Methods for cardiovascular risk assessment

Cardiovascular risk is defined as the probability of developing CVDs within a time-period or lifetime, after accounting for risk factors.[243] Cardiovascular risk assessment can be conducted either opportunistically or systematically. Cardiovascular risk should be assessed for people with atherosclerotic CVD risk factors, type 2 diabetes, chronic kidney disease or familial hypercholesterolaemia. As increasing age is also an independent factor of cardiovascular risk, risk assessment should be conducted in men above 40 years and women above 50 years without any other established risk factors. According to the 2021 European Society of Cardiology on CVDs Prevention in Clinical Practice, the risk stratification is generally defined by age in apparently healthy individuals, is a presented in Table 14.[14]

Table 14. Classification of CVDs risk based on age in apparently healthy individuals

Classification	<50 years	50–69 years	≥70 years
Low-to-moderate CVD risk Risk factor treatment generally not recommended	<2.5%	<5%	<7.5%
High CVD risk Risk factor treatment should be considered	2.5% to <7.5%	5% to <10%	7.5% to 15%
Very high CVD risk Risk factor treatment generally recommended	≥7.5%	≥10%	≥15%

A stepwise approach to stratifying and managing cardiovascular risk should be adopted. The 2021 ESC guidelines on cardiovascular disease prevention in clinical practice can be referred to for risk stratification and management of cardiovascular risks for apparently healthy individuals and people with risk factors.[14]

Many risk-prediction charts have been developed over the years to estimate cardiovascular events. In 2008, the Framingham Heart Study (FHS) was renewed from the published version in 1991. It is widely used among white and black populations in the United States to predict cardiovascular risk.[244] The FHS considers seven risk factors and estimation of risk is divided into men and women.[244] The risk factors include age, total cholesterol, HDL cholesterol, systolic blood pressure, smoking status and diabetes.[244] More information about FHS 2008 can be found in "General cardiovascular risk profile for use in primary care: The Framingham Heart Study".[244]

In 2014, the American College of Cardiology along with American Heart Association launched the Pooled Cohort Equations (PCEs).[245] They are commonly used among white and African-American populations. The computation is separated into men and women, accounting for several risk factors such as age, total cholesterol, HDL cholesterol, untreated or treated systolic blood pressure, smoking status and diabetes. The estimation of atherosclerotic CVD events within 10 years can be predicted using PCEs.[245]

In 2020, the WHO published the "HEARTS technical package for cardiovascular disease management in primary health care: Risk-based CVD management", which provided a strategic approach for improving cardiovascular health for 21 countries.[246] This publication aims to guide policy-makers and programme managers across different sectors within health ministries to encourage the implementation of cardiovascular prevention primary care services.[246] According to the WHO, in 2020, the risk-prediction model can be divided into laboratory-based and non-laboratory-based charting. Laboratory-based charting is used for interventional decisions where laboratory facilities, and economic and human resources are accessible.[246] It also includes biochemical assays such as blood sugar and total cholesterol to quantify risk.[246] Non-laboratory-based charting estimates total cardiovascular risk without information on diabetes and total cholesterol. It only requires age, gender, smoking status, systolic blood pressure and body mass index for estimation.[246] The aim of non-laboratory-based charting is to support cardiovascular risk prediction in low-resource settings which have limited facilities or limited human and financial capacities.[246] Figure 4 is a flowchart for cardiovascular risk estimation. More information can be found in "HEARTS technical package for cardiovascular disease management in primary health care: risk-based CVD management".

In 2021, the European Society of Cardiology along with the SCORE2 working group updated the "SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe". This model is

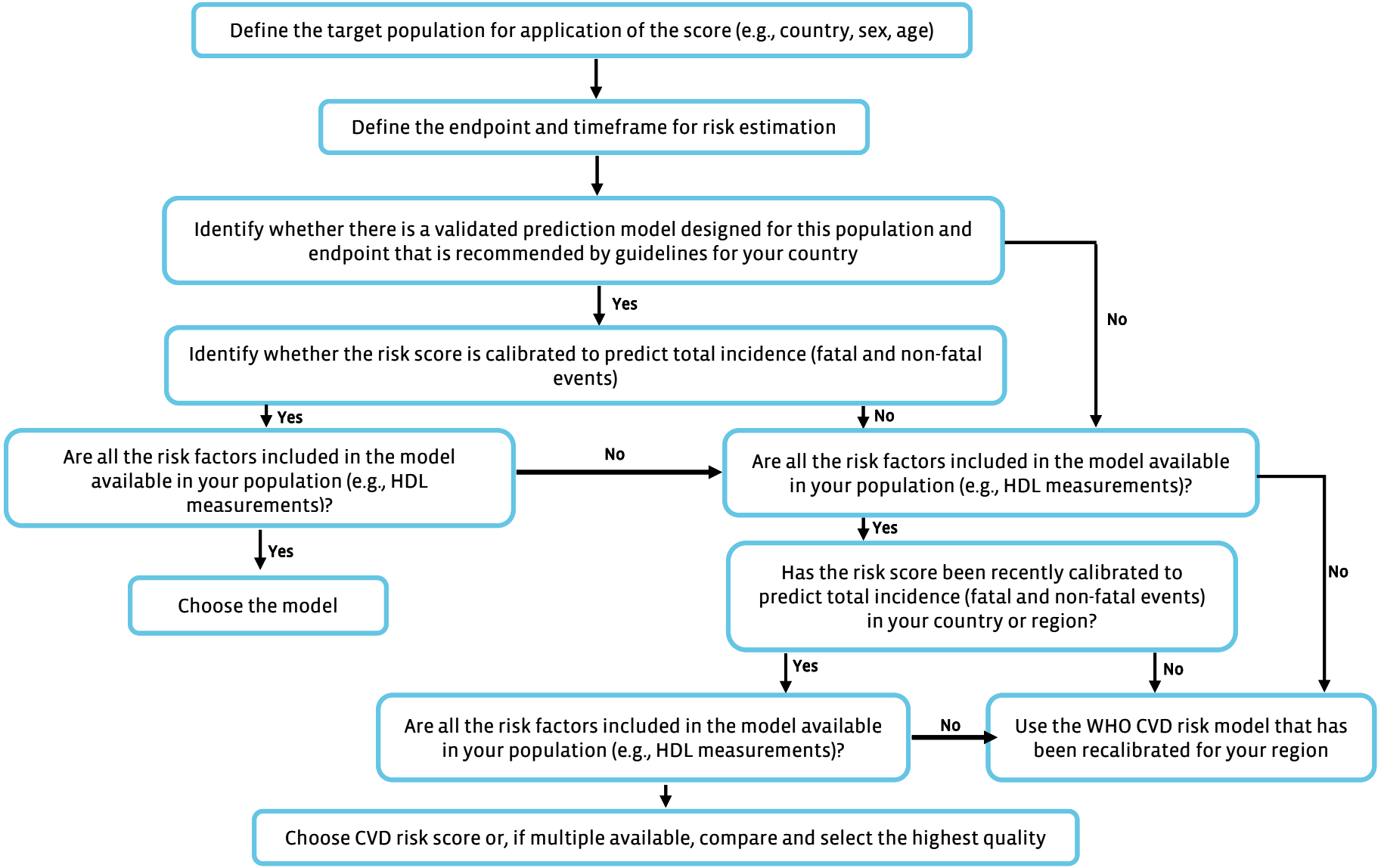
an updated version of the Systematic Coronary Risk Evaluation (SCORE) which was established from cohorts recruited before 1986. To predict cardiovascular risk, SCORE2 provides criteria, including gender, smoking status, a range of ages from 40 to 69 years, systolic blood pressure, total cholesterol and HDL cholesterol.[247] SCORE2 depicts distribution and proportion of fatal and non-fatal 10-year CVD events risk across European countries.[247] SCORE2-OP was also developed to predict cardiovascular risk for older people aged 70 years and above in four geographical risk regions (classified into low, moderate, high and very high risk). Table 15 summarises the characteristics of the different risk prediction models.

Table 15. Summary of characteristics of risk prediction models

Risk factors/parameters	Risk-prediction models				
	*SCORE2 and SCORE2-OP 2021	WHO 2020		*PCEs 2014	*FHS 2008
		Non-laboratory based	Laboratory-based		
Risk factors					
Age	•	•	•	•	•
Gender	•	•	•	•	•
Smoking status	•	•	•	•	•
Untreated/treated systolic blood pressure (SBP)	•	•	•	•	•
Total cholesterol	•		•	•	•
HDL cholesterol	•		•	•	•
Diabetes	•		•	•	•
BMI	•	•		•	•
Ethnicity	•			•	•
Country risk		•	•		
Population	Europe	21 countries	21 countries	USA	USA

*For abbreviations, see text

Figure 4. Flowchart on how to estimate cardiovascular risk (adapted from WHO "HEARTS technical package for cardiovascular disease management in primary health care: risk-based CVD management")[246]



5 Referral and interprofessional collaboration to support people with cardiovascular diseases

Pharmacists already play an important role in the primary and secondary prevention of CVDs.[248] This is done mainly through patient education and counselling, medication safety management, medication review, monitoring and reconciliation, detection, and control of specific CV risk factors.[137] Despite these positives, there is need to veer away from the "silo mentality" lens through which the medical profession has been traditionally viewed. Tackling chronic NCDs such as CVDs pragmatically and in a cost-effective manner requires the mobilisation of all available community resources. Interprofessional collaborations backed by innovative policies have been shown to promote achievement of the best possible healthcare outcomes for patients in our societies.[249, 250]

The Royal Pharmaceutical Society (UK) has identified five key models in which pharmacy teams can collaborate with other healthcare professionals to support the prevention and management of CVDs.[251] These include promoting prevention and healthy living as the first point of contact for patients in the community, early detection of CVD, pharmacist-led primary care network management of CVDs, acute hospital-based care as members of the multidisciplinary healthcare team, and pharmacists as critical players in discharge pathways for secondary care.

Furthermore, the US Centers for Disease Control advocates a team-based care strategy that ensures patients have two or more healthcare providers working collaboratively to achieve treatment goals.[252] Pharmacists are a core part of the team-based care strategy and through collaborative practice agreements (CPAs), pharmacists can make a tangible impact in the support of people with CVDs. CPAs are formal agreements where a licensed healthcare provider makes a diagnosis, supervises patient care and refers the patient to a pharmacist under a structured protocol which allows the pharmacist to perform certain patient care functions.[252] Ideally, CPAs are intended to expand health infrastructure by embedding pharmacists as important caregivers, subsequently reducing fragmentation of care, and ultimately easing access to care for cardiovascular patients. Some common services offered by pharmacists under CPAs include medication therapy management (MTM) and collaborative drug therapy management (CDTM).

Some of the key activities that pharmacists are involved in under MTM and CDTM that directly contribute to multidisciplinary team support for cardiovascular patients include:[137, 252]

- Medication therapy reviews and dose adjustment;
- Documentation and maintenance of patient medication records;
- Creation of medication-related action plans;
- Intervention and/or referral;
- Patient assessments, i.e., ordering appropriate laboratory tests;
- Initiation, monitoring and adjusting medication regimens based on targeted treatment goals; and
- Posthospital discharge follow-up and home visits for critical patients.[137]

There is evidence of the benefit of interprofessional collaboration through CPAs. This has been best demonstrated through the collaboration between the Australian government and the Pharmacy Guild of Australia.[249] The study conducted by Puspitasari and colleagues found that interprofessional collaboration improved patient outcomes, resulting in increased patient loyalty and improved demand for pharmaceutical care services.[249] Similar studies on interprofessional collaboration have also shown that such collaborative interventions result in lower costs of treatment and departing from such strategies causes a foreseeable deterioration in cardiovascular patient outcomes.[253, 254]

It is important to note that for these interprofessional relationships to be successful they need to be based on mutual respect and appreciation of the clear roles played by each healthcare professional.[255] Unfortunately, existing barriers such as lack of recognition of expanded pharmacist roles and lack of remuneration for MTM and CDTM services, have barred many pharmacists from promoting interprofessional collaboration.[255] However, it remains paramount for pharmacists to embed themselves as critical team players in CVD management and offer their MTM and CDTM services where necessary.[226]

6 CVD medicines

6.1 Pharmacological treatment of hypertension

The WHO guidelines on treatment of hypertension in adults[151, 256] recommend the use of either thiazide and thiazide-like diuretics, angiotensin converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), or long-acting calcium channel blockers (CCBs) for the initial management of hypertension. Treatment should be monitored to ensure target blood pressure is attained. Where blood pressure is not adequately attained, combination therapy can be considered.[151]

The therapeutic categories that can be used to manage hypertension are outlined in Table 16.

Table 16. Medication for hypertension

Therapeutic category	Mechanism of action	Examples of medicines in this category	Examples of common side effects	Potential medication interactions	Notes on patient counselling
Angiotensin-converting enzyme inhibitors (ACEIs)	Exert a haemodynamic effect by inhibiting the renin-angiotensin system, modulating sympathetic nervous system activity and increasing prostaglandin synthesis causing vasodilation and natriuresis.[257]	Captopril, cilazapril, enalapril, fosinopril, lisinopril, perindopril, quinapril, ramipril, zofenopril.	Chronic cough, metallic taste, hyperkalaemia, angioedema, syncope, hypotension.	ARBs. Increased risk of hyperkalaemia in those on potassium supplements and potassium-sparing diuretics.[74]	Do not use when patient has medical history of angioedema with ACEIs.[74] First-dose hypotension — first dose preferably taken at bedtime. Renal function and electrolytes should be checked before starting ACEIs (or increasing the dose) and monitored during treatment (more frequently if side effects mentioned are present). Contraindicated in pregnant women, patients with bilateral renal artery stenosis, and acquired or congenital solitary kidney and stenosis.[258]
Angiotensin II receptor blockers (ARBs)	Block angiotensin receptor, inhibiting the effects of angiotensin II.	Candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, valsartan.	Dizziness, light-headedness, vomiting, diarrhoea, hyperkalaemia, angioedema.	ACEIs. Increased risk of hyperkalaemia in those on potassium supplements.[74]	Contraindicated in pregnant women, patients with bilateral renal artery stenosis, and solitary kidney.[258]
Beta blockers	Competitively antagonise endogenous catecholamines by blocking their binding to receptor sites.	**Cardioselective (beta-1)**: acebutolol, atenolol, bisoprolol, esmolol, metoprolol, nebivolol. **Non-cardioselective (beta-1 and beta- 2):**	Dizziness, cold extremities, difficulty sleeping, nightmares, fatigue, impotence.	Nebivolol induces nitric oxide-induced vasodilatation.[74]	Monitor lung function. Avoid in patients with reactive airways disease.[74]

Therapeutic category	Mechanism of action	Examples of medicines in this category	Examples of common side effects	Potential medication interactions	Notes on patient counselling
		carvedilol (beta-1 and alfa-1), labetalol, pindolol, propranolol, sotalol, timolol.			
Calcium channel blockers	Selectively inhibit calcium influx through cellular membranes, thus reducing the rate and conduction of cardiac muscle.[259]	**Dihydropyridines:** amlodipine, barnidipine, felodipine, lacidipine, lercarnidipine, nicardipine, nifedipine, nimodipine, nitrendipine. **Non-dihydropyridines:** diltiazem, verapamil.	Headache, constipation, rash, nausea, flushing, oedema, drowsiness, hypotension.	Combination of non-dihydropyridines CCB and beta blockers can increase risk of bradycardia and heart block. Interactions with diltiazem and verapamil (CYP3A4 major substrate and moderate inhibitor).[74]	Potential dose-related pedal oedema, which is more common in women than men.
Thiazide or thiazide-like diuretics	Increase urine flow by inhibiting the sodium/chloride cotransporter located in the distal convoluted tubule.	Chlorthalidone, hydrochlorothiazide, indapamide, metolazone.	Dose-related side effects include blurred vision, dizziness, light-headedness, loss of appetite, headache and weakness, stomach upset, electrolyte disturbances, variations in plasma parameters: glucose, uric acid, lipids.		Monitor renal function. Monitor for hyponatraemia, hypokalaemia, and uric acid and calcium levels. Thiazides and related diuretics should not be used to treat gestational hypertension. Use with caution in patients with medical history of acute gout unless receiving uric acid therapy.[74]
Others medicines: aldosterone antagonist (spironolactone) and loop diuretics (furosemide and torasemide)	See Table 17				

6.2 Pharmacological treatment of heart failure

Pharmacological interventions are a mainstay in the management of heart failure. The American Academy of Family Physicians (AAFP) with the American College of Cardiology (ACC) and the American Health Association (AHA) provide guidance on the recommended treatments for heart failure based on functional classifications and associated symptoms, or lack thereof.[258, 260] The European Society of Cardiology (ESC) provides guidance on the pharmacotherapeutic management of heart failure, classified based on left ventricular ejection fractions (reduced ejection fraction, mid-range ejection fraction, and preserved ejection fraction). It is recommended that these pharmacological interventions are accompanied with appropriate non-pharmacological interventions to enhance therapy and ensure better treatment outcomes.[258] Notably, some of these medicines overlap with those used in the treatment of hypertension.

Both 2022 AHA/ACC/HFSA (Heart Failure Society of America)[260] and 2021 ESC[261] guidelines, according to new evidence, provide an update on the recommendations for the treatment of patients with heart failure focused on improving quality of care aligned with patients' interests. Among other recommendations guideline-directed medical therapy for heart failure with reduced ejection fraction (HFrEF) now includes four therapeutic groups to reduce mortality and/or hospitalisation. These are:

1. Beta blockers: mainly bisoprolol, carvedilol, and sustained-release metoprolol succinate. Beta blockers are recommended in patients with current or previous symptoms.

2. Mineralocorticoid receptor antagonists (MRAs): spironolactone and eplerenone. MRAs are recommended in patients with HFrEF and New York Heart Association (NYHA) class II to IV symptoms, if estimated glomerular filtration rate is >30 ml/min/1.73 m^2 and serum potassium is lower than 5.0 mEq/l. Notably, potassium, renal function, and diuretic dosing should be assessed at initiation and closely monitored thereafter to minimise risk of hyperkalaemia and renal failure.

3. Renin-angiotensin system Inhibition: with (i) an angiotensin receptor-neprilysin inhibitor (ARNI), (ii) angiotensin-converting enzyme inhibitors (ACEIs), or (iii) angiotensin II type I receptor blockers (ARBs):

- ARNIs are recommended for patients with NYHA class II to III symptoms;
- ACEIs are recommended for patients with previous or current symptoms of chronic HFrEF, when the use of ARNIs is not feasible;
- ARBs are recommended for patients with previous or current symptoms of chronic HFrEF who are intolerant to ACEIs due to cough or angioedema and when the use of ARNIs is not feasible; and
- ARNIs instead of ACEIs or ARBs is recommended for patients with NYHA class II to III symptoms who can tolerate these drugs.

4. Sodium-glucose cotransporter-2 (SGLT2) inhibitors: dapagliflozin, empagliflozin. SGLT2 inhibitors are recommended for patients with symptomatic chronic HFrEF with or without type 2 diabetes.

Other medicines that could be used in patients with HFrFE include:

- Loop and thiazide diuretics may be used in patients with hypervolemia (volume overload). This group is recommended in patients with HFrEF with signs or symptoms of congestion to alleviate heart failure symptoms, improve exercise capacity and reduce hospitalisations for heart failure.
- Funny current (I_f) inhibitor ivabradine should be considered in symptomatic patients with left ventricular ejection fraction (LVEF) of <35%, in sinusal rhythm and with a resting heart rate of >70 beats per minute, despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ARNI (or ACEI) and an MRA, to reduce the risk of heart failure hospitalisation and death; or who are unable to tolerate or have contraindications to a beta-blocker to reduce the risk of heart failure hospitalisation and death. Patients should also receive an ARNI (or ACEI) and an MRA.
- Digoxin may be used for patients with symptomatic HFrEF in sinus rhythm despite treatment with an ARNI (or ACEI), a beta-blocker and an MRA, to reduce the risk of hospitalisation (both all-cause and heart failure hospitalisations).

- Hydralazine/isosorbide dinitrate should be considered for black patients with LVEF <35% or with an LVEF <45% combined with a dilated left ventricle in NYHA class III–IV despite treatment with an ARNI (or ACEI), a beta-blocker and an MRA to reduce the risk of heart failure hospitalisation and death. Also, this combination may be used for patients with symptomatic HFrEF who cannot tolerate ACEI, an ARB or an ARNI.
- Vericiguat, a soluble guanylate cyclase receptor stimulator, may be used for patients in NYHA class II–V who have had worsening heart failure despite treatment with an ARNI (or ACEI), a beta-blocker and an MRA.
- Iron (ferric carboxymaltose) should be considered for iron deficiency, defined as serum ferritin <100 ng/ml or serum ferritin 100–299 ng/ml with transferrin saturation <20%.

Table 17 shows some pharmacological and clinic characteristics of the main medicines used in the treatment of patients with heart failure.

Table 17. Medicines for heart failure

Therapeutic category	Mechanism of action	Examples of medicines in this category (starting dose; target dose)	Common side effects	Potential medication interactions	Notes on patient counselling
Angiotensin-converting enzyme inhibitors (ACEIs)	Exert a haemodynamic effect by inhibiting the renin-angiotensin system. They also modulate sympathetic nervous system activity and increase prostaglandin synthesis, causing vasodilation and natriuresis.[257]	Captopril (6.25 mg *t.i.d.*; 50 mg *t.i.d*) Enalapril (2.5 mg *b.i.d.*; 10–20 mg *b.i.d.*) Lisinopril (2.5–5 mg *o.d.*; 20–35 mg *o.d.*) Ramipril (2.5 mg *b.i.d.*; 5 mg *b.i.d.*) Trandolapril (0.5 mg *o.d.*; 4 mg *o.d.*).	Chronic cough, metallic taste, elevated blood potassium levels, rash.	Chronic cough, metallic taste, hyperkalaemia, angioedema.[74]	Do not use when patient has medical history of angioedema with ACEIs.[74] Contraindicated in pregnant women, patients with bilateral renal artery stenosis, and acquired or congenital solitary kidney and stenosis.[258]
Angiotensin II receptor blockers (ARBs)	Block angiotensin receptor, inhibiting the effects of angiotensin II.	Candesartan (4 mg *o.d.*; 32 mg *o.d.*) Losartan (50 mg *o.d.*; 150 mg *o.d.*) Valsartan (40 mg *b.i.d.*; 160 mg *b.i.d.*)	Dizziness, light-headedness, vomiting, diarrhoea, hyperkalaemia, angioedema.	ACEI or direct renin inhibitors. Increased risk of hyperkalaemia in those on potassium supplements.[74]	Contraindicated in pregnant women, patients with bilateral renal artery stenosis, and solitary kidney.[258]
Angiotensin receptor-neprilysin inhibitor (ARNI)	Sacubitril inhibits the enzyme neprilysin, which is responsible for the degradation of atrial and brain natriuretic peptide, two blood pressure-lowering peptides that work mainly by reducing blood volume.[262]	ARNi is a medicine resulting from the combination of sacubitril and valsartan (24–49/26–51 mg *b.i.d.*; 97/103 mg *b.i.d.*)	Blood in urine, decreased frequency or amount of urine, difficult breathing, postural hypotension, increased thirst, irregular heartbeat, numbness or tingling in the hands, feet, or lips, angioedema.	ACEIs or direct renin inhibitors. Increased risk of hyperkalaemia in those on potassium supplements.[74]	Should not be used concomitantly with ACEIs or ARBs. It may cause hypotension or angioedema.[258] Contraindicated in pregnant women, patients with bilateral renal artery stenosis, and solitary kidney.[258] Monitor BP, potassium and renal function.
Beta blockers	Competitively antagonise endogenous catecholamines by	Bisoprolol (1.25 mg *o.d.*; 10 mg *o.d.*)	Dizziness, cold extremities, difficulty	Nebivolol induces nitric oxide-induced vasodilation.[74]	Avoid in patients with reactive airways disease.[74]

Therapeutic category	Mechanism of action	Examples of medicines in this category (starting dose; target dose)	Common side effects	Potential medication interactions	Notes on patient counselling
	blocking their binding to receptor sites	Carvedilol (3.125 mg *b.i.d.*; 25 mg *b.i.d.*) Metoprolol succinate controlled or extended release (12.5–25 mg *o.d.*; 200 mg *o.d.*) Nebivolol (1.25 mg *o.d.*; 10 mg *o.d.*)	sleeping, nightmares, fatigue.	Risk of bradycardia increases when co-administered with verapamil, diltiazem or ivabradine.	
Aldosterone antagonists	Block the effects of aldosterone, causing excretion of sodium by the kidneys and other glands, encouraging water loss, and a subsequent decrease in blood pressure and reduction in fluid around the heart.	Eplerenone (25 mg *o.d.*; 50 mg *o.d.*) Spironolactone (12.5–25 mg *o.d.*; 50 mg *o.d.*)	Dizziness, upset stomach, dry mouth, muscle spasms, swelling and tenderness of breast, skin rash.	Increased risk of hyperkalaemia in those using potassium supplements or using drugs that increase potassium levels, e.g., ACEIs and ARBs.[258]	Patients may be required to limit salt intake.
Sodium glucose cotransporter-2 inhibitors[263]	Inhibin sodium-glucose cotransporter type 2, causing glycosuria and osmotic diuresis. Also, in the vascular wall, reduced arterial stiffness, improved endothelial function, and reduced fluid overload; effects associated with a reduction in myocardial stretch, workload and risk of heart failure, providing cardiovascular protection.	Dapagliflozin (10 mg *o.d.*; 10 mg *o.d.*) Empagliflozin (10 mg *o.d.*; 10 mg *o.d.*)	Genitourinary infections Hypotension Limb amputation (low risk) Hypoglycaemia in patients with type 2 diabetes	Concomitant use of insulin or sulfonylurea therapy increases risk of hypoglycaemia. Canagliflozin-digoxin may result in an increase in digoxin levels. Concomitant use with diuretics may cause volume depletion.	Patients may be informed regarding glycosuria as indicator of effectiveness as well as risk of genitourinary infections.
Vasodilators	Bind to receptors on endothelial cells of the blood vessels, which	Hydralazine, isosorbide dinitrate.	Reflex tachycardia, headache, flushing, postural hypotension,	Should be avoided in patients taking monoamine oxide inhibitors, calcium channel	Should not be used concomitantly with phosphodiesterase

Therapeutic category	Mechanism of action	Examples of medicines in this category (starting dose; target dose)	Common side effects	Potential medication interactions	Notes on patient counselling
	stimulates calcium release, resulting in dilation of blood vessels.[264]		compensatory tachycardia, fluid retention.	blockers, heparin, phosphodiesterase inhibitors, aspirin, dihydroergotamine.	inhibitors, e.g., sildenafil, tadalafil, vardenafil. Alcohol may potentiate the effects of vasodilators and should be avoided.
Loop diuretics	Inhibition of the sodium/potassium/ chloride co-transporter (symporter) located in the thick ascending limb of the loop of Henle.[265]	Bumetanide, ethacrynic acid, furosemide, torasemide.	Dizziness, headache, gastrointestinal upset, hyponatraemia, hypokalaemia, ototoxicity, dehydration.	Interact with amphotericin B, digoxin, ACEIs, antidiabetic medicines, antifungal agents, dobutamine, and sotalol due to diuretic-associated hypokalaemia.[266] Interact pharmacodynamically with medicines like cephalosporins, ceritinib, levothyroxine, pixantrone, probenecid, lithium, non-steroidal anti-inflammatory drugs, sulfonylureas and herbal medicines.[266]	Monitor for hyponatraemia, hypokalaemia and uric aci, and calcium levels. Use with caution in patients with medical history of acute gout unless they are receiving uric acid therapy.[74] Due to the risk of ototoxicity, loop diuretics should be avoided in patients already taking medicines that can damage hearing, e.g., cisplatin, carboplatin, gentamicin and aspirin.
Thiazide diuretics	Increase urine flow by inhibiting the sodium/chloride cotransporter located in the distal convoluted tubule.	Hydrochlorothiazide, metolazone.	Dose-related side effects include blurred vision, dizziness, light-headedness, loss of appetite, headache and weakness, stomach upset.		Monitor for hyponatraemia, hypokalaemia, and uric acid and calcium levels. Use with caution in patients with medical history of acute gout unless they are receiving uric acid therapy.[74]

Therapeutic category	Mechanism of action	Examples of medicines in this category (starting dose; target dose)	Common side effects	Potential medication interactions	Notes on patient counselling
Cardiac glycoside (inotrope)	Induces an increase in intracellular sodium that drives an influx of calcium in the heart and causes an increase in contractility. Also has vagomimetic effects on the atrioventricular node, resulting in a decrease in heart rate.[267]	Digoxin.	Dizziness, blurred vision, diarrhoea, skin rashes, headache, loss of appetite.	Adverse effects are potentiated by NSAIDs, ACEIs, ARBs and ciclosporin. Macrolides and amiodarone cause digoxin overdose due to pharmacokinetic interactions. Enzyme-inducing medicines reduce the plasma concentrations of digoxin.	Has a narrow therapeutic window and therefore requires close therapeutic drug monitoring to avoid life-threatening cardiac adverse effects. Monitor serum electrolytes and renal function. For plasma-digoxin concentration assay, blood should be taken at least six hours after a dose.
Funny current (I_f) inhibitor in the sinoatrial node	Selectively and specifically inhibits the cardiac pacemaker current (I_f) that controls the spontaneous diastolic depolarization in the sinoatrial node, resulting in heart rate reduction.[268]	Ivabradine.	Dizziness, blurred vision, bradycardia, chest pain, atrial fibrillations.	Risk of bradycardia increases when co-administered with digoxin, amiodarone, beta blockers, verapamil or dilthiazem. Ivabradine is extensively metabolised by cytochrome P450 3A4; thus, its metabolism and plasma levels may be affected by inducers and inhibitors of the 3A4 enzyme.	Contraindicated in patients with atrial fibrillation and in pregnant women.[269]

6.3 Pharmacological treatment of dyslipidaemia

The management of dyslipidaemia is critical in preventing and managing atherosclerotic CVD. The European Society of Cardiology stresses the importance of conducting a total cardiovascular risk assessment as a guide to the selection of risk-based intervention strategies for lipid modification.[234] Similar to the management of hypertension, the effectiveness of the chosen treatment is guided by the achievement of predetermined therapeutic targets and goals.

The medication categories that can be used in the treatment of dyslipidaemias are outlined in Table 18.

Table 18. Medicines for dyslipidaemia

Therapeutic category	Mechanism of action	Examples of medicines in this category	Common side effects	Potential medication interactions	Notes on patients' counselling
Statins	Competitively inhibit the enzyme HMG-CoA reductase, a rate limiting step in cholesterol biosynthesis.[234]	Atorvastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin.	Gastro-intestinal disturbances, headache, myalgia, mild elevation in liver enzymes, proteinuria.	Induces or inhibits cytochrome (CYP) 450 enzymes, except pravastatin, rosuvastatin, and pitavastatin.[234] Interactions that lead to myopathy include those with: anti-infective agents (itraconazole, ketoconazole, erythromycin, clarithromycin, HIV protease inhibitors, etc). calcium channel blockers (verapamil, diltiazem, amlodipine), and others (gemfibrozil, amiodarone, ranolazine, danazol).[234]	Evening administration is preferable for most drugs but is not necessary for atorvastatin or rosuvastatin. Monitor liver function, renal function, thyroid function. Advise the patient to report any unexplained muscle pain, tenderness or weakness.
Cholesterol absorption inhibitors[270]	Interact with the Niemann-Pick C1-like protein 1 inhibiting intestinal uptake of dietary and biliary cholesterol.[234]	Ezetimibe.	Common: headache, runny nose, and sore throat. Less common: body aches, back pain, chest pain, diarrhoea, joint pain, fatigue, and weakness.	Concomitant use with statins increases risk of rhabdomyolysis.	Administered orally with or without meals (cholesterol-lowering diet). If patient is using bile acid sequestrants, ezetimibe may be administered 2 hours before or 4 hours after.

Therapeutic category	Mechanism of action	Examples of medicines in this category	Common side effects	Potential medication interactions	Notes on patients' counselling
Bile acid sequestrants	Bind to bile acids and prevent reabsorption of cholesterol into the blood.	Cholestyramine, colesevelam, colestipol.	Flatulence, dyspepsia, constipation, nausea.[235]		Consume food enriched with fibres.[234]
Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors	Inhibit PCSK9 enzyme enabling more efficient hepatic uptake of low density lipoproteins (LDL), decreasing serum LDL.[271, 272]	Alirocumab, evolocumab.	Itching at the site of injection and flu-like symptoms. Potential occurrence of neurocognitive effects.[234]	Potential occurrence of autoantibodies with long-term therapy.	
Lo Microsomal triglyceride transfer protein (MTP) inhibitors	Inhibits microsomal triglyceride transfer protein, thus preventing the formation of VLDL in the liver and of chylomicrons in the intestine.[234]	Lomitapide.	Gastro-intestinal side effects.		
Antisense apolipoprotein B (ApoB) synthesis inhibitor	Binds to a specific mRNA preventing the translation of ApoB protein and reducing the production of atherogenic lipids and lipoproteins[234, 272]	Mipomersen.	Injection site reactions, hepatic steatosis, liver enzyme elevation.		
Fibrates	Agonists of peroxisome proliferator-activated receptor-a (PPAR-a), causing a reduction in triglyceride levels.[234]	Bezafibrate, ciprofibrate, fenofibrate, gemfibrozil.	Myopathy, liver enzyme elevation, cholelithiasis.	Gemfibrozil inhibits the metabolism of statins through glucuronidation.	
Omega-3-acid ethyl esters	Interact with PPARs and decrease secretion of ApoB.[234, 272]	Eicosapentaenoic acid, docosahexaenoic acid.	Gastrointestinal disturbances, antithrombotic effects.	Antithrombotic effects may increase the propensity for bleeding, specifically aspirin and clopidogrel.	

Therapeutic category	Mechanism of action	Examples of medicines in this category	Common side effects	Potential medication interactions	Notes on patients' counselling
Niacin (nicotinic acid)	Inhibits diacylglycerol acyltransferase 2, resulting in decreased secretion of VLDL particles[234, 272]	Niacin (nicotinic acid).	Nausea and vomiting, abdominal pain, diarrhoea, liver damage, gout, skin flushing, dizziness, tachycardia.		
Cholesteryl ester transfer protein (CETP) inhibitors	Directly inhibit CETP, which induces an increase in high density lipoproteins[234]	Anacetrapib, dalcetrapib, evacetrapib, torcetrapib.	Unknown.		

In addition, there are novel medicines that have been developed and recommended by the 2018 ACC/AHA guidelines for cholesterol management as outlined in Table 19.[273]

Table 19. Novel medicines in the management of hypercholesterolaemia

Medicine	Mechanism of action	Common side effects	Notes on patients' counselling
Inclisiran	Small interfering RNA targeting hepatic PCSK9 (proprotein convertase subtilisin/kexin type 9) synthesis.	Myalgia, headache, fatigue, back pain, hypertension, dizziness.	If a dose is more than 3 months late, treatment should be reinitiated.
Evinacumab	Monoclonal antibody that inhibits angiopoietin-like protein 3 (ANGPTL3).	Nasopharyngitis, influenza-like illness, headache, rhinorrhoea.	
Gemcabene	Downregulation of hepatic apolipoprotein C-III mRNA expression and decrease of plasma apo C-III.	Unknown.	
ARO-ANG3	siRNA directed against ANGPTL3 mRNA.	Headache, respiratory tract infections, local injection site reactions.	
Bempedoic acid	Small molecule inhibitor of ATP-citrate lyase.	Small elevation in mean uric acid levels.	Monitor liver enzymes, uric acid level and for symptoms of gout

6.4 Antithrombotic therapy

Patients with CVD are at a high risk of developing thrombi due to multiple mechanisms that may include hyperactive platelets, hypercoagulable states and endothelial dysfunction.[274] This predisposes them to coronary artery disease that invariably deteriorates their overall treatment goals and quality of life. As such, antithrombotic agents play a critical role in secondary prevention of CVD.[275] The American College of Chest Physicians practice guidelines provide several antithrombotic strategies guided by the type of cardiovascular disease, the CHA_2D_2-VASc risk score, bleeding risk stratification based on PRECISE DAPT score, and the existence of any comorbidities.[276, 277] These strategies include single, dual and triple antiplatelet therapy.[276] The European Society of Cardiology also has provided guidance on antithrombotic therapies based on the type of cardiovascular diseases, bleeding risks and other comorbidities.

The medicines that can be used as antithrombotic therapy are outlined in Table 20.

Table 20. Medicines for antithrombotic therapy

Therapeutic category	Mechanism of action	Examples of medicines in this category	Common side effects	Notes on patient counselling
Antiplatelet medicines	Antagonise or impair any mechanism leading to blood platelet aggregation. This may include the phases of activation and shape change or following the dense-granule release reaction and stimulation of the prostaglandin-thromboxane system.[278]	Abciximab, acetylsalicylic acid (aspirin) in low dose, cangrelor, cilostazol, clopidogrel, dipyridamole, eptifibatide, prasugrel, ticagrelor, ticlopidine, tirofiban.	Headache, nausea, dyspepsia, nose bleeds, easy bruising, aspirin-induced asthma, haemorrhage, tinnitus, blood in stool/urine.	
Vitamin K antagonists (VKAs)	Impair the synthesis of several vitamin K-dependent coagulation factors resulting in a slow onset and offset of the anticoagulation effect.[279]	Acenocoumarol, dicoumarol, phenindione, phenprocoumon, warfarin.	Epistaxis, gastrointestinal bleeding, haematoma, melaena, syncope, fatigue.	Routine coagulation monitoring required to prevent fatal side effects.
Direct oral anticoagulants (DOACs)	Prevent coagulation through inhibiting key coagulation factors in the coagulation cascade, i.e., factor Xa or thrombin.[280]	Apixaban, dabigatran edoxaban, rivaroxaban.	Similar to VKAs. Have fewer side effects than VKAs and do not require routine coagulation monitoring.[281]	

6.5 Stable angina therapy

For patients with stable angina (chronic coronary syndrome), emphasis should be placed on optimising behavioural factors and medicines for secondary prevention to reduce the risk of CVD events and death, for instance lipid-lowering and antiplatelet agents. In addition, antianginal pharmacotherapy considered as first-line in the guidelines (beta blockers, short-acting nitrates or calcium channel blockers) should be initiated to improve angina symptoms.[282, 283] Also, ranolazine, ivabradine, nicorandil, long-acting nitrates and trimetazidine are recommended as second-line options.

Overall, the medicines used for patients with stable angina may be grouped as:[282-284]

- Medicines that reduce heart rate: beta-blockers, non-dihydropyridine calcium antagonists (verapamil and diltiazem) and ivabradine;
- Medicines that induce vascular smooth muscle relaxation: nitrates, dihydropyridine calcium antagonists (amlodipine, nicardipine) and nicorandil; and
- Metabolic modulators and late sodium current inhibitors: trimetazidine and ranolazine.

The main pharmacology and clinical characteristics of antianginal medicines are outlined in Table 21

Table 21. Pharmacology and clinical characteristics of antianginal medicines.[282-284]

Therapeutic category	Mechanism of action	Examples of medicines in this category	Common side effects	Potential medication interactions	Notes on patient counselling
Beta blockers	Competitively antagonise endogenous catecholamines by blocking their binding to receptor sites.	Atenolol, bisoprolol, carvedilol, metoprolol, nebivolol, propranolol.	Dizziness, cold extremities, difficulty sleeping, fatigue.	Nebivolol induces nitric oxide-induced vasodilation.[74]	Avoid in patients with reactive airway diseases.[74]
Calcium channel blockers	Selectively inhibit calcium influx through cellular membranes, thus reducing the rate and conduction of cardiac muscle.[259]	Dihydropyridines: amlodipine, barnidipine, felodipine, lacidipine, lercarnidipine, nicardipine, nifedipine, nimodipine, nitrendipine. Non-dihydropyridines: diltiazem, verapamil.	Headache, constipation, rash, nausea, flushing, oedema, drowsiness, hypotension.	Combination of non-dihydropyridines and beta blockers can increase risk of bradycardia and heart block. Interactions with diltiazem and verapamil (CYP3A4 major substrate and moderate inhibitor).[74]	Potential dose-related pedal oedema, which is more common in women than men.
Vasodilators	Bind to receptors on endothelial cells of the blood vessel, which stimulates calcium release, resulting in dilation of blood vessels.[264]	Short-acting nitrates: glyceryl trinitrate (nitroglycerine). Long-acting nitrates: isosorbide mononitrate, isosorbide dinitrate.	Reflex tachycardia, headache, flushing, postural hypotension, compensatory tachycardia, fluid retention.	Should be avoided in patients taking monoamine oxidase inhibitors, calcium channel blockers, heparin, phosphodiesterase inhibitors, aspirin, dihydroergotamine.	Should not be used concomitantly with phosphodiesterase inhibitor, e.g., sildenafil, tadalafil, vardenafil. Alcohol may potentiate the effects of vasodilators and should be avoided.
Metabolic modulators and late sodium current inhibitors	Selectively inhibit late sodium current relative to peak sodium channel current, resulting in decreases in sodium-dependent intracellular calcium overload.[285]	Ranolazine, trimetazidine.	Dizziness, light-headedness, dose-related QT prolongation.	Avoid concurrent use with CYP3A4 inducers and inhibitors.	Avoid in patients with hepatic diseases.
Funny Current Inhibitor (I_f)	Selectively and specifically inhibits the cardiac pacemaker current (I_f) that controls the spontaneous diastolic	Ivabradine.	Dizziness, blurred vision, bradycardia,	Risk of bradycardia increases when coadministered with digoxin, amiodarone, beta blockers, verapamil or diltiazem.	Contraindicated in patients with atrial

Therapeutic category	Mechanism of action	Examples of medicines in this category	Common side effects	Potential medication interactions	Notes on patient counselling
in the sinoatrial node	depolarisation in the sinoatrial node, resulting in heart rate reduction.[268]		chest pain, atrial fibrillations.	Ivabradine is extensively metabolised by cytochrome P450 3A4; thus, its metabolism and plasma levels may be affected by inducers and inhibitors of the 3A4 enzyme.	fibrillation and in pregnant women.[269]
Vascular smooth muscle relaxants	Nicorandil is a medicine used to treat and reduce chest pain caused by angina. It works by relaxing and widening blood vessels and increasing the blood and oxygen supply to the heart.	Nicorandil	Headaches, feeling dizzy or weak, nausea or vomiting, flushing.	Some medicines can lower blood pressure too much when they are taken with nicorandil. For example, medicines to treat hypertension or erectile dysfunction (e.g., sildenafil, tadalafil).	

7 Optimising medicine use

7.1 Prioritisation of professional pharmaceutical services

Ideally, in each pharmacist care situation the patient should receive a medicines use review (pharmacotherapeutic follow-up). However, due to the complexity and limited time for this professional service in the context of practice, it is a difficult target. Therefore, it is necessary to define the risk of not achieving the therapeutic goals (according to the patient's clinical situation and complexity of drug therapy regimen) and the professional pharmaceutical service more adequate for reducing this risk in a specific patient.[286, 287] Prioritisation according to the risk of a patient not achieving the therapeutic goals (pharmacotherapeutic risk) is a key strategy to increase the effectiveness of professional pharmaceutical services, which include all patient-oriented interventions (process and activities) carried out by the pharmacist, seeking to achieve the maximal possible benefit in terms of health, evidenced in the improvement of the patient's health outcomes and quality of life.[286, 287]

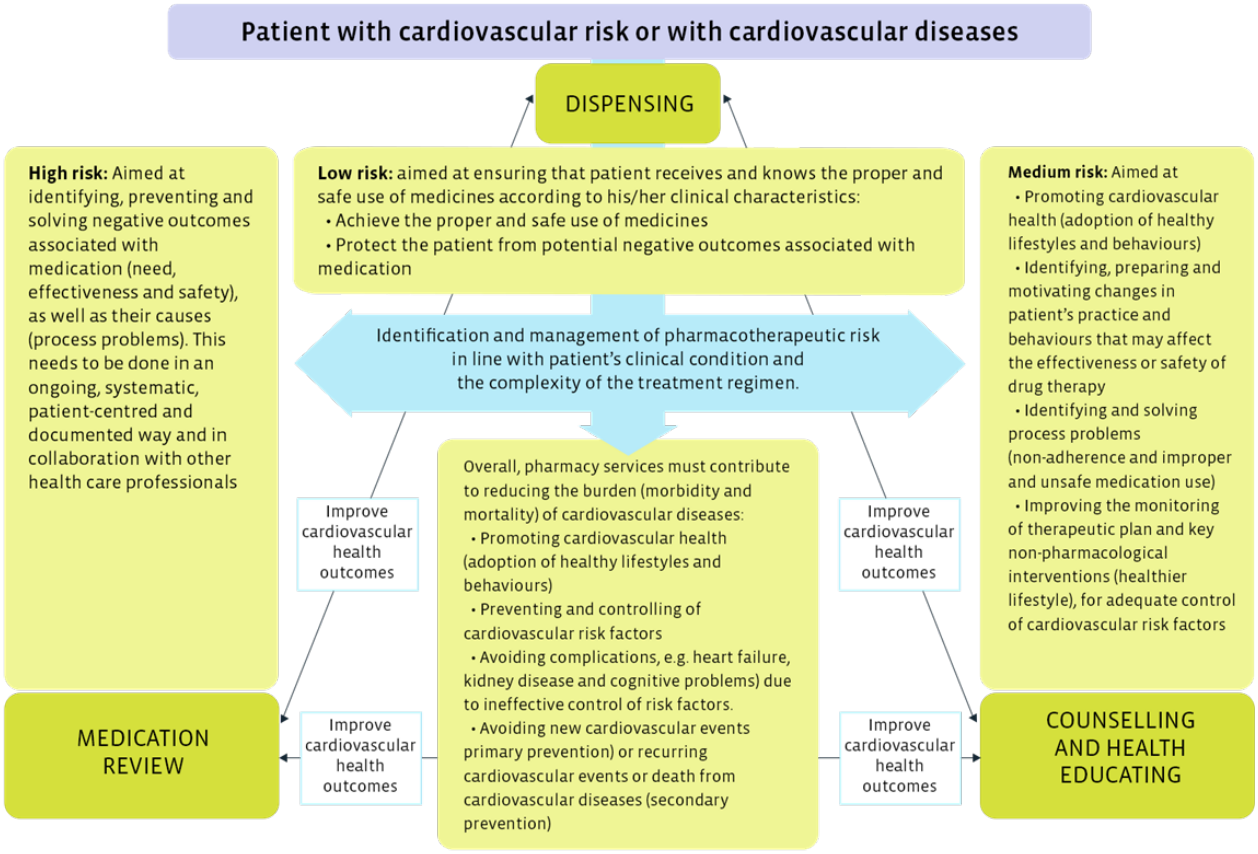
The combination of a patient's clinical risks with complexity of their medication therapy could be used to establish a predictive model to identify the patient's pharmacotherapeutic risk. Then, this pharmacotherapeutic risk is used to customise the professional pharmaceutical service more suitable to meet the patient's pharmacotherapeutic needs. Hence, it is important to prioritise and customise the professional service that a patient needs according to their pharmacotherapeutic risk.[286]

In addition, it is possible to define an increasing complexity level for the professional services according to demanded time, knowledge and skills, for instance, level 1: dispensing, level 2: counselling and health education, and level 3: medication review (pharmacotherapeutic follow-up):[286, 287]

1. **Dispensing** (level 1 for patients with low pharmacotherapeutic risk, requiring basic intervention, for instance, dispensing). Focused on ensuring that the patient receives and properly uses the medicines. The objectives are giving advice and achieving the proper use of the medicines and to protect the patient from the possible occurrence of negative outcomes associated with medication (NOM) by identifying, preventing and solving process medication-related problems (MRPs).
2. **Counselling and health education — promotion and prevention** (level 2 for patients with medium pharmacotherapeutic risk, requiring more than dispensing). Aimed at: (i) promoting cardiovascular health (adopting healthy lifestyles and behaviours); (ii) identifying, preparing and motivating patients to make behavioural changes that may affect the effectiveness or safety of medicines; (iii) identifying and solving process problems (non-adherence and improper and unsafety use of medicines); (iv) improving the monitoring and follow-up of key non-pharmacological interventions (towards healthier lifestyles) needed for the adequate control of CV risk factors; and (v) confirming that patients have the knowledge and skills needed to follow their pharmacological and non-pharmacological treatments and monitoring plans.
3. **Medication review** (level 3 for patients with high pharmacotherapeutic risk, requiring more than dispensing and counselling and health education). Focused on optimising pharmacotherapy use through identifying, preventing and solving NOM (necessity, effectiveness and safety), as well as identifying, preventing and solving MRPs in a continuous, systematised, documented way, in collaboration with other healthcare professionals while remaining centred to the patient.[61]

These three levels of professional pharmaceutical services should be aimed at optimising pharmacotherapy use and protecting the patient (minimising risk) from the presentation of NOM and MRP and, accordingly, at achieving the best possible health outcomes. In addition, the three levels must generate information for institutional pharmacovigilance or medicine safety programmes; therefore, the interventions and results achieved should be documented for each of the three levels.[286] Figure 5 illustrates the characteristics of the three types of services in patients with CV risk factors or with CVDs, which should be oriented according to the patient's pharmacotherapeutic risk.

Figure 5. Professional pharmaceutical services goals in patients with cardiovascular risk factors or with cardiovascular diseases, which should be oriented according to the patient's pharmacotherapeutic risk.



Adapted from: Amariles P. El paciente con factores de riesgo o con enfermedad cardiovascular en el contexto de la atención farmacéutica y el objetivo de desarrollo sostenible-3. Vitae. Vitae 28(Supl1):23-26. [in Spanish]. [accessed: 6 August 2022]. Available at: https://revistas.udea.edu.co/index.php/vitae/article/view/348083/20806693

7.2 Medication management for people living with CVDs

Medication management is a systematic process where healthcare providers ensure that prescribed medication regimens are optimal with regard to appropriateness, efficacy and safety while also promoting adherence to ensure holistic good health and reduce the need for acute care.[288] This may include, but is not limited to, identifying patient behaviours that may predispose them to adverse medicine events, or other important contextual factors that may limit adherence to prescribed medication. Ultimately, medication management should reduce medication errors and harm by ensuring the five rights are achieved i.e., right patient, right medicine, right dose, right route and right time.[289]

The medication management cycle is iterative and involves the following three key steps:[288]

1. **Medicines reconciliation**: Involves creating a complete list of a patient's medicines.
2. **Review of medical conditions**: Involves understanding the patient's current clinical status with regard to key health metrics.
3. **Addressing medication therapy problems**: Involves optimising medication regimens to achieve desired treatment goals and then working with the patient to promote adherence. Medication therapy problems are categorised into: indication problems, effectiveness problems, safety/side effect problems and adherence problems.

Medication management is especially important for CVD patients due to their increased likelihood of having comorbidities. This often precipitates the need for multiple pharmacological therapies, resulting in polypharmacy. To ensure the effective attainment of treatment goals, ensure adherence and reduce

occurrence of unpleasant or fatal side effects, close medication management between pharmacists and CVD patients is crucial.

Side effects arising from prescribed medication regimens occur frequently among CVD patients. This has been shown to increase morbidity, mortality and the overall cost of care.[290] Furthermore, the increased burden related to medication adverse effects has been shown to increase the negative impact on the patient's quality of life and that of their families or caregivers.[291] Eventually, this spurs non-adherence to the prescribed regimen resulting in poor outcomes, avoidable hospital admissions and higher healthcare costs — an unfortunate vicious cycle.[291] Therefore, it is imperative for pharmacists to understand the complex interplay between patient, disease and medication, and work closely with patients to predict and prevent known side effects from cardiovascular medicines. Additionally, pharmacists need to be at the forefront of patient education and promote open communication between themselves, patients and physicians. Such open communication has the potential to expose polypharmacy early and allows for quick initiation of corrective action that ensures patients can easily incorporate long-term medicines use into their daily lives.[291]

Cardiovascular medication management should be tailored based on a patient's disease progression, age, immune status and comorbidities. This creates special populations that may require unique considerations during treatment and medication management. These special populations include the elderly, people with diabetes, people living with HIV/AIDS, pregnant or breastfeeding women, and children.

The elderly: The elderly constitute a majority of CVD patients and medication management in this population is challenging owing to a number of factors. These include, but are not limited to, changes in organ function, weakened immune function and impaired drug pharmacokinetics and pharmacodynamics.[292, 293] The elderly are more likely to have multiple comorbidities that predispose them to polypharmacy.[293] Currently, there is a scarcity of data from clinical efficacy trials of cardiovascular medicines use among the elderly, and this has created obvious unpredictability in ascertaining the risks and benefits of prescribed cardiovascular therapies.[293] Regardless, pharmacists should generally expect the therapeutic and adverse effects of cardiovascular agents to be exaggerated in the elderly at normal therapeutic doses.[292] Therefore, it is recommended that careful therapy monitoring by multidisciplinary care teams is done to avert medication toxicities.[294] Additionally, slow, careful titration of medication is necessary during initiation and withdrawal. Where applicable, medication should be initiated only for compelling indications where benefit outweighs risk.[294]

People with diabetes: Diabetes is a common comorbidity among CVD patients. Medication management for both diseases requires tight control of blood glucose, blood pressure and lipids. Poor control of these means patient outcomes deteriorate, further worsening the patient's health status. A complex multi-level therapeutic approach is recommended for the prevention and management of CVD among diabetic patients.[295] Additionally, the integration of lifestyle interventions with pharmacological treatment provides a complete therapeutic strategy and better outcomes among CVD patients with diabetes.[295] Pharmacists can also make use of vascular protection mechanism, such as optimal blood pressure, cholesterol and HbA1C control, to ensure the attainment of good outcomes among CVD patients with diabetes.[294]

People living with HIV/AIDS: HIV/AIDS remains a huge burden in sub-Saharan Africa with many of the people living with HIV/AIDS susceptible to developing CVD through myriad risk factors.[294, 296, 297] The main concern in cardiovascular management of such people is medicine-medicine interactions between cardiovascular medication and antiretroviral therapy. A key role for pharmacists in medication management for this vulnerable population is identifying and understanding plausible pharmacokinetic interactions that may interfere with the effectiveness of cardiovascular medication. Once these have been identified, it may be necessary to initiate corrective measures or precautions, such as dose adjustment, close monitoring, medication withdrawal or patient counselling, to ensure treatment is optimised and foreseeable barriers to adherence are tackled.[294] Also, stigma and discrimination of people living with HIV/AIDS when it comes to receiving cardiovascular therapy is an emerging issue that requires healthcare providers to collaborate and ensure the continuum of care is maintained.[298, 299] Pharmacists should also be at the forefront of providing non-judgemental care to these patients as a way of supporting a team-based approach to CVD management.[298] The American Heart Association (AHA) provides a useful resource for clinicians who are managing CVD in this population, with pragmatic recommendations on how to prevent and treat CVD in the absence of demographic-specific, evidence-based information.[299]

Pregnant women: Pregnancy constitutes a period of drastic haemodynamic and metabolic changes that are designed to meet the increased metabolic needs of the mother and the fetus.[300] Some of these changes include an increase in blood volume and cardiac output, a reduction in blood pressure and an increased risk of vascular thromboembolic events due to a hypercoagulable state.[294, 301] These changes can result in myriad cardiac conditions that include hypertension, hypercholesterolaemia, arrhythmias, thromboembolic disease, valvular disease and cerebrovascular disease. The AHA recommends early involvement of a cardio-obstetrics team, including a pharmacist, to prevent maternal morbidity and mortality during and after pregnancy.[300] The European Society of Cardiology (ESC) recommends that cardiovascular treatment must be optimised for both mother and fetus and that the urgency of indication determines the necessity of medication treatment.[301] Some important considerations for cardiovascular medication during pregnancy and breastfeeding are as follows:[301]

- Vitamin K antagonists cross the placenta and are therefore contraindicated in the first trimester;
- Anticoagulants pose the risk of haemorrhagic complications for both mother and fetus, therefore vaginal delivery is contraindicated;
- Thrombolytics are contraindicated during pregnancy and peripartum, and should only be used in high-risk patients with severe hypotension and shock;
- Direct oral anticoagulants are largely not recommended for pregnant patients because they cross the placenta;
- Beta blockers are generally safe in pregnancy but are associated with fetal growth restrictions and hypoglycaemia;
- Angiotensin converting enzyme inhibitors and angiotensin receptor blockers are teratogenic and therefore contraindicated during pregnancy;
- Aldosterone antagonists are contraindicated during pregnancy;
- Diltiazem (a non-dihydropyridine calcium channel blocker) is teratogenic and is contraindicated in pregnancy, however verapamil is considered safe during pregnancy and is recommended as a second-line medication; and
- Statins are contraindicated in pregnancy and breastfeeding.

More up-to-date detailed information on medicines use and safety during pregnancy and breastfeeding can be found in the ESC guidelines for the management of hypertension in pregnancy and the WHO guideline for the pharmacological treatment of hypertension in adults.[256, 301]

Children: Children with diabetes, familial hypercholesterolaemia, Kawasaki disease, chronic kidney disease or congenital heart disease are at a high risk of developing CVD.[302] As such, intensive cardiovascular risk reduction is paramount and pharmacological therapy should be initiated where necessary. The recommended cardiovascular medicines are similar to those used by adults. However, important considerations need to be made with regard to dose reduction as per body surface area and the management of common side effects.[303] Therefore, treatment needs to be individualised depending on pathophysiology, status of heart function, severity of CVD, presence of end-organ damage and co-existing renal abnormalities.[303] The American Academy of Paediatrics Clinical Practice Guidelines for screening and management of hypertension in children and adolescents offer a deeper dive into evidence-based contextual medicine management among paediatric patients.[304]

7.3 Medication review

According to Pharmaceutical Care Network Europe (PCNE), "medication review is a structured evaluation of a patient's medicines with the aim of optimising medicines use and improving health outcomes. This entails detecting medicines-related problems and recommending interventions". PCNE has defined three types (levels) for medication review interventions according to information available to the pharmacist conducting this service:[61]

- Level 1 (simple): needs pharmacy dispensing data only;
- Level 2 (intermediate): in addition to pharmacy dispensing data, patient-supplied information (2a) or medical records (2b) needed; and
- Level 3 (advanced): needs access to the three information sources — pharmacy dispensing data, patient-supplied information and medical records.

Medication review must be provided on a regular basis according to a systematic and documented method carried out in collaboration with patients and other healthcare professionals. For example, the Dader method for pharmacotherapeutic follow-up is a systematic, patient-centred process that includes five steps and was developed by the Research Group of Pharmaceutical Care at the University of Granada, Spain,[305] and has been used for pharmacotherapeutic follow-up of patients with CVDs or with CV risk factors.[59] The interventions are based on the use of drug therapy records, the evaluation of an assessment form that registers all CV health problems and CV pharmacotherapy used to treat these medical conditions, and their assessment on a specific date. This assessment is used to identify any potential or actual negative outcomes associated with medication (NOM) and medication-related problems.[63] Once the relevant medication problems are identified, the necessary interventions are carried out to solve the identified NOM and are followed by a subsequent assessment of the achieved outcomes. Overall, some details regarding the five key steps of the Dader method for patients with CVDs or with CV risk factors are:[59, 287, 305]

- **Obtaining patient data related to CV medical problems and current medication therapy:** Patient-specific information regarding current health problems and pharmacotherapy used is obtained by interviewing the patient, reviewing the medication therapy and electronic clinical records (mainly medication history and results of clinical laboratory tests), and by interviewing other healthcare professionals. It is important to collect the necessary information to assess the type of prevention (primary or secondary) as well as the estimate of 10-year risk of CVDs (see sections 2.2, 3.1 and 4.6).
- **Completing the assessment form using the collected data**: Pairing of the patient's health problems (medical diagnostics and symptoms) with the current pharmacotherapy is the basic element to complete this assessment, which provides a global view of the patient's health status and its relationship to the pharmacotherapy used. An assessment form is interpreted and evaluated when all the necessary information is registered.
- **Assessing the patient's medication therapy outcomes**: The aim of this step is to assess if the desired therapeutic goals for controllable and major CV risk factors, for instance, hypertension, dyslipidaemia and diabetes, are achieved. It is important to note that the patient's therapeutic goals may be affected by both the type of prevention (primary or secondary) and by the CV risk assessed. For patients whose goals are not yet achieved, the pharmacist develops a therapeutic plan and interventions oriented to achieve the desired clinical outcomes.
- **Implementing the therapeutic plan by conducting an intervention intended to directly prevent or resolve any identified NOM:**[306] Once the pharmacist has identified concerns about NOM or medication-related problems, they interpret and analyse this information in the context of the clinical condition illustrated by the assessment form, taking into account factors such as the patient's CV risk, type of CV prevention, and the magnitude of increase in indicators of effectiveness of medication therapy, for instance blood pressure, LDL cholesterol, fasting plasma glucose and HbA1c levels. If the goal of the intervention is to modify a problem with lifestyle or with use of a medicine, the patient is the recipient of the intervention, whereas if the aim of the intervention is to modify medication therapy in either a quantitative (e.g., modifying dosage or frequency) or qualitative way (e.g., stopping, adding or changing any medicine), the physician is the recipient of the intervention.
- **Following and completing a new assessment form**: Conclusion of an intervention should generate a change in the patient's assessment, which must be completed in a scheduled follow-up. Thus, depending on whether NOM still exists, an additional therapeutic plan is carried out. This can be, for instance, informing the physician that medication therapy for hypertension or for hypercholesterolaemia has not been effective, thus the patient may need a modification in medication therapy, or providing the physician with information related to a need for medication therapy to address medical problems or for CVD prophylaxis.

In each follow-up appointment, patients must be provided with verbal and written counselling regarding CVD prevention (according to patient risk). In addition, blood pressure, lipid profile, body mass index, smoking status, physical activity and dietary habits need be evaluated during these appointments.

There are other models similar to the Dader method for medication review. For instance the Joint Commission of Pharmacy Practitioners in 2014 released the "Pharmacists' patient care process", which is a method supported by five patient-centred steps and "applicable to any practice setting where pharmacists provide

patient care and for any patient care service provided by pharmacists". Overall, some details regarding the five key steps of this process are:[307]

1. **Collect:** Patient-specific, necessary subjective and objective information is obtained and confirmed from the patient, patient records and other healthcare professionals. This information enables understanding of the patient's key medical and medication history and clinical condition. Patient-specific information collected includes: (i) lifestyle habits, preferences and beliefs, health and well-being goals, and socioeconomic factors that affect access to medicines; (ii) current pharmacotherapy and previous medication, including prescription and non-prescription medications, herbal products and dietary supplements; and (iii) significant health information, including medical history, test results and physical assessment.

2. **Assess:** According to information collected, the clinical effects of the patient's therapy in the context of the therapeutic goals must be assessed in order to identify, prioritise and solve problems and thus contribute to achieve optimal care. The assessment includes: (i) health and functional status, risk factors, health data, cultural factors, health literacy and access to medicines; (ii) immunisation status and the need for preventive care and other healthcare services, where appropriate; (iii) necessity and effectiveness (one or more medicines) and safety (each medicine) of the pharmacotherapy used for each health problem; and (iv) patient adherence and proper and safe use of medicines.

3. **Plan:** In collaboration with other healthcare professionals and the patient or caregiver, a patient-centred and evidence-based care plan is developed, which must be focused on: (i) solving NOM and medication-related problems identified for achieving clinical outcomes in the context of the patient's overall health care goals; (ii) motivating and engaging the patient through counselling and health education, empowerment and self-care; and (iii) arranging follow-up appointments.

4. **Implement:** In collaboration with other healthcare professionals and the patient or caregiver, the pharmacist implements the care plan, which involves: (i) addressing medication- and health-related problems; (ii) initiating, modifying, discontinuing or administering medication therapy as authorized; (iii) proviing counselling and health education, empowerment and self-care; and (iv) scheduling follow-up care as needed to achieve goals of therapy.

5. **Follow-up:** The effectiveness of the care plan must be monitored and evaluated, and, if applicable, it should be adapted in collaboration with other healthcare professionals or with the patient. This step is focused on monitoring: (i) the necessity and effectiveness (one or more medicines) and safety (each medicine) of the pharmacotherapy used for each health problem; and (ii) clinical endpoints and outcomes of care, mainly the progress to reaching the pharmacotherapy goals.

The US Centers for Disease Control and Prevention has released a specific pharmacists' patient care process to manage high blood pressure, which provides suggestions on how these five steps can be applied to managing patients with hypertension.[308]

Similarly, FIP supported the PCNE definition of medication review (MR) in its 2022 publication "Medication review and medicines use review. A toolkit for pharmacists, but suggested the inclusion of medication use review (MUR) as a subtype of MR, which is characterised by a partnership between pharmacists and patients to improve medicines use, consider patient preferences and, ultimately, optimise medication adherence. Thus, FIP states: "While both services are equally important in improving health outcomes, MR aims primarily at improving clinical outcomes and thus contributes to system-level efficiency in addition to encompassing medication adherence goals, whereas MUR is a service exclusively designed to improve medication adherence."[309] However, when step-by-step process and minimum information set are presented for MR, it is possible to identify a great similarly between these steps and the five steps previously detailed both for the Dader method and for the "Pharmacists' patient care process".

7.4 Digital health approaches in CVD management

Digital health is defined as the "use of digital, mobile and wireless technologies to support the achievement of health objectives".[310] The term can also be used to refer to the general use of information and communication technologies for health and is inclusive of both mHealth and eHealth.[310, 311] Digital health technologies have advanced rapidly over the past decade. Technologies such as electronic and mobile health platforms, wearable devices, sensors, telemedicine and artificial intelligence have provided myriad opportunities to improve access and delivery of quality healthcare services.[312] COVID-19 has further spurred the adoption and acceptance of digital health services, more so, in the prevention and management of CVDs.[313] Additionally, digital health technologies have allowed for patient empowerment, which is critical not only in promoting self-care in CVDs but also in ensuring the achievement of better health outcomes.[311] This has been illustrated in the management of hypertension, in which a systematic review of 28 studies reported positive impact of digital health innovations on reduction of blood pressure and improvement in quality of life. In addition, digital health approaches can also be utilised for the self-monitoring of blood pressure and to enhance self-management.[314]

The digital health space is ever evolving, and many interventions have been developed for diagnostic, monitoring and treatment purposes. However, the three main digital health interventions that have been most studied to date in the management of CVDs are text-messaging programmes, smartphone applications and wearable devices.

Text-messaging programmes: Text-messaging programmes have become a simple, innovative, convenient and inexpensive method of communicating with patients. They have shown usefulness in areas where internet connections are unavailable, and smartphone use is scarce. Text messages can also be sent in bulk, and easily automating this process has allowed for minimal human input. Studies on text-messaging programmes have shown positive improvements in modifying lifestyle behaviours such as smoking, physical inactivity, blood pressure, and weight management.[315-317] Research has also demonstrated the usefulness of text-messaging programmes in promoting medication adherence, an important cornerstone of CVD management.[318, 319] These studies also found that text-messaging interventions were engaging and useful for patients, leading to better clinical outcomes and translating into savings on medication costs.[311]

Smartphone applications: Smartphone apps are a little more sophisticated than text-messaging and they allow for more functionality and more services to be embedded in a single app. Apps have been used to educate patients, monitor adherence and provide automatic follow-up reminders.[311] Similar to text-messaging programmes, smartphone apps can also be used to promote lifestyle modifications and motivate patients to stay on track with their treatment. Studies conducted on the effectiveness of smartphone apps in CVD patients show their impact in improving blood pressure, body mass index, physical activity, waist circumference, cholesterol levels, smoking cessation and psychosocial well-being. This resulted in lower rehospitalisation rates and improved quality of life.[320-322]

Wearable devices: Wearable devices can capture information, perform data processing and provide outputs on relevant information. They are useful in providing real-time monitoring data on vital signs, physical activity and trackable behaviours. Consumer-based activity trackers have quickly caught on, and this has translated to an improvement in physical activity levels among those who have them.[323] Their impact on CVD patients has shown mixed results due to the quality of data that wearables provide when compared with standard medical equipment. Therefore, despite their usefulness in promoting physical activity, they have yet to demonstrate accuracy and robustness as monitoring devices.[324, 325]

The pharmacy profession has long been known for being an early adopter of new health technologies. Digital health technologies are no exception and, despite the acceleration of their use during the COVID-19 pandemic, community pharmacists had already been using social media and mobile health applications to deliver public health services and campaigns.[326] As the digital health space continues to expand, there is potential for the roles and responsibilities of pharmacists to shift in line with new patient needs. Since pharmacists are the most accessible healthcare professionals, there is a need to introduce and equip the "digital pharmacist" with knowledge and skills for the education and management of CVD patients through digital health technologies.[327] These technologies can be utilised alongside telepharmacy services. Telepharmacy is a convenient mode of service delivery to ensure continuity of care and monitoring for people living with CVDs. Furthermore, telepharmacy services also provide an avenue for people living with CVDs to seek clarifications on their medicines and health. In line with this, and as digital health technologies become more pervasive,

there will be a need to regulate the manufacturers of digital health technologies, especially those providing solutions for the management of chronic non-communicable diseases.[327]

7.5 Improving medication acceptance and adherence

Medicines are critical interventions in the management and treatment of cardiovascular disease. As a result, improving medication acceptance and adherence is important in ensuring positive health outcomes among CVD patients.[328] Acceptance refers to how medicines are used in the real-world setting, and this ranges from appropriate prescription by providers as per evidence-based guidelines to patient adherence to their medication.[328] Some useful metrics for acceptance of medication include the proportion of prescriptions that follow local treatment guidelines and the proportion of patients who adhere to their prescribed treatment regimens over a year.[328]

7.5.1 Prevalence and impact on non-adherence

Medication non-adherence has been termed as the most common potentially modifiable cause of inadequate control of CVDs.[329] A study by Barolleti and colleagues estimated the documented levels of non-adherence to medication among CV patients to be more than 60%.[330] A further study by Kolandaivelu and colleagues termed non-adherence to CV medication as a pandemic and a leading risk factor for treatment failure and poor outcomes in the management of CVD.[331] Despite the overall poor state of medication adherence globally, low- and middle-income countries are more affected and this has been narrowed down to regional variations in provider practices, cultural beliefs, resource limitations and varied public awareness.[331]

These findings are further backed by a cross sectional study conducted in Nigeria, which found that medication non-adherence was approximately 70%. Medication non-adherence was found to be associated with number of comorbidities, and specifically three comorbidities were found to be marginally associated.[332] A similar cross-sectional study conducted in Malaysia also shows a medication non-adherence prevalence level of 74% with fear of side effects, complex medication regimens and lack of information about illness cited as some of the common reasons for non-adherence.[333] It is important to note that despite the efforts made to determine the prevalence of medication non-adherence, accuracy of the data is difficult to gauge due to multivariate settings, lack of robust definitions, and lack of a gold-standard for screening medication non-adherence.[331]

The impact of medication non-adherence for patients with CVD include a reduction in the effectiveness of pharmacological treatment, increased risk of acute hospital admissions, increased morbidity and mortality, and an overall increase in the healthcare costs associated with managing CVD.[334] Furthermore, non-adherence confounds evidence-based practice, which results in inappropriate therapeutic escalation that potentially causes more harm than good.[331]

On a larger scale, the economic impacts of medication non-adherence are significant. An analysis from the United Kingdom showed that it costs an additional GBP 339 per non-adherent patient on antihypertensive medication.[335] When extrapolated, improving adherence would therefore result in a potential saving of over GBP 100m per year.[335] Similar research by Kleinsinger places the amount of preventable medical costs per year arising from medication non-adherence at USD 100bn.[336] These figures may appear arbitrary, however, they provide us with a rough picture of the scale to which a small health behaviour change can have a huge economic impact.

7.5.2 Measuring adherence

The key metric for determining adherence is simply the number of patients who have adhered to their prescribed treatments over a fixed period. Patients are considered adherent if they take more than 80% of their prescribed medicines over a given period.[337]

These data can be obtained through several methods.[338, 339]

- **Self-reporting by patients**: This is often conducted through questionnaires or structured interviews and is considered the most convenient, indirect, and efficient method to measure adherence among CV patients. This method is also low-cost and easy to apply in many settings.

- **Therapeutic medication monitoring by healthcare providers:** This comprises measurement of medicine concentrations in blood and is often done for medicines with narrow therapeutic windows. Despite its high accuracy, its overarching disadvantage is its invasive nature. As such, it is less practical in the pharmacy setting and on most CV medicines with wider therapeutic windows.
- **Electronic medication monitoring**: This method is considered as the "gold standard" for adherence measurement in chronic diseases.[338] The electronic monitors are broadly classified into oral medication monitors and inhaled medication monitors. Oral medication monitors, such as the electronic medicine event monitoring system, are more relevant to CV patients. These oral monitors record the date and time that medicine bottles are opened, and these data are shared with healthcare service providers. In addition to the oral medication monitors, smartphones are useful ways of monitoring medication adherence and they can be used to relay data from oral medication monitors to healthcare providers.[340]
- **Pick-up and refill rates from pharmacies:** Pharmacists play a central role in these methods and can calculate pick-up and refill rates for their CV patients. The prominent disadvantage of this method is the obvious subjectivity it holds. However, it remains an inexpensive and easily implementable method at pharmacy.[341]

It is important to note that the above stated methods of measuring adherence can be used for many other chronic diseases besides CVDs.[338]

Adherence can be measured with certain scales and some of the most frequently used ones include the Medication Adherence Report Scale and the Belief About Medicines Questionnaire.[339] Each of these adherence measurement methods has its own advantages and disadvantages. Therefore, it is important to determine validity and generalisability when choosing which method to use to measure medication adherence. A combination of methods is preferred to obtain useful clinical data.[339]

7.5.3 Reasons for non-adherence

Determining the exact cause of medication non-adherence is akin to trying to find a needle in a haystack — difficult but not impossible. There are myriad potential barriers that may prevent medication adherence, with some classifiable and others not. Despite their classification, the common denominator remains that non-adherence is common among cardiovascular patients due to the considerable number of medicines they are prescribed for all their ailments.

The factors that contribute to medication non-adherence can be classified as follows:[330]

- Socioeconomic factors, i.e., inadequate healthcare coverage, concerns about cost, poverty and unemployment, and substance or alcohol abuse;
- Communication barriers, i.e., illiteracy, mental illness, substance or alcohol abuse, old age, and differences in primary language between healthcare provider and patient; and
- Motivational barriers, i.e., poor understanding about one's illness, fear of toxicity or side effects and lack of perceived benefit from the medication prescribed.

These factors can be further translated and grouped into specific potential barriers to medication adherence. This grouping includes patient-related barriers, treatment-related barriers and other barriers.[336] See Table 22.

Table 22. Potential barriers to medication adherence

Patient-related	Treatment-related	Other
• Lack of motivation • Depression • Denial • Cognitive impairment • Medicine or alcohol abuse • Cultural issues • Low educational level • Alternate belief systems	• Complexity of treatment regimen • Side effects or fear of side effects • Cost • Time • Inconvenience • Treatment of asymptomatic disease	• Poor practitioner-patient relationship

Since reasons for non-adherence are multifactorial, successfully tackling it requires pragmatic multimodal interventions.

7.5.4 Adherence enhancing interventions

Pharmacist-led interventions are crucial in offering holistic care to patients with chronic diseases. In a study by Apikoglu and colleagues, pharmaceutical care interventions offered by community pharmacists led to a significant improvement in health outcomes for NCD patients in Turkey.[342] In a similar study on pharmacist reported interventions in Saudi Arabia, pharmacist-led interventions were shown to reduce prescribing errors and possible harm to patients.[343] Furthermore, pharmacists were considered critical players in ensuring patient safety through quality improvement initiatives.[343] Therefore, enhanced pharmacist involvement is key to improving medication adherence.[344]

When dealing with medication non-adherence, it helps to step back and not to focus solely on the barriers and factors stated above, but rather on the behaviour change that we are trying to foster. Promoting medication adherence is a behaviour change process that requires education, motivation, supportive tools, monitoring and evaluation.[336] Therefore, the best interventions around promoting medication adherence opt for a multifaceted systems approach as opposed to a unimodal strategy. Invariably, such high-level interventions will require input from and collaboration among many healthcare players. In any case, pharmacy-based interventions to improve medication adherence in CVD patients have been shown to be cost-effective and most economically viable with regard to returns on investments.[345] In addition, the implementation of community pharmacy-led services targeting medication adherence also resulted in positive clinical, humanistic and economic impacts.[346, 347]

Therefore, pharmacists remain critical players in enhancing medication adherence in the following ways:

- Pharmacists can conduct assessment interviews as a way of identifying adherence barriers. Identifying potential non-adherents is an important prerequisite to tackling medication non-adherence in the community or hospital setting.
- Community pharmacists can reach out to non-adherent patients and encourage them to make appointments for refills. This can be done through messaging or voice calls to remind or encourage them to collect and take their medicines as prescribed.[348] The pharmacist can use this opportunity to ask about any other potential causes of non-adherence.[255] This intervention aligns with evidence from a meta-analysis conducted by Thakkar and colleagues, which found that mobile phone messaging doubled the odds of medication adherence in patients with chronic illnesses.[319]
- Through medication therapy management and collaborative drug therapy management services, clinical pharmacists can identify, follow, educate and counsel non-adherent patients. They can also adjust patients' medication if needed to aid in adherence.[349] This is in line with the team-based approach recommended by the US Centers for Disease Control.[252]
- Pharmacists can employ motivational interviewing to help resolve patient ambivalence and enhance self-empowerment. The effectiveness of motivational interviewing in enhancing adherence was evidenced in a randomised study by Hedegaard and colleagues.[350]
- Where available, pharmacies should dispense or prescribe fixed dose combinations of cardiovascular medicines as a way of reducing patient pill burden and promoting compliance to prescribed medication regimens.[351]

Pharmacists are encouraged to explore more innovative solutions that tackle medication non-adherence among the areas and populations that they serve.

7.6 Evaluating and resolving medicines-related problems

The effectiveness of treatment and achievement of treatment goals among patients with CVD is largely dependent on the quick evaluation and resolution of medication-related problems (MRPs). Pharmaceutical Care Network Europe defines a MRP as an event or circumstance involving pharmacological therapy that potentially interferes with achieving desired therapeutic outcomes.[352] Patients with chronic diseases, such as

CVD or diabetes, take multiple medicines from varying pharmacological classes, and this increases the risk of MRPs occuring. The impact of not resolving MRPs promptly includes non-adherence, increased hospitalisation and subsequent avoidable socioeconomic burdens.[353]

MRPs are broadly classified into treatment effectiveness, adverse reactions, treatment costs and others.[352] For CVD patients, medication review is recommended for optimisation of medicines use.[354] In most clinical and community settings, pharmacists are usually best placed to identify MRPs and initiate required mitigation interventions.[355] However before intervening, pharmacists need to evaluate the cause(s) of the MRPs. To do this, pharmacists need to understand the eight most probable causes of MRPs. These include medication selection, medicinal form, dose selection, treatment duration, medicine use/administration process, logistics of prescribing and dispensing, patient behaviour, and other non-classifiable causes.[352] Notably, one cause may have multiple subcauses, and this is summarised in Table 23.[352]

Table 23. Primary causes and subcauses of medication-related problems

Primary cause	Subcauses
Medication selection	• Inappropriate/contraindicated medication • No indication for the medication • Inappropriate combination of medicines, or of medicines and food • Inappropriate duplication of therapeutic groups or active ingredients • Indication for medication treatment not noticed • Too many medicines prescribed for indication • More cost-effective medication available • Synergistic/preventive medicines required but not given • New indication for medication treatment present
Medicinal form	• Inappropriate selection of medicinal form
Dose selection	• Dose too low or too high • Dosage regimen not administered frequently enough or too frequently • No therapeutic medication monitoring • Pharmacokinetic problems • Improvement or deterioration of disease state requiring dose adjustment
Treatment duration	• Duration of treatment too short or too long
Medicine use/administration process	• Inappropriate timing of administration or dosing intervals • Medicine deliberately underused or overused • Medicine not administered at all • Wrong medicine administered • Medicine abused • Patient unable to use medicinal form as directed
Logistics of prescribing and dispensing	• Prescribed medicine not available • Prescribing error • Dispensing error
Patient behaviour	• Patient forgets to take medicine • Patient uses medicine unnecessarily • Patient eats food that interacts with medicine • Patient stores medicine inappropriately
Others	• Non-specified or obvious cause

Further to the causes stated above, medicine interactions and adverse medicine reactions are major concerns among CVD patients due to the overt risk of polypharmacy that treating these patients carries.[356] In fact, in a study by Patel and colleagues, it was observed that the potential for medicine-medicine interactions increases as the number of concomitant medicines increase.[357] Some common medicine-medicine interactions that occur with prescribed cardiovascular medication include the combination of an antiplatelet and anticoagulant (aspirin and rivaroxaban), combination of a statin with a CYP inhibitor (atorvastatin and clarithromycin), combination of angiotensin converting enzyme inhibitors and antiplatelets (captopril and aspirin) and combination of a statin with a calcium channel blocker (atorvastatin and diltiazem).[358] The presence of such harmful medicine-medicine interactions interferes with therapy goals, and results in an increase in adverse medicine reactions, morbidity and mortality. Therefore, avoiding the use of certain combinations of medicines ensures that adverse medicine reactions and events are prevented. However, sometimes is necessary combine some of these medicines.

Interactions between foods, supplements and other nutraceuticals may interfere with the effectiveness of cardiovascular medicines. For instance, grapefruit is a known CYP3A4 inhibitor and will interfere with the pharmacokinetic properties of cardiovascular medicines.

Pharmacists play a key role in screening patient prescriptions for medicine-medicine interactions through conducting medication reviews and classifying the potential causes of medication-related problems as shown above.[358] This then aids in guiding on which interventions will resolve the medication-related problem.

The resolution of MRPs can be done at several levels.[352] First, in countries where pharmacists are legally allowed to prescribe, they can appropriately prescribe medicines at the recommended doses and frequencies based on standard treatment guidelines or evidence-based practices.[352] Where pharmacists are not legal prescribers, they can propose interventions to prescribers, who may then approve the intervention.

Secondly, at the patient level, pharmacists can provide patient counselling to tackle patient behaviour problems. Additionally, they can speak to caregivers or guardians to ensure that the patient is monitored closely and adheres to prescribed medication. In cases where there is a language or literacy barrier, pharmacists can opt to provide written information only. If the pharmacist is unable to provide an appropriate intervention at this level, it is recommended that they refer the patient back to the prescriber.

Thirdly, at the medication level, pharmacists can resolve MRPs by changing the medication prescribed, adjusting doses, changing the medication formulation, changing the instructions for use, stopping inappropriate medication, or starting the patient on new medication. A combination of these interventions can be provided where necessary. It is important to note that these interventions are contextual, thus in countries where pharmacists are not prescribers, changes to prescribed medication can only be done by a medical doctor. Therefore, pharmacists can propose such interventions to legal prescribers, who may then approve them before they are implemented.

Finally, for unknown or unspecified causes, pharmacists can make use of the team-based approach and engage within multidisciplinary care teams to determine the best way forward. Pharmacists may also need to wear their pharmacovigilance hats and report any side effects through prescribed pharmacovigilance channels. A key component of resolving MRPs is monitoring the outcome of the instigated interventions. Thus, the process is iterative until the MRP is partially or totally solved.

Since the field of CV pharmacotherapy is ever evolving, new medicines with insufficient evidence-based clinical data may be prescribed to patients. Scott Pegler and colleagues recommend an analytic framework, i.e., safety, tolerability, effectiveness, price and simplicity (STEPS), that helps prescribers make better and balanced prescribing decisions for novel medicines.[359]

To further enhance CVD therapy at the patient and medication level, it helps to also view the patient through a pharmacogenomics lens.[360] Genomic variations have long been recognised as major contributing factors to variability in medication responsiveness. Over the past decade, our understanding of genetic determinants that influence response to cardiovascular medicines, such as statins, warfarin and clopidogrel, has improved significantly. This has opened new frontiers in personalised medicines and is expected to improve clinical outcomes and reduce medication toxicity. The availability and affordability of pharmacogenomics services may vary from country to country. However, pharmacists need to stay informed about research on new

approaches to medicine selection and dose prescription based on pharmacogenomics.[361] Additionally, they should be aware of the genetic tests used to determine individual CVD patient genomic variations, proper medication and dosage alterations. It is also crucial that pharmacists consider ethical guidelines when educating patients on these genetic tests.[361]

7.7 Developing treatment and monitoring plans

A treatment plan is a clear outline of a patient's disease, the goal of treatment, the treatment options for the disease, the expected length of treatment and any expected side effects. Treatment plans are a hallmark of CVD management and especially in medication therapy management and collaborative drug therapy management. Treatment plans are important because they act as a roadmap for the initiated therapeutic process and provide a way of measuring therapeutic effectiveness.

Pharmacists, and especially clinical pharmacists, can sit down with their patients and develop treatment and monitoring plans. This face-to-face interaction allows the pharmacist to observe visual cues to the patient's health problems and enhances the patient-pharmacist relationship.[362] The treatment and monitoring plan should be a collaborative effort between the patient and the pharmacist, and should be within the pharmacist's scope of practice or that agreed with other members of the multidisciplinary healthcare team.[362]

The first step in developing a treatment plan is to assess the patient. This assessment needs to be comprehensive and should focus not only on the disease state and progression, but also on the social, economic and psychological contexts.[362] These have the potential to be barriers to effective implementation of the treatment plan. Therefore, a holistic picture should be collected during this stage.

Once the pharmacist has captured the holistic patient-centred view, then goals and objectives need to be set. Both the pharmacist and the patient should clearly understand the goal(s) they are pursuing. Each goal, and subsequent objectives, needs to be defined, measurable and achievable. Often objectives can act as milestones for monitoring the treatment plan.

The final step is developing and initiating appropriate interventions, which may be pharmacological or non-pharmacological. These interventions should be evidence-based, aligned to national standard treatment guidelines and be within the pharmacist's scope of practice and competence.[362] Close monitoring is required to ensure that the patient adheres to prescribed interventions and that new or recurring medication-related problems are addressed. Periodic reviews must therefore be conducted. Furthermore, a team-based approach may be useful in ensuring the continuum of care is maintained.

Research by Breault and colleagues laid out the critical practical steps in implementing pharmacist-led treatment plans.[363] These include:

- Developing individual expertise related to one's scope of practice;
- Optimising roles, workflow and space to support implementation of treatment plans;
- Developing a treatment plan template that supports the care process;
- Scheduling time for care planning based on routine patient visits or overt patient need;
- Involving the patient in the treatment planning process to ensure goals and outcomes are patient-centred;
- Documenting and communicating specific responsibilities in the treatment plan process and
- Sharing treatment plan documentation with patients in a timely manner, which should include current medicines, agreed goals, health behaviour changes to be implemented, monitoring and follow-up plans.

Even as pharmacists develop patient-centred treatment plans, rational use of medicines needs to be stressed. Rational use involves correct and appropriate use of medicines so that the selection, dose and duration prescribed is in line with standard treatment guidelines.[364] This means that pharmacists must check the five rights of rational use when creating and implementing their treatment plans, i.e., right patient, right medicine, right dose, right route and right time. In addition to the five rights of rational use, pharmacist prescribers should always attempt to maximise clinical effectiveness, minimise harm, avoid wastage of scarce resources

and respect patient choice.[365] Many NCDs can be prevented or treated by rational prescription and use of available medicines.[364]

Irrational use of medicines results in avoidable morbidity and mortality, adverse medicine reactions, poor treatment outcomes and financial loss.[364] In low- and middle-income countries, such negative impacts are amplified by the lack of availability of medicines. Therefore, as pharmacists develop, implement and monitor treatment plans, it is important always to check that treatment falls within the five rights of rational use and adheres to the WHO criteria for rational use of medicines.[366]

7.8 Recommending or prescribing appropriate medicines therapy

In many countries around the world, pharmacist prescribing is legal.[367] Pharmacists may be supplementary prescribers or independent prescribers, with the former working with medical or dental practitioners within a specific clinical management plan, and the latter prescribing any medication independently for any condition within their scope of practice and competence.[368] Pharmacist prescribers play a critical role in meeting the needs of CVD patients and delivering high-quality, patient-centred, holistic care. This completes the continuum of care by incorporating medication therapy management and collaborative drug therapy management activities in the same basket. Furthermore, studies on the effects of pharmacist prescribing show that pharmacists are better at adhering to dosing schedules and make significantly fewer prescribing errors while promoting cost savings.[367, 369, 370]

The General Pharmaceutical Council (UK) provides key considerations for pharmacist prescribers.[368] First, it is paramount that pharmacists take responsibility for prescribing safely. This includes having all the necessary patient information before prescribing, prescribing only within the limits of their knowledge, skills and competence, and planning appropriate follow-up reviews to monitor medication prescribed.[368] Secondly, it is necessary for all prescribing pharmacists to maintain their competence in prescribing so as to provide safe, appropriate and updated care. The "Competency framework for all prescribers", a publication by the Royal Pharmaceutical Society (UK), is a useful resource on this.[371] Lastly, prescribing pharmacists must work and communicate effectively with other healthcare professionals to deliver safe and effective care.

Similarly to physicians, it is recommended that pharmacists adhere to this eight-step prescribing approach to minimise poor-quality and erroneous prescribing:[372]

1. Evaluate and clearly define the patient's problems;
2. Specify the therapeutic outcome or goal;
3. Select the appropriate medicine based on evidence-based treatment or standard treatment guidelines;
4. Initiate therapy with the appropriate details and always consider non-pharmacological interventions;
5. Provide the patient with complete information, instructions and warnings;
6. Evaluate therapy regularly, which may involve monitoring adherence, treatment results, and discontinuation if medication prescribed is ineffective;
7. Always consider medication costs when prescribing; and
8. Make use of computers and other tools to reduce prescribing errors.

Notably, pharmacist prescribers need to avoid prescribing in situations that may alter their objective clinical judgement, for instance, prescribing for themselves or for close family members.[368]

In addition to pharmacological therapy, nutraceuticals have proven to be useful in the prevention and treatment of CVD. In the spirit of offering holistic care to patients, pharmacists need to be aware of the evidence-backed nutraceuticals to augment pharmacological treatment of CVD.[373, 374] A summary list of these nutraceuticals is provided in Table 24.

Table 24. Nutraceuticals for the prevention and treatment of cardiovascular disease

Class	Examples	Indication
Sterols/stanols	Mainly found in fruits, cereals, seeds and nuts	Dyslipidaemia, hypertension,
Polyphenols/flavonoids	Mainly found in citrus fruits, vegetables, cereals, legumes, green tea, grapes, red yeast rice, honey, berries, and in beverages derived from these plant products	Dyslipidaemia, hypertension
Microalgae	Spirulina	Dyslipidaemia, hypertension
Vitamins	Vitamins C, D and E	Dyslipidaemia, hypertension
	Lycopene, found in papayas, tomatoes and watermelons	Dyslipidaemia, hypertension
	Garlic	Dyslipidaemia, hypertension

It is important to note that these products are not available in all countries and that they are not intended to replace the therapy prescribed by a doctor.

7.9 Stewardship of medicines supply, availability and affordability

Medicines are a critical intervention in the management of CVD. However, their availability, accessibility and affordability vary from country to country. A study by Mourik and colleagues, which comparatively analysed the availability and affordability of CVD medicines, found that overall availability was poor in low- and middle-income countries.[375] In addition to their poor availability, the cost of purchasing these medicines is higher than the individual daily wage in many LMICs. Because of this, treatment is still unaffordable for many.

Effective management of CVDs is dependent on the efficient supply, availability and affordability of medicines. Beyond their clinical roles, clinical and community pharmacists act as medicine custodians. Despite little research existing in the stewardship of CVD medicines, pharmacists play similar roles in this domain to those involved in antimicrobial stewardship.

In medicines supply, pharmacists are responsible for ensuring CVD medicines are safe and of high quality. This involves coordinating with pharmaceutical companies to provide medicines with the best quality, best price, and in sufficient quantities to avoid stock-outs. Pharmacists are responsible for assuring the quality of the purchased product and earmarking or segregating any substandard or counterfeit medicines. Additionally, pharmacists help maintain the quality of medicines received by ensuring they are stored under appropriate conditions at stores or warehouses until they are distributed or dispensed. This and many other roles are clearly outlined in the FIP publication on "Pharmacists in the supply chain".[376]

By monitoring supply chains, quantifying and forecasting need, and assessing the risks of stock-outs, pharmacists can ensure consistent availability and affordability of CVD medicines.[376] This ensures treatment is continuous and stock-outs or high prices are not blamed for treatment failure.

Finally, pharmacists ensure the rational use of CVD medicines, thus promoting sustainable supply chains.[377] This means analysing prescriptions for appropriateness to prevent polypharmacy. It also means conducting medication reviews to ensure medicines are administered at the right dose and in the right frequency to achieve therapeutic goals.[377] The impact of such reviews has been clearly demonstrated in a study by Dreijer and colleagues, where implementation of a multidisciplinary antithrombotic team that includes medication reviews by pharmacists resulted in a reduction of patients with anticoagulant-associated complications.[378] In some cases, pharmacists are also responsible for monitoring patients' medicines use to prevent wastage through expiry, abuse or disuse.

8 Measuring progress: clinical and economic outcomes metrics for CVD services

Concerns regarding the cost, access, and quality of care has driven health services researchers and practitioners to consider a more comprehensive model for medical decision making in healthcare settings.[379] When measuring the impact of professional pharmacy services in CVD, it is therefore important to consider the value these may add from the perspective of other stakeholders involved in patient care. This allows the attainment of a holistic and balanced overview of the service's impact and a better planning and sustainability assessment.

A commonly used approach in the evaluation of pharmacy and other services in healthcare settings is Kozma's ECHO (Economic, Clinical, Humanistic Outcomes) model.[379] The ECHO model illustrates the value of a service combining traditional clinical-based outcomes with additional measures of quality and economic efficiency in health care, supporting the optimisation of resources. It proposes evaluating:

- The service's clinical impacts (e.g., clinical outcomes), which are important from the perspective of the health care provider;
- The service's economic impacts (e.g., cost-effectiveness and cost-utility of the service), which are relevant from the policy maker and payer perspective; and
- The service's humanistic impacts (e.g., health-related quality of life), which are important from the patient perspective.

Examples of potential outcomes to be considered in CVD services according to this classification are outlined in Table 25.

Table 25. Application of the ECHO model to in cardiovascular disease services[379, 380]

Outcome type	Definition	Examples
Clinical	Medical events or changes in a health status that occur as a result of a pharmacist intervention or service	• Surrogate outcomes (i.e., clinical parameters): blood pressure, HbA1c, cholesterol levels, cardiovascular risk • Final outcomes (i.e., health-related events): heart attack, stroke, death
Economic	Direct, indirect and intangible costs associated with the intervention or service alternatives, which are often balanced against clinical or humanistic outcomes using pharmacoeconomic analyses	• Cost per quality adjusted life year • Cost per unit of benefit
Humanistic	Consequences of a pharmacist service on the patient's functional status, quality of life and often other patient-reported outcomes	• Patient health-related quality of life • Patient satisfaction

8.1 Clinical outcome measures for CVD services

8.1.1 Blood pressure levels

According to the European Society of Cardiology (ESC), hypertension is one of the most important preventable causes of premature morbidity and mortality.[14] Blood pressure levels can be easily measured and are routinely monitored in community pharmacies. In the latest guidelines, the ESC and the European Society of Hypertension recommend that blood pressure in clinical settings should be measured in standardised conditions using a validated device. Patients should sit for five minutes before the measurements. A cuff appropriate for the patient's arm circumference should be used. In the first measurement, blood pressure should be measured in both arms, and if differences are observed, the arm with the higher values should be used as the reference for future measurements. Three measurements should be undertaken one or two minutes apart. The first reading should be disregarded, and the level should be recorded as the average of the second two blood pressure readings.[14, 75] The systolic and diastolic blood pressure measurements should be

checked against the values described in Table 8 to determine whether additional pharmacist or other healthcare professional care is needed.

8.1.2 Cholesterol levels

Dyslipidaemias are characterised by elevated triglycerides, LDL cholesterol and low HDL cholesterol. Unfavourable blood lipid levels are directly associated with increased CVD risk, and the monitoring of the aforementioned indicators when evaluating the impact of pharmacy services in CVD patients should be considered. The current approach in lipids management is primarily focused on lowering LDL levels.

Different accurate, fast and automated methods are available for the measurement of these indicators in community pharmacy, and these usually involve taking a small blood sample from the patient's finger. No fasting is required but results should be interpreted with care in patients with metabolic syndrome, diabetes or hypertriglyceridaemia.[14] It should be noted that different regulations exist worldwide with regard to point-of-care testing.

8.1.3 Cardiovascular risk

Cardiovascular risk refers to the probability of suffering a CV event in the future. The ESC strongly recommends the use of risk prediction models in order to enhance healthcare and CVD prevention.[247] Different risk models are available and have been validated in different populations and regions, using data on a range of CVD risk factors. These models usually estimate an individual 's risk over a 10-year period and allow the identification of people at a higher risk and the implementation of preventive strategies. For example, the SCORE2 (Systematic Coronary Risk Estimation 2), an updated version of SCORE, predicts a 10-year fatal and non-fatal CVD risk in individuals in Europe without previous CVD or diabetes aged 40–69 years. Risk indicators including sex, age, systolic blood pressure, non-HDL cholesterol and smoking status are needed.[247] Pharmacists can easily calculate an individual's CVD risk through the aforementioned data. Online calculators and apps are available and can be accessed here and here.

It should be noted that validated algorithms and tools exist for given populations, countries or geographical regions. Pharmacists should therefore check the recommended tool for assessing CVD risk in their area and patient.

8.2 Economic outcome measures for CVD services

Pharmacoeconomics has traditionally been defined as the description and analysis of the costs and consequences of pharmaceuticals and pharmaceutical services, and its impact on individuals, healthcare systems and societies. A wide range of economic evaluations is used in health services and pharmacy practice research to determine the "value for money" of professional pharmacy services and basically compare the costs and consequences of healthcare interventions (e.g., the pharmacy service being evaluated vs usual care), with results being reported in terms of a cost per unit of effect.[381] A brief description of costs and consequences used in economic evaluations is provided below.

Costs: Costs are defined as the monetary value of the resources consumed by a programme or treatment alternative. Depending on the economic evaluation and the perspective adopted (e.g., payer, patient, societal), different costs can be considered. These have traditionally been classified into direct and indirect costs. Direct costs are the resources consumed in the prevention, detection or treatment of a disease (e.g., hospitalisations, medicines, GP visits, pharmacist care, supplies), whereas indirect costs are those costs that result from morbidity (i.e., costs incurred from productivity loss) and mortality (i.e., costs incurred due to premature death).[381]

Consequences: Consequences are defined as the effects, outputs and outcomes of the service or treatment chosen. The way in which consequences of a service are assessed represents the key distinction among the different economic evaluations available. For example, in cost-effectiveness analyses, consequences are expressed in terms of obtaining a specific therapeutic objective. In this type of economic evaluation of pharmacy services, it is common to use intermediate or surrogate outcomes (e.g., blood pressure, cholesterol levels) rather than final outcomes (e.g., stroke). On the contrary, in cost-utility analyses (CUAs) consequences

are usually expressed as quality-adjusted life-years (QALYs). QALYs represent the number of full years at full health that are valued equivalently to the number of years as experienced.[381] CUAs are usually expressed as a cost per QALY gained (or an alternative health state utility measurement). Considering the subjectivity around QALYs, there seems to be a lack of consensus on how utility should be measured. One of the most widely used tools in health services research to estimate QALYs is the EuroQoL EQ-5D-5L, although different versions of this tool are available for its use in research and clinical practice settings. Another economic evaluation worth mentioning is cost-benefit analysis, in which both costs and consequences are valued in monetary units.

9 Guidance for practice-based research on pharmacists' roles in CVDs

Pharmacists who wish to conduct practice-based research on the roles of pharmacists and CVD services should consider a variety of factors when developing their research and programme plans. A stepwise systematic approach should be adopted, starting from the identification of a problem and gap in service provision, to planning of a programme to address this gap, and subsequently to the implementation and evaluation of the programme.

9.1 Identification of problems and gaps

The first step to enhancing CVD services is to identify problems and gaps in the current practice. This step should be undertaken through in-depth analysis of local, national and regional data related to CVD services and the needs of communities. Quantitative data provide a comprehensive overview of the epidemiology and service utilisation rates for CVD management. Pharmacists should explore and obtain data from local sources such as national registries, and refer to global data sources such as the WHO Global Health Observatory and the World Bank.

Analyses of quantitative data should be coupled with the consideration of qualitative data through interviews, ethnographic research and focus group discussions. Qualitative research methods are useful for exploring facilitators and barriers to uptake of services and programmes. Pharmacists can initiate exploratory research for problems and gaps that have not been well-researched, so as to provide new insights to guide the planning and development of new interventions and programmes. Exploratory research is generally not structured and is open ended. It is also usually lower in cost and hence easier for pharmacists or pharmacies with minimal financial support to undertake.

9.2 Planning and development of programmes

9.2.1 Literature review

Literature review of primary research, policy papers and other documentations of best practices and implemented programmes can guide the planning and development of new CVD management programmes. Reviewing literature on facilitators and barriers to the implementation of similar programmes can allow pharmacists to mitigate any potential challenges.

9.2.2 Engagement of stakeholders

The planning and development of CVD-related programmes should involve multiple stakeholders, namely, healthcare providers, healthcare administrators, patients and caregivers. The Community Toolbox has outlined potential groups of stakeholders:[382]:

- Beneficiaries, e.g., patients, caregivers, a racial or ethnic group;
- Those directly responsible for the beneficiaries, e.g., family members, community workers, healthcare providers;
- Those who may be affected by the process or programme, e.g., employers, community members in residential estates, contractors;
- Government and policy makers;
- Media, healthcare administrators, healthcare management; and
- Those with an interest in the outcome, e.g., activists or community advocates, certain business community members, funders.

Key stakeholders and their interests should be identified during the planning of a programme. Stakeholders can then be divided into four groups: (i) high influence, high interest; (ii) low influence, high interest; (iii) high influence, low interest; and (iv) low influence, low interest. The Community Toolbox has outlined the details of engaging these stakeholders in the process of planning and development of a programme.[382]

9.2.3 Planning tools: RE-AIM and IRLM

RE-AIM and the IRLM (Implementation Research Logic Model) can be used to guide pharmacists on developing their programmes. RE-AIM is an acronym for reach, effectiveness, adoption, implementation, and maintenance (Table 26).[383]

Table 26. RE-AIM framework for programme planning[383]

Core element	Description
Reach	Who will take part in the programme?
Effectiveness	What are the results and outcomes?
Adoption	Where will the programme be implemented?
Implementation	How will the programme be delivered, including adjustments and adaptations?
Maintenance	When will the programme be reviewed?

The IRLM can be used to guide planning and evaluation of programmes. The core elements of IRLM include determinants of implementation, implementation strategies, mechanisms, and outcomes (Table 27).[384]

Table 27. Core elements of the Implementation Research Logic Model

Core element	Description
Determinants	Factors that may affect the success of the programme implementation (i.e., facilitators and barriers)
Implementation strategies	Supports or changes that increase the adoption of the programme
Mechanisms	Processes in which the strategy affects the outcomes
Outcomes	Indicators of the processes or clinical measures

9.3 Implementation and evaluation of programmes

Whether the implementation of CVD-related programmes into the community has been successful or not needs to be evaluated. Implementation outcomes include:[385]

- Acceptability — stakeholders are agreeable and satisfied with the programme;
- Adoption — the intention and action of the programme are undertaken;
- Appropriateness — outcomes are relevant to the community, setting and practice;
- Cost — the programme is cost-effective;
- Feasibility — the extent to which the programme can be successfully conducted; and
- Sustainability — the extent to which the programme can be maintained.

Pharmacists can play a role in evaluating the success of the roll-out of programmes targeted at managing CVDs. This evaluation process allows pharmacists to collect and analyse data about their programmes. Using these data, pharmacists can continuously improve on programme quality.

Most commonly used is the Model for Improvement, which consists of three questions followed by the PDSA (plan, do, study, act) cycle.[386] The three questions are:

- What are we trying to accomplish?
- How will we know that a change is an improvement?
- What change can we make that will result in an improvement?

The PDSA cycle is an iterative process whereby the changes are implemented, assessed and refined based on the data collected. Pharmacists can use data and research to continuously improve their programmes for the benefit of patients and important stakeholders involved in cardiovascular care.

10 Ethical considerations

Ethical principles should be considered while caring for people living with CVDs. These ethical principles include autonomy, beneficence, justice, and non-maleficence. Autonomy includes respect for the patient to be involved as one of the key stakeholders in making treatment and clinical decisions.[387] This is known as shared decision-making in the person-centred care paradigm, and takes into account an individual's beliefs, values, preferences and capabilities. Informed consent and respecting privacy and confidentiality therefore play a central role in the practice of shared decision-making.[387] Beneficence refers to acting in the best interest of the patient, maximising benefits and minimising risks and harms.[388] Justice encompasses equitability and distributive justice (a form of "do no harm"), in which all people should be treated similarly and limited resources should be distributed fairly.[388] Non-maleficence refers to avoid harming the patient or society.[388]

The healthcare paradigm for management of CVDs has shifted from a disease-oriented paradigm to one that is person-centric, and this implies the importance of engaging patients in making any clinical decision on treatments and procedures. This shared decision-making process can be multifaceted and conflict with different stakeholders' perspectives. From the physicians' and pharmacists' perspectives, clinical decisions should be guided by the best interest of the patient (beneficence), ensuring fair allocation of treatments to all patients (justice), and respecting the patient's values, beliefs, cultures and preferences (respect for the person).[388] However, from the patients' perspective, their beliefs, values and preferences may not always be in their best interest. Therefore, physicians and pharmacists have to communicate effectively with patients on all available treatment options and their benefits and risks, while acknowledging and being empathetic towards patients' values, beliefs and culture.

Building rapport and establishing trust with patients are pivotal to enhancing decisional capacity of the patient, and the foundation to establishing trust is respecting the privacy and confidentiality of the patient.[388] Privacy and confidentiality refer to the protection of personal information that healthcare providers gather in the course of caring for patients. Safeguarding privacy and confidentiality is governed by the principle of autonomy and respect for the person, and it is an obligation of the healthcare provider to ensure that confidential information is securely stored based on its sensitivity.[388] Pharmacists must ensure that privacy and patient confidentiality are safeguarded and, where disclosure of any confidential patient information is required, only the most limited information should be shared.

Obtaining informed consent is also essential in the care for people living with CVDs, and this falls under the principle of autonomy and respect for the person. Informed consent comprises communicating the treatment or procedure to the patient, ensuring quality understanding of the patient on what they will undergo, and obtaining authorisation from the patient to perform the communicated treatment or procedure without undue influence or coercion.[388] Fundamentally, the informed consent process should be person-centred, considering the individual's values, beliefs, needs and preferences. In the process, benefits and risks should be weighed and patients should be given free will to make voluntary decisions and authorise those decisions without any coercion.[389]

While safeguarding privacy and confidentiality, and obtaining informed consent, are key to respect for the person, pharmacists and healthcare providers may also need to weigh the importance of other ethical principles such as beneficence, justice and non-maleficence.[388] This may give rise to ethical dilemmas, especially where treatments proposed in the best interest of the patient come into conflict with the patient's beliefs, values and culture. CVD treatments often include primary and secondary prevention. For example, people living with atrial fibrillation who are prescribed anticoagulants for stroke prevention may not perceive the need for anticoagulants because they do not experience any symptoms, and this can lead to patients deciding against taking anticoagulants.[390] Pharmacists can play a role in providing medication and health education and subsequently work together with patients to jointly decide on the treatment regimen while respecting patients' beliefs and values. Pharmacists must consider ethical issues, including obtaining informed consent and safeguarding privacy and confidentiality when caring for people living with CVDs so as to ensure effective and efficient care.

11 Barriers to providing CVD services and facilitators to help overcome them

Pharmacists play an essential and complementary role in a collaborative care team for the management of CVDs. The healthcare delivery paradigm for the management of CVDs has shifted to one that is person-centred and collaborative. To ensure that the role of pharmacists is optimised in care delivery models for CVD management, it is important to assess barriers and facilitators to the delivery and implementation of pharmacist-led care services and subsequently identify strategies to overcome these barriers.

11.1 Barriers

11.1.1 Structural and system-level barriers

Involvement of pharmacists as part of a person-centred interprofessional collaborative care team in managing CVDs can be hindered by several structural and system-level barriers, as outlined below.[391]

Lack of comprehensive access to medical records: In many countries, pharmacists, especially in the community setting, do not have direct and comprehensive access to a patient's medical records and health information. This may hinder patient care, especially in optimising medication. People living with CVDs are often living with several other comorbidities and may also be experiencing polypharmacy issues. This signifies the importance of engaging pharmacists to optimise medication, address medicine-related problems and resolve any polypharmacy issues in a timely manner. However, without access to medical records, it will be challenging, if not impossible, for pharmacists to ensure efficacy and safety of medicines use and this may also prevent pharmacists from identifying care aspects that can be optimised.[392]

Time constraints and shortage of workforce: Pharmacists take on a wide array of responsibilities, ranging from direct patient care activities, such as medication management, to logistical, procurement and administrative responsibilities, such as ensuring medicines access. Coupled with these increasing responsibilities, many countries are also facing shortages of pharmacy staff and hence there is increased workload, leading to time constraints in engaging in CVD management activities and adequately addressing patients' needs.[393] Workforce shortages and time constraints were more prominent in low-resource countries, significantly limiting pharmacists' ability to engage in CVD management services, which require assessment of comorbidities, medication management, lifestyle counselling, and the addressing of other health concerns.[394] As the optimal management of CVDs relies heavily on self-management and lifestyle modifications, pharmacists can engage in activities that can empower patients to better manage CVDs. These activities and initiatives may be in the form of educational materials distributed to patients living with CVDs. Such initiatives will not take up too much contact time and hence should not add an additional work burden on pharmacists, while still allowing patients to benefit through optimal health education.

Remuneration: Pharmacist-led clinical services are not reimbursed or are poorly reimbursed in many countries, and this has limited the implementation of such services for the management of CVDs.[395] Delivery of person-centred services for managing CVD services requires additional time and effort from pharmacists. Person-centred services revolve around the patient as the key stakeholder in the shared decision-making process, and this implies that the pharmacist needs time to understand the patient's needs, values and beliefs, subsequently assessing their medicines use and medical histories before drawing up a management plan. Lack of remuneration is reported as a common barrier to the implementation of such multifaceted services.[396] Advocacy by pharmacist organisations for increased renumeration can enhance pharmacists' ability to provide cardiovascular-related services such as health education, medication management, and lifestyle counselling.

Inadequate consultation spaces: Lack of private counselling and consultation spaces in pharmacies is an established barrier to the provision of CVD services.[397] Providing a safe and convenient space that safeguards privacy and confidentiality will allow patients to share information about their health status and medicines more freely.[387] Pharmacists can erect structures to separate the pharmacy floor and an area for consultation, and this will at least provide some form of privacy for the patients. Alternatively, telepharmacy can be a novel approach to overcome this limitation in having a private space for consultation. As the management of CVDs

requires optimal self-management, follow-up by telephone allows pharmacists to monitor, educate and empower patients in self-management. Telepharmacy is convenient for patients and allows continual monitoring of patients to ensure efficacy and safety of treatment.

11.1.2 Patients' perceptions of pharmacists' roles

Management of CVDs has transformed towards a person-centric approach, which involves shared decision-making between patients and the healthcare team. This healthcare team is often collaborative, and studies have found that pharmacists, through providing medication-related expertise, can play an essential and value-added role in collaborative care teams.[398] Furthermore, positive outcomes of such collaborative care models have been established globally, and collaborative care models have also been found to be cost-effective.[398] However, implementing collaborative care models in real-world applications remains complex. One key factor to enable successful implementation of a person-centric care model that involves pharmacists is patients' perceptions of pharmacists' roles. The pharmacy profession has transformed from a product-centric profession to one that is service-centric, with pharmacists' roles expanding to the provision of direct patient care and supporting the management of CVDs through their expertise in medication. However, patients' perceptions of pharmacists' roles can be a barrier to the uptake of such services. For example, people in the UK viewed community pharmacists as a supplier of medicines and the trust level towards community pharmacists as a service provider remained low.[399] Therefore, there is a need to increase the awareness of the public towards the contemporary roles of pharmacists, specifically with regard to direct patient care and the support of CVD management.

11.2 Facilitators

11.2.1 Accessibility of pharmacists

Pharmacists are one of the most accessible healthcare providers and are often the first port-of-call for people living with CVDs. This accessibility provides convenience for people living with CVDs to seek health knowledge and skills promptly. Furthermore, being at the heart of communities where people with CVDs live allows pharmacists to perform screening, monitoring and follow-up for any self-management promptly. For example, self-monitoring of blood pressure and regulation of lifestyle are critical to ensuring optimal hypertension control; pharmacists can play a role in addressing lifestyle factors and medication-related factors that can affect blood pressure control. Community pharmacists are accessible and reliable for provision of pharmaceutical services, including health education, promoting appropriate medicines use and improving treatment adherence.[400]

11.2.2 Communication among interprofessional healthcare teams

While pharmacists are well-positioned to provide CVD services, they should collaborate and work collectively with the patient's primary healthcare team, including physician and nurses. To facilitate a person-centric care approach, coordination and continual communication among the healthcare providers remain essential to optimising clinical outcomes and health.[401] Communication can be in different forms, either through direct physical discussion or through documentation. Clear and detailed documentation in electronic medical records can enhance communication between the primary healthcare team and community pharmacists who can ensure continuity of care.[402] Communication among healthcare providers can allow for a more person-centric approach to coordination of care and enhance overall health outcomes.

11.2.3 Policies and legislation

Policies and legislation need to recognise the contemporary roles that pharmacists play in delivering CVD services. Appropriate policies and legislation can facilitate the integration of pharmacists' services into the CVD practice realm. In addition, policies and legislation should ensure that pharmacists are appropriately remunerated for the services that they provide. Furthermore, associations representing the pharmacy profession should work closely with government authorities and healthcare administrators to develop policies, guidelines and resources to encourage and guide pharmacists in providing CVD services.

12 Conclusions

With two cardiovascular diseases (namely ischaemic heart disease and stroke) leading the top causes of death globally, it is crucial that pharmacists increase their people-centred pharmaceutical services to people living with CVDs. Due to their accessibility, knowledge and skills, pharmacists are ideally positioned and qualified to provide holistic care to people with CVDs.

This handbook has described the various services through which pharmacists can play a role in improving the cardiovascular health of their communities. This includes their role as agents for patient health behaviour change, especially in relation to the adoption of a healthy lifestyle (e.g., through smoking cessation and weight management programmes) and other preventive services (e.g., recommending or implementing appropriate vaccinations), asking patients to take health status questionnaires, screening for CVDs, referring patients to additional care, working as part of interprofessional teams, optimising the use of medicines and improving adherence to treatments.

Pharmacists should consider how to integrate CVD services into their daily practice and how these services may benefit their patients, the community and the health system as a whole. Despite the acknowledged barriers that exist to implementing some of these services, there are many opportunities for pharmacists to increase their role as public health professionals and primary healthcare providers by taking steps towards preventing, identifying and managing the treatment of people living with CVDs. Both pharmacies and pharmacists are well-positioned to develop and implement structured and evidence-based CVD prevention strategies and patient-centred services that improve patient health outcomes in CVDs.

13 References

1. World Health Organization. Cardiovascular diseases (CVDs) [Internet]. 2021. updated [accessed: 21 March 2022]. Available at: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).
2. World Heart Federation. World Heart Observatory: Trends in Cardiovascular Disease [Internet]. updated [accessed: 8 August 2022]. Available at: https://worldheartobservatory.org/trends/.
3. World Health Organization, International Bank for Reconstruction and Development / The World Bank 2021. Tracking universal health coverage: 2021 Global Monitoring Report. [Internet]. 2021. [accessed: 8 August 2022]. Available at: https://cdn.who.int/media/docs/default-source/world-health-data-platform/events/tracking-universal-health-coverage-2021-global-monitoring-report_uhc-day.pdf?sfvrsn=fd5c65c6_5&download=true.
4. Perel P, Avezum A, Huffman M et al. Reducing Premature Cardiovascular Morbidity and Mortality in People With Atherosclerotic Vascular Disease: The World Heart Federation Roadmap for Secondary Prevention of Cardiovascular Disease. Glob Heart. 2015;10(2):99-110. [accessed: 19 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26213297.
5. van Driel ML, Morledge MD, Ulep R et al. Interventions to improve adherence to lipid-lowering medication. Cochrane Database Syst Rev. 2016;12:CD004371. [accessed: 8 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28000212.
6. Qureshi N, Da Silva MLR, Abdul-Hamid H et al. Strategies for screening for familial hypercholesterolaemia in primary care and other community settings. Cochrane Database Syst Rev. 2021;10:CD012985. [accessed: 8 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34617591.
7. World Heart Federation. World Heart Vision 2030: driving policy change. Forthcoming 2022.
8. World Health Organization. Cardiovascular diseases [Internet]. 2021. updated [accessed: 22 March 2022]. Available at: https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_1.
9. Roth GA, Mensah GA, Johnson CO et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990-2019: Update From the GBD 2019 Study. J Am Coll Cardiol. 2020;76(25):2982-3021. [accessed: 9 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33309175.
10. World Health Organization. Global Health Estimates: Life expectancy and leading causes of death and disability [Internet]. 2019. updated [accessed: 22 March 2022]. Available at: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates.
11. World Health Organization. The top 10 causes of death Geneva, Switzerland: World Health Organisation; 2020. updated [accessed: Available at: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death.
12. European Heart Network. European Cardiovascular Disease Statistics 2017: European Heart Network; 2017. updated [accessed: 26 June 2022]. Available at: https://ehnheart.org/cvd-statistics.html.
13. Mahmood SS, Levy D, Vasan RS et al. The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective. Lancet. 2014;383(9921):999-1008. [accessed: 23 March 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24084292.
14. Visseren FLJ, Mach F, Smulders YM et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2021;42(34):3227-337. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34458905.
15. Brown JC, Gerhardt TE, Kwon E. Risk Factors For Coronary Artery Disease. StatPearls. Treasure Island (FL)2022.
16. Francula-Zaninovic S, Nola IA. Management of Measurable Variable Cardiovascular Disease' Risk Factors. Curr Cardiol Rev. 2018;14(3):153-63. [accessed: 21 March 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29473518.
17. Li H, Sun K, Zhao R et al. Inflammatory biomarkers of coronary heart disease. Front Biosci (Schol Ed). 2018;10(1):185-96. [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28930526.
18. Caplan LR, Searls DE, Hon FK. Cerebrovascular disease. Med Clin North Am. 2009;93(2):353-69, viii. [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19272513.
19. Abdel Moneim A, Radwan MA, Yousef AI. COVID-19 and cardiovascular disease: manifestations, pathophysiology, vaccination, and long-term implication. Curr Med Res Opin. 2022;38(7):1071-9. [accessed: 4 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35575011.
20. Kleindorfer DO, Towfighi A, Chaturvedi S et al. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2021;52(7). [accessed: 5 May 2022]. Available at: https://www.ahajournals.org/doi/10.1161/STR.0000000000000375.
21. Aboyans V, Ricco J-B, Bartelink M-LEL et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS). European Heart Journal. 2018;39(9):763-816. [accessed: 11 May 2022]. Available at: https://academic.oup.com/eurheartj/article-pdf/39/9/763/25015217/ehx095.pdf.
22. Tran B. Assessment and management of peripheral arterial disease: what every cardiologist should know. Heart. 2021;107(22):1835-43. [accessed: 13 May 2022]. Available at: https://heart.bmj.com/content/107/22/1835.

23. Gerhard-Herman MD, Gornik HL, Barrett C et al. 2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2017;135(12):CIR.000000000000. [accessed: 11 May 2022]. Available at: https://www.ahajournals.org/doi/10.1161/CIR.0000000000000470.
24. Battinelli EM, Murphy DL, Connors JM. Venous thromboembolism overview. Hematol Oncol Clin North Am. 2012;26(2):345-67, ix. [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22463831.
25. World Health Organization. Noncommunicable diseases country profiles 2018 [Internet]. Geneva, Switzerland: World Health Organization; 2018. updated [accessed: Available at: https://apps.who.int/iris/handle/10665/274512.
26. World Health Organization. Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013-2020 [Internet]. Geneva, Switzerland: 2013. updated [accessed: Available at: https://apps.who.int/iris/handle/10665/94384.
27. United Nations. Transforming our world: the 2030 Agenda for Sustainable Development. 2015. [accessed: 1 August 2022]. Available at: https://sdgs.un.org/es/goals.
28. Hessel F. Burden of Disease. In: W K, editor. Encyclopedia of Public Health. Dordrecht: Springer; 2008. p. 94-6.
29. Mohebi R, Chen C, Ibrahim NE et al. Cardiovascular Disease Projections in the United States Based on the 2020 Census Estimates. J Am Coll Cardiol. 2022;80(6):565-78. [accessed: 29 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35926929.
30. Tsao CW, Aday AW, Almarzooq ZI et al. Heart Disease and Stroke Statistics-2022 Update: A Report From the American Heart Association. Circulation. 2022;145(8):e153-e639. [accessed: 22 March 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35078371.
31. Gheorghe A, Griffiths U, Murphy A et al. The economic burden of cardiovascular disease and hypertension in low- and middle-income countries: a systematic review. BMC Public Health. 2018;18(1):975. [accessed: 27 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30081871.
32. Schutte AE, Srinivasapura Venkateshmurthy N, Mohan S et al. Hypertension in Low- and Middle-Income Countries. Circ Res. 2021;128(7):808-26. [accessed: 27 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33793340.
33. Roth GA, Mensah GA, Fuster V. The Global Burden of Cardiovascular Diseases and Risks: A Compass for Global Action. J Am Coll Cardiol. 2020;76(25):2980-1. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33309174.
34. Duff S, Mafilios MS, Bhounsule P et al. The burden of critical limb ischemia: a review of recent literature. Vasc Health Risk Manag. 2019;15:187-208. [accessed: 1 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31308682.
35. Dzaye O, Razavi AC, Blaha MJ et al. Evaluation of coronary stenosis versus plaque burden for atherosclerotic cardiovascular disease risk assessment and management. Curr Opin Cardiol. 2021;36(6):769-75. [accessed: 1 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34620792.
36. Robinson JG, Williams KJ, Gidding S et al. Eradicating the Burden of Atherosclerotic Cardiovascular Disease by Lowering Apolipoprotein B Lipoproteins Earlier in Life. J Am Heart Assoc. 2018;7(20):e009778. [accessed: 1 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30371276.
37. Candelino M, Tagi VM, Chiarelli F. Cardiovascular risk in children: a burden for future generations. Ital J Pediatr. 2022;48(1):57. [accessed: 1 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35410281.
38. Noubiap JJ, Nansseu JR, Lontchi-Yimagou E et al. Global, regional, and country estimates of metabolic syndrome burden in children and adolescents in 2020: a systematic review and modelling analysis. Lancet Child Adolesc Health. 2022;6(3):158-70. [accessed: 1 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35051409.
39. GBD 2017 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1923-94. [accessed: 1 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30496105.
40. GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1223-49. [accessed: 1 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33069327.
41. Mannucci PM, Harari S, Franchini M. Novel evidence for a greater burden of ambient air pollution on cardiovascular disease. Haematologica. 2019;104(12):2349-57. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31672903.
42. de Bont J, Jaganathan S, Dahlquist M et al. Ambient air pollution and cardiovascular diseases: An umbrella review of systematic reviews and meta-analyses. J Intern Med. 2022;291(6):779-800. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35138681.
43. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020;16(4):223-37. [accessed: 1 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32024986.
44. Zhou B, Perel P, Mensah GA et al. Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. Nat Rev Cardiol. 2021;18(11):785-802. [accessed: 1 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34050340.

45. Brant LCC, Passaglia LG, Pinto-Filho MM et al. The Burden of Resistant Hypertension Across the World. Curr Hypertens Rep. 2022;24(3):55-66. [accessed: 2 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35118612.

46. Einarson TR, Acs A, Ludwig C et al. Economic Burden of Cardiovascular Disease in Type 2 Diabetes: A Systematic Review. Value Health. 2018;21(7):881-90. [accessed: 2 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30005761.

47. Ritsinger V, Jensen J, Ohm D et al. Elevated admission glucose is common and associated with high short-term complication burden after acute myocardial infarction: Insights from the VALIDATE-SWEDEHEART study. Diab Vasc Dis Res. 2019;16(6):582-4. [accessed: 2 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31476896.

48. Teufel F, Seiglie JA, Geldsetzer P et al. Body-mass index and diabetes risk in 57 low-income and middle-income countries: a cross-sectional study of nationally representative, individual-level data in 685 616 adults. Lancet. 2021;398(10296):238-48. [accessed: 2 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34274065.

49. Zambon A, Mello ESA, Farnier M. The burden of cholesterol accumulation through the lifespan: why pharmacological intervention should start earlier to go further? Eur Heart J Cardiovasc Pharmacother. 2021;7(5):435-41. [accessed: 2 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33119073.

50. Packard CJ, Young R, Ross K et al. Modelling total coronary heart disease burden and long-term benefit of cholesterol lowering in middle aged men with and without a history of cardiovascular disease. Eur Heart J Qual Care Clin Outcomes. 2017;3(4):281-8. [accessed: 2 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29044395.

51. Sinha DN, Suliankatchi RA, Gupta PC et al. Global burden of all-cause and cause-specific mortality due to smokeless tobacco use: systematic review and meta-analysis. Tob Control. 2018;27(1):35-42. [accessed: 2 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27903956.

52. Wang JL, Yin WJ, Zhou LY et al. Association Between Initiation, Intensity, and Cessation of Smoking and Mortality Risk in Patients With Cardiovascular Disease: A Cohort Study. Front Cardiovasc Med. 2021;8:728217. [accessed: 2 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34977166.

53. Duncan MS, Freiberg MS, Greevy RA, Jr. et al. Association of Smoking Cessation With Subsequent Risk of Cardiovascular Disease. JAMA. 2019;322(7):642-50. [accessed: 2 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31429895.

54. Yang JJ, Yu D, Shu XO et al. Reduction in total and major cause-specific mortality from tobacco smoking cessation: a pooled analysis of 16 population-based cohort studies in Asia. Int J Epidemiol. 2022;50(6):2070-81. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34999862.

55. Mendoza-Herrera K, Pedroza-Tobias A, Hernandez-Alcaraz C et al. Attributable Burden and Expenditure of Cardiovascular Diseases and Associated Risk Factors in Mexico and other Selected Mega-Countries. Int J Environ Res Public Health. 2019;16(20). [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31652519.

56. Bhagavathula AS, Shehab A, Ullah A et al. The Burden of Cardiovascular Disease Risk Factors in the Middle East: A Systematic Review and Meta-Analysis Focusing on Primary Prevention. Curr Vasc Pharmacol. 2021;19(4):379-89. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32525775.

57. Franco-Trigo L, Tudball J, Fam D et al. A stakeholder visioning exercise to enhance chronic care and the integration of community pharmacy services. Res Social Adm Pharm. 2019;15(1):31-44. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29496521.

58. Wolters M, van Paassen JG, Minjon L et al. Design of a Pharmacy Curriculum on Patient Centered Communication Skills. Pharmacy (Basel). 2021;9(1). [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33467691.

59. Amariles P, Sabater-Hernandez D, Garcia-Jimenez E et al. Effectiveness of Dader Method for pharmaceutical care on control of blood pressure and total cholesterol in outpatients with cardiovascular disease or cardiovascular risk: EMDADER-CV randomized controlled trial. J Manag Care Pharm. 2012;18(4):311-23. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22548691.

60. Allemann SS, van Mil JW, Botermann L et al. Pharmaceutical care: the PCNE definition 2013. International journal of clinical pharmacy. 2014;36(3):544-55. [accessed: 3 August 2022]. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24748506.

61. Griese-Mammen N, Hersberger KE, Messerli M et al. PCNE definition of medication review: reaching agreement. International journal of clinical pharmacy. 2018;40(5):1199-208. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30073611.

62. Moullin JC, Sabater-Hernandez D, Fernandez-Llimos F et al. Defining professional pharmacy services in community pharmacy. Res Social Adm Pharm. 2013;9(6):989-95. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23591411.

63. Committee of Consensus. Third consensus of Granada on drug-related problems (DRP) and negative outcomes associated with medication (NOM). Ars Pharm. 2007;48(1):5-17. [accessed: 6 August 2022]. Available at: https://revistaseug.ugr.es/index.php/ars/article/view/4974/4781.

64. Khettar S, Jacquin Courtois S, Luaute J et al. Multiprofessional intervention to improve adherence to medication in stroke patients: a study protocol for a randomised controlled trial (ADMED AVC study). Eur J Hosp Pharm. 2022;29(3):169-75. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32978218.

65. Ostbring MJ, Eriksson T, Petersson G et al. Effects of a pharmaceutical care intervention on clinical outcomes and patient adherence in coronary heart disease: the MIMeRiC randomized controlled trial. BMC Cardiovasc Disord. 2021;21(1):367. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34334142.

66. Hwang AY, Gums TH, Gums JG. The benefits of physician-pharmacist collaboration. J Fam Pract. 2017;66(12):E1-E8. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29202145.

67. Santschi V, Chiolero A, Colosimo AL et al. Improving blood pressure control through pharmacist interventions: a meta-analysis of randomized controlled trials. J Am Heart Assoc. 2014;3(2):e000718. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24721801.

68. Cheema E, Sutcliffe P, Singer DR. The impact of interventions by pharmacists in community pharmacies on control of hypertension: a systematic review and meta-analysis of randomized controlled trials. Br J Clin Pharmacol. 2014;78(6):1238-47. [accessed: 16 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24966032.

69. Hwang AY, Smith SM. Partnering With Pharmacists to Reduce Cardiovascular Risk in Outpatient Settings. J Am Heart Assoc. 2019;8(22):e014705. [accessed: 16 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31711389.

70. Martinez-Mardones F, Fernandez-Llimos F, Benrimoj SI et al. Systematic Review and Meta-Analysis of Medication Reviews Conducted by Pharmacists on Cardiovascular Diseases Risk Factors in Ambulatory Care. J Am Heart Assoc. 2019;8(22):e013627. [accessed: 2 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31711390.

71. Santschi V, Chiolero A, Burnand B et al. Impact of pharmacist care in the management of cardiovascular disease risk factors: a systematic review and meta-analysis of randomized trials. Arch Intern Med. 2011;171(16):1441-53. [accessed: 18 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21911628.

72. Alshehri AA, Jalal Z, Cheema E et al. Impact of the pharmacist-led intervention on the control of medical cardiovascular risk factors for the primary prevention of cardiovascular disease in general practice: A systematic review and meta-analysis of randomised controlled trials. Br J Clin Pharmacol. 2020;86(1):29-38. [accessed: 19 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31777082.

73. Rattanavipanon W, Chaiyasothi T, Puchsaka P et al. Effects of pharmacist interventions on cardiovascular risk factors and outcomes: An umbrella review of meta-analysis of randomized controlled trials. Br J Clin Pharmacol. 2022;88(7):3064-77. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35174525.

74. Whelton PK, Carey RM, Aronow WS et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2018;71(19):2199-269. [accessed: 4 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29146533.

75. Williams B, Mancia G, Spiering W et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). European Heart Journal. 2018;39(33):3021-104. [accessed: 21 March 2022]. Available at: https://doi.org/10.1093/eurheartj/ehy339.

76. Anker D, Tsuyuki RT, Paradis G et al. Pharmacists to improve hypertension management: Guideline concordance from North America to Europe. Can Pharm J (Ott). 2019;152(3):180-5. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31156731.

77. Anderegg MD, Gums TH, Uribe L et al. Pharmacist Intervention for Blood Pressure Control in Patients with Diabetes and/or Chronic Kidney Disease. Pharmacotherapy. 2018;38(3):309-18. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29331037.

78. World Health Organization. HEARTS technical package for cardiovascular disease management in primary health care: risk based CVD management Geneva, Switzerland: World Health Organisation; 2020. updated [accessed: 6 August 2022]. Available at: https://apps.who.int/iris/bitstream/handle/10665/333221/9789240001367-eng.pdf.

79. Amariles P, Gonzalez M, Sabater D. Actuación farmacéutica en Prevención Cardiovascular.: [Internet]. 2006. [accessed: 6 August 2022]. Available at: https://www.researchgate.net/publication/215898825_Actuacion_Farmaceutica_en_Prevencion_Cardiovascular.

80. American College of Cardiology. ASCVD Risk Estimator Plus: 2022. updated [accessed: Available at: https://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/.

81. Steltenpohl EA, Barry BK, Coley KC et al. Point-of-Care Testing in Community Pharmacies: Keys to Success From Pennsylvania Pharmacists. J Pharm Pract. 2018;31(6):629-35. [accessed: 16 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29034781.

82. Melton BL, Lai Z. Review of community pharmacy services: what is being performed, and where are the opportunities for improvement? Integr Pharm Res Pract. 2017;6:79-89. [accessed: 16 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29354554.

83. Steed L, Sohanpal R, Todd A et al. Community pharmacy interventions for health promotion: effects on professional practice and health outcomes. Cochrane Database Syst Rev. 2019;12:CD011207. [accessed: 16 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31808563.

84. Thurman W, Moczygemba LR, Barner JC et al. Priority community engagement strategies for cardiovascular health: A checklist for community pharmacists. J Am Pharm Assoc (2003). 2020;60(6):e133-e9. [accessed: 16 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32402677.

85. Gupta R, Yusuf S. Challenges in management and prevention of ischemic heart disease in low socioeconomic status people in LLMICs. BMC Med. 2019;17(1):209. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31767015.

86. Zolezzi M, Abdallah O, Sankaralingam S. Development and Evaluation of an Educational Program for Community Pharmacists on Cardiovascular Risk Assessment. Risk Manag Healthc Policy. 2020;13:623-32. [accessed: 18 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32607030.

87. Al Hamarneh YN, Johnston K, Marra CA et al. Pharmacist prescribing and care improves cardiovascular risk, but is it cost-effective? A cost-effectiveness analysis of the RxEACH study. Can Pharm J (Ott). 2019;152(4):257-66. [accessed: 16 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31320960.

88. World Health Organization. WHO Package of Essential Noncommunicable (PEN) Disease Interventions for Primary Health Care. [Internet]. Geneva, Switzerland: World Health Organisation; 2020. updated [accessed: 6 August 2022]. Available at: https://www.who.int/publications/i/item/who-package-of-essential-noncommunicable-(pen)-disease-interventions-for-primary-health-care.

89. Lopez-Melgar B, Fernandez-Friera L, Oliva B et al. Short-Term Progression of Multiterritorial Subclinical Atherosclerosis. J Am Coll Cardiol. 2020;75(14):1617-27. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32273027.

90. Lloyd-Jones DM, Hong Y, Labarthe D et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. Circulation. 2010;121(4):586-613. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20089546.

91. Ibanez B, Fernandez-Ortiz A, Fernandez-Friera L et al. Progression of Early Subclinical Atherosclerosis (PESA) Study: JACC Focus Seminar 7/8. J Am Coll Cardiol. 2021;78(2):156-79. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34238438.

92. Gupta R, Wood DA. Primary prevention of ischaemic heart disease: populations, individuals, and health professionals. Lancet. 2019;394(10199):685-96. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31448740.

93. U. S. Preventive Services Task Force, Mangione CM, Barry MJ et al. Behavioral Counseling Interventions to Promote a Healthy Diet and Physical Activity for Cardiovascular Disease Prevention in Adults Without Cardiovascular Disease Risk Factors: US Preventive Services Task Force Recommendation Statement. JAMA. 2022;328(4):367-74. [accessed: 30 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35881115.

94. Piepoli MF, Villani GQ. Lifestyle modification in secondary prevention. Eur J Prev Cardiol. 2017;24(3_suppl):101-7. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28618907.

95. Heath L, Jebb SA, Aveyard P et al. Obesity, metabolic risk and adherence to healthy lifestyle behaviours: prospective cohort study in the UK Biobank. BMC Med. 2022;20(1):65. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35164754.

96. Claas SA, Arnett DK. The Role of Healthy Lifestyle in the Primordial Prevention of Cardiovascular Disease. Curr Cardiol Rep. 2016;18(6):56. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27142061.

97. Boushey C, Ard J, Bazzano L et al. Dietary Patterns and All-Cause Mortality: A Systematic Review. USDA Nutrition Evidence Systematic Reviews. Alexandria (VA)2020.

98. Goyal P, Balkan L, Ringel JB et al. The Dietary Approaches to Stop Hypertension (DASH) Diet Pattern and Incident Heart Failure. J Card Fail. 2021;27(5):512-21. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33962741.

99. Yip CSC, Chan W, Fielding R. The Associations of Fruit and Vegetable Intakes with Burden of Diseases: A Systematic Review of Meta-Analyses. J Acad Nutr Diet. 2019;119(3):464-81. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30639206.

100. Caprara G. Mediterranean-Type Dietary Pattern and Physical Activity: The Winning Combination to Counteract the Rising Burden of Non-Communicable Diseases (NCDs). Nutrients. 2021;13(2). [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33525638.

101. Milesi G, Rangan A, Grafenauer S. Whole Grain Consumption and Inflammatory Markers: A Systematic Literature Review of Randomized Control Trials. Nutrients. 2022;14(2). [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35057555.

102. D'Esposito V, Di Tolla MF, Lecce M et al. Lifestyle and Dietary Habits Affect Plasma Levels of Specific Cytokines in Healthy Subjects. Front Nutr. 2022;9:913176. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35811952.

103. Semlitsch T, Krenn C, Jeitler K et al. Long-term effects of weight-reducing diets in people with hypertension. Cochrane Database Syst Rev. 2021;2:CD008274. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33555049.

104. Tajeu GS, Johnson E, Buccilla M et al. Changes in Antihypertensive Medication Following Bariatric Surgery. Obes Surg. 2022;32(4):1312-24. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35083703.

105. Iaccarino G, Franco D, Sorriento D et al. Modulation of Insulin Sensitivity by Exercise Training: Implications for Cardiovascular Prevention. J Cardiovasc Transl Res. 2021;14(2):256-70. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32737757.

106. Aune D, Schlesinger S, Leitzmann MF et al. Physical activity and the risk of heart failure: a systematic review and dose-response meta-analysis of prospective studies. Eur J Epidemiol. 2021;36(4):367-81. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33331992.

107. Liu JX, Zhu L, Li PJ et al. Effectiveness of high-intensity interval training on glycemic control and cardiorespiratory fitness in patients with type 2 diabetes: a systematic review and meta-analysis. Aging Clin Exp Res. 2019;31(5):575-93. [accessed: 21 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30097811.

108. Boule NG, Haddad E, Kenny GP et al. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. JAMA. 2001;286(10):1218-27. [accessed: 21 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11559268.

109. Kodama S, Tanaka S, Saito K et al. Effect of aerobic exercise training on serum levels of high-density lipoprotein cholesterol: a meta-analysis. Arch Intern Med. 2007;167(10):999-1008. [accessed: 21 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17533202.

110. Lemes IR, Turi-Lynch BC, Cavero-Redondo I et al. Aerobic training reduces blood pressure and waist circumference and increases HDL-c in metabolic syndrome: a systematic review and meta-analysis of randomized controlled trials. J Am Soc Hypertens. 2018;12(8):580-8. [accessed: 21 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29945775.

111. Palazon-Bru A, Hernandez-Lozano D, Gil-Guillen VF. Which Physical Exercise Interventions Increase HDL-Cholesterol Levels? A Systematic Review of Meta-analyses of Randomized Controlled Trials. Sports Med. 2021;51(2):243-53. [accessed: 21 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33064295.

112. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc. 2013;2(1):e004473. [accessed: 21 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23525435.

113. Lorenzo E, Szeszulski J, Shin CN et al. Relationship between walking for active transportation and cardiometabolic health among adults: A systematic review. J Transp Health. 2020;19. [accessed: 21 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34676154.

114. Lobczowska K, Banik A, Forberger S et al. Social, economic, political, and geographical context that counts: meta-review of implementation determinants for policies promoting healthy diet and physical activity. BMC Public Health. 2022;22(1):1055. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35619065.

115. Feigin VL, Brainin M, Norrving B et al. What Is the Best Mix of Population-Wide and High-Risk Targeted Strategies of Primary Stroke and Cardiovascular Disease Prevention? J Am Heart Assoc. 2020;9(3):e014494. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31983323.

116. Riegel B, Moser DK, Buck HG et al. Self-Care for the Prevention and Management of Cardiovascular Disease and Stroke: A Scientific Statement for Healthcare Professionals From the American Heart Association. J Am Heart Assoc. 2017;6(9). [accessed: 19 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28860232.

117. Thout SR, Santos JA, McKenzie B et al. The Science of Salt: Updating the evidence on global estimates of salt intake. J Clin Hypertens (Greenwich). 2019;21(6):710-21. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31033166.

118. Li S, Hou L, Zhu S et al. Lipid Variability and Risk of Cardiovascular Diseases and All-Cause Mortality: A Systematic Review and Meta-Analysis of Cohort Studies. Nutrients. 2022;14(12). [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35745179.

119. Lee SH, Kim MK, Rhee EJ. Effects of Cardiovascular Risk Factor Variability on Health Outcomes. Endocrinol Metab (Seoul). 2020;35(2):217-26. [accessed: 25 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32615706.

120. Kuang R, Liao Y, Xie X et al. Dynamic physical examination indicators of cardiovascular health: A single-center study in Shanghai, China. PLoS One. 2022;17(5):e0268358. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35550637.

121. Wei X, Zhang Z, Chong MKC et al. Evaluation of a package of risk-based pharmaceutical and lifestyle interventions in patients with hypertension and/or diabetes in rural China: A pragmatic cluster randomised controlled trial. PLoS Med. 2021;18(7):e1003694. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34197452.

122. Mantzari E, Reynolds JP, Jebb SA et al. Public support for policies to improve population and planetary health: A population-based online experiment assessing impact of communicating evidence of multiple versus single benefits. Soc Sci Med. 2022;296:114726. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35093794.

123. Barrett S, Begg S, O'Halloran P et al. The effect of behaviour change interventions on changes in physical activity and anthropometrics in ambulatory hospital settings: a systematic review and meta-analysis. Int J Behav Nutr Phys Act. 2021;18(1):7. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33413512.

124. Amini R, Rajabi M, Azami H et al. The effect of self-management intervention program on the lifestyle of postmyocardial infarction patients. J Educ Health Promot. 2021;10:145. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34222520.

125. Karunathilake SP, Ganegoda GU. Secondary Prevention of Cardiovascular Diseases and Application of Technology for Early Diagnosis. Biomed Res Int. 2018;2018:5767864. [accessed: 19 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29854766.

126. Jahangard-Rafsanjani Z, Hakimzadeh N, Sarayani A et al. A community pharmacy-based cardiovascular risk screening service implemented in Iran. Pharm Pract (Granada). 2017;15(2):919. [accessed: 19 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28690693.

127. World Health Organization. World Health Organization Model List of Essential Medicines, 21st List. Geneva: [Internet]. 2019. [accessed: 26 June 2022]. Available at: https://apps.who.int/iris/bitstream/handle/10665/325771/WHO-MVP-EMP-IAU-2019.06-eng.pdf.

128. World Health Organization. Prevention of cardiovascular disease : guidelines for assessment and management of total cardiovascular risk. Geneva, Switzerland: [Internet]. 2007. [accessed: 19 June 2022]. Available at: http://apps.who.int/iris/bitstream/handle/10665/43685/9789241547178_eng.pdf.

129. Kanai M, Toda T, Yamamoto K et al. A Mobile Health-Based Disease Management Program Improves Blood Pressure in People With Multiple Lifestyle-Related Diseases at Risk of Developing Vascular Disease- A Retrospective Observational Study. Circ Rep. 2022;4(7):322-9. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35860354.

130. Spring B, Pellegrini C, McFadden HG et al. Multicomponent mHealth Intervention for Large, Sustained Change in Multiple Diet and Activity Risk Behaviors: The Make Better Choices 2 Randomized Controlled Trial. J Med Internet Res. 2018;20(6):e10528. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29921561.

131. Bendtsen M. Heterogeneous treatment effects of a text messaging smoking cessation intervention among university students. PLoS One. 2020;15(3):e0229637. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32134977.

132. Asayut N, Olson PS, Kanjanasilp J et al. A community pharmacist-led smoking cessation intervention using a smartphone app (PharmQuit): A randomized controlled trial. PLoS One. 2022;17(3):e0265483. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35349576.

133. Buss VH, Leesong S, Barr M et al. Primary Prevention of Cardiovascular Disease and Type 2 Diabetes Mellitus Using Mobile Health Technology: Systematic Review of the Literature. J Med Internet Res. 2020;22(10):e21159. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33118936.

134. Hassen HY, Ndejjo R, Van Geertruyden JP et al. Type and effectiveness of community-based interventions in improving knowledge related to cardiovascular diseases and risk factors: A systematic review. Am J Prev Cardiol. 2022;10:100341. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35478931.

135. Sundararajan S, Thukani Sathanantham S, Palani S. The Effects of Clinical Pharmacist Education on Lifestyle Modifications of Postmyocardial Infarction Patients in South India: A Prospective Interventional Study. Curr Ther Res Clin Exp. 2020;92:100577. [accessed: 5 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32140190.

136. Fahs IM, Hallit S, Rahal MK et al. The Community Pharmacist's Role in Reducing Cardiovascular Risk Factors in Lebanon: A Longitudinal Study. Med Princ Pract. 2018;27(6):508-14. [accessed: 23 April 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29898452.

137. Omboni S, Caserini M. Effectiveness of pharmacist's intervention in the management of cardiovascular diseases. Open Heart. 2018;5(1):e000687. [accessed: 18 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29344376.

138. Amariles P. Consumo diario mínimo de 400 gramos de frutas y verduras - principio y meta de alimentación saludable y salud cardiovascular. Ars Pharmaceutica. 2022;63(1). [accessed: 6 August 2022]. Available at: https://scielo.isciii.es/pdf/ars/v63n1/2340-9894-ars-63-01-6.pdf.

139. Mayo Clinic. Strategies to prevent heart disease United States of America: Mayo Clinic; 2022. updated [accessed: 6 August 2022]. Available at: https://www.mayoclinic.org/diseases-conditions/heart-disease/in-depth/heart-disease-prevention/art-20046502.

140. Michos ED, Khan SS. Further understanding of ideal cardiovascular health score metrics and cardiovascular disease. Expert Rev Cardiovasc Ther. 2021;19(7):607-17. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34053373.

141. Fernandez-Alvira JM, Fuster V, Pocock S et al. Predicting Subclinical Atherosclerosis in Low-Risk Individuals: Ideal Cardiovascular Health Score and Fuster-BEWAT Score. J Am Coll Cardiol. 2017;70(20):2463-73. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29145946.

142. Fang N, Jiang M, Fan Y. Ideal cardiovascular health metrics and risk of cardiovascular disease or mortality: A meta-analysis. Int J Cardiol. 2016;214:279-83. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27085116.

143. Guo L, Zhang S. Association between ideal cardiovascular health metrics and risk of cardiovascular events or mortality: A meta-analysis of prospective studies. Clin Cardiol. 2017;40(12):1339-46. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29278429.

144. Kim S, Chang Y, Cho J et al. Life's Simple 7 Cardiovascular Health Metrics and Progression of Coronary Artery Calcium in a Low-Risk Population. Arterioscler Thromb Vasc Biol. 2019;39(4):826-33. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30700133.

145. Gomez-Pardo E, Fernandez-Alvira JM, Vilanova M et al. A Comprehensive Lifestyle Peer Group-Based Intervention on Cardiovascular Risk Factors: The Randomized Controlled Fifty-Fifty Program. J Am Coll Cardiol. 2016;67(5):476-85. [accessed: 18 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26562047.

146. Teo KK, Rafiq T. Cardiovascular Risk Factors and Prevention: A Perspective From Developing Countries. Can J Cardiol. 2021;37(5):733-43. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33610690.

147. Unger T, Borghi C, Charchar F et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension. 2020;75(6):1334-57. [accessed: 27 May 2022]. Available at: https://www.ahajournals.org/doi/10.1161/HYPERTENSIONAHA.120.15026.

148. Stergiou GS, Palatini P, Parati G et al. 2021 European Society of Hypertension practice guidelines for office and out-of-office blood pressure measurement. J Hypertens. 2021;39(7):1293-302. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33710173.

149. Lamirault G, Artifoni M, Daniel M et al. Resistant Hypertension: Novel Insights. Curr Hypertens Rev. 2020;16(1):61-72. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31622203.

150. Rossi GP, Bisogni V, Rossitto G et al. Practice Recommendations for Diagnosis and Treatment of the Most Common Forms of Secondary Hypertension. High Blood Press Cardiovasc Prev. 2020;27(6):547-60. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33159664.

151. Al-Makki A, DiPette D, Whelton PK et al. Hypertension Pharmacological Treatment in Adults: A World Health Organization Guideline Executive Summary. Hypertension. 2022;79(1):293-301. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34775787.

152. Tsakiridis I, Giouleka S, Arvanitaki A et al. Chronic hypertension in pregnancy: synthesis of influential guidelines. J Perinat Med. 2021;49(7):859-72. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33872475.

153. Brathwaite L, Reif M. Hypertensive Emergencies: A Review of Common Presentations and Treatment Options. Cardiol Clin. 2019;37(3):275-86. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31279421.

154. Hedayatnia M, Asadi Z, Zare-Feyzabadi R et al. Dyslipidemia and cardiovascular disease risk among the MASHAD study population. Lipids in Health and Disease. 2020;19(1). [accessed: 27 May 2022]. Available at.

155. Dixon DL, Khaddage S, Bhagat S et al. Effect of pharmacist interventions on reducing low-density lipoprotein cholesterol (LDL-C) levels: A systematic review and meta-analysis. J Clin Lipidol. 2020;14(3):282-92 e4. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32418821.

156. Authors/Task Force M, Guidelines ESCCfP, Societies ESCNC. 2019 ESC/EAS guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk. Atherosclerosis. 2019;290:140-205. [accessed: 21 March 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31591002.

157. Aronson D, Rayfield EJ. How hyperglycemia promotes atherosclerosis: molecular mechanisms. Cardiovascular Diabetology. 2002;1(1):1. [accessed: 18 May 2022]. Available at: https://pubmed.ncbi.nlm.nih.gov/12119059/.

158. Gleissner CA, Galkina E, Nadler JL et al. Mechanisms by which diabetes increases cardiovascular disease. Drug Discov Today Dis Mech. 2007;4(3):131-40. [accessed: 18 May 2022]. Available at: https://pubmed.ncbi.nlm.nih.gov/18695749/.

159. International Pharmaceutical Federation (FIP). Diabetes Prevention, Screening, and Management: A handbook for Pharmacists. [Internet]. 2021. [accessed: 15 May 2022]. Available at: https://www.fip.org/file/5071.

160. Kondo T, Nakano Y, Adachi S et al. Effects of Tobacco Smoking on Cardiovascular Disease. Circ J. 2019;83(10):1980-5. [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31462607.

161. Penín O, Rojo J, Penín A et al. [The influence of tobacco dependence on blood pressure control in people on antihypertensive drug treatment]. Farm Com. 2021;13(4):5-11. [accessed: 16 September 2022]. Available at: https://www.farmaceuticoscomunitarios.org/en/node/2997.

162. Csordas A, Bernhard D. The biology behind the atherothrombotic effects of cigarette smoke. Nat Rev Cardiol. 2013;10(4):219-30. [accessed: 4 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23380975.

163. Bialous S, Da Costa ESVL. Where next for the WHO Framework Convention on Tobacco Control? Tob Control. 2022;31(2):183-6. [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35241586.

164. Matthes BK, Robertson L, Gilmore AB. Needs of LMIC-based tobacco control advocates to counter tobacco industry policy interference: insights from semi-structured interviews. BMJ Open. 2020;10(11):e044710. [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33243822.

165. Kaur J, Rinkoo AV, Gouda HN et al. Implementation of MPOWER Package in the South-East Asia Region: Evidence from the WHO Report on the Global Tobacco Epidemic (2009-2021). Asian Pac J Cancer Prev. 2021;22(S2):71-80. [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34780141.

166. Lertsinudom S, Kaewketthong P, Chankaew T et al. Smoking Cessation Services by Community Pharmacists: Real-World Practice in Thailand. Int J Environ Res Public Health. 2021;18(22). [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34831660.

167. Thavorn K, Chaiyakunapruk N. A cost-effectiveness analysis of a community pharmacist-based smoking cessation programme in Thailand. Tob Control. 2008;17(3):177-82. [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18285385.

168. Carbone S, Canada JM, Billingsley HE et al. Obesity paradox in cardiovascular disease: where do we stand? Vascular Health and Risk Management. 2019;Volume 15:89-100. [accessed: 20 May 2022]. Available at: https://pubmed.ncbi.nlm.nih.gov/31118651/.

169. Cercato C, Fonseca FA. Cardiovascular risk and obesity. Diabetol Metab Syndr. 2019;11(1). [accessed: 20 May 2022]. Available at: https://dmsjournal.biomedcentral.com/articles/10.1186/s13098-019-0468-0.

170. Hijazi MA, Shatila H, El-Lakany A et al. Role of community pharmacists in weight management: results of a national study in Lebanon. BMC Health Serv Res. 2020;20(1). [accessed: 21 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7204056/.

171. Jordan M, Harmon J. Pharmacist interventions for obesity: improving treatment adherence and patient outcomes. Integr Pharm Res Pract. 2015:79. [accessed: 21 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7204056/.

172. Katzmarzyk PT, Friedenreich C, Shiroma EJ et al. Physical inactivity and non-communicable disease burden in low-income, middle-income and high-income countries. Br J Sports Med. 2022;56(2):101-6. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33782046.

173. Martins LCG, Lopes MVDO, Diniz CM et al. The factors related to a sedentary lifestyle: A meta-analysis review. J Adv Nurs. 2021;77(3):1188-205. [accessed: 21 May 2022]. Available at: https://pubmed.ncbi.nlm.nih.gov/33368524/.

174. Tam-Seto L, Weir P, Dogra S. Factors Influencing Sedentary Behaviour in Older Adults: An Ecological Approach. AIMS Public Health. 2016;3(3):555-72. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29546182.

175. Park JH, Moon JH, Kim HJ et al. Sedentary Lifestyle: Overview of Updated Evidence of Potential Health Risks. Korean J Fam Med. 2020;41(6):365-73. [accessed: 21 May 2022]. Available at: https://pubmed.ncbi.nlm.nih.gov/33242381/.

176. Strath SJ, Kaminsky LA, Ainsworth BE et al. Guide to the Assessment of Physical Activity: Clinical and Research Applications. Circulation. 2013;128(20):2259-79. [accessed: 22 May 2022]. Available at: https://www.ahajournals.org/doi/pdf/10.1161/01.cir.0000435708.67487.da.

177. Foster C, Shilton T, Westerman L et al. World Health Organisation to develop global action plan to promote physical activity: time for action. Br J Sports Med. 2018;52(8):484-5. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28724712.

178. Viegas R, Godinho CA, Romano S. Physical activity promotion in community pharmacies: pharmacists' attitudes and behaviours. Pharmacy Practice. 2021;19(3):2413. [accessed: 30 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8455122/.

179. Nam G-B. Exercise, Heart and Health. Korean Circ J. 2011;41(3):113. [accessed: 24 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3079129/.

180. NCD Alliance. Unhealthy diets and malnutrition: 2021. updated November 2021. [accessed: 27 June 2022]. Available at: https://ncdalliance.org/why-ncds/risk-factors-prevention/unhealthy-diets-and-malnutrition.

181. World Health Organization. HEARTS Technical package for cardiovascular disease management in primary health care: Healthy-lifestyle counselling: 2018. updated [accessed: Available at: https://apps.who.int/iris/bitstream/handle/10665/260422/WHO-NMH-NVI-18.1-eng.pdf?sequence=1.

182. Chareonrungrueangchai K, Wongkawinwoot K, Anothaisintawee T et al. Dietary Factors and Risks of Cardiovascular Diseases: An Umbrella Review. Nutrients. 2020;12(4):1088. [accessed: 24 May 2022]. Available at: https://pubmed.ncbi.nlm.nih.gov/32326404/.

183. Filippou CD, Tsioufis CP, Thomopoulos CG et al. Dietary Approaches to Stop Hypertension (DASH) Diet and Blood Pressure Reduction in Adults with and without Hypertension: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Adv Nutr. 2020;11(5):1150-60. [accessed: 24 May 2022]. Available at: https://pubmed.ncbi.nlm.nih.gov/32330233/.

184. International Pharmaceutical Federation (FIP). Nutrition and weight management services: A toolkit for pharmacists. [Internet]. 2021. [accessed: 19 May 2022]. Available at: https://www.fip.org/file/4986.

185. NCD Alliance. Trans Fat Free by 2023: Case Studies in Trans Fat Elimination: 2019. updated [accessed: Available at: https://ncdalliance.org/sites/default/files/resource_files/NCDA%20Trans%20Fats%20Acids_Case%20Studies_Web_single%20pages_FINAL.pdf.

186. World Health Organization. Global status report on alcohol and health 2018. [Internet]. 2018. [accessed: 27 June 2022]. Available at: https://ncdalliance.org/sites/default/files/resource_files/9789241565639-eng.pdf.

187. Maisch B. Alcoholic cardiomyopathy: The result of dosage and individual predisposition. Herz. 2016;41(6):484-93. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27582365.

188. Piano MR. Alcohol's Effects on the Cardiovascular System. Alcohol Res. 2017;38(2):219-41. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28988575.

189. Chiva-Blanch G, Badimon L. Benefits and Risks of Moderate Alcohol Consumption on Cardiovascular Disease: Current Findings and Controversies. Nutrients. 2019;12(1):108. [accessed: 24 May 2022]. Available at: https://www.mdpi.com/2072-6643/12/1/108/htm.

190. World Health Organization. Global strategy to reduce the harmful use of alcohol. Geneva, Switzerland: [Internet]. 2010. [accessed: 5 August 2022]. Available at: https://www.who.int/teams/mental-health-and-substance-use/alcohol-drugs-and-addictive-behaviours/alcohol/governance/global-alcohol-strategy.

191. Hattingh L, Tait R. Pharmacy-based alcohol-misuse services: current perspectives. Integr Pharm Res Pract. 2018;Volume 7:21-31. [accessed: 29 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5927143/.

192. Zhao SJ, Zhao HW, Du S et al. The Impact of Clinical Pharmacist Support on Patients Receiving Multi-drug Therapy for Coronary Heart Disease in China. Indian J Pharm Sci. 2015;77(3):306-11. [accessed: 5 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26180276.

193. Kamusheva M, Ignatova D, Golda A et al. The Potential Role of the Pharmacist in Supporting Patients with Depression – A Literature-Based Point of View. Integr Pharm Res Pract. 2020;Volume 9:49-63. [accessed: 25 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7049755/.

194. Wang Q, Wang X, Yang C et al. The role of sleep disorders in cardiovascular diseases: Culprit or accomplice? Life Sci. 2021;283:119851. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34324916.

195. Nikbakhtian S, Reed AB, Obika BD et al. Accelerometer-derived sleep onset timing and cardiovascular disease incidence: a UK Biobank cohort study. European Heart Journal - Digital Health. 2021;2(4):658-66. [accessed: 24 May 2022]. Available at: https://academic.oup.com/ehjdh/article/2/4/658/6423198.

196. Maness DL, Khan M. Nonpharmacologic Management of Chronic Insomnia. Am Fam Physician. 2015;92(12):1058-64. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26760592.

197. Abraham O, Schleiden LJ, Brothers AL et al. Managing sleep problems using non-prescription medications and the role of community pharmacists: older adults' perspectives. Int J Pharm Pract. 2017;25(6):438-46. [accessed: 27 May 2022]. Available at: https://pubmed.ncbi.nlm.nih.gov/28261882/.

198. Wazaify M, Elayeh E, Tubeileh R et al. Assessing insomnia management in community pharmacy setting in Jordan: A simulated patient approach. PLOS ONE. 2019;14(12):e0226076. [accessed: 27 May 2022]. Available at: https://pubmed.ncbi.nlm.nih.gov/31834888/.

199. Lum ZK, Nguyen AD, Szeto J et al. Spinning the globe from west to east: A mixed-method study to examine the impact of pharmacists on immunization advocacy and delivery in Asia Pacific. J Am Pharm Assoc (2003). 2021;61(5):605-13. [accessed: 28 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34023278.

200. Doherty MT, Aris E, Servotte N et al. Capturing the value of vaccination: impact of vaccine-preventable disease on hospitalization. Aging Clin Exp Res. 2022;34(7):1551-61. [accessed: 29 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35633477.

201. Restrepo MI, Reyes LF. Pneumonia as a cardiovascular disease. Respirology. 2018;23(3):250-9. [accessed: 29 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29325222.

202. Tralhao A, Povoa P. Cardiovascular Events After Community-Acquired Pneumonia: A Global Perspective with Systematic Review and Meta-Analysis of Observational Studies. J Clin Med. 2020;9(2). [accessed: 29 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32028660.

203. Blackburn R, Zhao H, Pebody R et al. Laboratory-Confirmed Respiratory Infections as Predictors of Hospital Admission for Myocardial Infarction and Stroke: Time-Series Analysis of English Data for 2004-2015. Clin Infect Dis. 2018;67(1):8-17. [accessed: 29 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29324996.

204. Ang LW, Yap J, Lee V et al. Influenza-Associated Hospitalizations for Cardiovascular Diseases in the Tropics. Am J Epidemiol. 2017;186(2):202-9. [accessed: 28 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28338806.

205. Warren-Gash C, Bhaskaran K, Hayward A et al. Circulating influenza virus, climatic factors, and acute myocardial infarction: a time series study in England and Wales and Hong Kong. J Infect Dis. 2011;203(12):1710-8. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21606529.

206. Kwong JC, Schwartz KL, Campitelli MA. Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection. N Engl J Med. 2018;378(26):2540-1. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29949484.

207. Warren-Gash C, Blackburn R, Whitaker H et al. Laboratory-confirmed respiratory infections as triggers for acute myocardial infarction and stroke: a self-controlled case series analysis of national linked datasets from Scotland. Eur Respir J. 2018;51(3). [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29563170.

208. Cheng Y, Cao X, Cao Z et al. Effects of influenza vaccination on the risk of cardiovascular and respiratory diseases and all-cause mortality. Ageing Res Rev. 2020;62:101124. [accessed: 29 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32683040.

209. Vardeny O, Claggett B, Udell JA et al. Influenza Vaccination in Patients With Chronic Heart Failure: The PARADIGM-HF Trial. JACC Heart Fail. 2016;4(2):152-8. [accessed: 29 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26746371.

210. Teresa Aguado M, Barratt J, Beard JR et al. Report on WHO meeting on immunization in older adults: Geneva, Switzerland, 22-23 March 2017. Vaccine. 2018;36(7):921-31. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29336923.

211. Ezequiel Zaidel SC, Gonzalo Pérez, Juan Pablo Costabel, Matías Failo, Andrés Rosende, Aldo Carrizo. Vacuna antineumocócica en adultos: encuesta a residentes de cardiología de argentina. Revista del Consejo Argentino de Residentes de Cardiología. 2014(124):101-4. [accessed: 3 August 2022]. Available at: http://www.revistaconarec.com.ar/contenido/art.php?recordID=MTAoMw==.

212. Martins Wde A, Ribeiro MD, Oliveira LB et al. Influenza and pneumococcal vaccination in heart failure: a little applied recommendation. Arq Bras Cardiol. 2011;96(3):240-5. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21271169.

213. Sosa Liprandi A, Zaidel EJ, Lopez Santi R et al. Influenza and Pneumococcal Vaccination in Non-Infected Cardiometabolic Patients from the Americas during the COVID-19 Pandemic. A Sub-Analysis of the CorCOVID-LATAM Study. Vaccines (Basel). 2021;9(2). [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33557082.

214. Frobert O, Gotberg M, Erlinge D et al. Influenza Vaccination After Myocardial Infarction: A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial. Circulation. 2021;144(18):1476-84. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34459211.

215. Kumbhani DJ. Influenza Vaccine to Prevent Adverse Vascular Events - IVVE Washington DC: American College of Cardiology; 2022. updated 3 April 2022. [accessed: Available at: https://www.acc.org/latest-in-cardiology/clinical-trials/2022/04/02/15/50/ivve#references-for-article.

216. Yedlapati SH, Khan SU, Talluri S et al. Effects of Influenza Vaccine on Mortality and Cardiovascular Outcomes in Patients With Cardiovascular Disease: A Systematic Review and Meta-Analysis. J Am Heart Assoc. 2021;10(6):e019636. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33719496.

217. Ma J, Mena M, Mandania RA et al. Associations between Combined Influenza and Pneumococcal Pneumonia Vaccination and Cardiovascular Outcomes. Cardiology. 2021;146(6):772-80. [accessed: 29 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34521082.

218. Liprandi AS, Liprandi MIS, Zaidel EJ et al. Influenza Vaccination for the Prevention of Cardiovascular Disease in the Americas: Consensus document of the Inter-American Society of Cardiology and the Word Heart Federation. Glob Heart. 2021;16(1):55. [accessed: 3 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34381676.

219. Bansilal S, Castellano JM, Fuster V. Global burden of CVD: focus on secondary prevention of cardiovascular disease. Int J Cardiol. 2015;201 Suppl 1:S1-7. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26747389.

220. van der Ham M, Bolijn R, de Vries A et al. Gender inequality and the double burden of disease in low-income and middle-income countries: an ecological study. BMJ Open. 2021;11(4):e047388. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33895719.

221. Amadi C, Lawal F, Ajiboye W et al. Opportunistic screening of cardiovascular disease risk factors in community pharmacies in Nigeria: a cross-sectional study. International journal of clinical pharmacy. 2020;42(6):1469-79. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32960427.

222. Muntner P, Shimbo D, Carey RM et al. Measurement of Blood Pressure in Humans: A Scientific Statement From the American Heart Association. Hypertension. 2019;73(5):e35-e66. [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30827125.

223. Shimbo D, Abdalla M, Falzon L et al. Role of Ambulatory and Home Blood Pressure Monitoring in Clinical Practice: A Narrative Review. Ann Intern Med. 2015;163(9):691-700. [accessed: 22 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26457954.

224. Benítez M, Torras J, Villasuso B et al. Diagnóstico. Criterios de seguimiento, control y derivación. Farm Com. 2022;14(Supl 2. Especial HTA):18-24. [accessed: 30 September 2022]. Available at: https://www.farmaceuticoscomunitarios.org/en/system/files/journals/3417/articles/guia-hta-03.pdf.

225. Parrilla I, Peña M, Rosinach J et al. Cribado. Fenotipos de hipertensión. Farm Com. 2022;14(Supl 2. Especial HTA):13-7. [accessed: 30 September 2022]. Available at: https://www.farmaceuticoscomunitarios.org/es/journal-article/cribado-fenotipos-hipertension.

226. Penín O, Villasuso B, Domenech M et al. [Guide for the approach of hypertension by the community pharmacist in the field of primary care: document of multidisciplinary consensus]. Madrid: SEFAC; 2022.

227. Albasri A, O'Sullivan JW, Roberts NW et al. A comparison of blood pressure in community pharmacies with ambulatory, home and general practitioner office readings: systematic review and meta-analysis. J Hypertens. 2017;35(10):1919-28. [accessed: 30 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28594707.

228. Sabater-Hernández D, de la Sierra A, Bellver-Monzó O et al. [Action guide for the community pharmacist in patients with hypertension and cardiovascular risk. A consensus document (extended version)]. Ars Pharmaceutica (Internet). 2011;52(2):38-58. [accessed: 16 September 2022]. Available at: https://revistaseug.ugr.es/index.php/ars/article/view/4723.

229. Penín O, Villasuso B, Rojo J et al. [KAIRÓS' project: ambulatory monitoring of blood pressure in community pharmacies. Monitoring and follow-up of blood pressure in hypertensive elderly patients under treatment]. Farm Com. 2018;10(2):21-6. [accessed: 16 September 2022]. Available at: doi: 10.5672/FC.2173-9218.(2018/Vol10).002.04.

230. Sabater-Hernandez D, Sendra-Lillo J, Faus MJ et al. Usefulness of blood pressure measurement by community pharmacists in the management of hypertension. J Manag Care Pharm. 2012;18(6):453-6. [accessed: 30 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22839686.

231. Sabater-Hernandez D, Sendra-Lillo J, Jimenez-Monleon JJ et al. Identifying masked uncontrolled hypertension in the community pharmacy setting. Blood Press Monit. 2015;20(3):138-43. [accessed: 30 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25591059.

232. Atar D, Jukema JW, Molemans B et al. New cardiovascular prevention guidelines: How to optimally manage dyslipidaemia and cardiovascular risk in 2021 in patients needing secondary prevention? Atherosclerosis. 2021;319:51-61. [accessed: 6 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33476944.

233. Pirillo A, Casula M, Olmastroni E et al. Global epidemiology of dyslipidaemias. Nat Rev Cardiol. 2021;18(10):689-700. [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33833450.

234. Mach F, Baigent C, Catapano AL et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J. 2020;41(1):111-88. [accessed: 4 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31504418.

235. Grundy SM, Stone NJ, Bailey AL et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;139(25). [accessed: 4 June 2022]. Available at: https://www.ahajournals.org/doi/10.1161/cir.0000000000000625.

236. Duren DL, Sherwood RJ, Czerwinski SA et al. Body Composition Methods: Comparisons and Interpretation. J Diabetes Sci Technol. 2008;2(6):1139-46. [accessed: 06 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2769821/.

237. World Health Organization. A healthy lifestyle - WHO recommendations: 2010. updated [accessed: Available at: https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi.

238. Roumie CL, Hung AM, Russell GB et al. Blood Pressure Control and the Association With Diabetes Mellitus Incidence. Hypertension. 2020;75(2):331-8. [accessed: 13 June 2022]. Available at: https://www.ahajournals.org/doi/10.1161/HYPERTENSIONAHA.118.12572.

239. Dorgalaleh A, Favaloro EJ, Bahraini M et al. Standardization of Prothrombin Time/International Normalized Ratio (PT/INR). Int J Lab Hematol. 2021;43(1):21-8. [accessed: 10 October 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32979036.

240. Elewa HF, AbdelSamad O, Elmubark AE et al. The first pharmacist-managed anticoagulation clinic under a collaborative practice agreement in Qatar: clinical and patient-oriented outcomes. J Clin Pharm Ther. 2016;41(4):403-8. [accessed: 9 October 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27144477.

241. Ingram SJ, Kirkdale CL, Williams S et al. Moving anticoagulation initiation and monitoring services into the community: evaluation of the Brighton and hove community pharmacy service. BMC Health Serv Res. 2018;18(1):91. [accessed: 10 October 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29415718.

242. Harper P, McMichael I, Griffiths D et al. The community pharmacy-based anticoagulation management service achieves a consistently high standard of anticoagulant care. N Z Med J. 2015;128(1422):31-41. [accessed: 10 October 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26411845.

243. Amouyel P, Deverly A. [Global cardiovascular risk: definition, evaluation and management strategies. Round table no. 1. XV]. Therapie. 2000;55(4):533-9. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/11098732.

244. D'Agostino RB, Sr., Vasan RS, Pencina MJ et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117(6):743-53. [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18212285.

245. Goff DC, Lloyd-Jones DM, Bennett G et al. 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk. Circulation. 2014;129(25_suppl_2):S49-S73. [accessed: 5 June 2022]. Available at: https://www.ahajournals.org/doi/pdf/10.1161/01.cir.0000437741.48606.98.

246. Campbell NRC, Ordunez P, Giraldo G et al. WHO HEARTS: A Global Program to Reduce Cardiovascular Disease Burden: Experience Implementing in the Americas and Opportunities in Canada. Can J Cardiol. 2021;37(5):744-55. [accessed: 7 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33310142.

247. SCORE2 working group and ESC Cardiovascular risk collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. Eur Heart J. 2021;42(25):2439-54. [accessed: 5 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34120177.

248. Chaudhri K, Hayek A, Liu H et al. General practitioner and pharmacist collaboration: does this improve risk factors for cardiovascular disease and diabetes? A systematic review protocol. BMJ Open. 2019;9(8):e027634. [accessed: 29 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31383700.

249. Puspitasari HP, Aslani P, Krass I. Challenges in the care of clients with established cardiovascular disease: lessons learned from Australian community pharmacists. PLoS One. 2014;9(11):e113337. [accessed: 25 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25409194.

250. Boykin A, Wright D, Stevens L et al. Interprofessional care collaboration for patients with heart failure. Am J Health Syst Pharm. 2018;75(1):e45-e9. [accessed: 29 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29273612.

251. Royal Pharmaceutical Society. Pharmacy: Helping to prevent and support people with Cardiovascular disease. [Internet]. 2019. [accessed: 27 May 2022]. Available at: https://www.rpharms.com/recognition/all-our-campaigns/policy-a-z/cardiovascular-disease.

252. Centers for Disease Control and Prevention. Best Practices for Cardiovascular Disease Prevention Programs: A Guide to Effective Health Care System Interventions and Community Programs Linked to Clinical Services. Atlanta, GA: [Internet]. 2017. [accessed: 22 July 2022]. Available at: https://www.cdc.gov/dhdsp/pubs/guides/best-practices/index.htm.

253. Mc Namara KP, Krass I, Peterson GM et al. Implementing screening interventions in community pharmacy to promote interprofessional coordination of primary care - A mixed methods evaluation. Res Social Adm Pharm. 2020;16(2):160-7. [accessed: 27 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31088777.

254. Carter BL, Doucette WR, Franciscus CL et al. Deterioration of blood pressure control after discontinuation of a physician-pharmacist collaborative intervention. Pharmacotherapy. 2010;30(3):228-35. [accessed: 27 May 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20180606.

255. International Pharmaceutical Federation (FIP). Beating non-communicable diseases in the community The contribution of pharmacists. The Hague: [Internet]. 2019. [accessed: 22 July 2022]. Available at: https://www.fip.org/file/4694.

256. World Health Organization. Guideline for the pharmacological treatment of hypertension in adults. Geneva: [Internet]. 2021. [accessed: 26 July 2022]. Available at: https://apps.who.int/iris/rest/bitstreams/1365359/retrieve.

257. DrugBank Online. Angiotensin-Converting Enzyme Inhibitors [Internet]. 2022. updated [accessed: 02 June]. Available at: https://go.drugbank.com/categories/DBCAT000415.

258. Chavey WE, Hogikyan RV, Van Harrison R et al. Heart Failure Due to Reduced Ejection Fraction: Medical Management. Am Fam Physician. 2017;95(1):13-20. [accessed: 23 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28075105.

259. DrugBank Online. Calcium Channel Blockers [Internet]. 2022. updated [accessed: 02 June]. Available at: https://go.drugbank.com/categories/DBCAT000574.

260. Heidenreich PA, Bozkurt B, Aguilar D et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145(18):e895-e1032. [accessed: 23 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35363499.

261. McDonagh TA, Metra M, Adamo M et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021;42(36):3599-726. [accessed: 23 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34447992.

262. Nicolas D, Kerndt CC, Reed M. Sacubitril/Valsartan. StatPearls. Treasure Island (FL)2022.

263. Rao S. Use of Sodium-Glucose Cotransporter-2 Inhibitors in Clinical Practice for Heart Failure Prevention and Treatment: Beyond Type 2 Diabetes. A Narrative Review. Adv Ther. 2022;39(2):845-61. [accessed: 23 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34881413.

264. Hariri L, Patel JB. Vasodilators. StatPearls. Treasure Island (FL)2022.

265. Feig PU. Cellular mechanism of action of loop diuretics: implications for drug effectiveness and adverse effects. Am J Cardiol. 1986;57(2):14A-9A. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/3511652.

266. Maideen NMP, Balasubramanian R, Muthusamy S. A Comprehensive Review of the Pharmacologic Perspective on Loop Diuretic Drug Interactions with Therapeutically Used Drugs. Curr Drug Metab. 2022. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35366769.

267. David MNV, Shetty M. Digoxin. StatPearls. Treasure Island (FL)2022.

268. Tse S, Mazzola N. Ivabradine (Corlanor) for Heart Failure: The First Selective and Specific I f Inhibitor. P T. 2015;40(12):810-4. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26681903.

269. Reed M, Kerndt CC, Nicolas D. Ivabradine. StatPearls. Treasure Island (FL)2022.

270. Sizar O, Nassereddin A, Talati R. Ezetimibe. StatPearls. Treasure Island (FL)2022.

271. Mazhar F, Haider N. Proprotein convertase subtilisin/kexin type 9 enzyme inhibitors: An emerging new therapeutic option for the treatment of dyslipidemia. J Pharmacol Pharmacother. 2016;7(4):190-3. [accessed: 02 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28163543.

272. Zodda D, Giammona R, Schifilliti S. Treatment Strategy for Dyslipidemia in Cardiovascular Disease Prevention: Focus on Old and New Drugs. Pharmacy (Basel). 2018;6(1). [accessed: 02 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29361723.

273. Su L, Mittal R, Ramgobin D et al. Current Management Guidelines on Hyperlipidemia: The Silent Killer. Journal of Lipids. 2021;2021:1-5. [accessed: 4 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8363437/.

274. Capodanno D, Angiolillo DJ. Antithrombotic Therapy for Atherosclerotic Cardiovascular Disease Risk Mitigation in Patients With Coronary Artery Disease and Diabetes Mellitus. Circulation. 2020;142(22):2172-88. [accessed: 04 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33253005.

275. Guillet B, Cayla G, Lebreton A et al. Long-Term Antithrombotic Treatments Prescribed for Cardiovascular Diseases in Patients with Hemophilia: Results from the French Registry. Thromb Haemost. 2021;121(3):287-96. [accessed: 04 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33099283.

276. Guyatt GH, Akl EA, Crowther M et al. Executive summary: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):7S-47S. [accessed: 04 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/22315257.

277. Chen WT, White CM, Phung OJ et al. Association between CHADS(2)risk factors and anticoagulation-related bleeding: a systematic literature review. Mayo Clin Proc. 2011;86(6):509-21. [accessed: 04 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21628615.

278. DrugBank Online. Antiplatelet agents [Internet]. 2022. updated [accessed: Available at: https://go.drugbank.com/categories/DBCAT000149.

279. Zirlik A, Bode C. Vitamin K antagonists: relative strengths and weaknesses vs. direct oral anticoagulants for stroke prevention in patients with atrial fibrillation. J Thromb Thrombolysis. 2017;43(3):365-79. [accessed: 04 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27896543.

280. De Caterina R, Ageno W, Agnelli G et al. The Non-Vitamin K Antagonist Oral Anticoagulants in Heart Disease: Section V-Special Situations. Thromb Haemost. 2019;119(1):14-38. [accessed: 04 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30597497.

281. Lane DA, Wood K. Cardiology patient page. Patient guide for taking the non-vitamin K antagonist oral anticoagulants for atrial fibrillation. Circulation. 2015;131(16):e412-5. [accessed: 22 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25901074.

282. Balla C, Pavasini R, Ferrari R. Treatment of Angina: Where Are We? Cardiology. 2018;140(1):52-67. [accessed: 30 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29874661.

283. Joshi PH, de Lemos JA. Diagnosis and Management of Stable Angina: A Review. JAMA. 2021;325(17):1765-78. [accessed: 30 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33944871.

284. Farmakis D, Andrikopoulos G, Giamouzis G et al. Practical Recommendations for the Diagnosis and Medical Management of Stable Angina: An Expert Panel Consensus. J Cardiovasc Pharmacol. 2019;74(4):308-14. [accessed: 30 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31356556.

285. Hale SL, Kloner RA. Ranolazine, an inhibitor of the late sodium channel current, reduces postischemic myocardial dysfunction in the rabbit. J Cardiovasc Pharmacol Ther. 2006;11(4):249-55. [accessed: 19 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17220471.

286. Amariles P. Estrategias para la priorización de servicios de atención farmacéutica: una aproximación a un marco conceptual para Colombia. Vitae 2015;22:45-7. [accessed: 6 August 2022]. Available at: https://revistas.udea.edu.co/index.php/vitae/article/view/24890/20266.

287. Faus MJ, Amariles P., Martinez-Martinez F, et al. Atención farmacéutica servicios farmacéuticos orientados al paciente: Armilla: Avicam; 2021.

288. Pellegrin K, Chan F, Pagoria N et al. A Statewide Medication Management System: Health Information Exchange to Support Drug Therapy Optimization by Pharmacists across the Continuum of Care. Appl Clin Inform. 2018;9(1):1-10. [accessed: 04 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29298450.

289. Hanson A, Haddad LM. Nursing Rights of Medication Administration. StatPearls. Treasure Island (FL)2022.

290. Faulx MD, Francis GS. Adverse drug reactions in patients with cardiovascular disease. Curr Probl Cardiol. 2008;33(12):703-68. [accessed: 04 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/19000586.

291. van der Laan DM, Elders PJM, Boons C et al. The impact of cardiovascular medication use on patients' daily lives: a cross-sectional study. International journal of clinical pharmacy. 2018;40(2):412-20. [accessed: 04 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29435910.

292. Ayan M, Pothineni NV, Siraj A et al. Cardiac drug therapy-considerations in the elderly. J Geriatr Cardiol. 2016;13(12):992-7. [accessed: 05 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28321243.

293. Schwartz JB, Schmader KE, Hanlon JT et al. Pharmacotherapy in Older Adults with Cardiovascular Disease: Report from an American College of Cardiology, American Geriatrics Society, and National Institute on Aging Workshop. J Am Geriatr Soc. 2019;67(2):371-80. [accessed: 22 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30536694.

294. Ministry of Health. Kenya National Guidelines for Cardiovascular Diseases Management. Nairobi: [Internet]. 2018. [accessed: 22 July 2022]. Available at: https://www.health.go.ke/wp-content/uploads/2018/06/Cardiovascular-guidelines-2018_A4_Final.pdf.

295. Patoulias D, Stavropoulos K, Imprialos K et al. Pharmacological Management of Cardiac Disease in Patients with Type 2 Diabetes: Insights into Clinical Practice. Curr Vasc Pharmacol. 2020;18(2):125-38. [accessed: 05 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32013815.

296. Hemkens LG, Bucher HC. HIV infection and cardiovascular disease. Eur Heart J. 2014;35(21):1373-81. [accessed: 05 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24408888.

297. Pandey A, Galvani AP. The global burden of HIV and prospects for control. Lancet HIV. 2019;6(12):e809-e11. [accessed: 05 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31439533.

298. Ashwitha SK, Jacob PA, Ajaj A et al. Management of cardiovascular diseases in HIV/AIDS patients. J Card Surg. 2021;36(1):236-43. [accessed: 05 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33225472.

299. Feinstein MJ, Hsue PY, Benjamin LA et al. Characteristics, Prevention, and Management of Cardiovascular Disease in People Living With HIV: A Scientific Statement From the American Heart Association. Circulation. 2019;140(2):e98-e124. [accessed: 05 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31154814.

300. Mehta LS, Warnes CA, Bradley E et al. Cardiovascular Considerations in Caring for Pregnant Patients: A Scientific Statement From the American Heart Association. Circulation. 2020;141(23):e884-e903. [accessed: 05 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32362133.

301. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J et al. 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J. 2018;39(34):3165-241. [accessed: 22 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30165544.

302. de Ferranti SD, Steinberger J, Ameduri R et al. Cardiovascular Risk Reduction in High-Risk Pediatric Patients: A Scientific Statement From the American Heart Association. Circulation. 2019;139(13):e603-e34. [accessed: 22 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30798614.

303. Rad EM, Assadi F. Management of hypertension in children with cardiovascular disease and heart failure. Int J Prev Med. 2014;5(Suppl 1):S10-6. [accessed: 05 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/24791185.

304. Flynn JT, Kaelber DC, Baker-Smith CM et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. Pediatrics. 2017;140(3). [accessed: 22 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28827377.

305. Pharmaceutical Care Research Group - University of Granada (Spain). Pharmacotherapy follow-up: the Dader Method (3rd revision: 2005). Pharmacy Practice 2006;4(1):44-53. [accessed: 6 August 2022]. Available at: http://scielo.isciii.es/pdf/pharmacy/v4n1/giaf.pdf.

306. Faus MJ, Sabater-Hernandez D, Amariles P. Types of pharmacist interventions intended to prevent and solve negative outcomes associated with medication [e-letter]. Pharmacotherapy. 2007;27:e51-e2. [accessed: 6 August 2022]. Available at: https://www.researchgate.net/publication/237546999_Types_of_Pharmacist_Interventions_Intended_to_Prevent_and_Solve_Negative_Outcomes_Associated_with_Medication.

307. Joint Commission of Pharmacy Practitioners. Pharmacists' Patient Care Process. Practitioners JCoP [Internet]. 2014. [accessed: 19 August 2022]. Available at: https://jcpp.net/wp-content/uploads/2016/03/PatientCareProcess-with-supporting-organizations.pdf.

308. Centers for Disease Control and Prevention. Using the Pharmacists' Patient Care Process to Manage High Blood Pressure: A Resource Guide for Pharmacists Atlanta: Centers for Disease Control and Prevention; 2016. updated [accessed: Available at: https://www.cdc.gov/dhdsp/pubs/docs/pharmacist-resource-guide.pdf.

309. International Pharmaceutical Federation (FIP). Medication review and medicines use review: A toolkit for pharmacists. The Hague, The Netherlands: [Internet]. 2022. [accessed: 6 August 2022]. Available at: https://www.fip.org/file/5100.

310. World Health Organization. Monitoring and evaluating digital health interventions: a practical guide to conducting research and assessment. Geneva: [Internet]. 2016. [accessed: 24 July 2022]. Available at: https://apps.who.int/iris/bitstream/handle/10665/252183/9789241511766-eng.pdf.

311. Santo K, Redfern J. Digital Health Innovations to Improve Cardiovascular Disease Care. Curr Atheroscler Rep. 2020;22(12):71. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33009975.

312. Islam SMS, Maddison R. Digital health approaches for cardiovascular diseases prevention and management: lessons from preliminary studies. Mhealth. 2021;7:41. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34345618.

313. Cowie MR, Lam CSP. Remote monitoring and digital health tools in CVD management. Nat Rev Cardiol. 2021;18(7):457-8. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33824486.

314. Wechkunanukul K, Parajuli DR, Hamiduzzaman M. Utilising digital health to improve medication-related quality of care for hypertensive patients: An integrative literature review. World J Clin Cases. 2020;8(11):2266-79. [accessed: 16 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32548157.

315. Scott-Sheldon LA, Lantini R, Jennings EG et al. Text Messaging-Based Interventions for Smoking Cessation: A Systematic Review and Meta-Analysis. JMIR Mhealth Uhealth. 2016;4(2):e49. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27207211.

316. Smith DM, Duque L, Huffman JC et al. Text Message Interventions for Physical Activity: A Systematic Review and Meta-Analysis. Am J Prev Med. 2020;58(1):142-51. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31759805.

317. Shariful Islam SM, Farmer AJ, Bobrow K et al. Mobile phone text-messaging interventions aimed to prevent cardiovascular diseases (Text2PreventCVD): systematic review and individual patient data meta-analysis. Open Heart. 2019;6(2):e001017. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31673381.

318. Adler AJ, Martin N, Mariani J et al. Mobile phone text messaging to improve medication adherence in secondary prevention of cardiovascular disease. Cochrane Database Syst Rev. 2017;4:CD011851. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28455948.

319. Thakkar J, Kurup R, Laba TL et al. Mobile Telephone Text Messaging for Medication Adherence in Chronic Disease: A Meta-analysis. JAMA Intern Med. 2016;176(3):340-9. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26831740.

320. Coorey GM, Neubeck L, Mulley J et al. Effectiveness, acceptability and usefulness of mobile applications for cardiovascular disease self-management: Systematic review with meta-synthesis of quantitative and qualitative data. Eur J Prev Cardiol. 2018;25(5):505-21. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29313363.

321. Morawski K, Ghazinouri R, Krumme A et al. Association of a Smartphone Application With Medication Adherence and Blood Pressure Control: The MedISAFE-BP Randomized Clinical Trial. JAMA Intern Med. 2018;178(6):802-9. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29710289.

322. Santo K, Singleton A, Chow CK et al. Evaluating Reach, Acceptability, Utility, and Engagement with An App-Based Intervention to Improve Medication Adherence in Patients with Coronary Heart Disease in the MedApp-CHD Study: A

Mixed-Methods Evaluation. Med Sci (Basel). 2019;7(6). [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31167489.

323. Brickwood KJ, Watson G, O'Brien J et al. Consumer-Based Wearable Activity Trackers Increase Physical Activity Participation: Systematic Review and Meta-Analysis. JMIR Mhealth Uhealth. 2019;7(4):e11819. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30977740.

324. Jo A, Coronel BD, Coakes CE et al. Is There a Benefit to Patients Using Wearable Devices Such as Fitbit or Health Apps on Mobiles? A Systematic Review. Am J Med. 2019;132(12):1394-400 e1. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31302077.

325. Perez MV, Mahaffey KW, Hedlin H et al. Large-Scale Assessment of a Smartwatch to Identify Atrial Fibrillation. N Engl J Med. 2019;381(20):1909-17. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31722151.

326. Crilly P, Hassanali W, Khanna G et al. Community pharmacist perceptions of their role and the use of social media and mobile health applications as tools in public health. Res Social Adm Pharm. 2019;15(1):23-30. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29501431.

327. Vatanka P, Lofton J. Re-envisioning the Pharmacist's Role in the Era of Digital Health—CPhA's Inaugural Digital Health Conference Contemp Pharm Pract. 2020;67(2):23-32. [accessed: 24 July 2022]. Available at: https://meridian.allenpress.com/jcphp/article/67/2/23/441307/Re-envisioning-the-Pharmacist-s-Role-in-the-Era-of.

328. Wirtz VJ, Kaplan WA, Kwan GF et al. Access to Medications for Cardiovascular Diseases in Low- and Middle-Income Countries. Circulation. 2016;133(21):2076-85. [accessed: 09 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27217433.

329. Marcum ZA, Zheng Y, Perera S et al. Prevalence and correlates of self-reported medication non-adherence among older adults with coronary heart disease, diabetes mellitus, and/or hypertension. Res Social Adm Pharm. 2013;9(6):817-27. [accessed: 09 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23291338.

330. Baroletti S, Dell'Orfano H. Medication adherence in cardiovascular disease. Circulation. 2010;121(12):1455-8. [accessed: 09 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20351303.

331. Kolandaivelu K, Leiden BB, O'Gara PT et al. Non-adherence to cardiovascular medications. Eur Heart J. 2014;35(46):3267-76. [accessed: 09 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25265973.

332. Ale OK, Busari AA, Irokosu ES et al. Medication nonadherence in Nigerian heart failure patients: A cross sectional study. J Clin Sci. 2021;18:155-60. [accessed: 09 June 2022]. Available at: https://www.jcsjournal.org/text.asp?2021/18/3/155/324400.

333. Ganasegeran K, Rashid A. The prevalence of medication nonadherence in post-myocardial infarction survivors and its perceived barriers and psychological correlates: a cross-sectional study in a cardiac health facility in Malaysia. Patient Prefer Adherence. 2017;11:1975-85. [accessed: 09 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29263654.

334. van der Laan DM, Elders PJM, Boons C et al. Factors Associated With Nonadherence to Cardiovascular Medications: A Cross-sectional Study. J Cardiovasc Nurs. 2019;34(4):344-52. [accessed: 09 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31045696.

335. Hughes D. Health and economic impact of non-adherence to preventative cardiovascular medicines. In: Camm JA, Lüscher TF, Maurer G, Serruys PW, editors. ESC CardioMed. 3rd ed: Oxford University Press; 2018.

336. Kleinsinger F. The Unmet Challenge of Medication Nonadherence. Perm J. 2018;22:18-033. [accessed: 09 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30005722.

337. Morrison A, Stauffer ME, Kaufman AS. Defining medication adherence in individual patients. Patient Prefer Adherence. 2015;9:893-7. [accessed: 26 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26170639.

338. Al-Hassany L, Kloosterboer SM, Dierckx B et al. Assessing methods of measuring medication adherence in chronically ill children-a narrative review. Patient Prefer Adherence. 2019;13:1175-89. [accessed: 09 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31413546.

339. Anghel LA, Farcas AM, Oprean RN. An overview of the common methods used to measure treatment adherence. Med Pharm Rep. 2019;92(2):117-22. [accessed: 09 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31086837.

340. Dayer L, Heldenbrand S, Anderson P et al. Smartphone medication adherence apps: potential benefits to patients and providers. J Am Pharm Assoc (2003). 2013;53(2):172-81. [accessed: 29 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23571625.

341. Rijcken CA, Tobi H, Vergouwen AC et al. Refill rate of antipsychotic drugs: an easy and inexpensive method to monitor patients' compliance by using computerised pharmacy data. Pharmacoepidemiol Drug Saf. 2004;13(6):365-70. [accessed: 29 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/15170765.

342. Apikoglu S, Selcuk A, Ozcan V et al. The first nationwide implementation of pharmaceutical care practices through a continuous professional development approach for community pharmacists. International journal of clinical pharmacy. 2022. [accessed: 25 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35699862.

343. Alzahrani AA, Alwhaibi MM, Asiri YA et al. Description of pharmacists' reported interventions to prevent prescribing errors among in hospital inpatients: a cross sectional retrospective study. BMC Health Serv Res. 2021;21(1):432. [accessed: 26 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33957900.

344. Simon ST, Kini V, Levy AE et al. Medication adherence in cardiovascular medicine. BMJ. 2021;374:n1493. [accessed: 26 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34380627.

345. Jacob V, Reynolds JA, Chattopadhyay SK et al. Pharmacist Interventions for Medication Adherence: Community Guide Economic Reviews for Cardiovascular Disease. Am J Prev Med. 2022;62(3):e202-e22. [accessed: 09 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34876318.

346. Consejo General de Colegios Oficiales de Farmacéuticos. Proyect: ADHERENCIA MED. Servicio de Adherencia Terapéutica.: [Internet]. 2019. [accessed: 30 September 2022]. Available at: https://www.farmaceuticos.com/wp-content/uploads/2020/02/2019-informe-resultados-adherenciamed.pdf.

347. García L, Moyá A, Díaz C et al. Tratamiento farmacológico y no farmacológico. Adherencia e inercia terapéutica. Farm Com. 2022;Sep 02;14(Supl 2. Especial HTA):25-38. [accessed: 30 September 2022]. Available at: https://www.farmaceuticoscomunitarios.org/es/journal-article/diagnostico-criterios-seguimiento-control-derivacion/full.

348. Jalal ZSMA, Smith F, Taylor D et al. Impact of pharmacy care upon adherence to cardiovascular medicines: a feasibility pilot controlled trial. Eur J Hosp Pharm. 2016;23(5):250-6. [accessed: 09 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31156861.

349. Sociedad Española de Farmacia Familiar y Comunitaria (SEFAC). ADHe+Dispensación,adherencia y uso adecuado del tratamiento:guía práctica para el farmacéutico comunitario.: [Internet]. 2017. [accessed: 30 September 2022]. Available at: www.sefac.org/sites/default/files/2017-11/Adherencia_0.pdf.

350. Hedegaard U, Kjeldsen LJ, Pottegard A et al. Multifaceted intervention including motivational interviewing to support medication adherence after stroke/transient ischemic attack: a randomized trial. Cerebrovasc Dis Extra. 2014;4(3):221-34. [accessed: 09 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/25598772.

351. Ogungbe O, Byiringiro S, Adedokun-Afolayan A et al. Medication Adherence Interventions for Cardiovascular Disease in Low- and Middle-Income Countries: A Systematic Review. Patient Prefer Adherence. 2021;15:885-97. [accessed: 29 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33953548.

352. Pharmaceutical Care Network Europe. Classification of Drug related problems. [Internet]. 2010. [accessed: 26 June 2022]. Available at: http://www.pcne.org/upload/files/11_PCNE_classification_V6-2.pdf.

353. Al Hamid A, Aslanpour Z, Aljadhey H et al. Hospitalisation Resulting from Medicine-Related Problems in Adult Patients with Cardiovascular Diseases and Diabetes in the United Kingdom and Saudi Arabia. Int J Environ Res Public Health. 2016;13(5). [accessed: 15 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27171100.

354. Huiskes VJ, Burger DM, van den Ende CH et al. Effectiveness of medication review: a systematic review and meta-analysis of randomized controlled trials. BMC Fam Pract. 2017;18(1):5. [accessed: 15 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28095780.

355. Reinau D, Furrer C, Stampfli D et al. Evaluation of drug-related problems and subsequent clinical pharmacists' interventions at a Swiss university hospital. J Clin Pharm Ther. 2019;44(6):924-31. [accessed: 15 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31408206.

356. Al-Jabi SW, Aldabe L, Alhaj-Asaad L et al. Assessment of drug interactions and their associated factors among patients with cardiovascular diseases: a cross-sectional study from the occupied Palestinian territory. The Lancet. 2021;398(S8). [accessed: 29 June 2022]. Available at: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01494-X/fulltext.

357. Patel VK, Acharya LD, Rajakannan T et al. Potential drug interactions in patients admitted to cardiology wards of a south Indian teaching hospital. Australas Med J. 2011;4(1):9-14. [accessed: 29 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23393498.

358. Akbar Z, Rehman S, Khan A et al. Potential drug-drug interactions in patients with cardiovascular diseases: findings from a prospective observational study. J Pharm Policy Pract. 2021;14(1):63. [accessed: 29 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34311787.

359. Pegler S, Underhill J. Evaluating the safety and effectiveness of new drugs. Am Fam Physician. 2010;82(1):53-7. [accessed: 15 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20590071.

360. Weeke P, Roden DM. Pharmacogenomics and cardiovascular disease. Curr Cardiol Rep. 2013;15(7):376. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23689943.

361. Howe LA. Pharmacogenomics and management of cardiovascular disease. Nursing. 2011;41 Suppl:1-7. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/21343749.

362. American Pharmacists Association, National Association of Chain Drug Stores Foundation. Medication therapy management in pharmacy practice: core elements of an MTM service model (version 2.0). J Am Pharm Assoc (2003). 2008;48(3):341-53. [accessed: 15 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/18595820.

363. Breault RR, Schindel TJ, Hughes CA. Pharmacist care planning services: What matters most. Can Pharm J (Ott). 2021;154(3):149-52. [accessed: 29 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34104267.

364. Kshirsagar NA. Rational use of medicines: Cost consideration & way forward. Indian J Med Res. 2016;144(4):502-5. [accessed: 29 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28256457.

365. Maxwell SR. Rational prescribing: the principles of drug selection. Clin Med (Lond). 2016;16(5):459-64. [accessed: 29 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27697811.

366. World Health Organization. Problems of Irrational Drug Use - Session Guide. [Internet]. 2010. [accessed: 29 June 2022]. Available at: https://www.paho.org/hq/dmdocuments/2010/3_IrrationalSG.pdf.

367. Poh EW, McArthur A, Stephenson M et al. Effects of pharmacist prescribing on patient outcomes in the hospital setting: a systematic review. JBI Database System Rev Implement Rep. 2018;16(9):1823-73. [accessed: 17 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30204671.

368. General Pharmaceutical Council. In practice: Guidance for pharmacist prescribers. [Internet]. 2019. [accessed: 17 June 2022]. Available at: https://www.pharmacyregulation.org/sites/default/files/document/in-practice-guidance-for-pharmacist-prescribers-february-2020.pdf

369. Hoti K, Hughes J, Sunderland B. An expanded prescribing role for pharmacists - an Australian perspective. Australas Med J. 2011;4(4):236-42. [accessed: 17 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23393515.

370. Rafferty E, Yaghoubi M, Taylor J et al. Costs and savings associated with a pharmacists prescribing for minor ailments program in Saskatchewan. Cost Eff Resour Alloc. 2017;15:3. [accessed: 17 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28400708.

371. Royal Pharmaceutical Society. A Competency Framework for all Prescribers. [Internet]. 2021. [accessed: 17 June 2022]. Available at: https://www.rpharms.com/resources/frameworks/prescribing-competency-framework/competency-framework.

372. Pollock M, Bazaldua OV, Dobbie AE. Appropriate prescribing of medications: an eight-step approach. Am Fam Physician. 2007;75(2):231-6. [accessed: 17 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/17263218.

373. Sosnowska B, Penson P, Banach M. The role of nutraceuticals in the prevention of cardiovascular disease. Cardiovasc Diagn Ther. 2017;7(Suppl 1):S21-S31. [accessed: 29 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28529919.

374. Alves QL, Camargo SB, Silva FD. Role of Nutraceuticals in the Prevention and Treatment of Hypertension and Cardiovascular Diseases. J Hypertens Manag. 2019;5(1). [accessed: 29 June 2022]. Available at: https://clinmedjournals.org/articles/jhm/journal-of-hypertension-and-management-jhm-5-037.php.

375. van Mourik MS, Cameron A, Ewen M et al. Availability, price and affordability of cardiovascular medicines: a comparison across 36 countries using WHO/HAI data. BMC Cardiovasc Disord. 2010;10:25. [accessed: 26 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/20534118.

376. International Pharmaceutical Federation (FIP). Pharmacists in the supply chain: The role of medicines expert in ensuring quality and availability. The Hague, the Netherlands: [Internet]. 2018. [accessed: 19 June 2022]. Available at: https://www.fip.org/file/1344.

377. Yamaguchi H. Roles of Cardiology Pharmacists. Yakugaku Zasshi. 2016;136(8):1121-3. [accessed: 19 June 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/27477728.

378. Dreijer AR, Kruip M, Diepstraten J et al. Effect of antithrombotic stewardship on the efficacy and safety of antithrombotic therapy during and after hospitalization. PLoS One. 2020;15(6):e0235048. [accessed: 24 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32584857.

379. Kozma CM, Reeder CE, Schulz RM. Economic, clinical, and humanistic outcomes: a planning model for pharmacoeconomic research. Clin Ther. 1993;15(6):1121-32; discussion 0. [accessed: 12 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8111809.

380. Garcia-Cardenas V, Rossing CV, Fernandez-Llimos F et al. Pharmacy practice research - A call to action. Res Social Adm Pharm. 2020;16(11):1602-8. [accessed: 12 August 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32919918.

381. Bungay KM, Sanchez LA. Types of economic and humanistic outcomes assessments. Pharmacoeconomics and Outcomes. 2nd ed. Kansas City: American College of Clinical Pharmacy; 2003.

382. University of Kansas. 8. Increasing Participation and Membership | Community Tool Box. [Internet]. updated [accessed: 20 September 2022]. Available at: https://ctb.ku.edu/en/increasing-participation-and-membership.

383. Kwan BM, McGinnes HL, Ory MG et al. RE-AIM in the Real World: Use of the RE-AIM Framework for Program Planning and Evaluation in Clinical and Community Settings. Front Public Health. 2019;7:345. [accessed: 20 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31824911.

384. Smith JD, Li DH, Rafferty MR. The Implementation Research Logic Model: a method for planning, executing, reporting, and synthesizing implementation projects. Implement Sci. 2020;15(1):84. [accessed: 20 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32988389.

385. Livet M, Haines ST, Curran GM et al. Implementation Science to Advance Care Delivery: A Primer for Pharmacists and Other Health Professionals. Pharmacotherapy. 2018;38(5):490-502. [accessed: 20 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29624704.

386. Berwick DM. A primer on leading the improvement of systems. BMJ. 1996;312(7031):619-22. [accessed: 20 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/8595340.

387. Krishnamurti T, Argo N. A Patient-Centered Approach to Informed Consent: Results from a Survey and Randomized Trial. Med Decis Making. 2016;36(6):726-40. [accessed: 25 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26964877.

388. Varkey B. Principles of Clinical Ethics and Their Application to Practice. Med Princ Pract. 2021;30(1):17-28. [accessed: 25 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32498071.

389. Grady C. Enduring and emerging challenges of informed consent. N Engl J Med. 2015;372(22):2172. [accessed: 25 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26017840.

390. Schafer A, Flierl U, Berliner D et al. Anticoagulants for Stroke Prevention in Atrial Fibrillation in Elderly Patients. Cardiovasc Drugs Ther. 2020;34(4):555-68. [accessed: 25 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32350792.

391. Alonso-Perales MDM, Lasheras B, Beitia G et al. Barriers to promote cardiovascular health in community pharmacies: a systematic review. Health Promot Int. 2017;32(3):535-48. [accessed: 30 September 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/26511943.

392. Craddock DS, Hall RG. Pharmacists without Access to the EHR: Practicing with One Hand Tied Behind Our Backs. Innov Pharm. 2021;12(3). [accessed: 26 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35601575.

393. Miller V, Nambiar L, Saxena M et al. Exploring the Barriers to and Facilitators of Using Evidence-Based Drugs in the Secondary Prevention of Cardiovascular Diseases: Findings From a Multistakeholder, Qualitative Analysis. Glob Heart. 2018;13(1):27-34 e17. [accessed: 26 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29146489.

394. MacCallum L, Mathers A, Kellar J et al. Pharmacists report lack of reinforcement and the work environment as the biggest barriers to routine monitoring and follow-up for people with diabetes: A survey of community pharmacists. Res Social Adm Pharm. 2021;17(2):332-43. [accessed: 25 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32327399.

395. San-Juan-Rodriguez A, Newman TV, Hernandez I et al. Impact of community pharmacist-provided preventive services on clinical, utilization, and economic outcomes: An umbrella review. Prev Med. 2018;115:145-55. [accessed: 26 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/30145351.

396. Tong B, Kapanen AI, Yuen J. Third-party Reimbursement of Pharmacist-Led Cardiovascular and Diabetes Preventive Health Services for Workplace Health Initiatives: A Narrative Systematic Review. Innov Pharm. 2021;12(1). [accessed: 26 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34007673.

397. El Hajj MS, Abu Yousef SE, Basri MA. Diabetes care in Qatar: a survey of pharmacists' activities, attitudes and knowledge. International journal of clinical pharmacy. 2018;40(1):84-93. [accessed: 25 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/29147964.

398. Lee JK, McCutcheon LRM, Fazel MT et al. Assessment of Interprofessional Collaborative Practices and Outcomes in Adults With Diabetes and Hypertension in Primary Care: A Systematic Review and Meta-analysis. JAMA Netw Open. 2021;4(2):e2036725. [accessed: 27 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33576817.

399. Ilardo ML, Speciale A. The Community Pharmacist: Perceived Barriers and Patient-Centered Care Communication. Int J Environ Res Public Health. 2020;17(2). [accessed: 27 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31952127.

400. Newman TV, San-Juan-Rodriguez A, Parekh N et al. Impact of community pharmacist-led interventions in chronic disease management on clinical, utilization, and economic outcomes: An umbrella review. Res Social Adm Pharm. 2020;16(9):1155-65. [accessed: 27 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31959565.

401. Boscart VM, Heckman GA, Huson K et al. Implementation of an interprofessional communication and collaboration intervention to improve care capacity for heart failure management in long-term care. J Interprof Care. 2017;31(5):583-92. [accessed: 27 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/28876202.

402. Kolla A, Lim S, Zanowiak J et al. The Role of Health Informatics in Facilitating Communication Strategies for Community Health Workers in Clinical Settings: A Scoping Review. J Public Health Manag Pract. 2021;27(3):E107-E18. [accessed: 27 July 2022]. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33512874.

International
Pharmaceutical
Federation

Fédération
Internationale
Pharmaceutique

Andries Bickerweg 5
2517 JP The Hague
The Netherlands
-
T +31 (0)70 302 19 70
F +31 (0)70 302 19 99
fip@fip.org
-
www.fip.org