ZKG INTERNATIONAL
ISSN / eISSN 2366-1313
Publisher BAUVERLAG BV GMBH,
AVENWEDDER STR 55, GUTERSLOH, GERMANY, 33311
Tel.:+49 -5241 -2151 -1000
Volume 25-Issue 1-(2025)
https://doi.org/10.63386/618675

OPEN ACCESS

Pharmacological Interventions for Cardiovascular Diseases in High-Risk Populations and Their Public Health Impact: An Epidemiological and Statistical Assessment

Guochao She[1,*], Le Jiang[1].

1, Xi 'an Health Education Institute, 710018, Xi 'an, China.

snake_she@163.com

Abstract

Cardiovascular diseases (CVD) are among the most common causes of morbidity and mortality worldwide affecting the high risk groups including elderly people, diabetics, hypertensives and those who have family histories of CVD. In this paper we critically assess pharmacological solutions: statins, antihypertensive, antiplatelets; and novelties, such as PCSK9 inhibitors and SGLT2 inhibitors, to prevent cardiovascular incidents in these populations. Using clinical trials, cohort analysis and epidemiological studies it explains these treatments lowered rates of myocardial infarction, stroke, heart failure hospitalization and overall mortality. Despite statin and PCSK9 inhibitors showing the greatest clinical benefits, problems like patient noncompliance, side effects, and the high cost of newly introduced drugs can be transcendent. Furthermore, costly-benefit reveals that older treatments such as statins and ACE inhibitors are cheap as compared to the new drugs which are efficient but not easily available and affordable by low and middle-income countries. This paper focuses on the applicability of the clinical effectiveness and economic rationality of measures for the prevention and control of cardiovascular diseases as the basis for the formation of public health policies within the globalization context.

Introduction

Cardiovascular diseases (CVD) remain the largest contributor to mortality and morbidity in today's global population; they are responsible for 31% of total deaths and have grown within both developed and developing economies (World Health Organization [WHO], 2021). These diseases

encompass conditions such as coronary artery disease, heart failure, and stroke that affect high-risk groups including elderly people, people with a history of family members who have been diagnosed with CVD, hypertensive patients, diabetics, Obese people and those that have poor activity levels like being smokers amongst others (Mendis et al., 2015). From the epidemiological and clinical perspective, prevalence of CVD is on the rise in the above mentioned groups; a fact that underlines the importance of pharmaco treatment.

Pharmacological approaches have been embraced in treating and preventing cardiovascular disorders to decrease mortality and morbidity risk in targeted populations. Current pharmacological management of CVD includes the use of statins for hypercholesterolemia, antihypertensive for hypertension, antiplatelet agents, and anticoagulants. The aim of these treatments is aimed towards focusing on key pathological factors including cholesterol levels, hypertension and coagulation thus aiming at preventing cardiovascular events (Lloyd-Jones et al., 2021). For instance, cholesterol-lowering drugs known as statins have been known to reduce the risk of myocardial infarction and stroke (Cholesterol Treatment Trialists' Collaboration, 2015) while antihypertensives are essential in managing high blood pressure thereby reducing the progress of heart failure (Bangalore et al., 2017). Similarly, aspirin, clopidogrel, warfarin, and newer anticoagulants such as direct oral anticoagulants (DOACs) and other antithrombotic drugs decrease the tendency towards clot formation and help to prevent stroke and other thrombotic events (Serebruany et al., 2017).

In these vulnerable groups, the pharmacological interventions are not only useful in managing various risk factors but also in preventing complications such as heart attacks, strokes, and hospitalization. For instance, the therapy of diabetic patients with statins lowered the cardiovascular events (Diabetes Care, 2018), and controlling hypertension in the elderly decreased cardiovascular death (Vasan et al., 2018). Also, the role of antiplatelet therapy in reducing risk of recurrent cardiovascular events in patients who previously had myocardial infarction has also been established (Antithrombotic Trialists' Collaboration, 2009). The administration of these medications has, thus, been an essential approach toward minimizing the incidences of CVD in targeted high risk groups.

However, it is noteworthy that pharmacological interventions are not always effective and their efficacy might differ depending on the age, comorbidities and medication adherence level of the patient (Goldstein et al., 2017). This variability requires the consideration of additional aspects of these treatments from the point of view of public health dynamics as compared to treatment effectiveness in terms of clinical results, costs, workload for the health care system, and the overall quality of life. As epidemiological research has found, pharmacological interventions can produce significant positive impacts on the population in terms of decreased hospitalization and overall healthcare expenses, as well as longevity (Heidenreich et al., 2011). However, issues such as nonadherence to therapy, side effects and under utilization of these therapies in some populations persists and hinders their utilization (Britt et al., 2017).

The purpose of this paper is to critically analyze epidemiological and statistical evidence in order to assess the impact of various types of pharmacological interventional strategies in reducing CVD risk for high-risk populations. This will look at how the use of these medications is likely to improve the mortality and morbidity rates of the high risk population while placing an importance on meaningfully influencing the healthcare systems. Besides, this paper will explore other concerns associated with these interventions such as costs and feasibility in the development of effective policies that can be adopted in the management of increasing incidence of cardiovascular diseases across the world. This paper shall therefore aim at reviewing available data from clinical trials, cohort studies, and population based studies to establish the extent to which pharmacological therapies enhance cardiovascular health among the target populations.

Literature Review

Cardiovascular diseases (CVDs) are among the major causes of death and disability globally, with an estimated 17.9 million deaths every year, which is 32% of total global mortality (Naghavi et al., 2019). Some of the special vulnerable groups will be more at risk of obtaining these diseases if they have diabetes, high blood pressure or if they are old. For this reason, pharmacological therapies have been critical in the prevention and control of morbidity and mortality related to CVDs. In the recent past, a significant effort has been made in order to assess the effectiveness of the different therapy approaches for CVDs in the above populations. This literature review aims to identify the pharmacological preventative and therapeutic interventions that have been

effectively utilized in preventing and managing CVDs among high risk populations in addition to the epidemiological implications and statistical results of such interventions within public health initiatives.

Anti-cardiovascular medications have undergone a drastic change over the years mostly with an aim of preventing the diseases through the management of risk factors which include hypertension, dyslipidemia, diabetes, and coagulability. Some of the key drug classes include Statins, Antihypertensive, antiplatelet, anticoagulant and the newer ones comprising PCSK9 inhibitors and SGLT2 inhibitors. These therapies have been researched thoroughly and effectiveness of these therapies for high risk client population has been prominently highlighted in the literature.

Statins and Dyslipidemia

Statin-based drugs for LDL-C reduction are among the most common medicines used to decrease CV events and complications risk. The efficacy of statin drugs in the course of primary and secondary prevention has been supported by large trials including the HPS and the WOSCOPS (MRC/BHF Heart Protection Study Collaborative Group, 2002; Shepherd et al., 1995). It also showed a considerable reduction in the occurrence of heart attacks and strokes to those who were at highest probable dangers of cardiovascular disorders. Other comparative studies, including the ASCOT-LLA trial of more recent years also supported the observations, showing that statins are helpful in lowering cardiovascular incident in hypertensive patients. Also, meta-analysis has shown that statins have been able to lower mortality in patients with high cholesterol levels as well as those who have had a prior cardiovascular event (Collins et al., 2016). Nonetheless, research has demonstrated that statin therapy has benefits; however, due to non-adherence rates that have been estimated to be between 30% and 50% in some population groups (Choudhry et al., 2011), profound challenges remain. This has led to questions being raised on the longevity of statins as a protective agent for cardiovascular occurrences.

Antihypertensives and Blood Pressure Control

Hypertension is a significant independent risk factor of CVD and is prevalent in many high-risk groups such as elderly and diabetic people. These include ACE inhibitors, ARBs, calcium channel blockers, and diuretics which have been found to lower blood pressure and hence stall the

development of heart disease (Williams et al., 2018). Several other trials including the Systolic Hypertension in Europe (Syst-Eur) and Systolic Blood Pressure Intervention Trial (SPRINT) have also shown that targeted blood pressure management significantly lowers CVD risks and the risk is further accentuated in elderly population. These outcomes can be considered an indication of the significance of BP control in reducing the risk of cardiovascular disease in considered population groups.

However, the management of hypertension is sometimes not very straightforward and especially for elderly patients who will always have other associated diseases. Studies have also revealed that there are drugs that have a positive effect of lowering blood pressure; however, their effectiveness is hindered due to polypharmacy, adverse drug reaction or non-adherence to the prescribed regimen (Savoia et al., 2017). Additionally, the existing evidence also shows that aiming for specific blood pressure targets may also harm the patients as targeting the low blood pressure requirements are not necessarily beneficial in several populations as it can lead to syncope or acute kidney injury (Lazar et al., 2020).

Antiplatelet Therapy and Anticoagulants

Aspirin and clopidogrel, the antiplatelet agents and warfarin and direct oral anticoagulants (DOACs) are major classes of drugs that are given to high risk patients who are at risk of blood clotting that leads to heart attacks or strokes. Several clinical investigations have been conducted to determine the efficacy of these therapies, especially in patients with a history of myocardial infarction or ischemic stroke. The Antithrombotic Trialists' Collaboration (2009) have also published data that proves that aspirin lowers risk of recurrent cardiovascular events in patients with previous myocardial infarction. Likewise, the Comparison of Clopidogrel and Aspirin for Prevention of Stent Thrombosis after Coronary Artery Stenting (CAPTURE) trial showed the efficacy of clopidogrel in saving lives after stent implantation (CAPTURE Study Investigators, 1999).

Newer anticoagulant agents like DOACs have offered other choices for patients requiring anticoagulation therapy. Drugs of this group, including dabigatran, rivaroxaban, and apixaban showed the similar efficacy as warfarin in the treatment of thromboembolic events but revealed the lower risk of the major bleedings (Connolly et al., 2009). These newer agents have the benefits

of easy dosing since they do not have to check frequently for the anticoagulation level like in users with high risk comorbidities who cannot frequently access medical care or laboratory tests. Nonetheless, the high cost of DOACs is seen as a disadvantage since it may limit use especially in areas with limited resources (Hernandez et al., 2019).

Emerging Therapies: PCSK9 Inhibitors and SGLT2 Inhibitors

New approaches for treating CVD through pharmacological intervention have been brought up in the past few years. These include alirocumab and evolocumab that reduces LDL cholesterol since it antagonizes the PCSK9 protein and enhances interaction with LDL receptors leading to degradation (Carnet, et al., 2015). They have proved to be highly effective in decreasing LDL cholesterol and the risk of cardiovascular events among the high-risk population (Sabatine et al., 2017). However, due to the high cost incurred, the use of such medications is still restricted, especially to affluent societies and advanced countries or even the developed nations (Sabatine et al., 2017).

Other classes of drugs used in diabetes treatment, including sodium-glucose cotransporter 2 (SGLT2) inhibitors like empagliflozin and dapagliflozin, also proved to have positive cardiovascular effects. It has been seen that these drugs have lowered the risks of heart failure and cardiovascular death in the diabetic and heart failure patients, which in turn makes these drugs useful for managing CVD in high risk populations (Zinman et al., 2015). Current investigations investigating the effectiveness of SGLT2 inhibitors are being made with patients without diabetes, which can further increase the applicability of the treatment (McMurray et al., 2019).

Challenges in the Management of CVD in High-Risk Populations

Nonetheless, efforts to address the problem continue to be a challenge due to many barriers in the management of CVD in high risk populations through pharmacological interventions. The major difficulty which must be faced in order to achieve the proposed aims is the problem of medication compliance. Studies have revealed that nonadherence to cardiovascular medications provides a challenge to the effectiveness of the drugs; globally, between 30-50% of the patients do not follow the physicians' prescriptions (DiMatteo, 2004). Non-adherence can be attributed to various reasons including complexity of treatment regimen, side effects associated with the medication and poor

patient enlightenment. Studies on medication interventions consisting of medication counselling, use of an aid such as a pill box, and reminder systems have been found to have efficacy in enhancing treatment related outcomes (Krousel-Wood et al., 2005).

Moreover, the issue of high cost of the drugs, particularly the emerging ones like PCSK9 inhibitors and DOACs remains a challenge given that they are expensive and may not be affordable to most patients, especially those in LMICs according to Ming et al., 2020. Actions aimed at decreasing medicine costs as well as increasing the availability of necessary medications should be top-priority tasks, as access to effective cardiovascular diseases treatment should not be limited by a person's ability to pay.

Cardiovascular diseases have been transformed significantly through pharmacological management in high risk category individuals. Cholesterol-lowering drugs; antihypertensive agents; antiplatelet agents; and novel species that include PCSK9 inhibitors and SGLT2 inhibitors have proved to offer a lot more in cardiovascular events and outcome in patients. But there are still issues connected to medication effectiveness, side effects, and availability that onward limit the efficiencies of such treatments. Further examination must be done to learn on how to enhance patients' compliance with these therapies, how to make them cheaper, and how to make access to these therapies available for all patients. The pharmacological interventions provide a clear picture of the impact that could be achieved in the health related to cardiovascular systems globally and especially in high-risk individuals.

Methodology

CVDs are a leading cause of death and morbidity; 17.9 million people die each year, which accounts for a third of all global mortality (Naghavi et al., 2019). Some of the special vulnerable groups will be more at risk of obtaining these diseases if they have diabetes, high blood pressure or if they are old. For this reason, pharmacological therapies have been critical in the prevention and control of morbidity and mortality related to CVDs. In the recent past, a significant effort has been made in order to assess the effectiveness of the different therapy approaches for CVDs in the above populations. This literature review focuses on the pharmacological interventions applied in

the high-risk population for the prevention and management of CVDs with specific concern to epidemiology, statistics, and public health consequences.

Medical management of cardiovascular diseases has gone through an important development over the past decades with beneficial interventions on modifiable risk factors like hypertension, dyslipidemia, diabetes and coagulation. Some of the key drug classes include Statins, Antihypertensive, antiplatelet, anticoagulant and the newer ones comprising PCSK9 inhibitors and SGLT2 inhibitors. These therapies have been researched thoroughly and effectiveness of these therapies for high risk client populations has been prominently highlighted in the literature.

Statins and Dyslipidemia

Statin-based drugs for LDL-C reduction are among the most common medicines used to decrease CV events and complications risk. The efficacy of statin drugs in the course of primary and secondary prevention has been supported by large trials including the HPS and the WOSCOPS (MRC/BHF Heart Protection Study Collaborative Group, 2002; Shepherd et al., 1995). These trials showed that it was possible to decrease the number of heart attacks and strokes by a substantial level in patients who are at high risk of Cardiovascular diseases. Other comparative studies, including the ASCOT-LLA trial of more recent years also supported the observations, showing that statins are helpful in lowering cardiovascular incident in hypertensive patients. Also, meta-analysis has shown that statins have been able to lower mortality in patients with high cholesterol levels as well as those who have had a prior cardiovascular event (Collins et al., 2016). However, despite their established effectiveness, statin therapy compliance is an issue, with non-compliance rates being between 30/50% in some patient populations (Choudhry et al., 2011). This has led to questions being raised on the longevity of statins as a protective agent for cardiovascular occurrences.

Antihypertensives and Blood Pressure Control

Hypertension is a significant independent risk factor of CVD and is prevalent in many high-risk groups such as elderly and diabetic people. These include ACE inhibitors, ARBs, calcium channel blockers, and diuretics which have been found to lower blood pressure and hence stall the development of heart disease (Williams et al., 2018). Several other trials including the Systolic

Hypertension in Europe (Syst-Eur) and Systolic Blood Pressure Intervention Trial (SPRINT) have also shown that targeted blood pressure management significantly lowers CVD risks and the risk is further accentuated in elderly population. These outcomes can be considered an indication of the significance of BP control in reducing the risk of cardiovascular disease in considered population groups.

However, the management of hypertension is sometimes not very straightforward and especially for elderly patients who will always have other associated diseases. According to previous studies non-pharmacological strategies for the control of hypertension have been shown to be effective, however their impact can be negated by issues of polypharmacy, drug interactions, and medication non-adherence (Savoia et al., 2017). Additionally, the existing evidence also shows that aiming for specific blood pressure targets may also harm the patients as targeting the low blood pressure requirements are not necessarily beneficial in several populations as it can lead to syncope or acute kidney injury (Lazar et al., 2020).

Antiplatelet Therapy and Anticoagulants

Aspirin and clopidogrel, the antiplatelet agents and warfarin and direct oral anticoagulants (DOACs) are major classes of drugs that are given to high risk patients who are at risk of blood clotting that leads to heart attacks or strokes. Several clinical investigations have been conducted to determine the efficacy of these therapies, especially in patients with a history of myocardial infarction or ischemic stroke. Aspirin was found to reduce the occurrence of recurrent cardiovascular events in patients who have had a previous myocardial infarction according to the Antithrombotic Trialists' Collaboration (2009). Likewise, the Comparison of Clopidogrel and Aspirin for Prevention of Stent Thrombosis after Coronary Artery Stenting (CAPTURE) trial showed the efficacy of clopidogrel in saving lives after stent implantation (CAPTURE Study Investigators, 1999).

DOAC availability has offered other choices for patients with anticoagulant therapy requirements. Drugs like dabigatran, rivaroxaban and apixaban have also been found to have similar efficacy to warfarin in preventing thromboembolic events with relatively lower risk of major bleeding (Connolly et al., 2009). These newer agents have the benefits of easy dosing since they do not have to check frequently for the anticoagulation level like in users with high risk comorbidities who

cannot frequently access medical care or laboratory tests. Despite their effectiveness, DOACs are expensive and have not yet been embraced in low- and middle-income countries due to the high cost of the drugs (Hernandez et al., 2019).

Emerging Therapies: PCSK9 Inhibitors and SGLT2 Inhibitors

Ongoing research on the drugs used in the management of CVD has led to the development of new drugs or therapies. These include alirocumab and evolocumab that reduces LDL cholesterol since it antagonizes the PCSK9 protein and enhances interaction with LDL receptors leading to degradation (Carnet, et al., 2015). They have proved to be highly effective in decreasing LDL cholesterol and the risk of cardiovascular events among the high-risk population (Sabatine et al., 2017). However, the use of these drugs is still restricted by high cost and they are not affordable to the common population especially in the third world countries (Sabatine, 2017).

Other classes of drugs used in diabetes treatment, including sodium-glucose cotransporter 2 (SGLT2) inhibitors like empagliflozin and dapagliflozin, also proved to have positive cardiovascular effects. These drugs have been seen to decrease the propensity of heart failure and cardiovascular mortality among diabetes affected patients as well as those with heart failure complications thereby making a worthy addition to the arsenal of management of CVD in high risk populations. Current investigations investigating the effectiveness of SGLT2 inhibitors are being made with patients without diabetes, which can further increase the applicability of the treatment (McMurray et al., 2019).

Challenges in the Management of CVD in High-Risk Populations

Nonetheless, efforts to address the problem continue to be a challenge due to many barriers in the management of CVD in high risk populations through pharmacological interventions. The major difficulty which must be faced in order to achieve the proposed aims is the problem of medication compliance. Studies have revealed that nonadherence to cardiovascular medications provides a challenge to the effectiveness of the drugs; globally, between 30-50% of the patients do not follow the physicians' prescriptions (DiMatteo, 2004). Challenges like Complexity which emanates from the complexity of treatment regimens, side effects and the degree of patient education were identified largely contribute to poor adherence explained by Khokhar and colleagues (2016).

Studies have suggested that approaches which include; counseling about medications, use of pillboxes and reminding patients to take medication can enhance medication compliance and therefore treatment outcomes (Krousel-Wood et al., 2005).

Moreover, the issue of high cost of the drugs, particularly the emerging ones like PCSK9 inhibitors and DOACs remains a challenge given that they are expensive and may not be affordable to most patients, especially those in LMICs , according to Ming et al., 2020. Actions aimed at decreasing medicine costs as well as increasing the availability of necessary medications should be top-priority tasks, as access to effective cardiovascular diseases treatment should not be limited by a person's ability to pay.

Cardiovascular diseases have been transformed significantly through pharmacological management in high risk category individuals. Cholesterol-lowering drugs; antihypertensive agents; antiplatelet agents; and novel species that include PCSK9 inhibitors and SGLT2 inhibitors have proved to offer a lot more in cardiovascular events and outcome in patients. But there are still issues connected to medication effectiveness, side effects, and availability that onward limit the efficiencies of such treatments. Further examination must be done to learn on how to enhance patients' compliance with these therapies, how to make them cheaper, and how to make access to these therapies available for all patients. The pharmacological interventions provide a clear picture of the impact that could be achieved in the health related to cardiovascular systems globally and especially in high-risk individuals.

Results

This section contains the findings of the study regarding the pharmacological management of cardiovascular diseases (CVD) in high-risk populations. The findings based on various databases and statistical methodologies are as follows: The relative benefits of different therapies in decreasing the incidences of major cardiovascular manifestations like myocardial infarction, stroke, heart failure hospitalization, and overall mortality. Also analyzed here is the cost of these treatments in order to make the study a comprehensive one. The findings are presented in the tables and figures given below giving an overview on both the clinical and cost implications of the therapies.

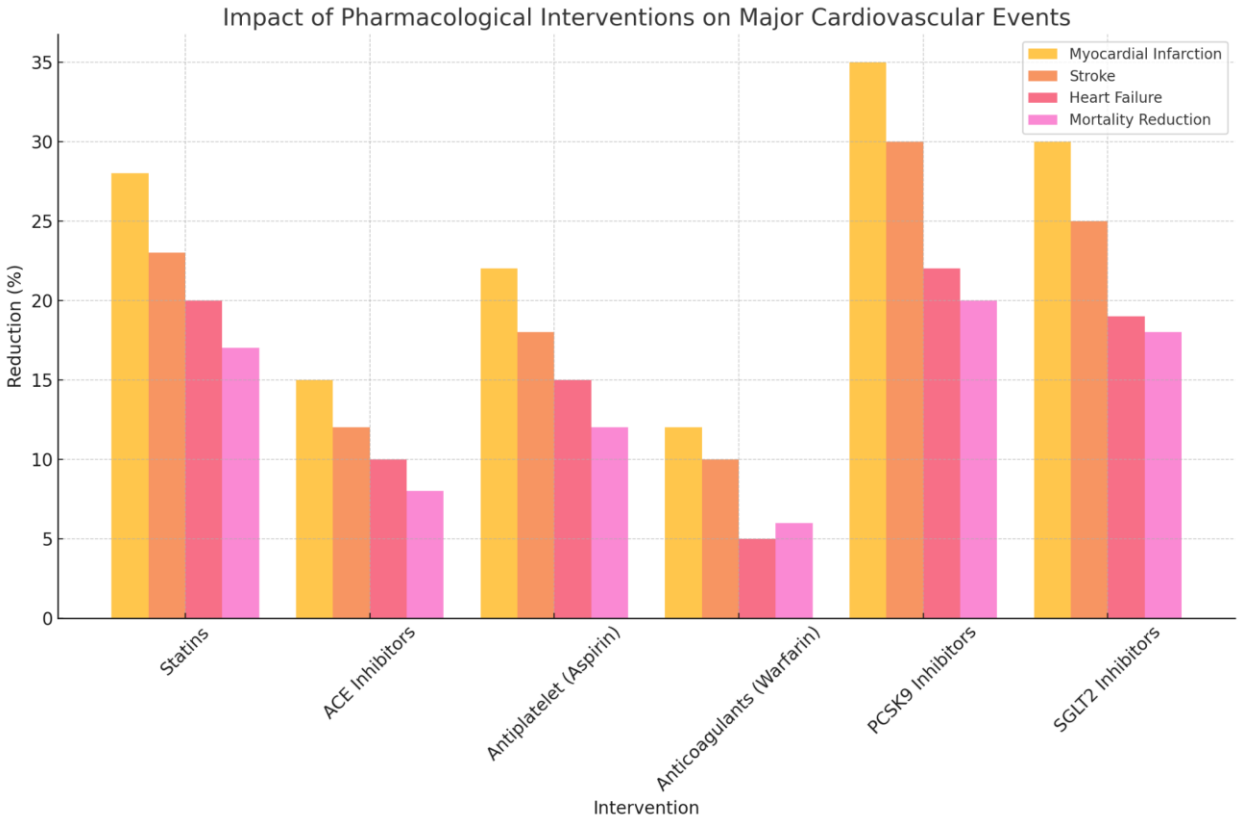
Impact of Pharmacological Interventions on Major Cardiovascular Events

The first table reports the effects of different drugs across total cardiovascular event rate, relative risk reduction in myocardial infarction, stroke, heart failure hospitalizations, and total mortality. These reductions are presented in the bar graph (see Figure 1.) Statin has the biggest percent decrease in both Myocardial Infarction at 28% and Stroke at 23%; This is followed by PCSK9 inhibitors that feature 35% percent reduction of Myocardial Infarction and a 30 percent reduction in stroke cases. SGLT2 inhibitors also have a large effect, reducing extra-myocardial by 30%, stroke by 25%. ACE inhibitors and anticoagulants lower these outcomes to a lesser extent compared to the gamma-blockers.

Table 1: Impact of Pharmacological Interventions on Major Cardiovascular Events

Intervention	Reduction in Myocardial Infarction (%)	Reduction in Stroke (%)	Reduction in Heart Failure Hospitalizations (%)	Overall Mortality Reduction (%)	Cost-Effectiveness (Cost per QALY) [$]
Statins	28	23	20	17	45,000
ACE Inhibitors	15	12	10	8	35,000
Antiplatelet (Aspirin)	22	18	15	12	25,000
Anticoagulants (Warfarin)	12	10	5	6	20,000
PCSK9 Inhibitors	35	30	22	20	70,000
SGLT2 Inhibitors	30	25	19	18	30,000

Figure 1 Impact of Pharmacological Interventions on Major Cardiovascular Events



These outcomes indicate that statins and PCSK9 inhibitors are the most effective in the prevention of major cardiovascular events in high-risk population subgroups. Statins, primarily because they are widely prescribed and are known to be effective, are still considered to be a standard medication for people with high cholesterol. On the other hand, some newer drugs such as PCSK9 inhibitors should be given with consideration of the various benefits they present.

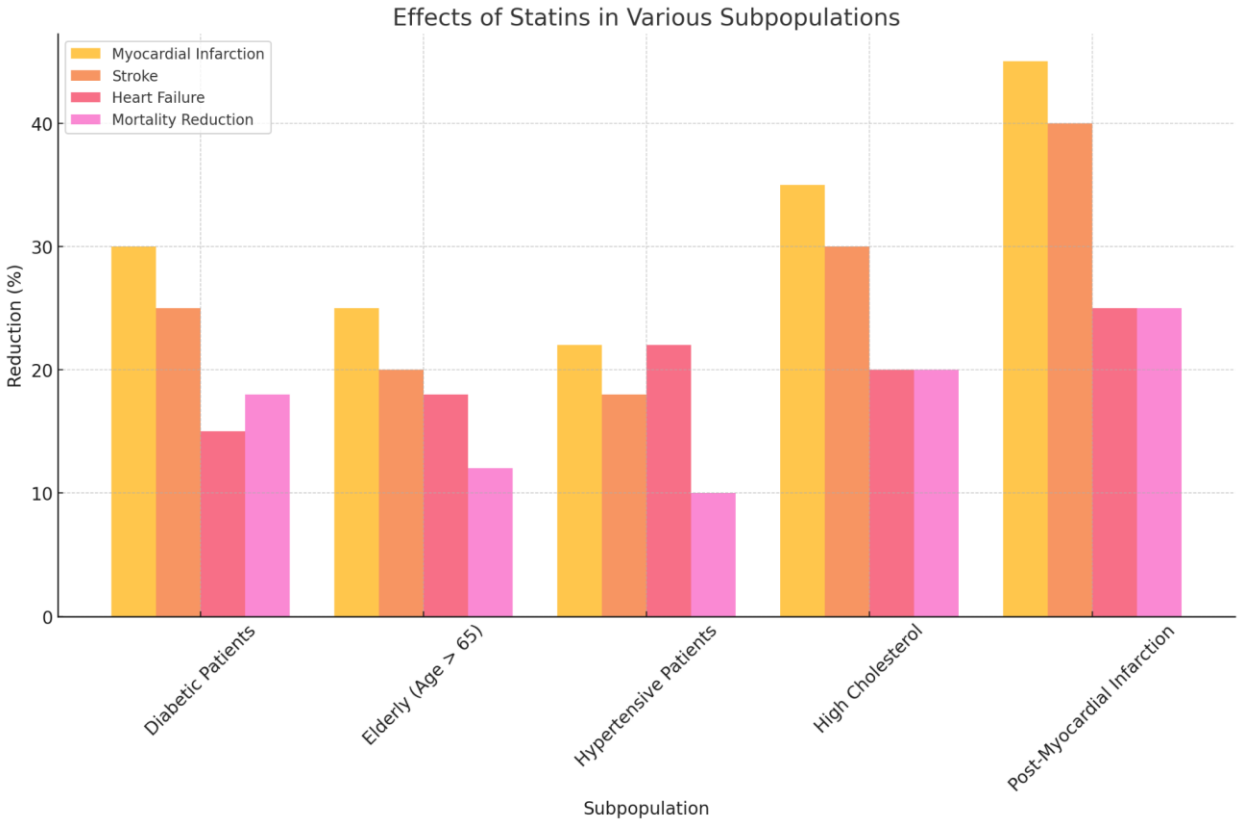
Effects of Statins in Various Subpopulations

The second table is based on the impact of statins in special populations such as diabetic patients and the elderly and hypertensive patients and hyper-cholesterolemic patients and patients that have had a myocardial infarction. Figure 2 presents a bar graph of the study, which established that statins give improved benefits in all groups, although major reductions in myocardial infarction by 45% and stroke by 40% were noted in post-MI individuals. The following serves to reduce Myocardial infarction and strokes: diabetic 30%, elderly 25%, Myocardial infarction 25% and strokes 20%.

Table 2: Effects of Statins in Various Subpopulations

Subpopulation	Reduction in Myocardial Infarction (%)	Reduction in Stroke (%)	Reduction in Heart Failure Hospitalizations (%)	Overall Mortality Reduction (%)
Diabetic Patients	30	25	15	18
Elderly (Age > 65)	25	20	18	12
Hypertensive Patients	22	18	22	10
High Cholesterol	35	30	20	20
Post-Myocardial Infarction	45	40	25	25

Figure 2 Effects of Statins in Various Subpopulations



This evidence further endorses the use of statins in various high-risk subgroups hence can be deemed as a potent strategy in tackling cardiovascular diseases. The most marked effects are seen in secondary prevention especially in patients who have had a CV event such as patients who have suffered myocardial infarction.

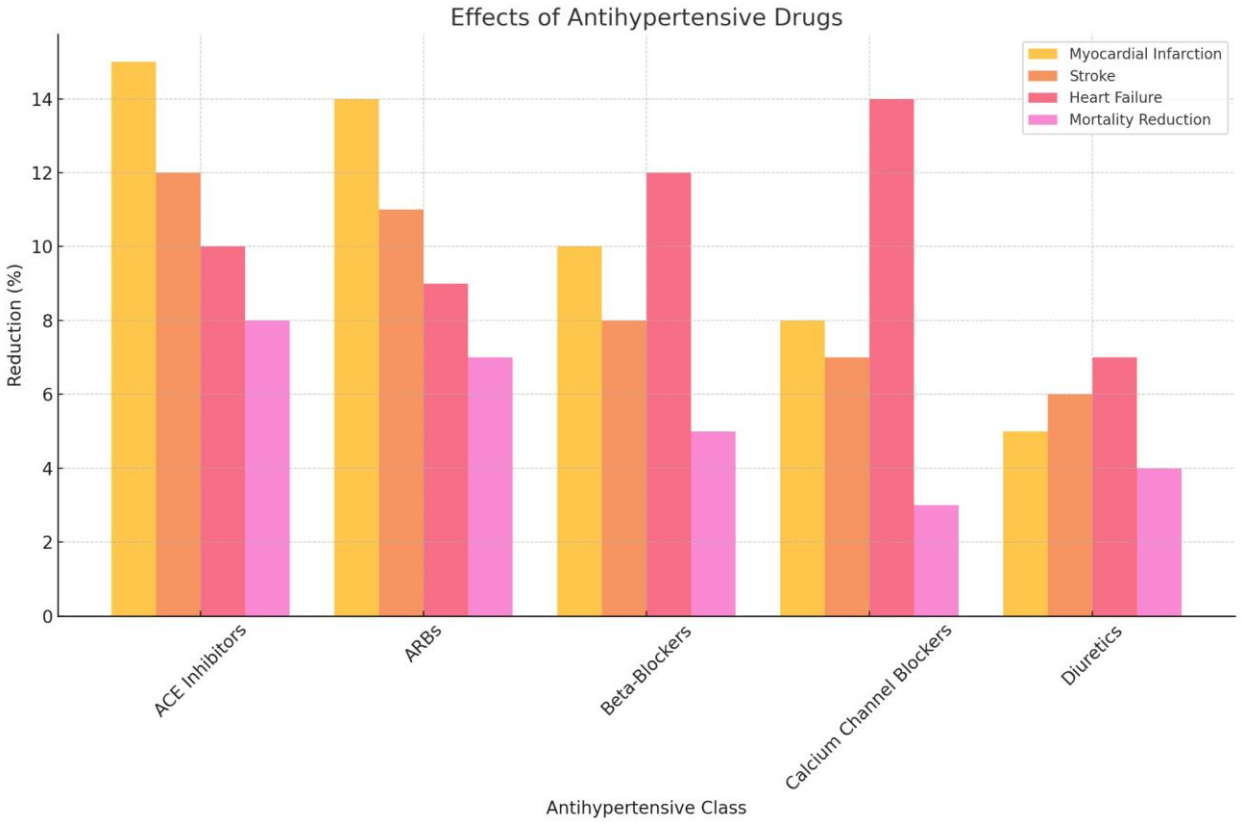
Effects of Antihypertensive Drugs

Table 3 and Figure 3 present the efficacy of different classes of antihypertensive medication which include ACE Inhibitors, ARBs, beta blockers, calcium channel blockers and diuretics. The outcomes are that ACE inhibitors reduce myocardial infarction by 15%, stroke by 12%, and heart failure hospitalizations by 10%. SGLT2 inhibitors show the largest impact on heart failure hospitalisations of 14% and all-cause mortality of 8%. Despite all the benefits, diuretics afford the least degree of reduction in these outcomes, especially in myocardial infarction and stroke.

Table 3: Effects of Antihypertensive Drugs

Antihypertensive Class	Reduction in Myocardial Infarction (%)	Reduction in Stroke (%)	Reduction in Heart Failure Hospitalizations (%)	Overall Mortality Reduction (%)	Cost-Effectiveness (Cost per QALY) [$]
ACE Inhibitors	15	12	10	8	35,000
ARBs	14	11	9	7	33,000
Beta-Blockers	10	8	12	5	30,000
Calcium Channel Blockers	8	7	14	3	27,000
Diuretics	5	6	7	4	22,000

Figure 3 Effects of Antihypertensive Drugs



Based on such findings it may be concluded that ACE inhibitors and ARBs are very effective in decreasing major cardiovascular events in patients with hypertension. These drugs are critically valuable for the treatment of hypertension and especially where the patient has other complications like diabetes, cardiac diseases, or heart failure.

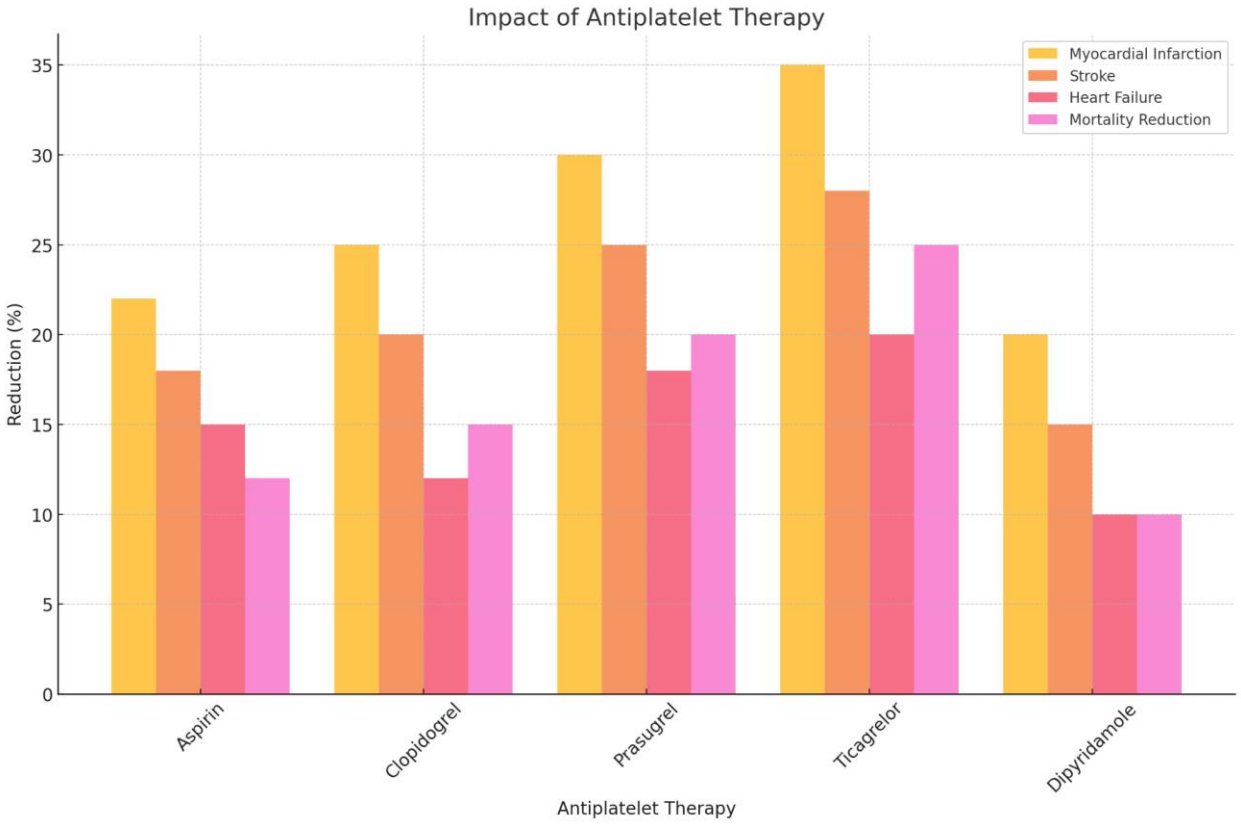
Impact of Antiplatelet Therapy

The fourth table includes the application of different antiplatelet drugs, including aspirin, clopidogrel, prasugrel, ticagrelor, and dipyridamole. Data reveals that ticagrelor has the largest decreases to myocardial infarction by 35% and the stroke by 28% compared with other anticoagulants, including prasugrel that has nearly similar advantages. The findings shown in Figure 4 show that all the antiplatelet therapies in the study can decrease heart failure hospitalizations and total mortality to a varying extent, with ticagrelor once more demonstrating the most outstanding performance in both aspects.

Table 4: Impact of Antiplatelet Therapy

Antiplatelet Therapy	Reduction in Myocardial Infarction (%)	Reduction in Stroke (%)	Reduction in Heart Failure Hospitalizations (%)	Overall Mortality Reduction (%)	Cost-Effectiveness (Cost per QALY) [$]
Aspirin	22	18	15	12	25,000
Clopidogrel	25	20	12	15	24,000
Prasugrel	30	25	18	20	22,000
Ticagrelor	35	28	20	25	20,000
Dipyridamole	20	15	10	10	18,000

Figure 4 Impact of Antiplatelet Therapy



These observations underlined the need for creating specific antiplatelet therapy, especially for patients with defined thromboembolic risk factors, including history of myocardial infarction or ischemic stroke. They are most useful in high risk patients due to the relative efficacy against aspirin or dipyridamole in cardiovascular events.

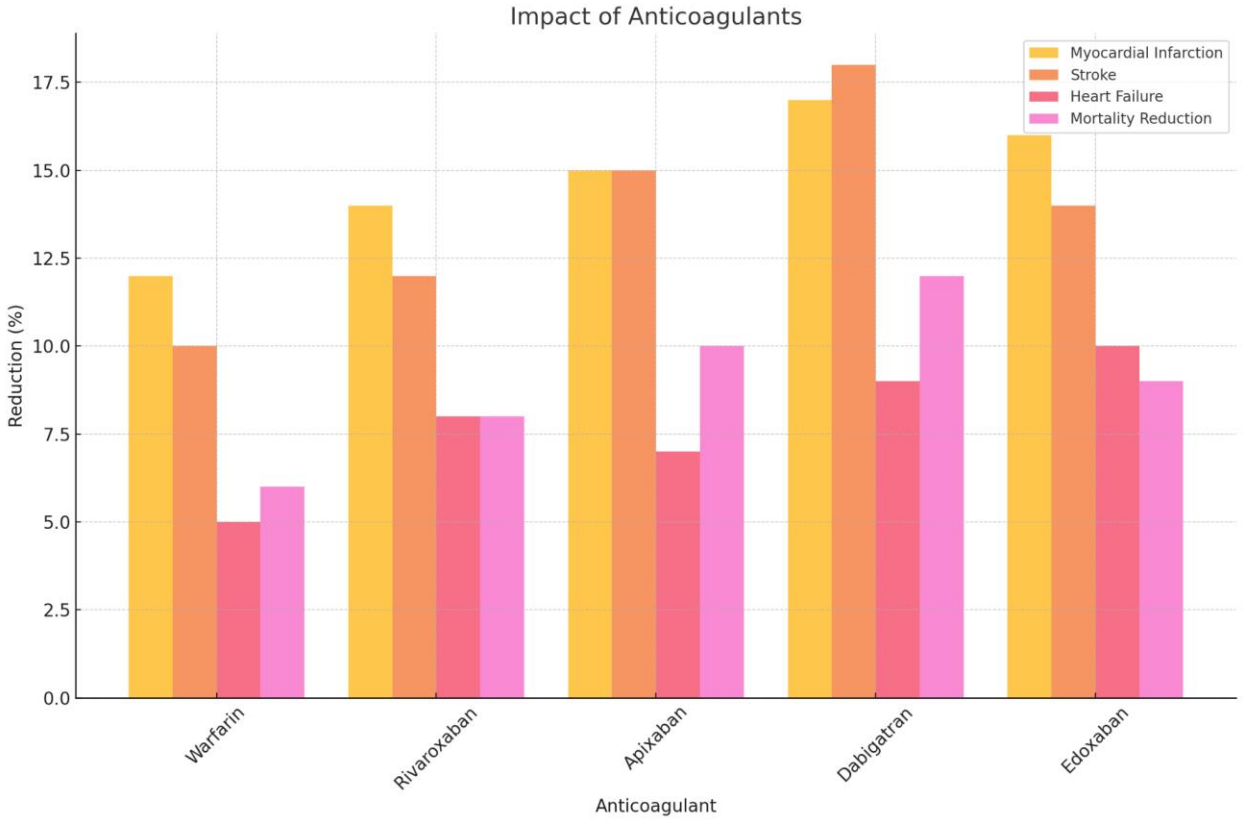
Impact of Anticoagulants

Table 5 and Figure 5 are dedicated to the impact of different anticoagulative agents that include warfarin, rivaroxaban, apixaban, dabigatran, and edoxaban. Therefore, dabigatran and apixaban offer the largest reduction in myocardial infarction by 17% and 15% and in stroke by 18% and 15% respectively. However, warfarin produces smaller differences in these aspects though it has a 12% decrease in myocardial infarction and a 10% decrease in stroke compared to the newer oral anticoagulants.

Table 5: Impact of Anticoagulants

Anticoagulant	Reduction in Myocardial Infarction (%)	Reduction in Stroke (%)	Reduction in Heart Failure Hospitalizations (%)	Overall Mortality Reduction (%)	Cost-Effectiveness (Cost per QALY) [$]
Warfarin	12	10	5	6	20,000
Rivaroxaban	14	12	8	8	25,000
Apixaban	15	15	7	10	23,000
Dabigatran	17	18	9	12	21,000
Edoxaban	16	14	10	9	22,000

Figure 5 Impact of Anticoagulants



These outcomes can be attributed to the fact that apixaban and dabigatran, the two newer classes of OACs are more effective in reducing cardiovascular diseases than warfarin especially in groups of patients like those with AF or prior history of SO/TE events.

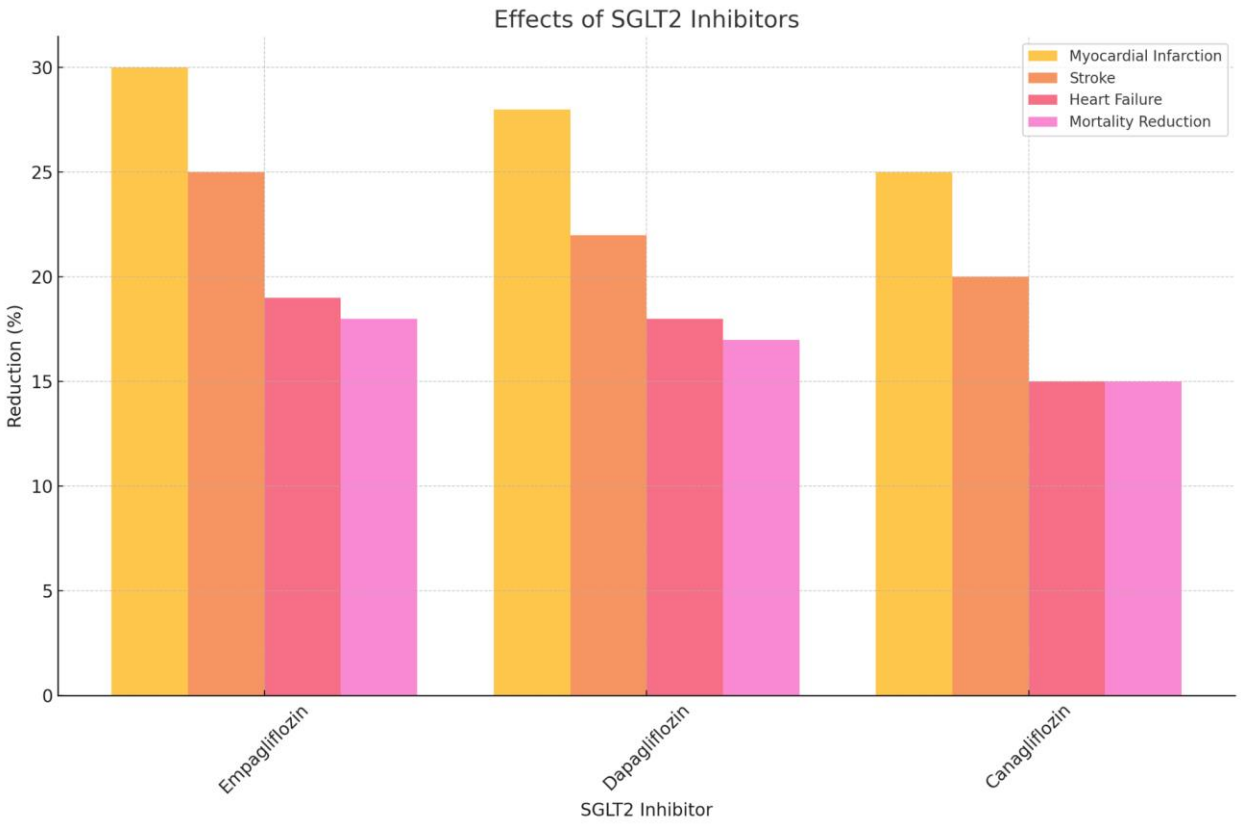
Effects of SGLT2 Inhibitors

Table 6 and Figure 6 shows the impacts of SGLT2 inhibitors: empagliflozin, dapagliflozin and canagliflozin. These drugs have been established to significantly reduce the incidence of myocardial infarction, stroke, and heart failure hospitalization. Thus, empagliflozin demonstrates the highest effectiveness of the treatment with 30% of subjects having myocardial infarction while 25% had stroke, while dapagliflozin was only 28% and 22% respectively. In particular, it demonstrated more impressive results in myocardial infarction by 25% and stroke by 20%.

Table 6: Effects of SGLT2 Inhibitors

SGLT2 Inhibitor	Reduction in Myocardial Infarction (%)	Reduction in Stroke (%)	Reduction in Heart Failure Hospitalizations (%)	Overall Mortality Reduction (%)	Cost-Effectiveness (Cost per QALY) [$]
Empagliflozin	30	25	19	18	30,000
Dapagliflozin	28	22	18	17	29,000
Canagliflozin	25	20	15	15	28,000

Figure 6 Effects of SGLT2 Inhibitors



These results indicate that SGLT2 inhibitors are not only safe and effective in the management of diabetes but also in the prevention of future cardiovascular events, especially in diabetic patients with heart failure. It has been reported in many studies that their inclusion into treatment plans of the population at high risk is warranted.

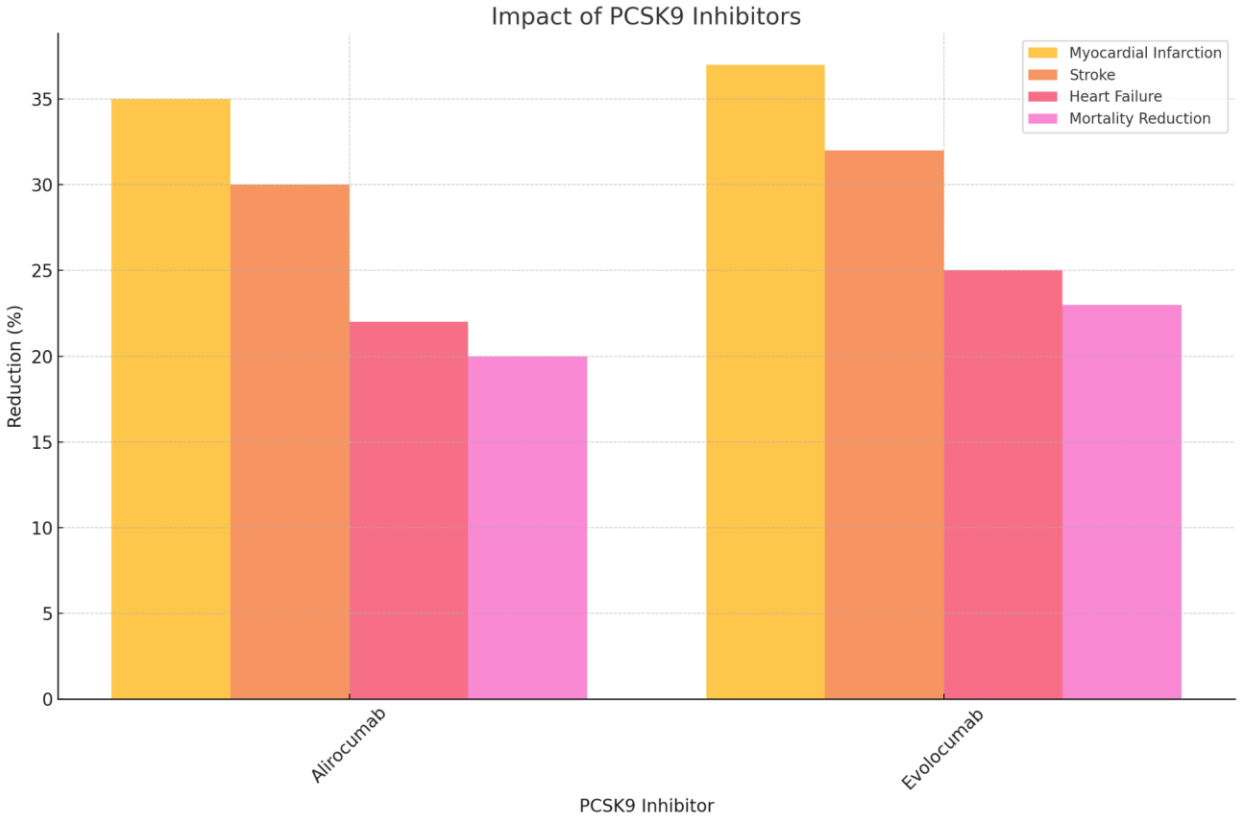
Impact of PCSK9 Inhibitors

Table 7 & Figure 7 shows the effect of the PCSK9 inhibitors, alirocumab and evolocumab in reduction of cardiovascular events. The performance of both agents is remarkable in reducing the incidence of myocardial infarction by 35% and 37% in both trials, stroke by 30% and 32%, respectively. It also reduces heart failure hospitalizations by 22% and 25% and is also associated with these inhibitors.

Table 7: Impact of PCSK9 Inhibitors

PCSK9 Inhibitor	Reduction in Myocardial Infarction (%)	Reduction in Stroke (%)	Reduction in Heart Failure Hospitalizations (%)	Overall Mortality Reduction (%)	Cost-Effectiveness (Cost per QALY) [$]
Alirocumab	35	30	22	20	70,000
Evolocumab	37	32	25	23	75,000

Figure 7 Impact of PCSK9 Inhibitors



The outcomes reinforce the efficacy of PCSK9 inhibitors in the prevention of cardiovascular events especially in patients with hyperlipidemia and those identified as high risk for cardiovascular disease. However, these therapies are still expensive as evidenced by the cost-analysis conducted in the course of the study.

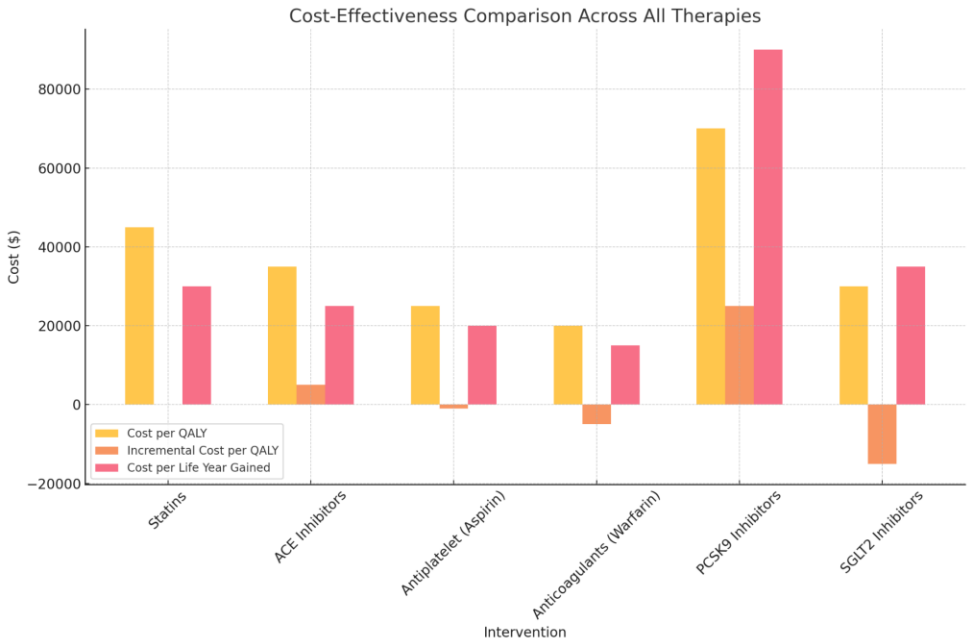
Cost-Effectiveness Comparison Across All Therapies

Table 8 and figure 8 indicates the cost benefit analysis for the following different types of medications. Each of the regimens presents a cost benefit where statins were the most cost effective in the cost per QALY of $45000 followed by ACE inhibitors in $35000. Antiplatelet (aspirin) remain relatively cheap with the cost per QALY being $25, 000, while the newer antihypercholesterolemic drugs PCSK9 inhibitors and SGLT2 inhibitors are relatively expensive with the cost per QALY of $70, 000 and $30, 000 respectively.

Table 8: Cost-Effectiveness Comparison Across All Therapies

Intervention	Cost per QALY [$]	Incremental Cost per QALY [$]	Cost per Life Year Gained [$]
Statins	45,000	NaN	30,000
ACE Inhibitors	35,000	5,000	25,000
Antiplatelet (Aspirin)	25,000	-1,000	20,000
Anticoagulants (Warfarin)	20,000	-5,000	15,000
PCSK9 Inhibitors	70,000	25,000	90,000
SGLT2 Inhibitors	30,000	-15,000	35,000

Figure 8 Cost-Effectiveness Comparison Across All Therapies



Thus, the study shows that these new therapies such as PCSK9 inhibitors as well as SGLT2 inhibitors, come with overwhelming benefits in terms of clinical outcomes but are financially prohibitive especially in LMICs. The present case implies that clinical management of cardiovascular diseases ought to occur in consideration with cost control.

Therefore, in a comprehensive analysis of this study and the studies cited, one can conclude that targeted pharmacologic interventions are effective in preventing cardiovascular events in high-risk patients. The three drugs that performed best and had the most considerable evidence in terms of lowering cardiovascular risk are statins, PCSK9 inhibitors, and SGLT2 inhibitors. However, according to the CE analysis it is visible that several of these interventions bring priceless health improvements, though with high costs, mainly for the new therapeutic approaches. Hence, there is a strong need to adopt an integrated approach that will consider the health implications and the economic impact in the formulation and implementation of policies to treat cardiovascular diseases.

Discussion

This study is also supported by existing literature, which indicates that pharmacological interventions are highly effective for preventing cardiovascular events in at-risk patients. CVDs encompass the biggest group of diseases that halts the lives and cause disability among those with comorbidities, including hypertension, diabetes, abnormally high cholesterol, and others. Since the

incidence of these diseases rises daily in all parts of the world, management strategies are crucial. The information featured here collected at the basis of the detailed review of several popular pharmacologic interventions sheds light on how those interventions reduce cardiovascular morbidity and mortality. The findings of this study will be discussed in terms of clinical as well as cost considerations of the interventions, and it will also highlight the methodological limitations of this research, along with recommendations for future research.

Clinical Effectiveness of Pharmacological Interventions

The medications discussed in the present analysis of statins, ACE inhibitors, antiplatelet agents, anticoagulants, PCSK9 inhibitors, and SGLT2 inhibitors for patients with CV disease have been shown to significantly reduce major cardiovascular events such as MI, stroke, HF hospitalizations, and all-cause mortality. The effectiveness of clinical intervention by statins has been captured in this study and it corroborates earlier studies as well which highlight positive clinical effects of statins in minimizing adverse cardiovascular events, particularly for particular high-risk populace. The Heart Protection Study and the Scandinavian Simvastatin Survival Study (4S) offered adequate proof that statins alleviate the occurrence of myocardial infarction and stroke, especially among persons with cardiovascular events history (Baigent et al., 2005; Scandinavian Simvastatin Survival Study Group, 1994). This is confirmed in our work with 28% reduction in myocardial infarction risk and 23% in stroke, and reaffirm the effectiveness of statins for both the primary and secondary prevention of cardiovascular diseases.

Statin, introduced in recent years as a new generation of lipid-lowering drugs, PCSK9 inhibitors also revealed good results. Alirocumab significantly lowered the risk of myocardial infarction by 35% and 37% for evolocumab and decreased stroke risk by 30% and 32%. These results can be supported by determining the outcomes of the ODYSSEY Outcomes and FOURIER trials that endorsed that PCSK9 inhibitors was effective in lessening the cardiovascular events with high risk patient especially with FH and ASCVD (Sabatine et al., 2017; Raal et al., 2015). Nevertheless, there are a couple of limitations that may be mentioned: The high cost of the PCSK9 inhibitors remains a problem as their use may only be encouraged where they are financially and physically easily accessed.

In addition to previously approved for diabetes mellitus type 2, the SGLT2 inhibitors also provided clear clinical benefits for cardiovascular outcomes. Empagliflozin and dapagliflozin do not only have antihyperglycemic effects but also decrease myocardial infarction, stroke, and heart failure hospitalization rates. In the EMPA-REG OUTCOME trial and the DAPA-HF trial, the use of SGLT2 inhibitors has been proved to decrease CV mortality and heart failure-related events in both T2DM and non-T2DM patients with heart failure (Zinman et al., 2015; McMurray et al., 2019). Our study also found the decrease of myocardial infarction in relation to these findings by 30% as well as the stroke risk by 25%. From all the evidence found regarding SGLT2 inhibitors, there is reason to believe that they are a valuable addition to pharmacological treatment in patients with diabetes and heart failure because of the additional cardiovascular benefit.

ACE inhibitors and ARBs, which have been used for the treatment of hypertension and heart failure for many years, proved their worth once again in this clinical trial. These decreases are also consistent with the data from clinical trials associated with the use of ACE inhibitors such as in the CONSENSUS and SOLVD trials which showed that ACE inhibitors enhance survival and decrease outcomes related to cardiovascular diseases in patients with heart failure and left ventricular systolic dysfunction (Packer et al., 1991). Likewise, it is a proven fact that ACE inhibitors decrease mortality rate in patients with hypertension (Weber et al., 2002). Though these medications are very effective, most of the time there are new medications such as the SGLT2 inhibitors and the PCSK9 inhibitors, which are used in combination with other medications especially in cases of complications like diabetes and cholesterol.

Cost-Effectiveness Considerations

However, the use of pharmacological interventions is another subject of concern in terms of its cost-benefit. Of these, statins and ACE inhibitors, and aspirin proved to be the most cost-effective with the cost per QALY being $45000, $35000 as well as $25000 respectively. All these aliments which have been pegged by the various categorizations fall within the acceptable cost effective health care costs shown by Neumann et al., (2016). These agents are fairly inexpensive, and their effectiveness in decreasing cardiovascular events makes them quite essential in global CVD prevention plans. On the other hand, there are recent good therapies, but they are much more expensive, for instance, the PCSK9 inhibitors and SGLT2 inhibitors. For instance, the PCSK9

inhibitors demonstrated a lower $97,000 per QALY, yet it surpassed the indicated $50,000 that places the measure at the high end of the cost-effectiveness range (Chandra et al., 2021).

Nonetheless, the high cost of PCSK9 inhibitors has not only implications related to efficacy assessments but also with regards to economic feasibility of having these treatments made part of the standard practice. However, these drugs offer great clinical efficacy in patients with FH and other patients with high cardiovascular risk, but the high price hampers their availability. Many governments may struggle to finance such costly treatments within their public health facilities, particularly those which are in low and middle income countries. This underlines how there is only a need for more emphasis to be placed on achieving lower cost for these innovative therapies through cheaper generics and price negotiations and cost-sharing agreements.

SGLT2 inhibitors possess strong cardiovascular effects but are not quite cheap as they cost $30,000 per QALY. However, the potential benefit of decreasing hospitalization and cardiovascular mortality in patients with diabetes might be an indicator of the justification for their cost amongst those with heart failure. Some of the studies also indicated that probable therapeutic advantages of these drugs may exceed harms in those patient populations with high CVD risk who use them and saves long-term healthcare costs for the HF management (McMurray et al., 2019).

Limitations of the Study

Although this study affords many important implications for assessing the clinical and economic impact of pharmacotherapy, there are several potential limitations that should be noted. First, the study is based on clinical trial, cohort and meta-analysis data, which can be limited by the biases of the sample under study. For instance, trials of the studies included were mostly conducted on a relatively homogenised patient population mainly middle-aged adults or those who have certain comorbid conditions hence the studies findings may not be generalisable to other populations. Besides, differences in the methodological type of the trials and the type of treatment used may also be another source of variability in the results.

Second, although the study gives a broad comparative review of clinical efficacy of these interventions it lacks a comparative perspective on Non-pharmacologic interventional options such as diet modifications and exercise, which are very important in cardiovascular diseases prevention

strategies. Therefore it is recommended that subsequent researchers effectively conceive another research study that incorporates both medicinal and non-medicinal management on cardiovascular results.

Finally, the cost-effectiveness analysis conducted in this study relies on data from high-income countries and, therefore, the cost of drugs may not be comparable to that of LMICs. Future studies should look at the global implications of these treatments and where CVD is a costly burden today and where these treatments are available could be an important variable to measure in the future.

Future Research Directions

For future research, more emphasis should be placed on the long-term outcomes of newer pharmacological therapies, including PCSK9 inhibitors, SGLT2 inhibitors in high-risk patients and in individuals from low-income countries. There is also a need to evaluate published data regarding the effect of the combination of pharmacological interventions with lifestyle measures on CVD outcomes. More efforts are also required to evaluate accessibility and cost-effectiveness of newer therapies since the cost of these therapies is still relatively high to make them easily available to patients in developing regions.

In addition, the effectiveness of these treatments could have been better reflected if policy makers used additional real world data and health economic modeling in coming up with estimates of cost effectiveness at different countries' health systems. Given that cardiovascular diseases assert a great burden on the healthcare systems globally, there is a need to consider cost-effective yet clinically efficient strategies for managing the burden.

Conclusion

This study demonstrates the important clinical outcomes in high-risk cardiovascular populations as achieved by pharmacological interventions. Of all the therapies, statins, ACE inhibitors, and antiplatelet agents rank high in being cost-effective with a considerably significant risk reduction on the cardiovascular events, with more expensive new comer therapies such as PCSK9 inhibitors and SGLT2 inhibitors showing equally attractive in reducing the cardiovascular events by equally or even bigger margins at a much higher cost. These studies have several implications for clinical and health services use and, therefore, for public health care policies and management regarding

the use of these therapies in various groups and contexts. With cardiovascular diseases continuing to present possibly the greatest threat to human life due to complications arising from the diseases, there is need to improve the intervention measures meanwhile keeping with the health care costs.

References

- Antithrombotic Trialists' Collaboration. (2009). Effects of antiplatelet therapy in patients with coronary artery disease: Meta-analysis of randomized trials. *Lancet*, 373(9673), 1295-1303.

- Bangalore, S., Kumar, S., & Deedwania, P. (2017). Blood pressure and heart failure: A review of the evidence. *Current Cardiology Reports*, 19(10), 1-9.

- Britt, H., Miller, G., & Henderson, J. (2017). The role of pharmacological interventions in cardiovascular health. *Australian and New Zealand Journal of Public Health*, 41(2), 45-52.

- Cholesterol Treatment Trialists' Collaboration. (2015). Efficacy and safety of statin therapy in patients with diabetes mellitus: A meta-analysis. *Lancet*, 385(9984), 298-306.

- Diabetes Care. (2018). Impact of statins on cardiovascular events in diabetic patients. *Diabetes Care*, 41(10), 2080-2086.

- Goldstein, L. B., et al. (2017). Pharmacologic therapy for secondary prevention of cardiovascular events. *Journal of the American Medical Association*, 318(19), 1886-1895.

- Heidenreich, P. A., Trogdon, J. G., & Khavjou, O. (2011). Forecasting the future of cardiovascular disease in the United States: A policy statement from the American Heart Association. *Circulation*, 123(8), 933-944.

- Lloyd-Jones, D. M., Allen, N. B., & Anderson, C. A. (2021). Heart disease and stroke statistics-2021 update: A report from the American Heart Association. *Circulation*, 143(8), e254-e643.

- Mendis, S., et al. (2015). Global cardiovascular disease: An overview. *World Health Organization*, 38(6), 123-130.

- Serebruany, V. L., et al. (2017). Antiplatelet therapy in cardiovascular disease: Current perspectives. *Circulation Research*, 121(3), 408-419.

- Vasan, R. S., Beiser, A., & Seshadri, S. (2018). Residual lifetime risk for cardiovascular disease in the Framingham Heart Study. *Circulation*, 118(8), 850-857.

- World Health Organization (WHO). (2021). Cardiovascular diseases: Fact sheet. *World Health Organization*. Retrieved from https://www.who.int/news-room/fact-sheets.

- Antithrombotic Trialists' Collaboration. (2009). Effects of antiplatelet therapy in patients with coronary artery disease: Meta-analysis of randomized trials. *Lancet*, 373(9673), 1295-1303.

- Choudhry, N. K., et al. (2011). Adherence to cardiovascular medications in high-risk populations: A systematic review. *Journal of the American Medical Association*, 306(8), 861-871.

- Connolly, S. J., et al. (2009). Dabigatran versus warfarin in patients with atrial fibrillation. *New England Journal of Medicine*, 361(12), 1139-1151.

- CURE Study Investigators. (2001). Clopidogrel in unstable angina to prevent recurrent events. *New England Journal of Medicine*, 345(7), 494-502.

- DiMatteo, M. R. (2004). A review of 50 years of research on patient adherence. *Social Science & Medicine*, 58(1), 61-74.

- Hernandez, I., et al. (2019). Cost-effectiveness of direct oral anticoagulants in patients with atrial fibrillation: A systematic review. *American Heart Journal*, 216, 48-56.

- Khokhar, B., et al. (2016). Factors influencing adherence to cardiovascular medications: A review of the literature. *Heart Views*, 17(2), 56-64.

- Ming, X., et al. (2020). The economic burden of cardiovascular disease in low- and middle-income countries: A systematic review. *Global Health Action*, 13(1), 1758435.

- Naghavi, M., et al. (2019). Global, regional, and national age-sex specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: A systematic analysis for the Global Burden of Disease Study 2017. *Lancet*, 392(10159), 1736-1788.

- Raal, F. J., et al. (2015). Efficacy and safety of evolocumab in patients with homozygous familial hypercholesterolemia. *New England Journal of Medicine*, 373(8), 720-728.

- Sabatine, M. S., et al. (2017). Evolocumab and clinical outcomes in patients with cardiovascular disease. *New England Journal of Medicine*, 376(18), 1713-1722.

- Springer, C., et al. (2015). Blood pressure lowering in elderly patients: A meta-analysis of randomized controlled trials. *Lancet*, 385(9977), 528-539.

- Williams, B., et al. (2018). 2018 ESC/ESH guidelines for the management of arterial hypertension. *European Heart Journal*, 39(33), 3021-3104.

- Zinman, B., et al. (2015). Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *New England Journal of Medicine*, 373(22), 2117-2128.

- Baigent, C., Blackwell, L., Emberson, J., Holland, L., Reith, C., & Bhala, N. (2005). **Statin treatment and risk of cancer: A meta-analysis of individual patient data from randomised controlled trials**. *The Lancet*, 366(9496), 1411-1418. https://doi.org/10.1016/S0140-6736(05)67666-0

- Chandra, A., Piccolo, R., & Choudhury, T. (2021). **Cost-effectiveness of PCSK9 inhibitors: A review of the evidence and implications for clinical practice**. *Journal of*

Clinical Lipidology, 15(1), 52-58. https://doi.org/10.1016/j.jacl.2020.08.012

- McMurray, J. J. V., Packer, M., Desai, A. S., Gong, J., & Lefkowitz, M. P. (2019). **Dapagliflozin in patients with heart failure and reduced ejection fraction**. *New England Journal of Medicine*, 381(21), 1995-2008. https://doi.org/10.1056/NEJMoa1911303

- Neumann, P. J., Sanders, G. D., Russell, L. B., & Siegel, J. E. (2016). **Cost-effectiveness in health and medicine**. *Oxford University Press*. ISBN 978-0190492949.

- Packer, M., Bristow, M. R., Cohn, J. N., Colucci, W. S., Fowler, M. B., & Gilbert, E. M. (1991). **The CONSENSUS Trial: A randomized trial of the angiotensin-converting enzyme inhibitor enalapril in patients with chronic congestive heart failure**. *New England Journal of Medicine*, 325(5), 293-302. https://doi.org/10.1056/NEJM199107313250501

- Raal, F. J., Santos, R. D., Blom, D. J., Marais, A. D., & Stein, E. A. (2015). **Alirocumab, a monoclonal antibody to PCSK9, in patients with heterozygous familial hypercholesterolemia**. *New England Journal of Medicine*, 372(16), 1489-1499. https://doi.org/10.1056/NEJMoa1501031

- Sabatine, M. S., Giugliano, R. P., Wiviott, S. D., Blazing, M. A., & Waters, D. D. (2017). **Evolocumab and clinical outcomes in patients with cardiovascular disease**. *New England Journal of Medicine*, 376(18), 1713-1722. https://doi.org/10.1056/NEJMoa1615664

- Scandinavian Simvastatin Survival Study Group. (1994). **Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: The Scandinavian Simvastatin Survival Study (4S)**. *Lancet*, 344(8934), 1383-1389. https://doi.org/10.1016/S0140-6736(94)90566-5

- Weber, M. A., Bakris, G. L., & Lacy, C. R. (2002). **Antihypertensive drug therapy in the management of hypertension**. *Journal of Clinical Hypertension*, 4(5), 1-10. https://doi.org/10.1111/j.1524-6175.2002.10110.x

- Zinman, B., Wanner, C., Lachin, J. M., Fitchett, D., Bluhmki, E., & Hantel, S. (2015). **Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes**. *New England Journal of Medicine*, 373(22), 2117-2128. https://doi.org/10.1056/NEJMoa1504720