Perceived impact of reimbursement policies on accessibility to PCSK9 inhibitors in the South African private healthcare sector.

BY

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DECLARATION

I Plossie Ngobeni hereby declare that this research report is my own work except as indicated in the references and acknowledgement. It has not been submitted in the past for any other degree or examination in this or any other university.

…….

(Signature of candidate)

At…....……. day of …….2024

DEDICATION

To my best friend and supportive grandmother, Gelly Ngobeni.

ACKNOWLEDGEMENTS

“For I know the plans I have for you, declares the Lord, plans to prosper you, and not to harm you, plans to give you hope and a future” Jeh 29:11

My utmost gratitude goes to my family, friends and colleagues who have shown unwavering support throughout out this journey. It would not have been possible without having every single one of them in my corner. I do not take it lightly and will be sure to pay it forward.

To my supervisor, Dr Totowa, thank you for holding my “sweaty little paw”. Your guidance and tenacity to deliver excellency came in handy during this journey.

To all the respondents who contributed to this research, I thank and appreciate you.

ABSTRACT

The South African private healthcare sector is confronted with the challenge of the limitation of adoption and access to proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i), a cholesterol-lowering medicine. At the heart of this is the complex nature of the reimbursement policies that are failing to yield favourable outcomes for patients, investors and practitioners alike. The long-term implications of these current medical reimbursement policies include resistance to medical cover, a decline in innovative drug adoption, a decline in optimal medical outcomes, decline in human capital development, loss in productivity, global drug companies pulling out of the South African market, and an extra financial burden to the patients.

This study, employing a qualitative approach, aims to investigates barriers limiting adoption and access to PCSK9i in the South African private healthcare sector with a focal focus on reimbursement policies implemented by medical funders and insurances. The study also explores the market access and commercial success of PCSK9i hindered by reimbursement policies. Through semi-structured interviews as the main method of primary data collection, and using a thematic analysis, the explores the barriers, challenges and burdens that impede market access and entry for the PCSK9i and how this affects the economy, commercial success and stakeholders involved.

The findings of this study indicate that reimbursement policies can have far-reaching impacts on businesses and the economy, affecting everything from cost management and innovation to employee satisfaction and market dynamics. Businesses must carefully navigate these policies to optimize their operations and remain competitive in the marketplace. Finally, the study proposes evidence-based recommendations for broadening accessibility to PSCK9i. These include encouraging medical funders to adopt a “risk-sharing” concept, value-based healthcare, patient advocacy groups, and review single exit pricing regulations. The significance of these recommendations is their potential to aid policy makers and other important stakeholders in decision making and ensuring access to the most deserving hypercholesteremia population.

Key words: PSCK9i, private healthcare, reimbursement policies, South Africa

Table of Contents

LIST OF FIGURES 8

LIST OF TABLES 8

CHAPTER 1: OVERVIEW OF THE STUDY 9

1.1 Introduction 9
1.3 Statement of the Problem 11
.4 Research purpose statement 12
1.5 Research questions 12
1.6 Research objectives 13
1.7 Assumptions, limitations and delimitations 13
1.8 Significance of the study 14
1.9 Outline of the study 15
1.9 Chapter summary 16

CHAPTER 2: LITERATURE REVIEW 17

2.1 Introduction 17
2.2 The innovative drug market access landscape 17
2.3 Innovative drug market access Then and Now. 18
2.4 What market access looks like in developed vs emerging markets. 18
2.5 Emerging stakeholders in PCSK9i market access 19
2.5.1 Payor (reimbursement policies) 19
2.5.2 Patients 19
2.5.3 Pharmacies and Physicians 19
2.5.4 Regulatory 20
2.5.5 Pharmaceutical firms 20
2.6 Barriers limiting access to PCSK9i. 20
2.6.1 Reimbursement policies 20
2.6.2 Single exit pricing 22
2.7 Reimbursement policies that limit access to innovative drugs in South Africa can have several potential impacts on the country's Gross Domestic Product (GDP), both direct and indirect. 22
2.8 Strategies reimbursement policies can implement to broaden access. 24
2.8.1 Value based reimbursement. 24
2.8.2 Outcome-based agreements 24
2.8.3 Patient assistance programs 24
2.8.4 Stakeholder engagement and collaboration 25
2.8.5Tiered pricing and differential reimbursement 25
2.9 Imperative aspects of market access and commercial success of innovative drugs 25
2.9.1 Pricing and reimbursement 26
2.9.3 Monitoring and Adaption 26
2.9.4 Stakeholder Engagement 26
2.9.5 Value shaping and demonstration 26
2.9.6 Market analysis, strategy and entry 27
2.9.7 Conceptual framework 27
2.3 Theoretical framework of the study: Institutional Theory 28

CHAPTER 3: DATA COLLECTION AND ANALYSIS 30

3.INTRODUCTION 30
3.1. RESEARCH METHODOLOGY 30
3.2 RESEARCH DESIGN 31
3.3 DATA COLLECTION METHODS 31
3.4 POPULATION AND SAMPLING 32
3.5 POPULATION 32
3.6 DATA COLLECTION AND ANALYSIS 34
3.7 STRENGTHS OF THE METHODOLOGY 35
3.7.1 CREDIBILITY 35
3.7.2 CONFIRMABILITY 35
3.7.3 DEPENDABILITY 35
3.7.4 TRANSFERABILITY 36
3.7.5 ETHICAL CONSIDERATIONS 36
3.8 ADMINISTRATIVE LIMITATIONS 36
3.9 CONCLUSION 37

CHAPTER 4: FINDINGS AND DISCUSSIONS 38

4. INTRODUCTION 38
4.1 FINDINGS 38
4.2 DISCUSSION OF KEY FINDINGS 40
4.2.1FACTORS LIMITING ACCESS TO PCSK9 INHIBITORS IN THE SOUTH AFRICAN PRIVATE HEALTHCARE SECTOR 40
4.3 STRATEGIES TO BROADEN ACCESS TO PCSK9 INHIBITORS. 44
4.4 CONCLUSION 47

CHAPTER 5: SUMMARY, RECOMMENDATIONS, AND CONCLUSION 48

5. INTRODUCTION 48
5.1 SUMMARY OF THE RESEARCH 48
5.2.1 TO IDENTIFY BARRIERS LIMITING ACCESS TO THE PCSK9 INHIBITORS. 49
5.2.2 ASSESS THE LONG-TERM CLINICAL AND ECONOMIC IMPLICATIONS OF THESE BARRIERS. 49
5.2.3 TO PROPOSE EVIDENCE-BASED RECOMMENDATIONS FOR BROADENING ACCESS TO PSCK9 INHIBITORS. 50
5.3 CONTRIBUTIONS 51
5.3.1 PRACTICAL CONTRIBUTIONS 51
5.3.2 THEORETICAL CONTRIBUTION 51
5.4 LIMITATIONS 51
5.4.1 DATA AVAILABILITY 51
5.4.2 SAMPLE SIZE 52
5.4.3 BIAS 52
5.4.4 TEMPORAL FACTORS: 52
5.5 RECOMMENDATIONS 52
5.6 OVERALL CONCLUSION 53

BIBLIOGRAPHY 54

LIST OF FIGURES

- Figure 1.1……10
- Figure 1.2……13
- Figure 3.1……25

LIST OF TABLES

- Table 4.1……33

CHAPTER 1: OVERVIEW OF THE STUDY

1.1 Introduction

Understanding the impact of reimbursement policies on accessibility to proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) in the South African private healthcare sector is essential for informing evidence-based decision-making by policymakers, healthcare providers, insurers, and pharmaceutical companies. PCSK9i are a class of drugs that reduce low-density lipoprotein (LDL). Hajar (2019) highlights the history of PCSK9 dates back to research by French and Canadian scientists who discovered that a gain-of-function mutation in a particular gene that is found on chromosome 1 was responsible for familial hypercholesterolemia. This means that the disorder could be passed down through families. Over the years, numerous scientific findings have led to the development of important strategies that are aimed at inhibiting the protein responsible for hypercholesterolemia through (Hajar, 2019)the use of monoclonal antibodies (Hajar, 2019). This has led to the development of PCSK9i, which are currently the recommended “appropriate second-line or third-line agents or as an alternative therapy in cases of complete statin intolerance, for patients with established atherosclerotic CVD or familial hypercholesterolemia with persistent hypercholesterolemia” Despite studies demonstrating the efficacy of PSCK9i in South Africa (Klug and Raal, 2020) there are some complexities regarding their accessibility and adoption. While this is may be due in part to their exorbitant and thus prohibitive costs (Blom., 2020) other factors including their reimbursement policies are a huge factor.

The prevalence of hypercholesteremia in South Africa is 76.7% (Masilela, 2022). This kind of health burden has a huge impact on the economy and essentially gross domestic product (GDP) markers. Loss in productivity can invite unfavourable economic bottlenecks such as an increased unemployment rate, and loss in special skills that drive and empower the economy. With the high prevalence of hypercholesteremia as outlined, it is imperative to broaden access to safeguard the economy, preserve special skills, and to attract global pharmaceutical companies to invest in the South African economy.

Reimbursement policies delineate the terms under which PCSK9i are covered, encompassing eligibility criteria, pricing structures, and reimbursement mechanisms (Blom., 2020). The implementation of these policies carries significant ramifications for patient access to PCSK9i, as well as the financial sustainability of healthcare providers, insurers and essentially impedes the economic growth of an emerging country like South Africa.

Reimbursement policies that limit access to innovative drugs can have complex and multifaceted impacts on South Africa's GDP, affecting healthcare expenditure, productivity,

innovation, human capital development, and international competitiveness (Bruen *et al*., 2016). Policymakers must carefully balance the need to control healthcare costs with the imperative to ensure timely access to effective treatments that can improve health outcomes and support economic growth.

In the context of South Africa's demography, most persons with hypercholesteremia and familial hypercholesteremia (FH) are black (Marais, 2019). Assuming that 80% of untreated hypercholesteremia and FH persons will experience coronary disease before the age of 60 years, there are 160 000 at-risk persons in whom early treatment could save many life-years (Marais, 2021). Therefore, understanding the impact of medical reimbursement policies on the accessibility to PCSK9i is imperative. As the South African private healthcare sector strives to balance the demands of a growing hypercholesteremia population with limited resources, the role of reimbursement policies in shaping access to innovative therapies such as PCSK9i becomes a pivotal area of investigation.

Figure 1.1: South Africa's total number of PSCK9 inhibitors applications in November 2023.

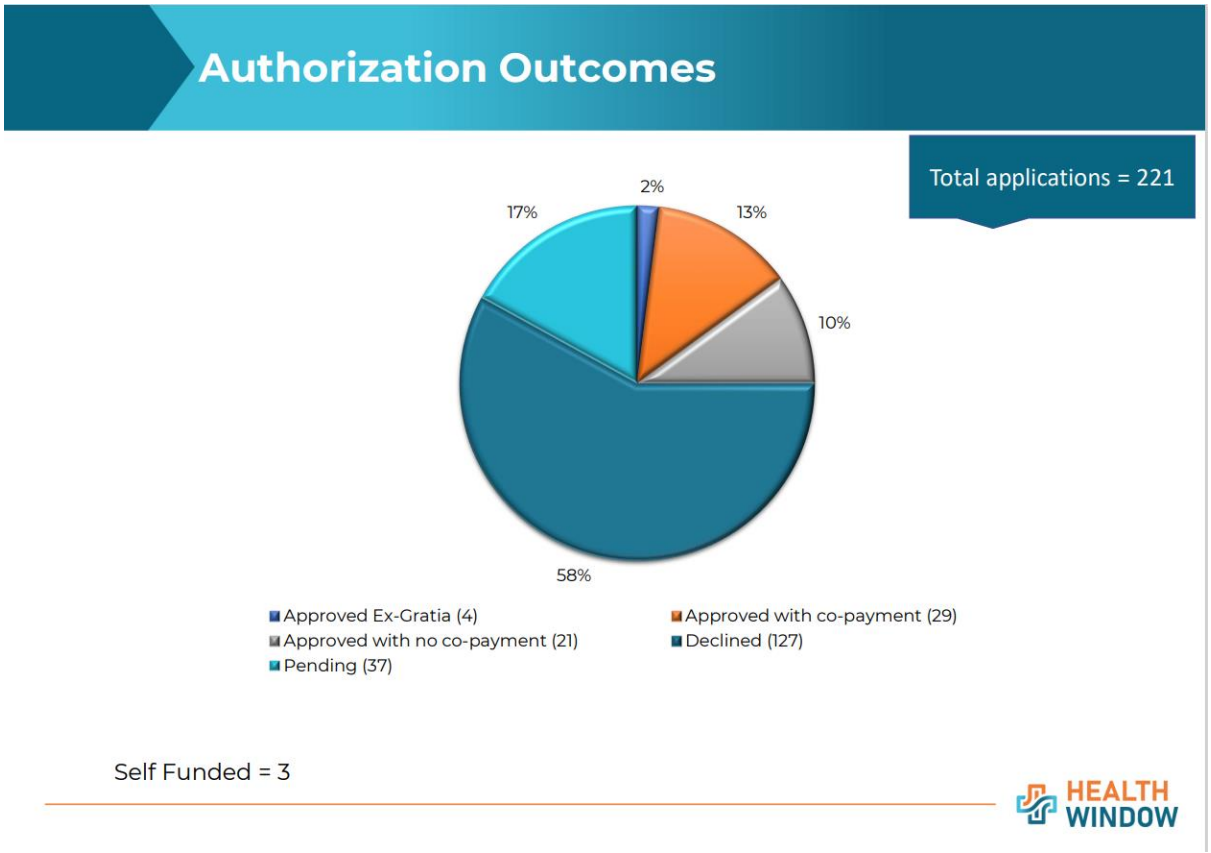


Image sourced from HEARTBEAT SA November report.

The private healthcare sector only covers 18% of the South African population (Mhlanga, 2020), however the prevalence and hypercholesteremia population is far bigger than what is displayed on figure 1.1. This report merely focuses on the private sector for the convenience

of data availability. Out of 221 applications for PCSK9i in the month of November 2023, only 9% applications were approved and fully funded by the medical funders, 13% approved with a 50% co-payment, 16% are pending cases and 58% are declined (Heartbeat SA PSP).

This study seeks to investigate the root causes of high declines, exorbitant co-payments and pending cases that are most likely to be declined Additionally, the study aims to investigate the complexities surrounding reimbursement policies for PCSK9i, exploring their influence on market access, economy, pharmaceutical industry success factors, product adoption and more importantly, the research and development pipeline of innovative drugs. By examining the interplay between policy frameworks, regulation, and pharmaceutical strategies, this study seeks to identify opportunities for improving the accessibility and affordability of PCSK9i while ensuring the long-term sustainability of the healthcare system.

PCSK9i	New class of drugs that lower low-density lipoprotein.
Private Healthcare	Largely funded through individual contribution to medical aid.
Reimbursement Policies	Fixed amount of money per covered individual paid in advance to healthcare provider.
South Africa	A country on the southernmost tip of the African continent.

1.3 Statement of the Problem

Despite the proven efficacy of PCSK9i in managing hypercholesterolemia, challenges related to reimbursement policies, high costs, drug pricing regulations, and inadequate awareness persist, hindering widespread access and adoption to these innovative drugs (Bruen et al., 2016). By understanding the multifaceted nature of these challenges and identifying effective solutions, this research seeks to contribute valuable insights to policymakers, healthcare professionals, and pharmaceutical stakeholders, facilitating the optimization of cardiovascular care and the reduction of the South African burden of hypercholesterolemia.

Despite the proven efficacy of PCSK9 inhibitors in managing hypercholesterolemia, challenges related to reimbursement policies, high costs, drug pricing regulations, and inadequate awareness persist, hindering widespread access to these innovative drugs. This research aims to investigate and propose comprehensive strategies that address reimbursement policies, innovative drug cost, economic, regulatory, and educational barriers, with the goal of enhancing access to PCSK9 inhibitors for eligible patient populations. By understanding the multifaceted nature of these challenges and identifying effective solutions, this research seeks to contribute valuable insights to policymakers, healthcare professionals,

and pharmaceutical stakeholders, facilitating the optimization of cardiovascular care and the reduction of the global burden of hypercholesterolemia.

LDL-Cholesterol is a major risk factor for cardiovascular disease, which is the leading cause of death in South Africa. Specialized therapies for LDL-Cholesterol are often expensive and may not be accessible to all patients. Reimbursement policies play a critical role in determining the affordability and accessibility of specialized LDL-Cholesterol therapies in the private healthcare sector in South Africa.

Treating cholesterol has become extremely complex due to various molecules available. With this said, innovative molecules like the PSCK9i have brough about a solution in curbing life threatening consequences of high cholesterol such as strokes. The main stumbling block remains to be access. Medical funders are adamant in including these innovative molecules into their formulary lists, making it almost impossible for medical aid beneficiaries to access these lifesaving molecules. PCSK9i are not offered to all patients with high LDL-Cholesterol but rather those that are resistant to the traditional statins which are readily available to the LDL-Cholesterol patient population. PCSK9i were developed with the intention of lowering LDL-Cholesterol in the niche population that suffers from elevated and uncontrolled levels.

This research seeks to investigate possible access options that all stakeholders can successfully adopted to ensure that these monoclonal antibodies are accessible to the deserving patient. By bridging the gap, more elevated LDL-Cholesterol cases will be curbed, leading to a drop in deaths caused by uncontrolled LDL-Cholesterol. Opening access for this market will result in better clinical outcomes, more volumes sold as product adoption will increase, price reduction as this could possibly invite more market entrants.

.4 Research purpose statement

The study seeks to investigates barriers limiting adoption and access to PCSK9i in the South African private healthcare sector with a focal focus on reimbursement policies implemented by medical funders and insurances. The study also explores the market access and commercial success of PCSK9i hindered by reimbursement policies.

1.5 Research questions

The questions that will guide this research include:

- What are the barriers to PCSK9i market access and commercial success in an emerging market like South Africa?
- What key strategies can reimbursement policies implement to broaden PCSK9i market access?

1.6 Research objectives

The primary objectives of this research are:

- To Investigate the barriers that limit access and adoptability to PCSK9 inhibitors.
- To assess the long-term economic implications of these policies on all stakeholders involved in ensuring access (medical insurers, pharmaceuticals, regulatory.

1.7 Assumptions, limitations and delimitations

One of the primary limitations of this study is the potential insufficiency of data specifically focused on reimbursement policies and the accessibility of PCSK9i in the South African private healthcare sector. The perception of respondents regarding the impact of reimbursement policies on PCSK9i accessibility may be influenced by various biases, including personal experiences, beliefs, and interests. Reimbursement policies and healthcare dynamics are subject to change over time due to legislative, regulatory, and economic factors. Therefore, the findings may be limited by the temporal context in which data is collected.

This study assumes that reimbursement policies pertaining to PCSK9i in the South African private healthcare sector are implemented consistently across different private healthcare facilities and insurance providers. Differences in policy interpretation and implementation may influence the perceived impact on accessibility. Additionally, this study recognises that while perceptions provide valuable insights, they may not always align with objective measures of accessibility to PCSK9i in the South African private healthcare sector.

This study delimits its scope to the private healthcare sector and thus, excludes the public sector. While the public sector plays a significant role in healthcare delivery in South Africa, focusing exclusively on the private sector allows for a more targeted examination of reimbursement policies and accessibility dynamics within this context.

Figure 1.2: Problem tree to systematically analyse the cause-and-effect relationship of limited access to PCSK9 inhibitors in the South African private healthcare.

Impact
- Poor adoption and access to innovative drugs.
- Poor International reputation & investment.
- Productivity loss
- Reduced human capital development.
- Increased healthcare expenditure

Main Problem
- Reimbursement Policies limiting access to PCSK9 inhibitors.

Root Causes -To be Analyzed.

1.8 Significance of the study

Hypercholesterolemia is a significant risk factor for cardiovascular diseases, with a high prevalence of 76.7% in South Africa (Masilela, 2022). PCSK9i represent a novel and effective therapeutic option for managing hypercholesterolemia, especially in patients with familial hypercholesteremia (Marais, 2021) or those intolerant to traditional lipid-lowering therapies. However, despite their clinical efficacy, accessibility to PCSK9i in the South African private healthcare sector may be hindered by factors such as reimbursement policies. Investigating the perceived impact of these policies on accessibility is crucial for understanding access barriers and identifying opportunities for improvement in healthcare expenditure.

Access to innovative therapies like PCSK9i should be equitable across different segments of the population. However, disparities in healthcare access and affordability may exist, particularly in the private healthcare sector where access is often dependent on insurance coverage and financial means. By examining the influence of reimbursement policies on PCSK9i accessibility, this research can contribute to efforts aimed at promoting healthcare equity and ensuring that all eligible patients have access to effective treatments, regardless of socio-economic status (Delobelle, 2013).

1.9 Outline of the study

This research report is into five chapters. These are outlined as follows:

Chapter 1: Introduction

This chapter provides a background and introduction of the study. It outlines the rationale and significance for the study and gives a comprehensive overview of the study aim, objectives and research questions that guide the realisation of the said objectives. The chapter also outlines the problem statement as well as the assumptions, limitations and delimitations.

Chapter 2: Literature review

This chapter provides a comprehensive review of contemporary literature on PCSK9i as an instrument for the management of hypercholesterolemia, as well as an overview of the South African private health landscape in relation to this. Theoretical and legislative frameworks for PCSK9i access and reimbursement policies are explored.

Chapter 3: Research methodology

This chapter details the research methodology and design that was used in the study. It provides an overview of the sample population and sampling techniques that were used in the study. The data collection methods, data analysis techniques, as well as the strengths of the utilized methodology are outlined. Ethical considerations related to the research are also discussed.

Chapter 4: Findings and discussions

This chapter provides the results/findings of the study from the semi-structured interviews and secondary data that was utilised in the study. It also provides a comprehensive discussion in which the findings of the study are analysed and interpreted.

Chapter 5: Summary, recommendations and conclusion

The final chapter of this study provides a summary of the findings, linked to the study's aims and objectives as outlined in the introductory chapter. It further provides recommendations for strengthening reimbursement policies in the South African private healthcare sector to ensure accessibility and adoption of PCSK9 inhibitors**.** Potential areas for further study are also explored.

1.9 Chapter summary

This chapter provided a comprehensive summary of the research objectives and how it aims to investigate the barrier impeding accessibility to PCSK9i indicated for hypercholesteremia. It also highlights the high prevalence of hypercholesteremia in South Africa and why it is imperative to ensure access to innovative and noble therapies like the PCSK9i. This chapter outlines the background, statement of the problem, research purpose statement, research questions, objectives and finally the limitations, delimitations and assumptions.

Chapter 2: Literature review

2.1 Introduction

This literature review aims to unpack the empirical evidence reported in prior literature related to this study, with the purpose of investigating barriers limiting adoption and access to PCSK9i in the South African private healthcare sector with a focal focus on reimbursement policies implemented by medical funders and insurers. The study also explores the market access and commercial success of PCSK9i hindered by reimbursement policies. Lastly, an empirical review aids to investigate and propose comprehensive strategies that address economic, regulatory, and educational barriers, with the ultimate goal of enhancing access to PCSK9i for eligible patient populations. This literature review examines the existing body of research on how medical reimbursement policies may act as barriers to accessing innovative care in South Africa, with a specific focus on challenges related to affordability, coverage limitations, and regulatory frameworks.

2.2 The innovative drug market access landscape

With the world economy in decline, governments in developing countries are attempting to rein in their escalating healthcare expenditure (World Health Organization, 2023), which has led to a significant increase in focus on market access. Government regulations pertaining to the approval of new products have become more stringent as a result. Consequently, the obstacles that pharmaceutical businesses have in effectively addressing the unique issues raised by different government agencies, regulatory bodies, and stakeholders are growing. However, because only the biggest pharmaceutical corporations can afford to fund the substantial research and development needed and take on the associated financial risk, the process of developing new medications has been limited to them (Llamas, 2015). This has seriously harmed patients in need by significantly delaying the release of innovative products into the market (Raposo, 2020). The need for market access functions is growing, particularly in emerging nations where the ever-changing and complex healthcare landscape makes it difficult to approve and adopt new products. Additionally, emerging markets are today's growth engines (Riley, 2023), thus success in these areas is crucial for most pharmaceutical organisations. Pharmaceutical firms have historically relied heavily on research and development, marketing, and sales to achieve commercial success (Llamas, 2015). In order to increase product acceptance, this conventional market access strategy, which is highly linear, entails interacting with doctors, pharmacists, and regulatory agencies (Zarei *et al*., 2022). However, it only covers price and reimbursement operations. On the other hand, we describe market access as a procedure that guarantees quick and continuous access to the

product at the appropriate cost for all eligible patients. This is a broad notion that encompasses various tasks from the corporate, marketing, supply chain, legal, and medical aspects of a corporation (Kumar, 2014)

2.3 Innovative drug market access Then and Now.

Pharmaceutical firms have historically placed a strong emphasis on the push approach to guarantee the commercial success of their goods. To approve a medicine, one had only to provide the regulatory bodies with information on its safety, effectiveness, and tolerability. After receiving permission, the medication was distributed by pharmacies and promoted to the intended doctors (Raposo, 2020). Pharmacies, regulatory bodies, and doctors were the only parties with whom market access could be achieved. However, over the years, market access has taken a turn, and it is mostly reliant on two important and determining factors. The first is that South Africa has significant growing rates of chronic illness, an ageing population, and rising expenses for novel treatments that are all contributing to rising healthcare costs (Solanki *et al*., 2019). The second is a challenging environment for reimbursement and pricing. These two factors have led to change in market access dynamics and stakeholders involved in ensuring access and commercial success of innovative drugs (Kumar, 2014).

2.4 What market access looks like in developed vs emerging markets.

Developed markets have seen a steady increase in the relevance of the market access role as regulatory and reimbursement policies have become more cognizant of the need for value over current treatments (Kumar, 2014). According to Corvino *et al*., (2022) pharmaceutical firms are beginning to integrate the market access function as a core component of their businesses in order to manage this ever-changing regulatory landscape. Still, very few businesses today have a specialised market access team with well-defined roles and duties. Instead, a divided model is currently used by most pharmaceutical corporations, with sales, marketing, and regulatory divisions sharing responsibility for market access (Kumar, 2014). On the other hand, for developing markets the structure of market access remains inferior to that of developed markets. Nonetheless, the importance of market access functions has grown as a result of shifting healthcare regulations and the market environment. In spite of this, pharmaceutical firms are now concentrating on distinct aspects of market access, such as price, channel, stakeholders, and government bodies, without taking a comprehensive approach to address all aspects at once (Kumar, 2014). Furthermore, compared to developed economies, these markets have more complicated healthcare laws and regulatory

frameworks. As a result, pharmaceutical companies struggle to pinpoint the appropriate parties to involve in the medication approval procedure (Kumar, 2014)

2.5 Emerging stakeholders in PCSK9i market access

Jeffery (2009) highlights gaining entry to a market entail interacting with all of its constituents as well as many stakeholders who have an influence on the commercialization process as a whole. Customised procedures and features are therefore necessary to involve various stakeholders in an efficient manner.

2.5.1 Payor (reimbursement policies)

Without a question, the most prominent stakeholder is the payer. When it comes to the cost and reimbursement of any new medication, the payer has the most influence. Payers receive advice from specialised health technology evaluation organisations regarding formulary and reimbursement choices. Payers also actively contribute to the development of treatment protocols and impact doctors' prescribing practices. Payers are essential to a new product's commercial success and will continue to rule the market access situation (Kumar, 2014).

2.5.2 Patients

Patients should be prepared to ask questions about the rationale behind a drug's price (Rajkumar, 2020) as they are more knowledgeable about available treatment options today. This is because patients must pay co-payments, which make them payers as well as absorb the added expense of expensive medications (Raposo, 2020). Furthermore, patients are demanding a cure rather than just treatment and are more anxious now than they were in the past about the drug's efficacy. Indeed, if there is no compensation or only a partial reimbursement, the significance of the drug's effectiveness will grow even more (Kumar, 2014).

2.5.3 Pharmacies and Physicians

Pharmacies are important players that have the power to affect drug access by dictating whether a medicine is available for purchase at retail or through personal payment (Seeley and Singh, 2021). Pharmacies may also be able to influence brand preference through replacement in reimbursement situations. Product success depends on knowing how they dispense and getting the most amount of shelf space. According to Kumar (2014) and García-Goñi (2022) physicians have experienced a gradual decline in significance within the market access value chain over time. The increasing measures of austerity have had a significant

impact on their prescribing behaviour. It will be difficult for businesses to properly interact and explore areas of shared interest as they battle to spend quality time with these crucial traditional channels (Kumar, 2014).

2.5.4 Regulatory

Regulatory is a complicated group of parties who have a significant influence on healthcare policy and the creation of the legal framework that pharmaceutical companies must work within (e.g., setting price and reimbursement rules). They are the payers in some nations, they control the pharmaceutical industry, and they will always have a big say. To prosper in the market, pharmaceutical businesses will need to manage this very difficult collection of stakeholders efficiently (Kumar, 2014).

2.5.5 Pharmaceutical firms

Pharmaceutical firms have shifted from using conventional drug development strategies to address the massive health concerns that lie ahead. Part of the burden for discovering answers falls on the pharmaceutical sector, which is a major role in the medication development process and access (Stevens, 2017).

2.6 Barriers limiting access to PCSK9i.

2.6.1 Reimbursement policies

Decisions made by the authorities at the Council for Medical Schemes (CMS) govern access to certain medical care for private healthcare patients (CMS, 2024). Such decisions can either foster access to medical care or hamper the opportunity to healthcare access. Involves pharmacy and therapeutics (P&T) committees or other authorized decision-makers who are responsible for evaluating drugs and devices translating the available evidence into decisions for prescribing, availability, and reimbursement of drugs and devices. Reimbursement policies use these evaluations to make decisions on what products to include in formularies, at what price, and for whom. The decision-making process also encompasses decisions about which tools to use to attempt to affect provider choices/prescribing and manage utilization, such as formulary tier placement (which may affect patient cost sharing), prior authorization, step therapy, and quantity limits (Bruen, 2016). Medical reimbursement policies in South Africa often impose coverage limitations on innovative treatments, further exacerbating access barriers. For example, certain medications or procedures may only be reimbursed under specific conditions or for certain patient populations, limiting their accessibility to those who meet stringent criteria. Research

by Govender et al. (2020) identified discrepancies between clinical guidelines and reimbursement policies, leading to inconsistencies in access to innovative care for patients with chronic conditions. Systems and processes within reimbursement policies that impede access include:

2.6.1.1 Formulary restrictions

Payers establish formularies, lists of approved medications, and often tier them based on cost and clinical efficacy. PCSK9i may be placed in higher tiers, requiring patients to pay higher co-payments or coinsurance, or they may be excluded entirely from the formulary, necessitating special authorization or out-of-pocket payment (Park, 2019).

2.6.1.2 Step therapy

Step therapy mandates that patients try and fail less expensive or alternative treatments before receiving coverage for more costly medications like PCSK9i. Patients must first attempt treatment with conventional therapies such as statins. Only if these treatments are ineffective or result in adverse effects, they may be eligible for coverage of PCSK9i (Nayak, 2014).

2.6.1.3 Coverage determination criteria

Payers establish criteria for determining coverage of PCSK9i based on clinical evidence, cost-effectiveness, and patient characteristics. Coverage decisions may consider factors such as LDL cholesterol levels, cardiovascular risk factors, prior treatment history, and comorbidities to determine eligibility for reimbursement (Singer, 2004)

2.6.1.4 Quantity limits

Payers may limit the quantity or duration of coverage for medications to control costs and discourage overutilization. Patients may be restricted to a certain number of doses or a specified duration of treatment with PCSK9i, requiring reauthorization for continued coverage beyond the limit (Bruen, 2016).

2.6.1.5 Utilization review

Payers conduct utilization reviews to assess the appropriateness, necessity, and efficiency of healthcare services and treatments. Payers may conduct retrospective reviews of PCSK9i prescriptions to identify outliers or patterns of overutilization, prompting further investigation or intervention (Bruen, 2016).

These processes and systems within reimbursement policies are implemented to manage costs, promote appropriate utilization, and ensure that patients receive effective and medically necessary treatments while maintaining the financial sustainability of healthcare systems.

However, they can also present challenges for patients and healthcare providers in accessing and providing innovative therapies like PCSK9i.

2.6.2 Single exit pricing

The government introduced the Single Exit Price (SEP) for medicines in 2004 for all prescription medicine (Naidoo, 2021). This has posed with both advantages and obviously disadvantages for a middle-income country such as South Africa. The SEP has fostered pricing transparency in the private healthcare sector. On the other hand, these kinds of regulations take away the opportunity for Pharmaceuticals to meet the patient in need for a lifesaving therapy such as being able to donate, rebate and discount as stipulated in Section 18a and b. These regulations make medicine even more unaffordable for the average middle-income South African. The single exit price (SEP) mechanism in South Africa lists the maximum price that a medicine can be charged at. Dispensers may charge an additional dispensing fee depending on the price of the medicine. The Medicines and Related Substances Act allows for the following charges (excluding VAT). To overcome this barrier, SAHPRA (South African Health Products Association) could consider a different approach such as Alberta model. Alberta introduced their generic policy where new generic entries start at 70% of the brand if there is only one generic entrant, and then subsequent generic medicines that entered the market were priced at 50%, 25% and 18% respectively of the originator (Moodley and Suleman, 2019). The first generic entrant keeps the advantage for one year after which the 50% price applies. The savings through agreements with manufacturers using this model is expected to be $3.8 billion over three years to all payers.

Regulatory frameworks governing medical reimbursement in South Africa are complex and may contribute to access barriers for innovative care. In South Africa and globally, the process of gaining approval for reimbursement of new treatments can be lengthy and bureaucratic, delaying access for patients in need (EFPIA, 2023). The availability of reasonably priced pharmaceutical items has consequences for community health and can lead to beneficial social development. Adherence to regulatory mandates contributes to the development of pharmaceutical businesses' products, which are vital to healthcare since they prevent and treat diseases, thereby saving and improving people's lives (Jagun, 2018).

2.7 Reimbursement policies that limit access to innovative drugs in South Africa can have several potential impacts on the country's Gross Domestic Product (GDP), both direct and indirect.

2.7.1 Healthcare expenditure

Limiting access to innovative drugs through reimbursement policies may lead to higher healthcare costs in the long run. If patients cannot access effective treatments, they may experience prolonged illness or complications, resulting in increased healthcare utilization, hospitalizations, and healthcare spending. Higher healthcare costs can strain public and private healthcare budgets, potentially crowding out investment in other areas and negatively impacting overall economic productivity (Bedir, 2016).

2.7.2 Productivity loss

When patients are unable to access innovative drugs due to reimbursement restrictions, they may experience decreased productivity and impaired quality of life. Chronic illnesses or uncontrolled conditions can lead to absenteeism from work, reduced work productivity, and disability. These productivity losses can have ripple effects throughout the economy, reducing output and economic growth potential (Russell, 2004).

2.7.3 Innovation and research investment

Limiting access to innovative drugs may disincentivize pharmaceutical companies from investing in research and development (R&D) activities in South Africa. If the market for innovative drugs is constrained due to reimbursement policies, pharmaceutical companies may redirect their investment to markets with more favourable reimbursement environments. This could stifle innovation, hinder the development of new treatments, and limit South Africa's ability to benefit from advances in medical science, ultimately impacting GDP growth (Schoonveld, 2016).

2.7.4 Human capital development

Access to innovative drugs can contribute to better health outcomes and improved human capital development. When individuals can effectively manage their health conditions with innovative treatments, they are more likely to remain productive members of the workforce, contributing to economic growth. Conversely, restrictions on access to innovative drugs may compromise human capital development by exacerbating health disparities and limiting individuals' potential contributions to the economy (Bedir, 2016).

2.7.5 International reputation and investment.

Reimbursement policies that limit access to innovative drugs may affect South Africa's international reputation as a destination for healthcare investment and medical tourism. Countries with restrictive reimbursement policies may be perceived as less favourable environments for pharmaceutical companies and investors, potentially deterring foreign direct investment and collaboration in the healthcare sector. This could have implications for South

Africa's competitiveness and ability to attract investment, impacting GDP growth in the long term (Bedir, 2016).

Overall, reimbursement policies that limit access to innovative drugs can have complex and multifaceted impacts on South Africa's GDP, affecting healthcare expenditure, productivity, innovation, human capital development, and international competitiveness. Policymakers must carefully balance the need to control healthcare costs with the imperative to ensure timely access to effective treatments that can improve health outcomes and support economic growth.

2.8 Strategies reimbursement policies can implement to broaden access.

Reimbursement policies play a crucial role in determining access to innovative drugs within a healthcare system. To broaden access to innovative drugs while maintaining cost-effectiveness and sustainability, policymakers can consider implementing several strategies (Stevens, 2017).

2.8.1 Value based reimbursement.

By putting value-based pricing and reimbursement models into place, it is possible to make sure that the cost of novel medications accurately represents their therapeutic value and patient benefits. This method entails evaluating the long-term effects of medications on patient health and quality of life, as well as their cost-effectiveness and therapeutic outcomes. Policymakers can ensure patient affordability and accessibility while encouraging the development and adoption of cost-effective medicines by matching reimbursement with the value provided by novel pharmaceuticals (de Silva Etges, 2023).

2.8.2 Outcome-based agreements

Pharmaceutical companies and payers can reduce financial risk associated with novel medications while maintaining patient access by implementing outcome-based agreements. These contracts usually include performance-based pricing structures, in which payment is contingent upon predetermined treatment efficacy or clinical outcome measures. Payers can negotiate lower costs for novel pharmaceuticals and increase affordability while encouraging manufacturers to prove the benefit of their goods by sharing the risk with them and linking reimbursement to actual treatment outcomes (Vlaanderen, 2019)

2.8.3 Patient assistance programs

Implementing patient assistance programs and financial support mechanisms can help mitigate out-of-pocket costs and improve affordability for patients who face financial barriers to accessing innovative drugs. This may include offering subsidies, co-payment assistance, or reimbursement vouchers to eligible patients, as well as facilitating access to patient assistance programs offered by pharmaceutical manufacturers. By providing targeted financial support to vulnerable populations, policymakers can ensure that all patients have equitable access to innovative treatments regardless of their ability to pay (Colon, 2020)

2.8.4 Stakeholder engagement and collaboration

Building consensus and facilitating the creation of long-term reimbursement policies that strike a balance between access, affordability, and innovation can be achieved by encouraging stakeholder engagement and collaboration among legislators, payers, pharmaceutical companies, healthcare providers, and patient advocacy organisations. Policymakers can address issues, find areas for improvement, and foster confidence in the reimbursement system by incorporating important stakeholders in decision-making processes and requesting feedback from a range of viewpoints (Houlihan-lokey, 2023).

2.8.5Tiered pricing and differential reimbursement

Access to novel pharmaceuticals for a variety of patient populations can be ensured by implementing tiered pricing and differential reimbursement schemes, which can assist overcome economic hurdles. This method entails modifying payment rates in accordance with variables like the severity of the patient's illness, income level, or clinical necessity. Policymakers may guarantee access to breakthrough therapies for the most disadvantaged while preserving cost-effectiveness and justice in reimbursement by customising reimbursement to the unique needs of patients and healthcare providers (Moradpour, 2023).

By implementing these strategies, policymakers can broaden access to innovative drugs within a healthcare system while promoting affordability, value, and sustainability. These approaches can help address the unmet medical needs of patients, improve health outcomes, and drive innovation in the pharmaceutical industry, ultimately contributing to the advancement of healthcare and the well-being of society.

2.9 Imperative aspects of market access and commercial success of innovative drugs

Market access aims to strike a compromise between target patient populations' access and the requirement for optimal pricing and reimbursement. It also describes the funding and prescription practices needed for a drug to be commercially viable while fulfilling the ultimate

objective of healthcare, which is to treat illnesses and enhance patient outcomes. (Houlihan-lokey, 2023). Finding the right balance for all parties involved promotes future expansion and serves as a catalyst for the study and creation of innovative, intricate treatments. Below are few interconnected components imperative for market access and commercial success for innovative drugs:

2.9.1 Pricing and reimbursement

Ensures a clear pricing strategy and executes effective reimbursement negotiations to guarantee that a product is priced competitively. Precise pricing eventually increases the market potential and rate of product uptake by striking a balance between the needs of patients' affordability and the manufacturer's sustainability (Bruen, 2016). Reduces complicated facts, communicates important product features, draws attention to support from stakeholders, and provides payors (reimbursement policies) with an overview of the product's total value proposition through efficient, interesting communication channels that facilitate smooth payor and manufacturer interactions (Houlihan-lokey, 2023).

2.9.3 Monitoring and Adaption

Updates the market access strategy in response to the ongoing changes in the landscape by monitoring market data, assessing the effects of pricing and reimbursement, monitoring regulatory changes, and putting the necessary modifications to the market access approach into practice (Houlihan-lokey, 2023).

2.9.4 Stakeholder Engagement

Fosters connections and partnerships with patients, patient advocacy organisations, and healthcare professionals by addressing stakeholder concerns, presenting the value proposition of the product, and facilitating evidence-based dialogues. Through these initiatives, the target market is better understood, the product is supported more strongly, there is a greater chance of increased market access, and payors have more support (Houlihan-lokey, 2023).

2.9.5 Value shaping and demonstration

Gives a thorough grasp of the target market (including landscape, patient need, regulatory environment, competitive outlook, etc.), making it possible to create a customised market access plan that specifies the best options for reimbursement, pricing, and market entry (Houlihan-lokey, 2023).

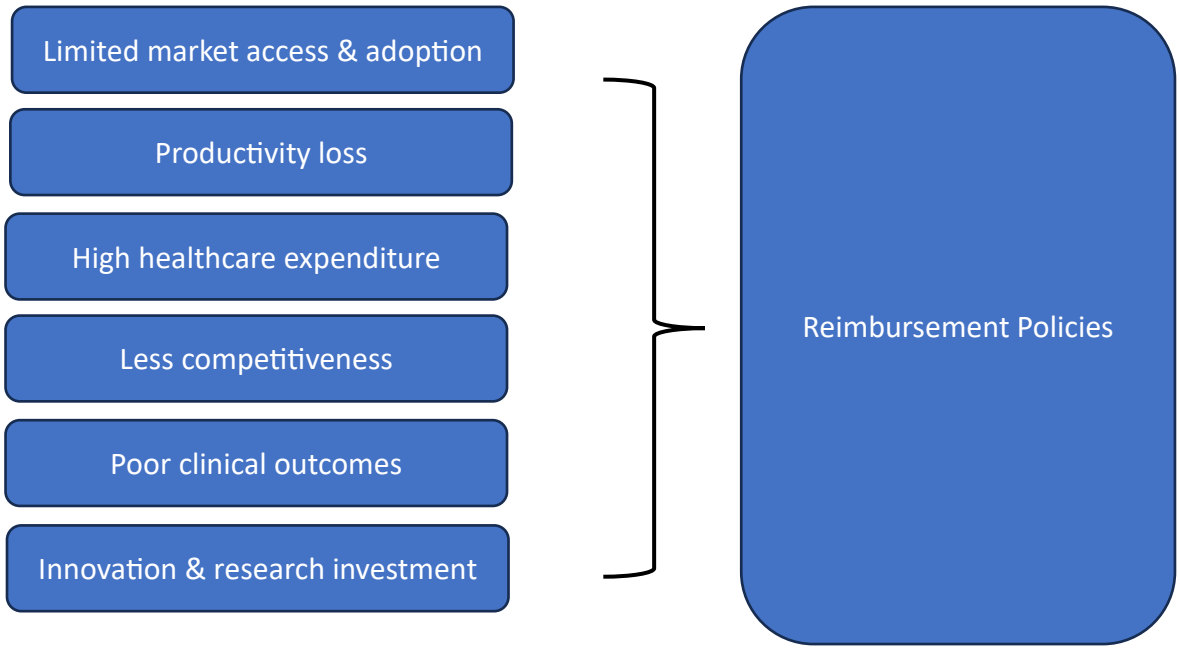
2.9.6 Market analysis, strategy and entry

Updates the market access strategy in response to the ongoing changes in the landscape by monitoring market data, assessing the effects of pricing and reimbursement, monitoring regulatory changes, and putting the necessary modifications to the market access approach into practice (Alt, 2018). Gives a thorough grasp of the target market (including landscape, patient need, regulatory environment, competitive outlook, etc.), making it possible to create a customised market access plan that specifies the best options for reimbursement, pricing, and market entry (Houlihan-lokey, 2023).

2.9.7 Conceptual framework

Below is a conceptual framework outlining the factors influencing the accessibility of PCSK9i reimbursement policies play a critical role in shaping the landscape of healthcare economics, particularly in the pharmaceutical industry. This conceptual framework outlines the impact of reimbursement policies on the economy, pharmaceuticals, and product adoption in the South African private healthcare sector.

Figure 3.1: *The relationship between reimbursement policies and accessibility to innovative drugs (PCSK9i)*



As illustrated in Figure 3.1, the impact of PCSK9i reimbursement policies in South Africa have an adverse impact on both stakeholders and the entire value chain of the said medications. This impact includes poor clinical outcomes for patients, high healthcare expenditure, less competitiveness, lack of incentive for innovation and investment in research and development (R&D) as well as limited market access and adoption.

The economic impact of the existing reimbursement policies for PCSK9i in South Africa is significant by influencing the cost and availability of pharmaceuticals and healthcare services, reimbursement policies effectively determine the physical health of the country's population, both the economically active and the inactive. Scholars such as Remes *et al*., (2020) have demonstrated that poor health reduces global GDP by at least 15% - a number which increases exponentially in developing countries that already have poor economic outcomes.

2.3 Theoretical framework of the study: Institutional Theory

According to Vinz (2022) and George (2023) a theoretical framework is "a foundational review of existing theories that serves as a roadmap for developing arguments utilised in research" and serves to justify and contextualise a research undertaking. The study seeks to investigates barriers limiting adoption and access to PCSK9i in the South African private healthcare sector with a focal focus on reimbursement policies implemented by medical funders and insurances. The study also explores the market access and commercial success of PCSK9i hindered by reimbursement policies. It relies on Institutional Theory to explain the complexities embedded in the access and adoption of PCSK9i in the South African private healthcare system. De Jonge (2015) defines institutional theory as a theory that explains why organisational structures and practices become entrenched, as well as how and why change occurs. Other scholars contend that institutional theory "provides suitable frameworks for examining the nature of external demands and the behaviour of organisations" (Eriksson *et al*, 2023: 129). According to Scott as quoted in Debroux (2010) there are three pillars on which societies are built: the regulative, the normative and the cognitive. The regulative pillar is formal and legally codified, while the normative pillar includes non-codified perceptions and attitudes that are present in societies.

Institutional Theory is prominent in the analysis of value-based reimbursement programme (VBRP) globally. According to Eriksson *et al*. (2023) VBRPs in European and American healthcare systems is reflective of the institutional contexts of these geographies. These contexts inform the orientation of healthcare systems, with the USA slowly moving away from fee-for-service approaches and while healthcare in European countries is primary focused on the coordination of care among providers. Institutional Theory is also relevant to this study, in great part because it not only explains the challenges of reimbursement under study, but also theorises how institutions converge over time (Eriksson *et al*, 2023). This is especially relevant to the socio-political context of South Africa where the inequities

of healthcare provision have sharpened contradictions is so far as placing the spotlight on the challenges confronted by the private healthcare system across the value chain.

Chapter summary

This chapter provides an analysis of contemporary debates and reflections on the perceived and material impact of reimbursement policies on accessibility to PCSK9 inhibitors in the South African private healthcare sector. It also outlines Institutional Theory as a framework guiding the study.

Chapter 3: Data collection and analysis

3.Introduction

In this chapter, the methodology and its strengths are discussed. The data source and study population are identified. The interview questions and respondents' profiles are discussed. The analysis plan's specifics are given, and data management is emphasised. The chapter concludes by discussing ethical consideration and limitations.

3.1. Research methodology and Research paradigm.

A qualitative research approach is adopted in this research report. Qualitative research is an iterative process in which improved understanding to the scientific community is achieved by making new significant distinctions resulting from getting closer to the phenomenon studied (Aspers, 2019). This approach was carefully selected to provide insights and understanding from treating cardiologists, pharmaceutical personnel's and reimbursement administrative clerks when seeking approval from medical funders. It may also be used in informing the development of interventions or in understanding barriers and facilitators to their successful implementation. (Denny, 2018).

This research aims to investigate the challenges and barriers (funders and their reimbursement policies) experienced by cardiologists when treating hypercholesteremia, pharmaceutical companies, and most importantly, patient treatment outcomes. Qualitative research approach is best fitting for this research as it is characterized as inductive (Saunders, 2007), where the researcher begins by gathering information from participants and develops this information into themes. These themes are then developed into broad patterns, theories, or generalizations. Lastly, it will be compared with personal experiences or with the existing literature related to the topic (Bahari, 2010).The adopted research approach seeks to guide in answering the following primary question below:

- What are the barriers to PCSK9i market access and commercial success in an emerging market like South Africa?
- What key strategies can reimbursement policies implement to broaden PCSK9i market access?

Epistemological assumptions can be regarded as a question of what is (or should be) regarded as acceptable knowledge in a discipline. Interpretivism is also often associated with the view of phenomenology (Bahari, 2010). Interpretivism considers that humans and knowledge are inseparable and relativist ontology and subjective epistemology are considered (Junjie &

Yingxin, 2022).Taking into consideration the aim and scope of this research, the interpretivism paradigm is apt. As such, the interpretivism paradigm has been employed in this research because of its richness in context, authenticity of details and narrative quality in the efforts to generate inductive generalizations from the themes and relationships identified from treating physicians, patients, and pharmaceutical companies to develop new theories as part of the study (Penaloza, Viscont, & Toulouse, 2020). It has also been established that interpretivism may be influenced by subjective bias of the researcher (Junjie & Yingxin, 2022), and as such, ethics and tackling ethical issues are essential to qualitative research and will be enclosed later in sections to follow.

3.2 Research design

This study adopted an in-depth semi-structured interview research design, which is an appropriate method for investigating how reimbursement policies set out by the council of medical schemes affect the treatment practice of healthcare professionals into advocating for the appropriate therapy for the treatment of hypercholesteremia in the private healthcare sector. Interviews can be unstructured, highly structured, or semi-structured, the latter being most common (Eppich, 2019). In-depth interview research design is appropriate for this study as it allows the researcher to gain valuable insight from carefully selected participants. This method allows the researcher an opportunity to investigate complicated phenomena, comprehend human viewpoints, and produce in-depth insights that contribute to a deeper understanding (Showkat, 2017) of impact of reimbursement policies on accessibility to PCSK9i in the private healthcare sector SA. Furthermore, in-depth interview research design has been commonly used in the healthcare sector.

The interview research method was adopted in this research because of its ability to foster an insightful and in-depth feedback from carefully selected interviewee's. This research method also allows for a deeper understanding of topic, and therefore encouraging constructive answers to the research questions.

3.3 Data collection methods

Data collection plays an important role in answering research questions and accomplishing the objective of a study. In this research, the data collection method was carefully selected to capture the necessary data on the impact of reimbursement policies on accessibility to specialized therapies like PCSK9i. The targeted interviewees include prescribing cardiologists, cardiology research consultant, access managers, sales representatives,

marketing managers at a pharmaceutical company, and formulary managers at the councils of medical insurance. The primary data collection method adopted was semi-structured interviews. Through non-probability purposive sampling, selected interviewees were engaged to gain insightful feedback for the purpose of answering the research questions. Interviews normally include a smaller population than other research methods (Showkat, 2017). To capture a comprehensive understanding and in-depth knowledge, a vast range of expertise was selected to acquire information that is rich and inclusive of all stakeholders impacted by reimbursement policies when treating dyslipidaemia with limited access to PSCK9i.

3.4 Population and sampling

Due to the impracticality of accessing an entire population, studies are done using representative samples of the population. Conclusions made from samples are meant to be extrapolated to the entire population, and occasionally even to the future. Consequently, the sample must be representative of the population. The easiest way to guarantee this is to use a representative and adequate sample The sample must also be of a sufficient size, meaning neither too large nor too little (Andrade C. , 2020).

South Africa's private healthcare provides health care to 20% of the population and is responsible for almost 50% of overall health care spending (Govender et al, 2021). The three big players in private healthcare include: Netcare, Life and Mediclinic, with almost 80% presence in South Africa the study's focus is mainly on reimbursement policies set out by the Council for Medical Schemes (CMS) that have become a barrier to access certain specialized therapies that have been approved by Section 21. The target population included formulary managers at the CMS These include the dominant players in the industry, namely: Bestmed 72.7%, Gems 70%, and Discovery 67% (Bruen, 2016). Treating cardiologists responsible for prescribing specialized hypercholesteremia treatment, cardiology research consultant, representatives at pharmaceutical companies, access managers, and lastly PSCK9i brand managers.

3.4.1 Population

The population for this study was carefully determined by accessibility and feasibility of reaching respondents. The selection was guided by emerging stakeholders in innovative drug accessibility as stipulated in literature review. The focal focus for this research was specifically the private healthcare sector with a very close investigation in cardiology. Four face to face interviews were conducted with top PSCK9 inhibitor prescribers in the private hospitals situated in Johannesburg. In total, 15 semi-structured in-depth interviews were conducted.

Each interview was 15-20 minutes long on average. The study kept a very niche number of interviews, with a depth of experience in the industry, to extract valuable and insightful knowledge about accessibility to innovative and noble therapies indicated in hypercholesteremia. Most stakeholders affected by restricted access to novel medications like PCSK9i are included in the study. Due to the Protection of Personal Information Act (Act no 4 of 2013) and the research principle of confidentiality and anonymity, this study does not include any patient details and any systems applied in the private healthcare facilities.

3.4.2 Sample Size

Failure to reach data saturation has an impact on the quality of the research conducted and hampers content validity. The aim of a study should include what determines when data saturation is achieved, for a small study will reach saturation more rapidly than a larger study. Data saturation is reached when there is enough information to replicate the study when the ability to obtain additional new information has been attained, and when further coding is no longer feasible (Fusch Ph D, 2015). The projected sample size was 11, and fortunately 15 were realized, this was because the study hadn't reached saturation and hence the study needed to employ more respondents. The respondents were chosen using non-probability sampling. The sample is chosen because of the convenience of the investigator. Often the respondents are selected because they are at the right place at the right time (Acharya, 2013).

Table 1: Respondents sample and demographics

Sample	Demographics	#
Cardiologists	▪ Cardiologists at Netcare Sunninghill and Linksfield. ▪ Over 20 years' experience in cardiology and treating hypercholesteremia.	4
PCSK9 inhibitor brand manager	▪ Launched PCSK9 inhibitors in South Africa. ▪ 7 years in brand management ▪ PCSK9 inhibitors market strategies, communication and trend analysis	1
Head of Access	▪ Facilitate the reimbursement process in the healthcare market. ▪ 3 years in access management. ▪ Maintain and build relationships with key opinion leaders to ensure successful market access.	1

Pharmacist	▪ Ensure that medicines prescribed to patients are suitable, within the law, and accessible.	1
Head of Medical Affairs	▪ Formulate long-term strategies to improve drug and other medical devices information delivery and education. ▪ 11 years' experience in medical affairs for three renowned pharmaceuticals in the industry.	1
Reimbursement clerk	▪ Liaise with medical funders to ensure reimbursement and access to treatment. ▪ 6 years' experience at Dr Angels practice.	2
PCSK9i representatives	▪ Promote PCSK9 inhibitors throughout South Africa in the private healthcare sector. ▪ Maintain and build relationships with cardiologist. ▪ Various years of experience ranging from 2 years to 10 years.	5

3.6 Data collection and analysis

Purposive sampling technique was employed. Purposeful sampling, which is a non-probability selection strategy, therefore, the research only chose respondents who meet the study's objectives. This technique works well in a small population and helps the researcher filter out irrelevant responses that do not meet the context and objective of the study (OBILOR, 2023). There are many ways in which qualitative data can be analysed, such as adopting either an inductive analysis, content analysis, thematic analysis, basic interpretive, and discourse analysis (Lester, 2020). 15 semi-structured interviews were conducted in this study, out of the 15 interviews, 5 interviews were conducted face-to-face and were recorded using a voice recorder. The remaining 10 semi-structured interviews were conducted and conducted via Microsoft teams. This method encouraged much more detailed information as compared to other forms of data collection methods like surveys, questionnaire etc. Semi-structured interviews foster an in-depth understanding of the topic (Showkat, 2017). Moreover, the interactive nature of the semi-structured interviews allowed room for free responses from the respondents which in turn inspired new ideas and areas for further investigation. Facts on topics during the semi-structured interviews were captured in their natural form (Kakilla, 2021). In-depth interview enables researcher to study behaviour of the participant (Showkat, 2017). Semi-structured interviews allow the researcher to sass out certain energies, A well-presented semi-structured interview can ideally draw upon the interviewee's inner voice (Kakilla, 2021). A set of 5 interview questions served as the basis for the semi-structured interviews, questions were twigged based on respondents' designation and experience. Thematic analysis was used to analyse data, because of its theoretical flexibility allows researchers across a range

of disciplines to engage disciplinary theories and perspectives. Potentially generating a more meaningful and relevant analysis for a given field. Accordingly, thematic analysis can result in a theory-driven or data-driven set of findings and engage a range of research questions (Lester, 2020).

3.7 Strengths of the methodology

Robust, knowledgeable, and extensively documented qualitative research is what makes it good. Like quantitative research, qualitative research is interpretive and naturalistic, but it is also methodical, requiring a rigorous procedure of problem identification, data collection, analysis, explanation, evaluation, and interpretation. Therefore, it is crucial to guarantee the rigour and quality of qualitative research when conducting it (Nassaji, 2020).

3.7.1 Credibility

Credibility in qualitative research becomes evident whenever the researcher develops works that can be in the process of problematizing of the matter, through coherency with the theoretical foundations of the case (Abdalla, 2018). This study will adopt data triangulation research by collecting data in diverse cycles of time and from different sources, to obtain in-depth knowledge about the research topic. The study included interviews with long serving cardiologists, with middle and top leaders at various pharmaceutical companies, reimbursement clerks and pharmacist. This vast range of experiences and feedback fostered a rich data triangulation. Data triangulation can reveal a social phenomenon's complexity by providing a fuller picture, while in-depth interviews and a 'slow' interview technique can enhance data quality (Jentoft, 2019).

3.7.2 Confirmability

Confirmability is "concerned with establishing that data and interpretations of the findings are not figments of the inquirer's imagination, but are clearly derived from the data (Anney, 2014), and refers to reporting research findings as being the views that have been extracted from the interviewees and are not influenced by any other view. To ensure confirmability guiding questions were avoided, and respondents shared their honest point of view based on their personal experiences and knowledge.

3.7.3 Dependability

Dependability is the stability, reliability, and consistency of the study methodology and results across time. It focuses on determining to what extent the study's findings would hold true if the

investigation were to be replicated. To ensure dependability, data was only collected (Nassaji, 2020). To ensure dependability, data was collected to a point of saturation and hence 3 more interviews were conducted to ensure dependability, and that any other researcher would arrive at similar findings.

3.7.4 Transferability

Transferability focuses on the likelihood that the results will apply other contexts or populations that are comparable. This research will include Rich and thorough descriptions of the research context, participants, and research procedure to enable readers to compare the study context with other contexts of interest (Nassaji, 2020). Transferability was ensured through including detailed responses in chapter 4 and 5. Respondents detailed demographics and how the data was collected, has also been provided.

3.7.5 Ethical considerations

Responsible research includes a report on ethical issues such as voluntary participation, informed consent, confidentiality, anonymity, and potential for harm. The researcher applied and obtained ethical clearance from the Wits Business School to take accountability for adhering to ethical principles and safeguarding both the respondents and the researcher. This research does not include any patient details and nor does it interview any patients. Data collection only began once clearance certificate was obtained. To ensure voluntary participation, respondents were not pressurised into participating in interviews. Respondents were issued with consent and information sheets. To ensure consents from respondents, consent forms were either shared prior to the interview or a verbal consent was obtained before the interview could commence. (Bell, 2022) highlights the importance of anonymity and confidentiality in qualitative research. Although some of the interviewees may be known to the researcher, respondents were assured that their identity and responses was safeguarded will not be disclosed.

3.8 Administrative limitations

Limitations represent weaknesses within the study that may influence outcomes and conclusions of the research. Administrative limitations in research refer to obstacles or constraints faced during the administrative parts of performing research investigations. These restrictions may appear at any point during the research process and influence the efficacy, calibre, and productivity of research management (Ross, 2019).

Attaining approval from Aspen to conduct the study took longer than anticipated and that forced the researcher to push out interviews. Also, cardiologists' availability was a challenge

as two of the cardiologists were either in theatre or consulting. Appointments needed to be rescheduled three times. Eventually interviews took place and the feedback was impactful.

3.9 Conclusion

This chapter focused on the research methodology, design and the method used to collect data. The strength of the methodology, ethical considerations and the limitations were discussed.

Chapter 4: Findings and discussions

4. Introduction

This chapter presents the findings of the study. The respondents were asked questions (see Annexure1.2) based on their designation and how their respective mandates contributed to ensuring accessibility to innovative therapies indicated in hypercholesteremia. The questions were asked with the aim of addressing and unpacking the impact of medical reimbursement policies on accessibility to PCSK9i, the regulatory, market access, commercial, marketing & brand management, clinical outcome, economic impact, international competitiveness, R&D. These questions were critical in answering the two main research questions:

- What are the barriers to PCSK9i market access and commercial success in an emerging market like South Africa?
- What key strategies can reimbursement policies implement to broaden PCSK9i market access?

4.1 Findings

The practice of finding themes or central concepts in unstructured qualitative data is known as thematic analysis. Thematic analysis, then, entails identifying patterns in data, with emerging themes serving as the basis for qualitative analysis's categories (Clarke, 2017). Table 4.1 is a demonstration of the interview questions, key literature review concepts that were discussed in chapter 2 and the emergent themes from the qualitative data gathered.

Table 4.1: interview questions, literature review, and emerging themes.

Interview question	Literature	Emerging themes
In your opinion, what limits market access for innovative drugs like PCSK9i in South Africa?	"Healthcare systems are facing barriers related to high out-of-pocket cost for patients and/or barriers regarding the decision-making process and the effects of reimbursement decisions i.e., restricted, delayed or denied access, particularly the latter for socialized systems with coverage scheme (Wahlster, 2015)."	Reimbursement policies Drug cost Physicians' inertia Outdated CMS guidelines Administrative burden Regulatory Lack of collaboration

What are the perceived long-term Economic and Clinical implications of limited access to PCSK9i?	"Consequences of nonadherence due to limited access include worsening condition, increased comorbid diseases, increased health care costs, and death. Nonadherence results from many causes; therefore, no easy solutions exist (Chisholm-Burns, 2012)."	Poor clinical outcomes Increases healthcare expenditure. Productivity loss Competitiveness R&D
How do these access barriers impede on the objectives of all stakeholders involved in ensuring access to PCSK9i?	There is an urgent need for accessible and improved treatments - to reduce mortality and avoid scenarios in which resistance becomes the norm rather than the exception. (Cox, 2015).	Increased healthcare burden Poor drug adoption Growth Sustainability Poor health economy
What strategy could be implemented to broaden market access?	"There is a significant potential for reducing out-of-pocket healthcare expenditure, highlighting the need for patient as well as prescriber education (Khanijo, 2020)." "For hypercholesterolemia, a high level of medication adherence was associated with lower disease-related medical costs (Sokol, 2005)."	Patient advocacy group Synergized optimal processes. Funder risk sharing Value based healthcare. Update CMS guidelines Affordable drug cost
How important is market access for innovative drugs in an emerging market?	"The communication of value for complex products, combined with the extremely nuanced healthcare marketplace, emphasizes the essential nature of market access specialists." (Houlihan-lokey, 2023)	Prevent strokes and MI. Maximise market potential. Sustainability Better health economy Clinical solutions

What challenges do you foresee and what is your plan of action?	"Focus on value within the assessment and appraisal of drugs continues to be jeopardized by financial drives as the side of industry and at the side of the payers" (Pauwels, 2016)	Decrease in innovative drugs in SA. Global pharmaceutical firms pulling out of SA market. Increased health burden
What are the indicators of successful market access?	"One critical area is the communication of a drug's value to key healthcare stakeholders, to expand patient access to therapies at equitable prices. In the life sciences community, the process is referred to as market access." (Houlihan-lokey, 2023)	Market access to innovative drugs for the right patient at the right time and affordable cost.

4.2 Discussion of key findings

PCSK9i have emerged as a ground-breaking class of drugs for managing hypercholesterolemia, particularly in patients with familial hypercholesterolemia or those intolerant to traditional lipid-lowering therapies. Despite their efficacy, access to PCSK9i has been a concern due to factors such as, reimbursement challenges, high costs, and limited awareness.

4.2.1Factors limiting access to PCSK9 inhibitors in the South African private healthcare sector

4.2.1.1 Reimbursement policies and processes.

The need for medical funders to change their reimbursement models emerged as the respondents reflected on their unique engagements, and encounters with the funders in their respective roles and provinces. The most common response was that reimbursement policies needed to be reviewed for better clinical outcomes, and accessibility to innovative hypercholesteremia like the PCSK9i This finding is presented on Table 4.1 and Table 4.2, and thirteen out of fourteen research respondents spokes about reimbursement policies with identifiable references including the following quotes:"

"I think the medical aids have a mindset of an insurance company rather than a health medical aid companies. They focus on covering minimum payment benefits rather than focusing on up-to-date therapies that potentially could give better health economic data, better time returned to living better quality of life."

As stipulated by research respondents, medical funders need to consider reviewing their reimbursement policies to ensure better access for deserving patients. The research also found that medical funders operated in silo's and that they are offshore insured for hospital admissions and hence it is easier to get admitted for a surgical procedure then it is get preventive medication such as the PCSK9i. It is evident that the countries are following similar models with a focus on pricing measures, reimbursement measures, and measures directly affecting the patients. It is our opinion that most of the measures are focused on ensuring the sustainability of the payer's funds and less are those that stimulate faster access(Tachkov, 2023)

4.2.1.2 Research & Development/ Innovative drug cost

Most respondents mentioned that access to innovative drugs like the PCSK9i was a twofold conundrum between reimbursement policies and drug cost. They also acknowledged that innovative drugs were costly due to extensive research and development that went into producing these innovative drugs, this is what some of the respondents had to say about drugs costs:

"They go into research and development of these products and those costs cannot be avoided. You know, if we didn't have research and development, we wouldn't have these new novel products coming out that are able to treat patients for these complex diseases."

As indicated by the research respondents, innovative drug cost is a barrier to access. To support this, (Prasad, 2017) found that drugs are most unaffordable in economically developing nations, such as India and China. Not only are launch prices high and rising, but individual drug prices are often escalated during exclusivity periods. High drug prices harm patients, often directly through increased out-of-pocket expenses, which reduce levels of patient compliance and lead to unfavourable outcomes.

4.2.1.3 Lack of Stakeholder engagement and Collaboration

The lack of stakeholder mapping and collaboration also emerged from the interviews. Stakeholders involved in ensuring market access, entry and commercial success are not collaborating. They are often operating in silos. To ensure access to innovative drugs and healthcare, the stakeholders need to collaborate to understand each stakeholders' interests, perspective and future goals. They will be able to form synergies to achieve similar goals. This is reiterated by an interviewee who asserted:

"So almost if you want to call it doing a funder stakeholder mapping, understanding who the players are, how they fit together and looking at who is the more influential, influential funder. So and then once we had that footprint in place was going and saying who do we need to talk to and we are two key strategies. Obviously, you have to talk to the big guys, but then we were saying what about having the conversation with the little guys as well, showing them their value, showing them, they can have an impact because it might be a case that certain patients might be directed to certain funders that are actually on board and willing to fund them."

Building relationships and establishing collaborations with healthcare professionals, patient advocacy groups, and patients by communicating the product's value proposition, addressing stakeholder concerns, and holding evidence-based discussions, is crucial. These efforts contribute to a deeper understanding of the target market, enhance support for the product, increase the likelihood of expanded market access, and provide additional backing for payors. Payor communication distils complex datasets, conveys key product benefits, highlights stakeholder support, and outlines the overall value proposition of the product to payors through effective, engaging communication channels that lead to seamless payor and manufacturer negotiations (Houlihan-lokey, 2023).

4.2.1.4 Poor International reputation and investment

Another emerging topic amongst the respondents was the fact that a couple of global pharmaceutical firms have exited the South African market because of the commercial viability and return on investment (ROI). They have instead given distribution rights to local companies. They expressed scepticism about launching certain drugs in South Africa owing to the regulatory framework as well as socio-economic challenges such as high levels of crime, unemployment and institutional instabilities within the state. This demonstrates that South Africa's international reputation has taken a hit. The implications of this are significant. For one thing, with limited investments, we could struggle to access curable innovative drugs to the rare diseases informed by our gene diversity. This is reiterated by an interviewee who asserted:

"So the longer term impact is pharmaceutical companies will just withdraw themselves from the country and maybe they all use companies like Aspen to distribute the innovative pharmaceuticals. But even in that, still the longer term is eventually certain drugs just won't be available in a country like South Africa. And I mean that results in patients needing to look at medical tourism."

The argument for imports is stronger because they are more economical. Labour, power, and water expenses were mentioned as examples of input costs that were greater in South Africa. Additionally, some interviewees mentioned that for some Indian enterprises, the South African market seems limited and does not offer substantial volumes for higher front-end investment (Horner, 2021).

4.2.1.5 Single exit pricing (Section 22G)

Eight out of fourteen respondents mentioned how the single exit pricing regulation was a stumbling block to patients accessing innovative drugs. Often, pharmaceutical companies are in no position to discount or altar prices to meet a specific patient need. In 1996 the Government introduced the National Drug Policy outlining among other policies, the intention to establish a pricing committee to regulate medicine prices, create transparency in the pricing structure from manufacturer, wholesaler, distributor and providers of service, as well as to ensure a non-discriminatory pricing system.[5] The Medicines and Related Substance Control Amendment Act 90 of 1997, implemented on 2 May 2003, banned the offer of discounts and rebates to patients and healthcare providers (bonusing section 18G) and establishing a pricing committee (section 22G)(Moodley, 2019). This finding is presented on Table 4.1 Thirteen out of fifteen research respondents spoke about reimbursement policies with identifiable references including the following quotes:

"This whole concept of single exit price, which is a determinant drug law, but then it is a statutory thing, but if the industry can negotiate with state, the single exit price does not exist. Nicholas the NHI director was there, and I do agree with him, he said that whatever is available in private should be available in state too".

As indicated by the research respondents, single exit pricing can pose as a threat to innovative drug accessibility and essentially treating patients to acceptable clinical targets. The single exit pricing regulation needs to be reviewed, similarly (Gray, 2014) conceded that the single exit price mechanism, with annual adjustments, may need reconsideration and refinement. Proposals for external reference pricing are in the final stages of preparation. Greater use of pharmacoeconomic evaluations will help to inform rational selection and reimbursement policies, especially as the country moves towards a National Health Insurance model.

4.2.1.5 Clinical inertia

The need for physicians to proactively manage hypercholesteremia emerged as research respondents unpacked the bottlenecks limiting access to PCSK9i. Four out of thirteen respondents shared a similar perspective. Actively treating hypercholesteremia requires physicians to closely monitor LDL-C baseline levels, to motivate for innovative drugs, and to prevent events like strokes and heart attacks. This finding is presented on table 4.1,

Research respondents frequently mentioned that access to innovate drugs like the PCSK9i will require more than just updated reimbursement policies and that it effectively treating hypercholesterolemia requires a holistic approach and more importantly physicians that will manage and treating hypercholesteremia proactively. (Phillips, 2001) explains that limitations in managing such problems are often due to clinical inertia—failure of health care providers to initiate or intensify therapy when indicated. Clinical inertia is due to at least three problems: overestimation of care provided; use of “soft” reasons to avoid intensification of therapy; and lack of education, training, and practice organization aimed at achieving therapeutic goals.

4.3 Strategies to broaden access to PCSK9 inhibitors.

Strategies to broaden access to PCSK9i were thoroughly discussed by research respondents. The research respondents mentioned the following as strategies to increase access to PCSK9i:

- Adopt value-based healthcare.
- Adopt funder risk sharing.
- Review single exit pricing.
- Affordable drug cost
- Patient advocacy group

These findings are presented on table 4.1 and table 4.2, and are supported by the following quotes:

4.3.1 Value-based healthcare

Broadening access to PCSK9i will require synergies amongst all stakeholders involved. To date, all four stakeholders (pharmaceuticals’, doctors, hospitals, medical funders) are operating in silos. Value-based healthcare relies on the measurement of health outcomes that are meaningful to patients. Central to the value-based healthcare approach is the concept of patient-centred care, which involves engaging patients in decision-making, understanding

their preferences and values, and tailoring care plans to meet their individual needs. This shift from a provider-centric to a patient-centric model fosters a collaborative relationship between patients and healthcare providers, leading to better adherence to treatment plans and improved outcomes (Zanotto, 2021). This type of approach could be the change that the South African healthcare sector yearns for and more especially for patients facing barriers to innovative care and treatment.

4.3.2 Affordable drug cost

Affordable drug costs in South Africa yield multiple benefits, ranging from improved access to innovative drugs like the PCSK9i and disease management to positive economic and public health outcomes. By ensuring that essential medications are accessible and affordable to all segments of society, both in the public and private healthcare sector. Affordable drug costs can stimulate pharmaceutical innovation by increasing demand for medications and incentivizing research and development efforts focused on addressing unmet medical needs. A robust market for affordable medications encourages competition among pharmaceutical companies, leading to the development of new and more cost-effective treatments. This will promote health equity, economic prosperity, and overall well-being for South Africa as a whole.

4.3.3 Patient advocacy group

Patient advocacy groups varying in size, resources, and stages of development could be the solution to be heard by the medical funders, most of their obstacles to reaching their objectives persist due to a lack of financing and ignorance of the condition. Although there are support tools available to make research more accessible, their usefulness is frequently contingent upon factors such as finance, sustainability, PAG maturity, and collaborators' degree of investment. Notwithstanding the existence of extant support mechanisms, there are obstacles pertaining to the initiation and maintenance of patient-centric research initiatives (Patterson, 2023). Empowering patients with improved access to PCSK9i aligns with the goal of ensuring that advancements in medical science translate into tangible benefits for those who need them most.

4.3.5 Funder risk sharing model.

One of respondents mentioned the adoption of a risk sharing model, which could help alleviate risk from all stakeholders involved in ensuring access to PCSK9i. The risk sharing model involves financial arrangement between medical funders and healthcare providers (such as

hospitals, clinics, or physicians) aimed at sharing the financial risk associated with providing healthcare services. This model is designed to align incentives between payers and providers, promote cost-effective care delivery, and improve patient outcomes. Typically, both parties share the financial risk associated with achieving the agreed-upon performance metrics. This means that if the provider delivers high-quality, cost-effective care and meets performance targets, they both stand to benefit financially. However, if performance falls short, both the provider and the payer may incur financial losses. All health system collects, manages, and distributes resources. Sufficient resources must be generated, risks must be pooled effectively, and resources must be distributed to services that use health expenditures more economically in order to achieve health goals more effectively (Ahangar, 2018).

The insured patient communicates with both their medical service providers and the private healthcare insurer. Collaboration between the private healthcare insurer, their medical service providers, and other important stakeholders has been included in the concept of risk sharing. Because the insured claimant is positioned between these two influential parties, the patient will be impacted by their activities, even if they are well-intentioned and compliant with their contractual obligations (Orros, 2007). To achieve this, the medical funders, pharmaceuticals, CMS, hospitals will have to form synergies around a desired clinical outcome, which will in the long run translate in cost saving.

4.3.6 Review single exit pricing regulation

Single exit pricing may reduce the incentive for pharmaceuticals and retailers to invest in efficiency improvements or and more importantly access to innovative drugs like the PCSK9i. Since prices are fixed, there may be less motivation to develop new products, improve distribution channels, or invest in cost-saving technologies. Furthermore, single exit pricing restricts the ability of suppliers and retailers to implement flexible pricing strategies based on factors such as demand, seasonality, or regional differences in costs. This lack of flexibility may hinder efforts to optimize pricing and revenue generation. The single exit price regulation can limit competition among PCSK9i producing pharmaceutical companies since all products are sold at the same price. This reduction in competition may lead to reduced innovation, fewer product offerings, and less incentive and essentially limit access to PCSK9i to deserving patients. Additional studies in this area indicate that single exit pricing might not be enough to provide accessible, reasonably priced healthcare (Moodley R. &., 2019). These strategies will require a multifaceted approach to combat the challenges and barriers limiting access to life saving drugs like the PCSK9i.

4.4 Conclusion

This chapter presented and discussed research findings. Discussions included, factors limiting access to innovative drugs like PSCK9 inhibitors and strategies to broaden access.

Chapter 5: Summary, recommendations, and conclusion

5. Introduction

This chapter presents the summary of the findings, conclusions and recommendations based on the data analysed in the previous chapter. Some limitations have been identified and discussed. The perceived impact of reimbursement policies on accessibility to PCSK9i in the South African private healthcare sector was researched by investigating the barriers and challenges limiting access to innovative and noble drugs like the PCSK9i.

5.1 Summary of the research

This research aims to investigate and propose comprehensive strategies that address reimbursement policies, innovative drug cost, economic, regulatory, and educational barriers, with the goal of enhancing access to PCSK9i for eligible patient populations. By understanding the multifaceted nature of these challenges and identifying effective solutions, this research seeks to contribute valuable insights to policymakers, pharmaceutical firms, and healthcare professionals, facilitating the optimization of market access, cardiovascular care and the reduction of the global burden of hypercholesterolemia.

The objectives of this study were to:

- To identify barriers limiting access to the PCSK9 inhibitors.
- Assess the long-term health and economic implications of these barriers.
- To propose evidence-based recommendations for broadening accessibility to PSCK9 inhibitors.

This was achieved through conducting semi-structured interviews which were about 20 to 40 minutes on average. A total 15 interviews were conducted, with a vast range of experiences and knowledge about the industry. Data was analysed using thematic analysis due to its theoretical flexibility.

5.2 Conclusion of main findings

The study investigated the impact of reimbursement policies on accessibility to PCSK9i in the South African private healthcare sector. The study had a focal focus on the private healthcare sector due to availability of data and convivence compared to the public healthcare sector. The study excluded other health conditions and focused solely on hypercholesteremia, which is successfully treated by PCSK9i. The conclusions are based on respondents' experiences,

knowledge and exposure in either treating hypercholesteremia, seeking reimbursement from medical funders, promoting PCSK9i or dispensing these noble and innovative medications. The conclusions are also supported by empirical literature review on factors and barriers limiting access to PCSK9i. Overall, this study concludes that reimbursement policies, drug costs, regulatory, lack of collaboration amongst imperative stakeholder, international reputation and investment and clinical inertia are the main stumbling blocks to PSCK9i accessibility. It emphasises the need for a more inclusive approach like value-based healthcare, which has been successful implemented in other parts of the world, showing better clinical outcomes and broader access to PCSK9i.

5.2.1 To identify barriers limiting access to the PCSK9 inhibitors.

The first objective was to identify barriers limiting access and the adoption of the PCSK9i in the South African private healthcare sector. The present research found that reimbursement policies and innovative drug cost remain to be the most critical barriers impeding access to PCSK9i. Besides reimbursement policies and cost, the research also found that lack of stakeholder collaboration, business units operating in silos at the funder level, global companies are recently exiting the South African market, clinical inertia, outdate council of medical schemes, administration burden and drug regulations in South Africa have a significant impact on access to PCSK9i. These findings coupled with the existing literature confirms that the South African healthcare sector, still has a huge gap in achieving better clinical outcomes.

5.2.2 Assess the long-term clinical and economic implications of these barriers.

The second objective was to assess the long-term health and economic implications of not treating hypercholesteremia to clinical targets. The research found that Hypercholesterolemia is a leading risk factor for cardiovascular diseases, and a major health concern. By improving access to effective medications like PCSK9i, this research coupled with existing literature has the potential to contribute to the prevention and management of cardiovascular diseases, thereby reducing the overall burden on healthcare expenditure. Higher healthcare costs can strain public and private healthcare budgets, potentially crowding out investment in other areas and negatively impacting overall economic productivity (Krug et al.,2018) Chronic illnesses or uncontrolled conditions can lead to absenteeism from work, reduced work productivity, and disability (Fouad et al, 2017). These productivity losses can have ripple effects throughout the economy, reducing output and economic growth potential. Despite South Africa and the broader sub-Saharan Africa market having untapped potential (Conway et al, 2019). If the market for innovative drugs is constrained due to reimbursement policies, pharmaceutical

companies may redirect their investment to markets with more favourable reimbursement environments. This could stifle innovation, hinder the development of new treatments, and limit South Africa's ability to benefit from advances in medical science, ultimately impacting GDP growth. According to the European Parliament (2023) restrictions on access to innovative drugs may compromise human capital development by exacerbating health disparities and limiting individuals' potential contributions to the economy. Countries with restrictive reimbursement policies may be perceived as less favourable environments for pharmaceutical companies and investors, potentially deterring foreign direct investment and collaboration in the healthcare sector. This could have implications for South Africa's competitiveness and ability to attract investment, impacting GDP growth in the long term.

5.2.3 To propose evidence-based recommendations for broadening access to PSCK9 inhibitors.

The third objective was to propose evidence-based recommendations for broadening access to PCSK9i. The study found that access to PCSK9i requires a multifaceted approach that addresses economic, regulatory, and educational aspects. By fostering collaboration, advocating for policy changes, and promoting awareness, stakeholders can collectively contribute to overcoming barriers and ensuring that this innovative class of drugs reaches the patients who stand to benefit the most. Most respondents were in favour of value-based healthcare approach (Zanotto, 2021) which centralises patients' clinical outcomes, around the patients' needs are stakeholders that are in sync to achieve best possible clinical outcomes. According to the findings, this approach combats stakeholders operating in silos and only looking after their piece of the pie, but rather fosters an inclusive environment which shares similar interests and objectives, which is essentially to achieve better clinical outcomes. Respondents and literature also recommended the need for initiating educational campaigns targeted at both patients and healthcare professionals can raise awareness about the benefits of PCSK9i, leading to increased demand and, subsequently, improved access. The study also determined that the current Council of Medical Schemes guidelines were 20 years outdated. It is thus prudent to engage with the Council to review and update its guidelines and possibly incorporate the PCSK9i into its Prescribed Minimum Benefit (PMB) drug list to alleviate physician inertia, raise awareness and encourage proactive prescription in eligible patients. Another critical intervention is = to engage in advocating for the inclusion of PCSK9i in medical funders formularies, ensuring broader coverage. Encouraging collaboration between pharmaceutical companies, healthcare providers, and insurers to facilitate price negotiations to make PCSK9i more affordable.

5.3 Contributions

There are two contributions to this study: theoretical and practical. The contribution is covered in full in the discussion that follows.

5.3.1 Practical contributions

In conclusion, this research on the perceived impact of reimbursement policies on PCSK9 inhibitor accessibility in the South African private healthcare sector is justified by its clinical significance, implications for healthcare equity and policymaking, relevance to clinical practice, and contribution to addressing knowledge gaps in the field. By examining stakeholder perceptions and experiences, this research has the potential to inform evidence-based interventions aimed at improving access to PCSK9i and optimizing cardiovascular care in South Africa. Previous studies (Van Zyl, 2013) on the association of LDLR and PCSK9i variants with LDL-C levels in a black South African population have laid an important foundation. It is necessary to extend this inquiry into the equity dimensions of drug access and adoption.

5.3.2 Theoretical contribution

This study provides a notably theoretical contribution to the literature about reimbursement policies in the South African private healthcare sector, adoption and accessibility of PCSK9i, barriers limiting access and evident based recommendations to broaden access to PCSK9i to achieve better clinical outcomes for patients diagnosed with hypercholesteremia. This study could aid prospective and already existing stakeholders in making informed decisions around broadening access.

5.4 Limitations

This research study had 4 major research limitations, namely: data availability, sample size, bias, and temporal factors.

5.4.1 Data availability

One of the primary limitations to this research is the potential scarcity of data, more especially data to perform a comparison against the public healthcare sector. The fact that PCSK9i haven't really been fully adopted or rather, there has been a lot of declines from the medical funders, it makes it difficult to source sufficient data and to also depict trends in the hypercholesteremia industry.

5.4.2 Sample size

Although the study reached data saturation, it was quite a challenge to get respondents to commit to interviews due to their busy schedules and commitments. It would have been beneficial to have included respondents from other markets where the PCSK9i have been adopted, so to share best practice and provide a comprehensive comparative analysis. s,

5.4.3 Bias

The perception of stakeholders regarding the impact of reimbursement policies on PCSK9i accessibility may be influenced by various biases, including personal experiences, beliefs, and interests. Efforts to minimize bias through data and investigator triangulation and reflexivity, are essential, though they do not eliminate subjectivity.

5.4.4 Temporal factors:

Legislative, regulatory, and economic considerations can cause changes in reimbursement policies and healthcare dynamics over time. The temporal context in which the data are gathered may limit the study's conclusions and cause it to miss newly developing trends.

5.5 Recommendations

There are several factors that this study did not fully explore which further studies can pick up on in enhancing access to PCSK9i to achieve better clinical outcomes which will translate in better health economy, market access, innovative drug adoption and commercial success. This report suggests that all stakeholders involved in broadening market access to innovative drugs to collaborate, share interests and look at the bigger picture which is essentially a better healthcare system that is accessible, competitively priced and always has clinical outcomes of its beneficiaries at the forefront. Future recommendations for further research include:

- Perform a health economic analysis to assess the cost-effectiveness of various PCSK9i reimbursement plans in the South African private healthcare market. This could entail simulating the possible effects of different reimbursement strategies, including risk-sharing plans, value-based pricing, or tiered formularies, on the budget, savings, and health outcomes.

5.6 Overall Conclusion

In conclusion, affordable innovative drug costs in South Africa yield multiple benefits, ranging from improved access to medications and disease management to positive economic and public health outcomes. By ensuring that essential medications are accessible and affordable to all segments of society, South Africa can promote health equity, economic prosperity, and overall well-being for its population.

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Appendices

Appendix 1.1: Consent form for all participants

Appendix 1.2: Participants information sheet

Appendix 1.3 Respondents demographic information sheet

Appendix 1.4 Interview guide

University of the Witwatersrand,
Wits Business School
Faculty of Commerce, Law, and Management

Good day

My name is Plossie Ngobeni. I am a Master's in Business Administration student at the University of the Witwatersrand, Johannesburg.

My supervisor is Dr Jacques Totowa. I am conducting a research study about the impact of reimbursement policies on the adoption and accessibility to PSCK9i.

The study title is "The perceived impact of reimbursement policies to accessibility of PCSK9 inhibitors in the South African private healthcare sector.

I am inviting you to take part in an interview. If you decide to take part, your participation in this research study will last about approximately 10-15 minutes . The interview will take place at Aspen Pharmacare in Woodmead or at your practice.

Data will be deleted after 5 years. Only the I researcher will have access to the data. During the research activity, I will need to ask for typical barriers you are faced with when prescribing, and promoting PCSK9i.

The interview will be confidential and anonymous. When I share the results of the research study, I will not include your name or anything else that could identify you. With your permission, other researchers may use the data collected from this research study, but your name and any personal information will not be used or passed on.

If you decide to take part in the research study, it should be because you want to volunteer. You do not have to take part. You can stop being in the study at any time. You do not have to answer any questions if you do not want to. You will not get any direct benefits if you choose to join the research study. You will not lose any services, benefits or rights you would normally have if you decide not to join. Taking part in the research study will not cost you anything. You will not be paid for being in this research study.

This research study will be written up as a research report. If you have any questions during or afterwards about this research study, feel free to contact me or my supervisor on the details listed below. If you have any concerns or complaints about the ethical procedures of this research study, you are welcome to contact the University Human Research Ethics Committee (Non-Medical), telephone +27(0) 11 717 1408, email hrecnon-medical@wits.ac.za.

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Participant Consent Form

The perceived impact of reimbursement policies on accessibility to PCSK9 inhibitors in the South African private healthcare sector.

Plossie Ngobeni

I, ..., agree to participate in this research project.
I agree to the following:
(Please circle the relevant options below)
The research study was explained to me. I understand what this study is about.
YES NO
I understand that I can volunteer to take part in the study YES NO
I agree that the interview/focus group/other activity may be audio recorded
YES NO
I agree that direct quotations from my interview/focus group/other activity may be used by the researcher in their research report/ manuscript/book chapter
YES NO
I agree that my participation will remain anonymous (my name or other identifying data will not be used by the researcher in their research report/manuscript/book chapter)
YES NO
I agree that other researchers may use the information I provide in my interview/focus group/other activity (depending on their own ethics clearance being obtained) but my name and any personal information will not be used or passed on
YES NO

Signature……..
Name of participant…….

Date……

Signature……

Plossie Ngobeni……

Date…….

Annexure 1.3 *Respondents sample and demographics*

Sample	Demographics	#
Cardiologists	▪ Cardiologists at Netcare Sunninghill and Linksfield. ▪ Over 20 years' experience in cardiology and treating hypercholesteremia.	4
Brand manager	▪ Launched PCSK9iin South Africa. ▪ 7 years in brand management ▪ PCSK9i market strategies, communication and trend analysis	1
Head of Access	▪ Facilitate the reimbursement process in the healthcare market. ▪ 3 years in access management. ▪ Maintain and build relationships with key opinion leaders to ensure successful market access.	1
Pharmacist	▪ Ensure that medicines prescribed to patients are suitable, within the law, and accessible.	1
Head of Medical Affairs	▪ Formulate long-term strategies to improve drug and other medical devices information delivery and education. ▪ 11 years' experience in medical affairs for three renowned pharmaceuticals in the industry.	1
Reimbursement clerk	▪ Liaise with medical funders to ensure reimbursement and access to treatment. ▪ 6 years' experience at Dr Angels practice.	2
Brand Marketers	▪ Promote PCSK9i throughout South Africa in the private healthcare sector. ▪ Maintain and build relationships with cardiologist. ▪ Various years of experience ranging from 2 years to 10 years.	5

Annexure 1.4 Interview Guide

Question	Comment
Please outline your role in ensuring market access. (how does your role support market access)	
In your opinion, what limits market access for innovative drugs like Repatha (PCSK9i)	
How important is market access for Repatha?	
What are the long -term economic and health implications? (of limited access)	
What strategy have you implemented in broadening market access?	
What challenges do you foresee and what is your plan of action?	
What are the indicators of successful market access?	
What challenges have you encountered with market access?	