DEPARTMENT OF PUBLIC HEALTH
RESEARCH REPORT

VARIATION IN PRICES OF MEDICINES USED IN THE MANAGEMENT OF HIV, TYPE 2 DIABETES MELLITUS, AND HYPERTENSION IN SOUTH AFRICA'S PRIVATE SECTOR, 2022.

A research report submitted to the University of the Witwatersrand, Johannesburg, School of Public Health (Faculty of Health Sciences), in partial fulfilment of the requirements for the degree of Master of Public Health in Health Economics.

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DECLARATION

I, Nyaradzai Matanyaire declare that this research report is my own, unaided work. It is being submitted for the degree of Master of Public Health at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at another University.

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ABSTRACT

Background: There is significant variation in the price of medicines used to manage chronic diseases in the private health sector in South Africa. Understanding pricing structures can aid in reducing out-of-pocket payments, enhancing access, and improving medicine affordability. This study aimed to investigate the sources of variation in private sector single exit price (SEP) of medicines used in the management of Human Immunodeficiency Virus (HIV), type 2 diabetes mellitus (diabetes), and hypertension.

Methods: This was a cross-sectional quantitative study design using private sector price data published on the Medicine Price Registry (MPR) as of July 11, 2022. To quantify the variation in SEP, the mean, median, and range was calculated for each Anatomical Therapeutic Chemical group (ATC) at level two (ATC2) and active ingredient. Decomposition using Shorrocks' method was used to examine the contribution of price sub-components, namely manufacturer fees and logistics fees to medicine price variations. Field's inequality decomposition was used to understand the contribution of non-pricing-related factors such as origin of manufacturer and generics to medicine pricing variations.

Results: Varying patterns were observed across disease classes, with HIV medicines showing the highest variability and overall highest average SEP per unit. Anti-hypertensives showed the least variation in SEP per unit. Variation in manufacturing costs consistently drove price inequalities across the three disease groups, overshadowing logistics fees. Field's decomposition unveiled significant contributors to price disparities, such as drug class and origin of manufacturer. For example, hypertension medication pricing was affected by the number of available brands, while HIV medicine price variation was mostly influenced by combination formulations.

Conclusions: The findings reveal the complex nature of medicine pricing in South Africa, impacted by regulatory policies and market dynamics. Considerable medicine price variation for HIV, diabetes and hypertension medicines was attributable to both pricing and non-pricing related factors. Policies to control prices of medicines should encompass both, including direct price controls, regulatory frameworks, and generic medicine policies. Policies that promote generic substitution can shift demand towards more cost-effective alternatives, contributing to more uniform pricing and increased access.

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LIST OF ABBREVIATIONS

ARV	Antiretroviral
ATC code	Anatomical Therapeutic Chemical code
CPI	Consumer Price Index
DPCO	Drug Price Control Order
EML	Essential Medicines List
GDP	Gross Domestic Product
HCTZ	Hydrochlorothiazide
HIV	Human Immunodeficiency Virus
Log fee	Logistics fees
MPC	Medicine Pricing Committee
MPR	Medicine Price Registry
NDOH	National Department of Health
NDP	National Drug Policy of South Africa
NHI	National Health Insurance
OECD	Organisation for Economic Co-operation and Development
OOP	Out of Pocket
PPI	Purchaser Price Index
PPP	Purchasing Power Parity
R&D	Research and Development
SAHPRA	South African Health Products Regulatory Authority
SAMF	South African Medicines Formulary
SAPC	South African Pharmacy Council
SDG	Sustainable Development Goal
SEMDSA	Society for Endocrinology, Metabolism and Diabetes of South Africa
SEP	Single Exit Price
STG	Standard Treatment Guidelines
UHC	Universal Health Coverage
UN	United Nations
VAT	Value Added Tax

1. CHAPTER ONE: INTRODUCTION

1.1. BACKGROUND

The United Nations, through Sustainable Development Goal (SDG) target 3.8, strives to attain universal health coverage (UHC), while ensuring financial risk protection and access to quality essential health care services (United Nations, 2018). Attaining UHC means that individuals should not face financial distress when seeking healthcare services, therefore, direct payments at the point of service must be minimised or eliminated. In low- and middle-income countries, direct payments can be remarkably high, reaching up to 90% of health expenditure (Bigdeli *et al*., 2015). Controlling the overall cost of health services is necessary to increase affordability and therefore encourage health-seeking behaviour.

For any health system to effectively address its main health challenges, ensuring the availability and provision of medicines is crucial. However, approximately 50% of the global population lacks access to essential medicines especially in Africa and Asia (World Health Organization, 2020). High medicine prices, inequitable access, and excessive spending on medicines are the driving factors behind this disparity (World Health Organization, 2008). A mere 15% of the world's population consumes about 90% of pharmaceuticals produced globally, with per capita spending on pharmaceuticals in high-income countries estimated to be a hundred times higher than in low-income countries (World Health Organization, 2008). In developing countries, medicine expenditure constitutes a sizeable portion (20-60%) of all health expenditures, while in the Organization for Economic Co-operation and Development (OECD) and European countries, it averages 18 and 20% respectively (World Health Organization, 2023). Interestingly, healthcare spending, including pharmaceuticals, closely correlates with a country's Gross Domestic Product (GDP), countries with a lower GDP are at higher risk of undersupply of pharmaceuticals as they have lower healthcare expenditure than those with higher GDPs (IMS Institute for Healthcare Informatics, 2015).

The cost of medication poses a significant financial burden on individuals, primarily due to direct/out-of-pocket (OOP) payments. In many developing countries, OOP payments are the primary method used to pay for medicines, with medication expenses often ranking second after food expenses in household spending (World Health Organization, 2023). As a result, many households struggle to afford essential medications. The disparity in both accessing and

spending on essential medicines further deprives less privileged populations of their basic right to good health.

Variation in medicine pricing particularly for different brands of the same medicine may be an indicator of pricing irregularities which can make medicines unaffordable and hinder access. There is therefore a need to understand price regulation methods and how they can assist in controlling medicine prices.

1.2. LITERATURE REVIEW

The following section gives information on mechanisms of medicine price regulations in a global context before giving the South Africa medicine pricing context. The medicine pricing regulations that South Africa has employed are discussed in detail.

1.2.1. Regulating Medicine Pricing

Medicine pricing is a crucial factor affecting access to medicines globally (Xiphu and Mpanza, 2004) and its regulation is essential. The impact of pricing on access to medicines is noted on a global scale, but the practices adopted in regulating medicine prices differ from country to country. This has warranted the need for pricing control mechanisms guided by medicine pricing policies. A medicine pricing policy is a set of guiding principles for managing the prices of medicines to be used by any organisation in health services (World Health Organization, 2020b). Research indicates that certain factors, such as price regulation frameworks, central purchasing, and promotion of generic use are associated with lower medicine prices (Daalen *et al.*, 2021). Given the significant impact of pharmaceutical costs on healthcare expenditures, interventions to control these prices are essential. The following section presents information on medicine pricing controls with some country specific examples. It is then followed by presentation of South Africa's medicine price regulation background.

Regulatory frameworks and direct price control policies include reference pricing, mark-up regulations and tiered pricing. Reference pricing is the practice of benchmarking medicine prices to those of other countries or purchasing authorities based on a set of clear factors as determined by the purchasing authority. These include, affordability, countries with comparable Gross Domestic Product (GDP), similar health funding models and similar medicines indications (World Health Organization, 2020b). This strategy is used in the Netherlands to establish maximum allowable prices by comparing local product prices with

those in foreign markets (Rietveld and Haaijer-Ruskamp, 2002). Despite complexities due to variations in dosage forms and trade names, this approach led to a 20% reduction in pharmaceutical prices in 1996 when it was introduced (Rietveld & Haaijer-Ruskamp, 2002). In 2014, Morocco enacted reforms to lower medicine prices, which included referencing prices against those of seven other countries, harmonising pricing rules, and adjusting profit margins. These reforms led to reduced prices for over 25% of medicines (Cheikh *et al.*, 2021).

Mark-up regulation refers to the measures that are used to control additional charges in the supply chain following establishment of manufacturing costs. Controlling margins and mark-ups is crucial in regulating medicine prices across different stages of the supply chain. Pharmacies often adhere to fixed percentage mark-ups, tiered mark-ups, and tiered professional fees, disincentivising the sale of expensive medicines (Mackintosh *et al.*, 2016). In China, the National Development and Reform Commission (NDRC), which oversees different pharmaceutical pricing policies, requires that medicine prices for all essential medicines are capped. The NDRC monitors the compliance of pharmaceutical companies and healthcare providers to these caps (Fang, 2015). The WHO recommends that medicine price regulations be used in conjunction with other pricing policies to yield better outcomes (World Health Organization, 2020b). However, the effectiveness of medicine price regulation depends on legislative frameworks, post-implementation monitoring, and compliance (World Health Organization, 2020b).

Policies promoting generic substitution, coupled with educational efforts, aim to reduce medicine expenditure. Despite their importance, generic availability in Africa remains below 40% (Mackintosh *et al.*, 2016). In countries like the US, generics contribute to over 80% of sales within the first year of market entry, driving competition and influencing retail prices (Mackintosh *et al.*, 2016). Yet, the effectiveness of standalone generic policies varies across countries. High-income countries with more open markets tend to have higher initial generic prices compared to those with stricter regulations. Scandinavian nations employ mandatory generic substitution alongside price regulation for effective pricing management (Daalen *et al*., 2021). In South Korea, generic medicines are priced according to an 'equal medicine, equal pricing policy', where generics are all priced the same, at 53.6% of the originator medicine cost (Kwon and Godman, 2017). Meanwhile, France implemented a prescriptive pricing policy and has extra measures such as, permitting the delisting of medicines with high prices (Sermet

et al., 2010). Promotion of the use of cost-effective generic options in France, led to a reduction of costs of about 450 million Euros per year in the period of 2003 to 2007(Kwon and Godman, 2017).

The use of a single purchaser to procure medicines on behalf of many purchasing authorities often leads to more competitive medicine prices (US Department of Health and Human Services, 2018; World Health Organization, 2020b). In the United States, bulk purchasing by the government resulted in significant discounts of nearly 50% compared to prices at local pharmacies, highlighting the impact of centralised procurement systems on medicine prices (Rietveld and Haaijer-Ruskamp, 2002).

In the USA, pharmaceutical companies have flexibility in setting initial drug prices due to open market entry. In contrast, in the UK, prices are negotiated between the government and drug manufacturers, resulting in significant cost reductions, particularly for cancer drugs. This led to a remarkable 42% decrease in the initial cancer drug prices in the UK compared to the USA, showing the impact of government intervention in pricing negotiations and improving access to vital medications (Savage *et al*., 2017).

The above examples illustrate various interventions for controlling medicine pricing, highlighting that a uniform approach is not suitable due to the varied economic contexts and unique healthcare requirements of each country. Thus, a combination of multiple interventions is often the preferred strategy to optimise price controls. For example, Canada's adoption of the Alberta model in 2014 predicted substantial savings of close to four billion Canadian dollars over a three-year period through capped generic entry prices and progressive reductions over time (Hollis and Grootendorst, 2015). The Alberta model is a generic policy that prescribes the pricing of generic entrants based on their order of introduction to the market (Hollis and Grootendorst, 2015). The first generic entrant on the market is priced at 70% of the originator and holds this privilege for a year before being set to 50% of the originator price, the second entrant is priced at 50% and subsequent entrants are priced lower (Hollis and Grootendorst, 2015).

Many countries have implemented medicine price regulation to enhance the affordability and accessibility of medications. However, inadequate legislative frameworks, limited post-

implementation evaluations, and non-compliance with existing policies can undermine the effectiveness of such regulations (Abdel *et al*., 2017).

1.2.2. Medicine Pricing in South Africa.

South Africa is a middle-income country with a per capita expenditure on health of 489 United States dollars (USD) and a health spending of about 8.1% of the GDP (The World Bank, 2023). This is higher than the OECD recommended level of 5% of GDP as expenditure on health.

The healthcare system in South Africa consists of the public sector which caters for about 82% of the population using only about 24% of the national drug expenditure and a much smaller private sector that caters for the rest of the population but has access to 76% of the drug expenditure (Mcintyre and Ataguba, 2014). The public sector is mostly utilised by individuals of lower socioeconomic status who cannot afford the high costs of private health care as most public services are offered free of charge. The per capita spending in the public sector is much lower than that in the private sector. The two sectors acquire medicines through different channels, through the SEP system for medicines regulated by the SEP for the private sector and through a public tender bidding system for the public sector. In South Africa, the state's tender process for procuring medicines is managed by the National Department of Health (NDOH) and follows strict guidelines to ensure fair and transparent sourcing. Tenders are advertised publicly, allowing pharmaceutical companies to bid by submitting proposals that meet specified criteria, including price, quality, and compliance with manufacturing standards. Submitted bids undergo evaluation for technical and financial aspects to ensure sufficient capacity and cost-effectiveness. This structured process helps maintain an affordable, reliable supply of essential medicines for public health facilities, enhancing medicine accessibility while maintaining strict quality standards.

In South Africa's private healthcare sector, funding primarily comes from private medical insurance and direct/out-of-pocket payments(McIntyre, 2010; Bangalee and Suleman, 2015). However, private medical insurance often falls short in coverage, requiring individuals to supplement with out of pocket (OOP) payments or copayments in cases where the cost of medicines is more than what is reimbursed, for benefit exclusions, and when annual benefits are depleted. The excessive cost of medicines exacerbates OOP expenses, as medical scheme funders typically cap payment limits based on medicine reference pricing indices (McIntyre,

2010). This limitation can impede access to essential medications, potentially affecting health outcomes.

Prior to 1994, the pharmaceutical market in South Africa was largely unregulated in terms of medicine pricing, allowing pharmaceutical companies significant discretion in setting prices (Gray & Vawda, 2016). This lack of strict regulation contributed to high medicine costs and limited accessibility for many South Africans, as companies could establish prices with minimal oversight (Harrison, 2009). In addition, import tariffs and restrictions on promotion of use of generic medicines further impacted affordability and access in the private sector, exacerbating health inequities across socioeconomic groups. Generic alternatives were not widely promoted due to regulatory and market barriers (Gray & Vawda, 2016).

Innovator companies dominated the market for pharmaceuticals, and they influenced prescribing and dispensing patterns through sampling, bonusing, rebates, discounting, and other perverse incentives (Organization for Economic Co-operation and Development, 2018). This allowed price discrimination to the detriment of the poor and marginalised patients who ended up making more direct/OOP payments or forgoing treatment (Organization for Economic Co-operation and Development, 2018). Because of these serious health system disparities and exceedingly high medicine costs, South Africa developed the National Drug Policy (NDP) in 1996 (South African Government, 1996).

The NDP was developed to address deficiencies in the pharmaceutical sector and guide how pharmaceutical services would be managed in the country. Its economic objective was to lower the price of medicines in both private and public sectors to improve access to healthcare particularly for previously disadvantaged populations (South African Government, 1996). To promote cost containment of medicines, measures stipulated by the NDP included the establishment of a Medicines Pricing Committee (MPC) to monitor activities related to medicine pricing, to increase the transparency of the pricing process, and to increase affordability and improve access (South African Government, 1996). The pricing components introduced by the NDP including transparency in medicine pricing, regulation of private sector mark-ups and the establishment of the SEP, which was later introduced in 2004, this incorporated distribution logistics fees (South African Government, 1996) . The NDP also introduced the promotion of generic substitution. The Medicines and Related Substances Act was amended to ban bonusing, discounting and rebates. Further amendments to legislation

led to prohibition of incentives and provisions allowing companies other than innovator companies to import medicines (South African Government, 1996; Organization for Economic Co-operation and Development, 2018).

In 2004, the SEP for all buyers (final sellers) except the government/state was introduced to promote transparency and uniform pricing of medicines by manufacturers (Ondo, 2019). It is the only pricing system for all buyers in the private sector (community, institutional etc), before the addition of regulated dispensing fees for the patient. The SEP comprises of manufacturer fees, logistics fees, and Value Added Tax (VAT). It is applicable only to scheduled medicines (schedules 1 to 7) according to the Medicines and Regulated Substances Act.

The manufacturer price is determined by the manufacturer or importer of a medicine or scheduled substance and includes costs incurred before release for distribution, such as R&D, raw materials, and production. Logistics fees are subsequently added for distribution of final product to wholesalers. They are determined through negotiation between the manufacturer/importer and the logistics service provider of the medicines. Logistics fees usually account for 10-15% of the final medicine price, however, due to the lack of transparency between involved parties, manufacturers may inflate their fees which in turn inflates logistics fees such that negotiated savings on logistics fees accrue back to the manufacturer (National Department of Health, 2012; Bangalee and Suleman, 2015). Value added Tax (VAT), is the final component of the SEP and is currently set at 15% in South Africa.

At the point of dispensing medicines to a patient, a professional fee in the form of dispensing fee is added to the stipulated SEP. Dispensing fees are regulated and determined by a formula outlined and published in the government gazette (Government of the Republic of South Africa, 2015). This formula sets the maximum dispensing fee that can be added to the SEP, with dispensers having the option to charge amounts up to this maximum amount.

The Minister of Health determines, annually, the extent to which all private medicine prices may be adjusted through consideration of the relevant economic indicators and the need to ensure availability and accessibility of medicines (Government of the Republic of South Africa, 2015). The government oversees price regulation by setting the SEP for each medicine each year and ensuring that dispensers adhere to the specified price limit for each medicine and that the dispensing fee remains within the capped amount (Moodley and Suleman, 2019).

Following the implementation of SEP, the private sector became a regulated market with a more transparent pricing system (SEP introduction and banning of perverse incentives) resulting in lower prices of medicines compared to the prices before its implementation (Ondo, 2019). The introduction of SEP and banning of incentives adversely affected the profit margins of retailers and was not well accepted in the beginning (Organization for Economic Co-operation and Development, 2018; Ondo, 2019). One study analysed the impact of South Africa's SEP policies and regulatory measures on the pricing of a selection of generic medicines from 1999 to 2014 and it found that the implementation of SEP resulted in an increase from about 43% to 111% in the price gap between originator and lowest priced generic in the studied basket (Moodley and Suleman, 2019). This was due to generics responding to price regulation and their prices dropping significantly while originator medicines did not respond equally (Moodley and Suleman, 2019), confirming that originator brands are not responsive to price competition (Gray, 2009; Bangalee and Suleman, 2015). Consequently, some originator brands were withdrawn from the market post-2004 due to their inability to compete on price (Gray, 2009).

While the policy changes led to a reduction in medicine prices, significant pricing disparities persisted among generics and between originators and generics. Achieving uniformity in pricing remains a challenge it is still unclear how some determinants of medicine prices such as manufacturer and logistics fees are set (Xiphu & Mpanza, 2004). Uniformity in pricing ensures that people have consistent access to affordable medicines regardless of their socio-economic status and where they source their medicines.

A study looking at the variation in SEP between originator and generic medicines used to manage three common cancers found that there was considerable variation in prices of different brands of cancer medicines in the private sector in South Africa and that the SEP differences between the highest and the lowest priced brands of the same medicine could be as high as 97.3% (Mattila, Babar and Suleman, 2021). Aspen faced legal challenges regarding their cancer medications (Leukeran, Alkeran, and Myleran) and Pfizer was similarly challenged over their lung cancer drug, Xalkori, due to the higher prices of these drugs in South Africa compared to the global market (Bangalee and Suleman, 2018). The case of Hazel Tau vs. GlaxoSmithKline and Boehringer Ingelheim in 2002 also proved the extent of excessive pricing in South Africa and the impact it had on access to life-saving antiretroviral medicines (Organization for Economic Co-operation and Development, 2018). The settlement of that

case led to a decrease in prices of antiretrovirals by over 11% per annum between 2011-2015 and contributed to the increase in access to antiretroviral treatment (OECD, 2018).

In South Africa's private sector, despite policy changes over the years, medicine prices remain high and unpredictable, lacking transparency in their determination (Bangalee and Suleman, 2016, 2018). This poses a barrier to accessing medicine for those who rely on private healthcare. The cost of medicine is crucial for private healthcare users, whether they are insured or not, as it affects their ability to afford necessary treatment.

The proposed implementation of NHI in South Africa which seeks to address the lack of equity of access to health services in South Africa, will focus on a single purchaser, single payer approach (Department of Health, 2015). Procurement of pharmaceuticals will be based on price negotiations between the purchaser and pharmaceutical companies(Mashile, 2020). This approach may achieve a reduction of prices of pharmaceuticals by leveraging its bulk purchasing power as the public sector has, in the current tender procurement system(Mashile, 2020). However, a risk exists in that, pharmaceutical companies have an obligation to achieve a certain level of return on investments so, moving from the current two-tier system to the NHI proposed system is not a guarantee that the price of pharmaceuticals will drop drastically.

Market segmentation in South Africa allows pharmaceutical companies to implement different pricing strategies for the public and private sectors which impacts medicine pricing and accessibility. In the public sector, the government operates as a bulk purchaser, enabling it to negotiate lower prices with pharmaceutical companies through tender processes (Gray & Vawda, 2016). These bulk procurement mechanisms, combined with government incentives, enables securing of essential medicines at substantially lower prices. In contrast, the private sector lacks centralized purchasing power, leading to higher medicine prices. Through market segmentation, pharmaceutical companies can maintain premium prices in the private market, where a different consumer base with higher disposable income and private health insurance can absorb higher costs. It thus enables companies to maximize profits in the private sector while supporting public health goals through lower-cost drug availability in the state sector (McIntyre, Thiede and Birch, 2007).

Understanding the factors influencing medicine pricing in the private sector is essential for developing policies that ensure fair access to affordable essential medicines and services.

1.3. PROBLEM STATEMENT

Prices of various brands of the same medicines vary significantly in the private health sector in South Africa particularly between originator brands and the lowest priced generics. Reducing these price variations will lead to more uniform pricing and understanding of the contributory factors will help inform policies that will lead to lower medicine prices and increased affordability.

1.4. JUSTIFICATION

The study investigated the components of the Single Exit Price (SEP) in South Africa and how they contribute to price variation in South Africa's private health sector. This is because of the wider scope of medicine brands available in this sector. It focused on understanding the pricing of medicines in the private sector to which the SEP policy applies and not the government/state sector where a tendering policy is used. The private sector encompasses private medical insurances and direct payments / OOPs. Despite the adoption of different regulations and policies, notable variations in medicine prices persist, accompanied by a lack of transparency in pricing. Conducting research on medicine pricing variation in South Africa will assist in the development of NHI in South Africa, centred on the equitable provision of healthcare for all South Africans as it can inform the sources of price variations and how to correct them to procure medicines at lower prices.

An understanding of the pricing structures and sources of price variation will help us understand why different branded medicines with the same active ingredients have huge cost differences. Obtaining accurate information on medicine pricing will allow for fair bargaining of prices from manufacturers, ensuring affordability of medicines in South Africa and assist in the attainment of SDG 3. It will provide tangible data to inform drug policymaker decisions. In addition, it will provide relevant health economics centred approaches which may be useful in NHI implementation in South Africa.

The study focused only on pricing of medicines for 3 disease classes, HIV, diabetes and hypertension due to their importance in terms of prevalence in South Africa and the high economic burden they pose. In South Africa, HIV, diabetes, and hypertension are among the most prevalent chronic conditions, impacting millions of individuals and placing a high burden on healthcare resources (Statistics South Africa, 2020). Meanwhile, non-communicable

diseases like diabetes and hypertension are soaring, contributing to a high rate of morbidity and mortality in the country (Statistics South Africa, 2020). Chronic disease treatment, therefore, demands a sustainable and affordable approach to medicine pricing to ensure that both public and private healthcare sectors can meet demand without compromising quality or access. Investigating the pricing of medicines for HIV, diabetes, and hypertension in South Africa is crucial in addressing the challenges of affordability and accessibility. Understanding pricing dynamics can guide policy reforms aimed at making essential medicines more affordable and reducing the long-term healthcare costs associated with these chronic conditions.

1.5. RESEARCH QUESTION.

What is the range of variation in SEP for medicines used to treat HIV, diabetes and hypertension in adults in South Africa and what factors influence the price variations in the private health sector in South Africa based on pricing data as of July 2022.

1.6. RESEARCH AIM

To describe, quantify and investigate the reasons for the variation in pricing of medicines used in the management of three common adult chronic diseases in South Africa.

1.7. RESEARCH OBJECTIVES

I. To quantify the range of variation in private sector SEP in South Africa for oral medicines used to treat HIV, diabetes, and hypertension as of July 2022.
II. To investigate how manufacturer fees and logistics fees contribute to private sector medicine SEP variation for HIV, diabetes, and hypertension oral medicines.
III. To summarise the non-pricing related factors which contribute to private sector medicine price variation for HIV, diabetes, and hypertension oral medicines.
IV. To analyse whether non-pricing related factors explain the variation in private sector medicine prices for HIV, diabetes, and hypertension medicines.

2. CHAPTER TWO: METHODOLOGY

This study is a secondary data, cross-sectional analysis of the SEP dataset published on the 11th of July 2022 on the Medicines Pricing Registry (MPR) which reflects the SEP of medicines in South Africa as at that date. This dataset, which was the most recent during the protocol development stage of this research, is the primary data source with no additional primary data collected for this study. The primary SEP dataset will be described before presentation of the methods for secondary study.

2.1. PRIMARY STUDY

The SEP data is published regularly and made publicly available on the MPR which is found on the National Department of Health (NDOH) website. The SEP raw data is available from the MPR website.

2.1.1. Study Design.

The SEP datasets have been provided over time and therefore the primary data constitute a longitudinal study design.

2.1.2. Study Setting.

Medicine prices for all scheduled medicines that are available to the SA private health care sector.

2.1.3. Study Population.

Prices of medicines in the private sector are adopted from the MPR website. The version published on the 11th of July 2022 forms the primary study population. It contains 17 883 entries of various medicines (South African Department of Health, 2022).

2.1.4. Study Sample

There is no sampling in the primary data. All medicines that are registered in SA and require an SEP are included in the dataset.

2.1.5. Data collection

Data on SEP was derived from the MPR. It is the duty of the Pricing committee to ensure that the SEP is defined by all manufacturers for all medicines that are registered in SA (South African Department of Health., 2022). Medicine manufacturers/principal applicants, through an obligatory process, periodically submit SEP data for their SA registered medicines to the

NDOH. The NDOH then collates and publishes this data on the MPR in MS Excel format. All updates on SEP are approved by the Pharmaceutical Evaluation Unit of the NDOH. The datasets are published on the MPR together with previous versions and are available publicly. (South African Department of Health., 2022).

2.2. SECONDARY STUDY

2.2.1. Study Design

This secondary study is a cross-sectional analysis of the SEP dataset published on the 11th of July 2022.

2.2.2. Study Setting

Medicine prices for medicines that are available to the SA private health care sector.

2.2.3. Study Population

Medicine prices of medicines in the private sector adopted, from the MPR website as published on the 11th of July 2022.

2.2.4. Study Sample

The study sample includes registered oral medicines for adults used in the management of the three highly prevalent adult chronic conditions in SA, namely, diabetes, hypertension, and HIV. Oral medications were chosen as the study's focus to as they offer the widest selection of generic options. In addition, oral medications are the most common form of treatment for these conditions, making them the most representative and practical choice for examining pricing trends in the context of the diseases studied. The selection of medicines was based on the South African Medicines Formulary (SAMF) listing and the treatment guidelines of the respective clinical societies for diabetes (Society for Endocrinology, Metabolism and Diabetes of South Africa- SEMDSA) (SEMDSA Type 2 Diabetes Guidelines Expert Committee, 2017), hypertension (Southern African Hypertension Society) (Seedat YK, Rayner BL and Veriava Y, 2014)and HIV (Southern African HIV Clinicians Society) (Nel *et al.*, 2023). Medicines for diabetes and hypertension are also regulated by the Council for Medical Schemes under prescribed minimum benefit (PMB) guidelines. In the case of HIV management, medical schemes must align with the STG and EML used by the public sector, ensuring equivalent treatment options between private and public sectors.

The inclusion criteria were an active product ingredient with at least five brands available on the SA market and medicines that are regulated using the SEP structure limited to adult, oral dosage form medicines only. The selection of medicines with at least five available brands aimed to ensure a representative sample with sufficient generic alternatives, indicating products that have been on the market for a long time and have stabilized. Analysing pricing at the peak of market forces influence, such as immediately after a patent expires when competition is limited, could lead to distorted and exaggerated variations. This approach is believed to facilitate a more meaningful comparison of pricing trends across different options, offering insights into the competitive dynamics of the market and the availability of affordable alternatives. The exclusion criteria were medicines that are exempt from SEP regulations in SA (unscheduled and zero scheduled medicines), non-oral dosage form medicines and liquid dosage form medicines and unregistered medicines including Section 21 medicines. Section 21 medicines are not registered by SAHPRA but can be obtained via a special exemption according to Section 21 of the Medicines and Related Substances Act 101 of 1965, as amended (SAHPRA, 2021).

2.2.5. Data Management

Data analysis was conducted using Stata software.

Step 1: Downloading the relevant SEP data.

A JSON version of the July 2022 dataset was downloaded in MS Excel format from the MPR website (South African Department of Health., 2022). This version of the data was used as it can be manipulated to remove incomplete records and duplications. The dataset contained twenty-one variables detailing the Applicant/Manufacturer's details and the details of registered medicines as well as the breakdown of the medicine price components.

Step 2: Data cleaning

The data downloaded in MS excel format was imported into Stata (17 MSI) (StataCorp LP, College Station, TX, USA). Stata is a statistical package and was used to clean and analyse the data. The original dataset contained 17 883 observations. The original dataset was in a long format, meaning that each registered product had multiple rows in the dataset for each active ingredient. It was then converted to a wide format wherein each product was presented in a single row with multiple active ingredients. The study sample data (medicines of interest) were extracted in Stata, first by dropping medicines with the irrelevant ATC2 codes, then

irrelevant formulation types, and active ingredients based on the inclusion and exclusion criteria. Data for all discontinued medicines was omitted from the analysis. The resultant number of observations of interested that were used in the study was 730.

Step 3: Creating new variables and recoding.

To allow easier identification of a concatenated variable, combining active ingredient, strength and unit was constructed for each active ingredient. Further cleaning was done by dropping unnecessary variables, then recoding e.g. formulation type and pack size, encoding, and generating new ones e.g. origin of drug manufacturer/principal applicant. The manufacturer's origin was not specified in the MPR dataset. Instead, this information was obtained from various sources by investigating the parent manufacturing company. However, there was no further examination to identify which products were imported as finished goods or the sourcing of excipients, even for medicines produced locally. The price data for all available dosage forms of the selected medicines were collected and expressed in South African Rand (ZAR). The data was presented based on ATC level 4 (ATC4). The ATC classification system classifies the active substances in a hierarchy of five levels (World Health Organization Collaborating Centre for Drug Statistics and Methodology, 2022). Each ATC group is separated into a 2nd level denoting pharmacological or therapeutic group. Levels 3 and 4 are either chemical, pharmacological, or therapeutic subgroups while the 5th level is the chemical substance(World Health Organization Collaborating Centre for Drug Statistics and Methodology, 2022). Therefore, ATC level 5 is the most specific while level 2 is the least specific. ATC4 codes were trimmed to ATC2 level and irrelevant codes dropped, the ATC2 codes that were maintained for analysis are A10 (medicines used in the management of diabetes mellitus), Diuretics, C07, C08, C09 (medicines used in the management of hypertension) and J05 (medicines used in the management of HIV), (Refer to Appendix A for more detail). Medicines that had too few brands on the market to allow analysis were also dropped. New variables, prices (SEP of the medicine) and disease groups (classification according to active ingredient and strength) were generated before decomposing the two pricing components.

2.2.6. Explanation of variables for analysis

The variables of interest for the analysis to answer the set objectives are outlined and explained in the table below (Table 1).

Table 1: Variables for analysis

Variable	Variable type	Modifications to variable	Explanation of variable
Active ingredient	Categorical, nominal	Concatenated to create active ingredient+ strength+ unit	This is the international non-proprietary name of a medicine which is used to facilitate identification of pharmaceutical substances i.e., active pharmaceutical agent. Once concatenated, it included the amount of active ingredient per unit of medicine (strength)
Origin of manufacturer/principal applicant	Categorical, nominal	SA=0 Non-SA-1	Defines whether the pharmaceutical company that manufactures the medicine or the principal applicant that markets the medicine is of SA or non-SA origin.
ATC (Anatomical Therapeutic Chemical) code	Categorical, nominal	Trimmed from ATC4 to ATC2 format	Unique code assigned to a medicine based on the organ/system it that it works on and its mechanism of action.
Formulation type	Categorical, nominal	Recoded: Immediate release formulations =0 Modified/slow-release formulations=1	Oral dosage form formulation type refers to whether a medicine is immediate/normal release or modified release (extended, sustained or slow release). The pharmacokinetics differ depending on the release mechanism. Pricing also differs in most cases depending on the formulation type.
Logistics fee	Numerical, discrete		Fee charged by the manufacturer over and above the manufacturer fee.
Manufacturer price	Numerical, discrete		Price charged by manufacturer for production costs
Medicine pack size	Categorical	Recoded to distinguish bulk packs from ready packs: Pack sizes denoted as follows. 1-120=1(ready packs) 121+=0 (bulk packs)	Number of units in a single pack or container of medicine. Packs of below 120 tablets were defined as ready packs meaning ready-to-use packs. Bulk packs are packs of 121tablets or more.
Medicine proprietary name	Nominal		The brand name and strength of a medicine. Determined by manufacturer. The same compound made by different manufacturers will have different proprietary names.
SEP per unit (as defined in the dataset)	Numerical, continuous		Single exit price per single unit of a medicine (unit refers to a single, tablet/capsule). The SEP comprises a manufacturer price, fee-for-service logistics fees for distributors (capped using a tiering system), and Value-Added Tax (VAT) of 15% all divided by the pack size of the medicine.
Nappi (National Pharmaceutical Product Index) code	Numeric, nominal	Identifier variable, not changed	Unique code identifying a medicine, differs for every medicine by name, pack size and strength. No two medicines have the same Nappi code, this prevents duplication.

Variable	Variable type	Modifications to variable	Explanation of variable
Number of brands on market (frequency)	Numerical, continuous		Defines the number of brands available on the SA market for a particular active ingredient.
Originator or generic	Categorical	Generic=0 Original=1	Classifies medicine as originator or generic. Originator/innovator brands are medicines that contain an active ingredient that has not been authorised before, it is normally first available as a patented product. When the patent expires, generic manufacturers can manufacture the same active ingredient, to have the same characteristics in terms of safety, efficacy, route of administration and intended use, these are called generic medicine brands (generics). Generics are more affordable in comparison to originator brands.

2.3. DATA ANALYSIS

Analysis of data was conducted in Stata, version 18. The ATC level two (ATC2) for this analysis. The ATC2 level was preferred as it would have a significant number of medicines unlike higher, more specific levels which would be limiting for our analysis. Data analysis methods per objective are explained in detail below:

2.3.1. Objective 1: To quantify the variation in private sector SEP in South Africa for oral medicines used to treat HIV, diabetes, and hypertension.

To quantify the variation in SEP, the mean, median, standard deviation, minimum and maximum and range were calculated for each ATC2 group and for each active ingredient.

2.3.2. Objective 2: To investigate the components of pricing which contribute to private sector medicine price variation for HIV, diabetes, and hypertension oral medicines.

Decomposition analysis was used to answer Objectives 2 and 4. Decomposition is defined as the process of breaking down a complex into main determinants or causal components for analysis (Shorrocks, 2013). The first decomposition in Objective 2 using Shorrocks' methods, looked at the contribution of pricing related factors; manufacturer fees and logistics fee to the observed SEP price variations. The second decomposition, in Objective 4 used the inequality regression-based methods based on the Fields approach(Fiorio and Jenkins, 2007) to investigate the contribution of non-pricing related factors of the medicines. Using these two methods, we gained additional insights into the contributions of the pricing and non-pricing elements.

To understand how the various components of pricing which form the SEP impact on variation of medicine prices, we used the Source/Factor decomposition analysis using Shorrocks' approach to decompose the total price variation by price components using the inequality decomposition by factor components, Stata command "*ineqfac"*. The Shorrocks' method focuses on the contribution of different income sources to overall inequality, using a variance decomposition approach. his method allows for the identification of how each income source contributes to overall inequality, emphasizing the elasticity of each source with respect to the total (Shorrocks, 2013). These mathematical approaches provide a structured way to dissect income inequality and understand the underlying dynamics affecting it. The use of this analysis for this study therefore provided a decomposition of the variation of medicine price into variation contributions from each of the factor components of the total price: manufacturer fee and logistics fee (explanatory variables). VAT was excluded as it is a constant variable (STATA, 2009). This method was selected because it gives an exact decomposition of the contribution of each pricing components to the SEP per tablet/capsule (outcome variable) (Shorrocks, 2013). The proportionate contribution of manufacturer fees and logistics fees to variation of SEP per tablet or capsule for each medicine was presented.

2.3.3. Objective 3: To summarise the non-pricing related factors which contribute to private sector medicine price variation for HIV, diabetes, and hypertension oral medicines.

Other non-pricing related factors that can contribute to the observed variation in the SEP of medicine were summarised. These were formulation type, whether the medicine is an originator or generic brand, pack size of medicine, the number of brands available on the market, origin of manufacturer/principal applicant, drug class (based on mechanism of action) and drug combination.

2.3.4. Objective 4: To analyse whether non-pricing related factors explain the variation in private sector medicine prices for HIV, diabetes, and hypertension.

To decompose the contribution of other factors to the price variation, regression-based decomposition analysis using the Stata command "*ineqbrd"* was done (Fiorio and Jenkins, 2007). The "*ineqrbd"* command performs regression-based decomposition of the inequality in dependent variable into the contributions accounted for by each of independent variables (Fiorio and Jenkins, 2007). The formulae used are those proposed by Fields, of which the functional form for the income generating function is log-linear function (Manna and Regoli, 2012). The logarithm of the SEP per tablet or capsule was therefore used for the inequality

regression-based decomposition, as the income variable (in this case SEP) can be estimated well by a lognormal distribution (Fields, 2003; Tripathi, 2018). For the factor variables generic or originator, formulation type, pack size and drug class, the category with the lowest mean was used as the reference category. The Fields method uses a counterfactual approach to decompose changes in inequality into contributions from various factors, such as demographic changes and shifts in income distribution. This method typically employs regression analysis to estimate the contributions of different factors (Fields, 2003).

For the diabetes and hypertension groups, the factors that were decomposed, were number of brands on the market, origin of manufacturer/principal applicant, generic or originator, formulation type, pack size and drug class/combination. Biguanides, which are the group with the lowest mean SEP per tablet or capsule were used as the reference for diabetes group. For the hypertension group, a challenge was presented because drug classification for some of the drugs was difficult as they were combinations of different classes of drugs. To overcome this, drug class was recoded as follows: 0=diuretics, 1=B-blockers, 2=Ca+ channel blockers,3=ACE inhibitors, 4=ARBs, 5=other= combinations of different drugs from different classes. For the HIV group, formulation type, pack size and drug class were omitted in favour of a new explanatory variable called “combination” which denotes whether a medicine was a single agent or combination of medicines. This factor was added since most HIV medicines are combinations of more than one drug and price variations along that factor was probable.

3. CHAPTER THREE: RESULTS

This study undertook an examination of medicine price variations for medicines used to manage HIV, diabetes and hypertension in adults in the South African private sector, based on medicine pricing data published in July 2022.

3.1. Objective 1: Variation in private sector SEP in South Africa for oral medicines used to treat HIV, Type 2 diabetes and hypertension.

The table below (Table 2) summarizes key descriptive statistics, including the number of observations, mean, standard deviation, minimum, maximum and the range for each ATC2 group.

Table 2: Characteristics of SEP per unit for medicines used to manage diabetes, hypertension, and HIV in South Africa.

Disease	ATC2 group	n	Mean (ZAR)	SD	Min (ZAR)	Max (ZAR)	Range (ZAR)	Ratio of max: min
Diabetes n=168	A10 (Sulphonamides, Biguanides, DPP IV inhibitors	168	2.18	2.59	0.29	16.33	16.04	0.02
Hypertension n=444	C03 (Diuretics)	30	0.97	1.47	0.18	6.26	6.08	0.03
	C07 (B-blockers)	79	2.93	2.26	0.55	15.70	15.15	0.04
	C08 (Calcium channel blockers)	59	3.88	2.47	1.53	11.59	10.06	0.13
	C09(ACE-inhibitors, ARBs)	276	3.79	2.23	0.73	13.06	12.33	0.06
HIV n=118	J05 (Antiretrovirals)	118	10.58	6.70	0.77	32.63	31.86	0.02
	Total	730	4.32	4.46	0.18	32.63	32.45	0.01

**All monetary values depict the single exit price per tablet/capsule*

Of the 730 medicines selected, hypertension medicines were the most common, accounting for 444 observations (60.8%), followed by 168 (23%) for diabetes and 118 (16.2%) for HIV (Table2). The range (difference between the highest price item and the lowest priced item) was R32.45 per unit. Medicines used in the treatment of HIV (ATC2 group J05), had the highest variability in pricing, with an observed standard deviation of 6.7 and highest range of R31.86. HIV medicines also had the highest mean SEP per tablet/capsule at R10.58, and the highest maximum SEP per tablet/capsule across all groups at R32.63. The diuretics' standard deviation and range were also the lowest at 1.47 and 6.08 respectively, hence the smallest variation in medicine pricing across all groups. In general, hypertension medicine showed uniform pricing across the other ATC2 groups.

In the analysis of hypertension medications, comprising 28 single and 12 combination medicines, four ATC classes were investigated. Among these classes, calcium channel blockers showed the highest mean SEP per tablet/capsule at R3.88, while diuretics had the lowest at R0.97 (Table 2). Despite varied range values, the spread of SEP per tablet/capsule across beta-blockers, calcium channel blockers, ACE inhibitors and ARBs was comparable. Beta-blockers had the highest range, and calcium channel blockers, the highest standard deviation, suggesting that they showed the highest price variability among hypertension medicines. On the other hand, diuretics had the lowest range and standard deviation, diuretics therefore had the most uniformity of all hypertension medicines.

Table 3 below shows the characteristics of manufacturing price for medicines used to treat the three diseases by ATC2 group. Antiretrovirals, had the highest average manufacturing price per tablet/capsule while diuretics had the lowest. This was consistent with the pattern observed for SEP per unit. Variation in manufacturer fees was however highest in the beta-blockers group with a standard deviation of 7.82 and range of R61.04. Manufacturer fee variation was lowest in the diuretics group. Based on this, not only were diuretics the lowest priced medicine class, but they also displayed the most uniform pricing.

Table 3: Characteristics of manufacturing fees for medicine used to manage diabetes, hypertension, and HIV in South Africa.

Disease	ATC2 group	n	Mean	SD	Min	Max	Range
Diabetes n=168	A10 (Sulphonamides, Biguanides, DPP IV inhibitors	168	1.72	2.08	0.21	13.56	13.35
Hypertension n=444	C03 (Diuretics)	30	0.77	1.22	0.14	5.19	5.05
	C07 (B-blockers)	79	3.47	7.82	0.43	61.48	61.04
	C08 (Calcium channel blockers)	59	3.00	1.91	1.20	9.47	8.27
	C09 (ACE-inhibitors, ARBs)	276	3.00	1.79	0.59	10.42	9.83
HIV n=118	J05 (Antiretrovirals)	118	8.38	5.37	0.59	26.77	26.18
Total		730	3.53	4.33	0.14	61.48	61.34

**All monetary values depict the single exit price per tablet/capsule*

Logistics fees per tablet/capsule showed the highest average in the antiretrovirals group and the lowest average in the diuretics group (Table 4). The highest standard deviation and range,

as with manufacturing price was for beta-blockers and lowest for diuretics (Table 4). This was similar to the pattern observed in the other pricing components above.

Table 4: Characteristics of logistics fee for medicine used to manage diabetes, hypertension, and HIV.

	ATC2 group	n	Mean	SD	Min	Max	Range
Diabetes n=168	A10 (Sulphonamides, Biguanides, DPP IV inhibitors	168	0.18	0.21	0.03	1.09	1.07
Hypertension n=444	C03 (Diuretics)	30	0.08	0.06	0.01	0.25	0.23
	C07 (B-blockers)	79	0.44	1.18	0.05	9.22	9.18
	C08 (Calcium channel blockers)	59	0.39	0.48	0.10	3.06	2.96
	C09(ACE-inhibitors, ARBs)	276	0.30	0.22	0.02	1.80	1.78
HIV n=118	J05 (Antiretrovirals)	118	0.82	0.56	0.07	3.04	2.97
Total		730	0.37	0.54	0.01	9.22	9.21

**All monetary values depict the single exit price per tablet/capsule*

Further detail was analysed below, to quantify the of range of variation of the SEP per tablet/capsule by ATC2 group for each of the three diseases.

Diabetes

As shown in Table 5 below, 13 single agents were analysed for this disease class and no combination medicines were eligible for analysis. Glimepiride 4mg had the highest mean SEP per tablet/capsule at R8.75, there were 13 different preparations of this active ingredient. Among these, the lowest-priced one cost R6.17 per tablet, while the most expensive was R16.33 per tablet. This was the widest range for this ATC2 group and was coupled with the highest standard deviation. Based on this, the pricing of Glimepiride 4mg was the most variable.

In contrast, Metformin XR 500 had the lowest standard deviation, showing a high degree of uniformity in pricing. Metformin XR 1000mg, on the other hand, had the lowest range, indicating minimal variation between the highest and lowest-priced brands for this medicine. Within the Metformin 500mg category, the highest number of brands was found, and the standard deviation was among the lowest, suggesting relatively uniform pricing across the 29 available brands. Metformin showed an increase in pricing with strength, and price differences

based on formulation type, with extended-release tablets being more expensive than immediate-release ones (Table 5). Similar trends are observed for Glimepiride. Gliclazide had an interesting pattern, showing an increase in mean SEP per tablet/capsule from the 30mg to the 60mg strength, followed by an unexpected drop for the 80mg strength (Table 5). However, Gliclazide 80mg had almost double the number of brands on the market compared to the other strengths.

Table 5: Characteristics by active ingredient for medicine in ATC2 group, A10 used to manage diabetes.

ATC2 group	Drug class	Generic name+ strength	n	Mean (ZAR)	SD	Min (ZAR)	Max (ZAR)	Range (ZAR)
A10	**Sulphonamides**	Glibenclamide 5mg	13	1.36	2.01	0.29	5.78	5.50
		Gliclazide 30mg	6	1.35	0.57	1.02	2.42	1.40
		Gliclazide 60mg	8	2.37	0.89	2.02	4.57	2.55
		Gliclazide 80mg	13	1.15	0.13	0.92	1.39	0.47
		Glimepiride 1mg	13	2.69	0.74	1.83	4.65	2.82
		Glimepiride 1mg	13	5.25	1.38	3.48	8.83	5.35
		Glimepiride 4mg	13	8.75	2.93	6.17	16.33	10.16
	Biguanides	Metformin 500mg	31	0.49	0.10	0.31	0.81	0.50
		Metformin 850mg	29	0.92	0.20	0.61	1.47	0.87
		Metformin 1000mg	8	1.00	0.31	0.83	1.60	0.77
		Metformin XR 500mg	10	0.68	0.08	0.45	0.76	0.31
		Metformin XR 1000mg	6	1.93	0.13	1.85	2.12	0.28
	DPP-IV inhibitors	Vildagliptin 50mg	5	4.36	2.31	2.65	6.89	4.25

**All monetary values depict the single exit price per tablet/capsule*

Hypertension

Table 6 shows the characteristics of medicines for the hypertension group. The hypertension medicine with the highest mean SEP per tablet/capsule was Lercanidipine 20mg, a calcium-channel blocker, at R8.70 (Table 6). Atenolol 100mg stood out with the highest standard deviation and the widest range in SEP per tablet/capsule, at 2.67 and R14.17 respectively, the highest variability in the beta-blockers group and overall hypertension medicines. Conversely, HCTZ 25mg had the lowest standard deviation and range, indicating the most uniform pricing and least variation for this medicine. The cost of combination medicines in the group (Telmisartan/HCTZ and Valsartan/HCTZ), are less than the cost of single agents combined.

Table 6: Characteristics by active ingredient for medicines used to manage hypertension.

ATC2 group	Drug class	Generic name+ strength	n	Mean (ZAR)	SD	Min (ZAR)	Max (ZAR)	Range
C03	**Diuretics**	Furosemide 40mg	19	1.11	1.84	0.18	6.26	6.08
		HCTZ 25mg	11	0.73	0.26	0.54	1.22	0.68
C07	**B-blockers**	Atenolol 50mg	11	1.68	2.67	0.55	9.66	9.12
		Atenolol 100mg	10	2.98	4.51	0.91	15.70	14.79
		Bisoprolol 5mg	16	2.27	1.03	1.57	4.86	3.29
		Bisoprolol 10mg	16	3.8	1.54	2.71	7.68	4.97
		Carvedilol 6.25mg	9	2.96	1.48	1.84	6.75	4.91
		Carvedilol 12.5mg	10	3.05	1.45	2.21	7.04	4.83
		Carvedilol 25mg	9	3.86	1.30	2.86	7.04	4.18
C08	**Calcium-channel blockers**	Amlodipine 5mg	26	2.47	1.22	1.53	7.92	6.39
		Amlodipine 10mg	23	3.72	1.81	2.37	11.11	8.74
		Lercanidipine 10mg	6	6.65	1.13	5.56	8.69	3.13
		Lercanidipine 20mg	6	8.70	1.70	6.90	11.59	4.69
C09	**ACE-inhibitors**	Enalapril 5mg	13	1.21	0.25	0.73	1.57	0.84
		Enalapril 10mg	12	1.89	0.28	1.42	2.17	0.75
		Enalapril 20mg	10	3.04	0.71	1.97	3.97	2.00
		Lisinopril 5mg	9	1.42	0.45	0.87	2.01	1.14
		Lisinopril 10mg	9	1.66	0.82	0.87	2.84	1.97
		Lisinopril 20mg	12	2.55	1.27	0.87	4.33	3.46
C09	**ARBs**	Losartan 50mg	19	3.01	0.77	2.10	4.64	2.54
		Losartan 100mg	15	3.24	0.79	2.10	4.81	2.71
		Perindopril 4mg	15	2.80	1.51	1.68	7.14	5.46
		Perindopril 8mg	9	4.24	0.52	3.36	5.14	1.78
		Telmisartan 40mg	13	5.32	2.57	3.05	13.06	10.01
		Telmisartan 80mg	11	5.84	2.56	4.14	13.06	8.92
		Valsartan 80mg	12	4.61	2.48	1.96	11.76	9.80
		Valsartan 160mg	12	4.61	2.48	1.96	11.76	9.80
	Combinations (Calcium channel blocker+ ARB)/ ACE inhibitor+ diuretic/ ARB+ Diuretics/ ACE inhibitor+ diuretic/	Amlodipine5/Valsartan160	9	5.55	1.76	4.15	10.16	6.01
		Amlodipine10/Valsartan160	10	6.24	1.98	4.15	11.56	7.41
		Lisinopril10/HCTZ12,5	8	2.18	0.59	1.55	3.21	1.66
		Lisinopril20/HCTZ12,5	10	3.79	0.82	2.69	4.97	2.28
		Losartan 50/HCTZ12,5	15	3.34	0.79	2.64	5.20	2.56
		Losartan 100/HCTZ25	12	3.71	0.81	2.97	5.54	2.57
		Perindopril4/Indapamide1,25	8	4.025	1.34	3.05	6.23	3.18
		Telmisartan40/HCTZ12,5	6	5.43	4.12	2.88	12.95	10.07
		Telmisartan80/HCTZ12,5	6	5.43	4.12	2.88	12.95	10.07
		Valsartan80/HCTZ12,5	6	6.66	2.68	4.18	11.76	7.58
		Valsartan160/HCTZ12,5	6	6.14	1.56	4.18	8.60	4.42
		Valsartan160/HCTZ25	5	6.83	2.76	4.18	11.36	7.18

Generally, an increase in the strength of medicine corresponded to an expected increase in price as observed in most hypertension medicines. Interestingly, the 8mg strength of Perindopril was nearly double the price of the 4mg tablets on average (Table 6) while the price of Telmisartan 40/HCTZ 12.5 was identical to that of Telmisartan80/HCTZ 12.5 which had double the strength of Telmisartan. Some formulations with higher strength were cheaper on average, for instance Valsartan160/HCTZ12.5 was cheaper than Valsartan80/HCTZ12.5.

HIV

The analysis of 118 HIV medicines is presented in Table 7. This group had the highest standard deviation, SEP per tablet/capsule and range among all ATC2 groups included in this study, indicating substantial variability. Specifically, the combination Abacavir 600mg/Dolutegravir50mg/Lamivudine300mg had the highest SEP per tablet/capsule at R32.63 and the highest mean SEP per tablet/capsule at R26.15 (Table 7). It is also had a relatively high standard deviation. Efavirenz600mg/Emtricitabine200mg/ Tenofovir300mg had the highest range, R17.72 and the second highest standard deviation, which confirmed high variation in pricing of the brands of medicine containing that triple combination of medicines. Efavirenz 50mg as a single agent, on the other hand, had the lowest range and standard deviation (Table 7). Single agents in HIV medicines follow an expected trend of increasing SEP per tablet/capsule with strength. The triple combination, Dolutegravir 50mg/Lamivudine 300mg/Tenofovir 300mg showed the highest standard deviation at 5.3 and a relatively wide range, confirming pricing diversity.

In summary, the HIV medications within ATC2 group, J05 demonstrated diverse pricing patterns, with certain formulations exhibiting higher mean SEP per tablet/capsule and high variability. The combinations had higher mean SEP per tablet/capsule, with some showing considerable standard deviations, indicating pricing variation.

Table 7: Characteristics by active ingredient for medicine used to manage HIV.

ATC2 group	Drug class	Generic name+ strength	n	Mean (ZAR)	SD	Min (ZAR)	Max (ZAR)	Range (ZAR)
J05	**Antiretrovirals Single agents**	Efavirenz 50mg	5	1.61	0.28	1.20	1.97	0.77
		Efavirenz 200mg	7	3.95	1.30	2.41	6.22	3.81
		Efavirenz 600mg	11	7.07	2.22	3.59	10.96	7.37
		Lamivudine 150mg	5	5.98	4.21	0.77	10.34	9.57
		Nevirapine 200mg	10	4.62	1.08	2.60	5.35	2.75
	Double combination	Abacavir600mg/Lamivudine300mg	9	19.95	2.25	17.63	24.01	6.38
		Emtricitabine 200mg/Tenofovir300mg	13	13.25	4.59	8.35	23.31	14.96
		Lamivudine 150mg/Zidovudine300mg	7	5.17	1.83	3.16	7.03	3.87
	Triple combination	Abacavir 600mg/Dolutegravir50mg/Lamivudine 300mg	5	26.15	3.63	24.15	32.63	8.48
		Dolutegravir 50mg/Lamivudine300mg/Tenofovir300 mg	17	10.95	5.35	6.90	19.11	12.21
		Efavirenz600mg/Emtricitabine200mg/Tenofovir300mg	23	12.54	5.07	7.28	25.85	18.57
		Efavirenz600mg/Lamivudine300mg/Tenofovir300mg	6	10.87	2.51	7.84	14.01	6.17

**All monetary values depict the single exit price per tablet/capsule*

3.2. Objective 2: Investigation of components of pricing which contribute to private sector medicine price variation for HIV, Type 2 diabetes and hypertension oral medicines.

These results offer a detailed breakdown of how the components of medicine prices (logistics fees and manufacturing fees) contributed to the overall variation in medication prices following decomposition by factor components using Shorrocks' method. This method decomposed the overall inequality in pricing into the contributions from manufacturer and logistics fees and found that manufacturer fees were the main contributing factor to observed price variations, logistics fees played a secondary but significant role. It was interpreted as below:

Diabetes

Table 8: Price decomposition of diabetes medicines considering components of price only.

	Contribution to overall variation	
Generic name+ strength	**Logistics fee %**	**Manufacturing price %**
Gliclazide 30mg	8.22	91.78
Gliclazide 30mg	9.57	90.43
Gliclazide 60mg	9.50	90.51
Gliclazide 80mg	13.49	86.51
Glimepiride 1mg	-0.81	100.81
Glimepiride 1mg	-0.59	100.59
Glimepiride 4mg	-0.76	100.76
Metformin 500mg	8.95	91.05
Metformin 850mg	8.90	91.10
Metformin 1000mg	9.37	90.63
Metformin XR 500mg	9.28	90.73
Metformin XR 1000mg	15.23	84.77
Vildagliptin 50mg	7.13	92.88

As shown in Table 8 which is the decomposition results for diabetic medicines, across various medications, manufacturing price was consistently the primary factor driving price variation, often contributing over 90% to the overall inequality. Logistics fees had a smaller impact. The decomposition analysis revealed that manufacturing fees were the main factor driving price variation across different formulations of Gliclazide and Glimepiride (see Table 8). Logistics fees made a relatively smaller but still significant contribution to the price variation of Gliclazide. For Glimepiride, logistics fees had a negative contribution hence manufacturing price showed a contribution of over 100% (Table 8). The negative contribution of logistics fees suggests a minimal and inverse relationship between logistics fees and price variation. Rather than increasing price variation, logistics fees reduced it for this medicine. Overall, manufacturing price was the primary driver of price variation.

In the biguanides class, across various formulations of Metformin, the decomposition result was the same. Manufacturer fees were the primary contributor and logistics fee the secondary one. Metformin XR 1000mg had the highest overall contribution of logistics fee in explaining the price variation in this group of medicines.

Finally, for the GPP-IV inhibitor, Vildagliptin 50mg, like other medicines, manufacturing price is the major contributor to the overall variation prices while logistics fee made a secondary contribution.

Overall, the trends observed indicated a high degree of consistency in the factors influencing price variation for diabetes medicines, with manufacturing costs contributing the most to the observed price variation.

Hypertension

Across the various hypertension medications, as with diabetes medicines, manufacturing fees were the primary driver of price variation (Table 9). Table 9 shows that logistics fees also contributed but generally played a secondary role. Logistics fee contributions varied across medicines; Perindopril4/Indapamide1.25, showed a contribution of over 27%, the highest in the group, but was very low for Atenolol 50mg and 100mg at 2.67% and 2.61% respectively.

For Enalapril, the contribution of logistics fee to price variation decreased with increasing strength, 7.43% for Enalapril 5mg, 6.46% for Enalapril 10mg and 5.05% for the Enalapril 20mg. A similar trend was noted for Lisinopril, Losartan and Telmisartan.

Overall, the trends indicated that manufacturing fees are a crucial factor in determining the prices of hypertensive medicines, highlighting the importance of production-related factors in pricing dynamics.

Table 9: Decomposition of price components for hypertension medicines.

	Contribution to overall variation	
Generic name+ strength	**Logistics fee %**	**Manufacturing price %**
Furosemide 40mg	4.86	95.14
HCTZ 25mg	13.32	86.71
Atenolol 50mg	2.67	97.33
Atenolol 100mg	2.61	97.39
Bisoprolol 5mg	9.97	90.03
Bisoprolol 10mg	10.08	89.92
Carvedilol 6.25mg	15.12	84.89
Carvedilol 12.5mg	16.00	84.00
Carvedilol 25mg	17.65	82.35
Amlodipine 5mg	6.18	93.82
Amlodipine 10mg	7.37	92.63
Lercanidipine 10mg	4.77	95.23
Lercanidipine 20mg	10.61	89.40
Enalapril 5mg	7.43	92.57
Enalapril 10mg	6.46	93.54
Enalapril 20mg	5.05	94.95
Lisinopril 5mg	12.93	87.07
Lisinopril 10mg	12.58	87.43
Lisinopril 20mg	12.10	87.90
Losartan 50mg	9.56	90.44
Losartan 100mg	9.12	90.88
Perindopril 4mg	9.26	90.74
Perindopril 8mg	13.42	86.58
Telmisartan 40mg	6.84	93.16
Telmisartan 80mg	4.73	95.28
Valsartan 80mg	5.95	94.05
Valsartan 160mg	5.95	94.05
Amlodipine5/Valsartan160	5.20	94.80
Amlodipine10/Valsartan160	4.79	95.21
Lisinopril10/HCTZ12,5	11.19	88.81
Lisinopril20/HCTZ12,5	9.08	90.92
Losartan 50/HCTZ12,5	11.78	88.23
Losartan 100/HCTZ25	12.61	87.40
Perindopril4/Indapamide1,25	27.44	72.56
Telmisartan40/HCTZ12,5	8.15	91.85
Telmisartan80/HCTZ12,5	8.15	91.85
Valsartan80/HCTZ12,5	6.20	93.80
Valsartan160/HCTZ12,5	5.67	94.33
Valsartan160/HCTZ25	7.34	92.66

HIV

Table 10 presents a decomposition of price factors that influenced the variation in prices for different formulations of antiretroviral medicine used in HIV management. As with diabetes and hypertension medicines, manufacturing fees made the highest contribution to overall variation in medicine price. The largest contribution of manufacturer fees to price variation was observed for Abacavir 600mg/Dolutegravir50mg/Lamivudine300mg the logistics fees having a negative contribution to variation and therefore more uniformity in pricing. The largest contribution of logistics fees to price variation was observed for Efavirenz600mg/Lamivudine300mg/Tenofovir300mg at 16.56% while the least variation was for Abacavir600mg/Lamivudine300mg at 4.74%. Only the logistics fees of the triple combination Abacavir 600mg/Dolutegravir50mg/ Lamivudine300mg had a negative contribution (-0.81%).

Table 10: Decomposition of price components of HIV medicines.

	Contribution to overall variation	
Generic name+ strength	**Logistics fee %**	**Manufacturing price %**
Efavirenz 50mg	6.83	93.17
Efavirenz 200mg	6.62	93.38
Efavirenz 600mg	10.14	89.86
Lamivudine 150mg	5.12	94.88
Nevirapine 200mg	7.97	92.03
Abacavir600mg/Lamivudine300mg	4.74	95.26
Emtricitabine 200mg/Tenofovir300mg	15.57	84.43
Lamivudine 150mg/Zidovudine300mg	7.59	92.41
Abacavir 600mg/Dolutegravir50mg/Lamivudine300mg	-0.81	100.81
Dolutegravir 50mg/Lamivudine300mg/Tenofovir300mg	6.78	93.22
Efavirenz600mg/Emtricitabine200mg/Tenofovir300mg	8.70	91.30
Efavirenz600mg/Lamivudine300mg/Tenofovir300mg	16.56	83.44

Across the various formulations of antiretroviral medicines, manufacturing price consistently emerged as the primary driver of price variation while logistics fees generally played a secondary role.

In summary, across all 3 diseases, the consistent dominance of manufacturing price, ranging from about 72.56% to over 100% highlighted the importance of production-related factors in shaping the pricing dynamics of all medications, while logistics fees also contributed but to a lesser extent.

3.3. Objective 3: Description of non-pricing related factors which contribute to private sector medicine price variation for HIV, diabetes, and hypertension oral medicines.

There are other factors which might contribute to the price variation seen in medicine prices for the three conditions in South Africa. Possible factors, for which there is data in the SEP dataset are, the number of brands available on the market, the origin of the drug manufacturer/principal applicant, whether the medicine is an originator or generic medicine, formulation type, pack size, class of drug (based on the mechanism of action), and drug combination. The descriptive statistics for each of these components is presented in Table 11.

Table 11: Descriptive statistics for explanatory variables

Explanation variable		**DIABETES** (n=168)	**HYPERTENSION** (n=444)	**HIV** (n=118)
		%	%	%
Origin of manufacturer/ principal applicant	SA	44.64	48.42	25.42
	non-SA	55.36	51.58	74.58
Originator or generic	generic	88.1	89.86	88.98
	originator	11.9	10.14	11.02
Formulation type	immediate release	96.43	100.00	100.00
	modified release	3.57	0.00	0.00
Pack size	bulk (0)	11.9	3.15	0.00
	ready packs (1)	88.1	96.85	100.00
Disease specific variables **(Drug class/Drug combination)**		**Drug class.** (Biguanides=50% Sulphonamides=47.02%. DPP-IV inhibitors= 2.98%	**Drug class.** Diuretics=6.76% Beta-blockers=18.24%, Calcium-channel blockers=19.14%, Angiotensin-Converting-Enzyme (ACE) inhibitors=14.644% Angiotensin-receptor-blockers (ARB)=18.47% others/combinations=22.75%	**Drug combination.** Combination agents=67.8% Single agents=32.2%

Most of the medicines studied were not produced in South Africa with almost 75% of HIV being of non-SA origin (Table 11). Approximately 89% of all medicines studied were generics, while originator brands constituted a considerably smaller portion, approximately 11% of the medicines used to manage the three conditions in adults in South Africa.

As seen in Table 11 above, immediate release tablets were the most common across all three disease groups with hypertension and HIV medicines being solely immediate release formulations. Most medicines came in ready to use pack sizes of up to 120 tablets per pack, bulk packs were less common.

Most of the diabetes medicines fell into two drug classes, sulphonamides and biguanides while for hypertension there was an almost even distribution of medicines along the six classes. The impact of the above factors on price variations were investigated in Objective 4.

3.4. Objective 4: Analysis of other factors that may explain the variation in private sector medicine prices for HIV, diabetes, and hypertension medicines.

Decomposition analysis of non -pricing related factors and their contribution to price variation was investigated. The analysis was useful in helping us understand the determinants of the variation in the medicine prices for the diseases under study. It was based on the non-pricing related factors and was done by disease; the results of both the linear regression and Field's decomposition are presented per disease group, in the following sections.

Diabetes

Table 12: Linear regression and decomposition of non-price related factors on the pricing of medicines used to manage diabetes in South Africa.

Description	**Linear Regression R-squared=0.4561**		**Fields decomposition**
Logarithm of single exit price per tablet/capsule	**Coefficient**	**P value**	**Explained variance %**
number of brands on the market	-0.01	0.16	5.84
Origin (SA=0, non-SA=1)	0.30	0.01	2.29
Generic (generic=0, originator =1)	0.46	0.02	3.25
formulation type (immediate release formulations=0, modified/slow-release formulations=1)	-0.46	0.15	-0.18
pack size (1-120=1(ready packs), 121+=0 (bulk))	0.28	0.13	2.28
Sulphonamides	1.02	p<0.001	27.94
Drug class 2 (DPP-IV inhibitors e.g. vildagliptin)	1.21	0.001	4.19
constant	-0.49	0.103	
residual			54.39

The regression model shows that all the explanatory variables collectively explained a significant portion of the variation in the log of the single exit price per tablet/capsule (all p-values were lower than 0.05). The model's R-squared value of 0.4561 suggests that these variables accounted for approximately 45.61% of the variance in the dependant variable.

For the decomposition, the extent of contribution of all the factors were expressed as percentages of the total inequality. It showed that the residual component contributed 54.39% to the inequality, indicating unexplained variance while 45.61% was explained by the model as shown above (Table 12). Number of brands, origin, whether the medicine is an originator or generic medicine, pack size and drug classes 1 and 2 all contributed positively to the inequality, while formulation type contributed negatively. A negative contribution means that it contributed to price uniformity. Sulphonamides made the highest contribution to price variation (27.94%) followed by the number of brands on the market (5.84%) while formulation type made the least contribution to price variation with a negative contribution of -0.18%. This negative contribution translates to more uniformity of pricing.

Hypertension

Table 13: Linear regression and decomposition of non-price related factors on the pricing of medicines used to manage hypertension in South Africa.

Description	**Linear Regression R-squared=0.6578**		**Fields decomposition**
Logarithm of single exit price per tablet/capsule	**Coefficient**	**P value**	**Explained variance %**
number of brands on the market	-0.33	p<0.001	4.62
Origin (SA=0, non-SA=1)	0.06	0.19	0.76
Generic (generic=0, originator =1)	0.82	p<0.001	12.74
pack size (1-120=1(ready packs), 121+=0 (bulk))	0.23	0.13	2.14
B-blockers	1.15	p<0.001	-5.60
Calcium channel blockers	1.75	p<0.001	11.39
ACE inhibitors	0.85	p<0.001	-10.56
ARBs	1.74	p<0.001	20.81
Other- combinations	1.63	p<0.001	29.48
constant	-0.25	0.07	
residual			34.22

*Drug class 0=diuretics **sf is the slope coefficient from the regression of each factor on total variable.

As shown on Table 13, the regression model explained a significant portion of the variance in the logarithm of the SEP per tablet/capsule (R-squared = 0.6578), indicating that the included variables collectively contributed significantly to understanding the variation in medicine pricing. The number of brands on the market had a negative coefficient (-0.03), implying that as the number of brands of medicines on the market increased, pricing decreased. All other variables had positive coefficients. All variables excluding origin and pack size were statistically significant (p-values less than 0.05 in explaining price variation.

The decomposition analysis demonstrated that combinations, Angiotensin Receptor Blockers (ARBs), whether the medicine is an originator or generic medicine and drug class Calcium channel blockers, contributed the most to observed price variations. Origin contributed a very small proportion of 0.76% to observed price variations. While B-blockers and ACE inhibitors made negative contributions, -5.6% and -10.56% respectively. The decomposition model had a residual component of 34.22% (Table 13), indicating that there are other unaccounted factors influencing the dependant variable beyond those included in the model.

HIV

Table 14: Linear regression and decomposition of non-price related factors on the pricing of medicines used to manage HIV in South Africa.

Description	**Linear Regression R-squared=0.4665**		**Fields Decomposition**
Logarithm of single exit price per tablet/capsule	**Coefficient**	**P value**	**Explained variance %**
number of brands on the market	0.04	0.67	1.09
Origin (SA=0, non-SA=1)	0.23	0.06	3.28
Generic (generic=0, originator =1)	0.26	0.12	0.27
Combination (single agent=0, combination=1)	1.00	p<0.001	42.01
constant	1.21	p<0.001	
residual			53.35

The regression model included the variables number of brands, origin of principal applicant, whether the medicine is an originator or generic medicine, combination, or single agent products. Combination is the only variable that had a statistically significant coefficient ($p < 0.05$), indicating its importance in predicting the log of SEP per tablet/capsule. The R-squared value of 0.4665 suggests that the variables in the model collectively explained about 46.65% of the variation in log SEP per tablet/capsule.

The decomposition broke down the sources of variation in SEP per tablet/capsule. The residual component/unexplained variance that was not captured by the model's variables was 53.35%, therefore the model explained only 46.65% of the variation noted. Combination contributed the most to inequality (42.01%), followed by origin of principal applicant (3.28%) and number of brands on the market (1.08%). Whether or not the medicine was a generic contributed the least (0.27%) to the variation observed.

4. CHAPTER FOUR: DISCUSSION

The results of this study provide insight into medicine pricing dynamics for drugs used to treat diabetes, hypertension, and HIV. Policymakers, healthcare professionals, and patients must all understand the factors that influence pricing of pharmaceuticals as they directly impact patients' access to essential medications and the overall quality of medical care.

The observed discrepancies in medicine pricing across disease categories demonstrates the intricacies of pharmaceutical pricing dynamics. While some medicines, such as diuretics for hypertension, had relatively uniform pricing, others, particularly HIV medicines, had significant pricing variations. These variations could be influenced by regulatory factors, pricing-related factors like manufacturer and logistics fees, and other market-related characteristics such as generics on the market.

Medicines used in HIV management exhibited the highest variability in pricing while diuretics showed the most consistent pricing and were the least expensive group of medicines. Metformin, one of the earliest and commonly used medicines in diabetes management was very well priced. Its low price is attributable to the high number of available brands on the market leading to intense market competition coupled with its long time in the market. Newer medications are typically more expensive compared to older ones that have been subject to multiple market forces. A similar pricing pattern was observed in the hypertension group, where medications with numerous brands and more time on the market displayed more competitive and uniform pricing, for example, Ridaq (HCTZ), a long-standing hypertension medication, was the lowest priced hypertension medicine.

Consistent with earlier studies, our analysis showed that manufacturing fees were the primary factor determining price variation in each of the three disease categories. This is in line with recent research that demonstrates the significant role that production-related factors play in setting the price of pharmaceuticals (Gray, 2009). Logistics fees play a significant but secondary role, the factors that contribute to logistics fees such as transportation, storage, and distribution costs highlights the importance of supply chain management and the need for efficient supply chain practices to minimise price fluctuations. There is a lack of transparency in how both manufacturer and logistics fees are determined. An understanding of how these fees is determined would be useful in medicine price regulation. Over time,

research and development costs have been the biggest contributor to high manufacturing costs, particularly for originator medications (Wadee *et al*., 2020). This gives meaning to our findings that manufacturer fees were the biggest driver of observed price variations. It is unclear whether the logistics fee is consistently applied to all wholesale purchasers. As a result, the accuracy and relevance of the logistics fee recorded in the MPR are uncertain. This raises questions about whether breaking down the components of the SEP—specifically the contributions from the manufacturer price and the logistics fee—truly reflects their impact. The logistics fee might not be paid at all and could instead be kept by the manufacturer. Bangalee and Suleman have similarly emphasized the need for greater transparency in regulating the logistics fee (Bangalee and Suleman, 2015).

Most of the medicines studied were not produced locally, most, were generics, while originator brands constituted a considerably smaller portion, approximately 11% of the medicines used to manage diabetes, hypertension, HIV in South Africa. Immediate release tablets were also the most common with hypertension and HIV medicines comprising only immediate release formulations. Most medicines came in ready to use pack sizes of up to 120 tablets per pack, bulk packs were less common. Finally, non-pricing factors, origin, generic and pack size contributed the most to inequality in pricing for medicines used in the management of these three diseases.

Research and development of new medicines is a long and capital-intensive process. It is estimated that the average R&D cost for a new drug is USD 802 million (DiMasi, Hansen and Grabowski, 2003). The use of pharmacoeconomics during the R&D phase is likely to result in more efficient use of resources and provides a basis for justifying the product value (Miller, 2005). One of the most controversial issues for medicine manufacturers is that of medicine pricing. Ideally, a balance between the business case and the humanistic case needs to be achieved. The business case requires pharmaceutical innovation be incentivised through adequate compensation and attractive profits, to encourage investment in the medicine discovery and development. At the same time, the humanistic case requires the appreciation of the ethics around medicine pricing and access; medicines are not luxury goods, therefore, exposing medicines to free market pricing systems must be avoided (Mendoza, 2019).

In the case of South Africa, although the SEP was introduced with the intention of improving pricing transparency, recent data indicates that additional measures are required (Bangalee

and Suleman, 2015; Wadee *et al*., 2020).The potential impact of putting a cap on the logistics fees for 47 medicines was studied in 2013 (Bangalee and Suleman, 2015). However, it was found that only a third of medicines saw a price drop because of capping logistics fees while the majority, particularly medicines without generic alternatives, unexpectedly increased beyond the initial price. This was likely because of limited competition and manipulation of the market and warrants greater transparency of the pricing structures along the distribution chain and further focus on logistics fees costing (Bangalee and Suleman, 2015). The proposal to cap logistics fees faced opposition from smaller manufacturers, fearing a disadvantage against larger counterparts in fee negotiations(Bangalee and Suleman, 2015). While capping logistics fees may not be universally effective, selective implementation for non-generic medicines could be considered. A survey conducted in 2004 (Xiphu and Mpanza, 2004) highlighted the higher logistics fees associated with originator medicines compared to generics and found evidence of potential exploitation of logistics fees by pharmaceutical companies who used them as market incentive for wholesalers and distributors. The researchers proposed uniform logistics fee pricing for similar medicines to allow more uniform pricing (Xiphu and Mpanza, 2004).

The lack of transparency in medicine pricing is a widespread issue observed in many countries. A scoping review examining pricing transparency initiatives found that the impact of increased transparency on medicine prices was inconclusive(Ahmad, Makmor-Bakry and Hatah, 2020). For instance, in South Africa, transparency did not consistently result in lower medicine prices. This could be attributed to the absence of additional initiatives such as price negotiations, as seen in countries like Australia, New Zealand, Germany, and the United Kingdom(Ahmad, Makmor-Bakry and Hatah, 2020). In contrast, Ghana implemented measures to negotiate with pharmaceutical companies, resulting in VAT exemptions for selected medicines and subsequent price decreases(Ahmad, Makmor-Bakry and Hatah, 2020). Malaysia which has a similar private and public health system as South Africa attempted to increase price transparency to patients by making it mandatory to declare ex-manufacturer fees and recommended retail prices of medicines (Ahmad, Hatah and Makmor-Bakry, 2019). The impact of this over a 5-year period in 2011-2025 revealed a correlation between declared pricing and actual retail pricing for that period. Medicine prices also didn't increase drastically, showing the impact of accountability (Ahmad, Hatah and Makmor-Bakry, 2019). Poor

implementation of transparency measures can have unintended consequences such as inflated prices that don't accurately reflect actual medicine costs. This is because manufacturers and pharmaceutical industries can manipulate ex-factory, logistic, and wholesale prices (Ahmad, Makmor-Bakry and Hatah, 2020). This manipulation is a possible contributing factor to the price variations high medicine prices observed in South Africa but was beyond the scope of this study.

Our study further identified additional non-pricing related factors that contributed to medicine price variation. The findings are consistent with existing literature, which has highlighted the influence of other factors on medicine pricing dynamics (Bodhania, 2007). For example, the predominance of generic medicines in the market may contribute to competitive pricing pressures, leading to lower overall medicine prices. While the number of generics on the market is not an accurate predictor of lower medicine prices, having enough generics allows for impactful competition(Moodley and Suleman, 2019). The introduction of new generic competitors in the market exerts downward pricing pressure on existing generics, further extending this effect to originator brands (Bodhania, 2007). Consequently, the greater the number of available generic options for a given medication, the more competitive the pricing becomes for that drug (Moodley and Suleman, 2019), this is consistent with our findings that an increase in number of brands on the market resulted in a lower contribution to inequality and therefore more uniform pricing e.g. for Metformin and HCTZ.

In our study, most of the medicines we analysed were generic drugs (89%). While this is likely due to the inclusion and exclusion criteria used, it aligns with what we know about generics being helpful in increasing access to medicines because they usually cost less (IMS Institute for Healthcare Informatics, 2015). Policies promoting generic substitution result in a shift from more expensive originator brands to more cost-effective generic alternatives (IMS Institute for Healthcare Informatics, 2015).

By quantifying the influence of specific components, policymakers can prioritize policies that address important drivers of price disparities. For example, policies encouraging the use of generic pharmaceuticals or streamlining regulatory processes to minimize manufacturing costs may help alleviate price swings and enhance access to more cost-effective medications(Moodley and Suleman, 2019). Sound pharmaceutical policies will lead to better healthcare outcomes, but strategic long-term planning and regulation will assist in minimising

inefficiencies and maintaining lower mark-ups and increase access to medicines(Moodley and Suleman, 2019) .

The success of combining price regulation strategies is noted in India (Wadee *et al.*, 2020). India maintains low medicine prices through a price control mechanism overseen by the National Pharmaceutical Pricing Authority. The ceiling price for each drug is set at the weighted average price of brands with over 1% market share. Unlike South Africa, where local production is limited, India has the advantage of vast local manufacturing which encourages price competition among manufacturers therefore driving down medicine prices (Wadee *et al.*, 2020).This strategy may still work in South Africa because generics are common and many medicines have more than a few generic alternatives as seen by the high proportion of generic to originator brands in this study.

Finally, with the imminent implementation of NHI in South Africa, it is important to understand what the possible implications of NHI on medicine pricing may be. The procurement of medicines in the public sector is typically subject to minimal logistics fees or may even be exempt from them (Mashile, 2020). In contrast, our study has shown that logistics fees significantly influence medicine pricing in the private sector. Currently, there is a lack of transparency regarding how these fees are determined, which creates opportunities for manipulation. Unless appropriate regulatory measures are implemented to address this and ensure transparency, making it obligatory to pay logistics fees, the existing challenges are likely to continue. When NHI is introduced, it is unlikely that pricing will be exempt of logistics fees. This poses an additional expense which must be factored into medicine pricing. The NHI will therefore need to establish an effective way of pricing medicines. In addition, if under the NHI, the purchaser focuses solely on awarding medicine supply contracts based on price, it will require pharmaceutical companies to take further price reductions to remain relevant in the market(Mashile, 2020). This may have the unintended consequence of driving other manufacturers out of the SA market due to lack of operational viability. When this happens, supply options will decrease, and this can ultimately lead to stock availability challenges downstream. Security of supply needs to be guaranteed for NHI to be successful.

4.1. STUDY LIMITATIONS.

The SEP dataset from the MPR was of poor quality, with many missing observations and poor presentation format, a lot of time was therefore spent cleaning it and generating new variables for ease of analysis. In its raw form, this data is difficult to use, it would therefore be beneficial for the MPR datasets to be presented better, for instance presentation of data in the wide format, data completeness and uniform formatting for ease of reference for all parties that use it. Some observations had to excluded due to incomplete data or too few brands on the market to allow comparison which affected the scope of statistical analysis, this may have introduced bias into our results by omitting crucial information. Given the poor quality of the dataset, this limitation was addressed through the generation of many new variables from available data so that meaningful analyses could be done.

In analysing pricing components, it is crucial to recognize that logistics fees are not adequately regulated. As mentioned earlier, the reliability of the information published in the MPR database is uncertain. However, it was not feasible to interrogate or verify this data for all medicines included in the study, so the analysis relied on the published information.

For the second decomposition analysis, when categorising manufacturers into South African and non-South African origins, we might have missed variations due to different regions. For instance, medicines from India could be priced differently compared to those from Europe or other African regions. Furthermore, products registered by SAHPRA are linked to a locally licensed manufacturer or importer. However, many medicines, including those from South African companies, are imported as finished products or have components of the excipients being imported. These imports may represent a significant portion of the manufacturer's costs therefore the lack of further interrogation of these issues present a limitation. The data on origin of manufacturer was not readily available from the dataset and reference was made to other sources to determine the manufacturer’s origin. The inclusion of information on origin of manufacturer/ principal applicant to the MPR datasets would be beneficial for to any similar future studies.

Finally, the study was a cross-sectional analysis, which captures information at one specific point in time. Cross-sectional studies do not capture trends over time. Pricing of medicine is not a stagnant process, and changes do occur over time e.g. price reviews like the annual

increase or price revisions in response to market forces like new generic entrants. These factors impact pricing and price variations, but the effects will not be captured in a cross-sectional study.

4.2. CONCLUSION

This study examines the complex topic of medicine pricing in the private sector of South Africa, with a particular emphasis on medicines for diabetes, hypertension, and HIV. The results highlight variations in medication prices among the three diseases, which are mainly attributable to manufacturing expenses, logistics expenses and non-pricing related factors like origin of manufacturer, generic and number of brands on the market. Comprehensive policy interventions, such as increased transparency, regulatory reforms, and strategic purchasing frameworks, are needed to address these issues. To achieve sustainable healthcare results for all population segments, South Africa needs to progress towards equitable access to reasonably priced medicines for everyone, while maintaining market viability for the manufacturers. To support evidence-based decision-making and advance the control of pharmaceutical prices, ongoing research and policy assessment are essential. Further research examining a wider variety of pharmaceutical classes may provide a more thorough knowledge of the dynamics of medicine pricing.

5. CHAPTER FIVE: RECOMMENDATIONS

A number of recommendations flow from these analyses. The Pricing Committee should have greater power to enable negotiation of manufacturer fees directly with manufacturers, this should be done in conjunction with external reference pricing such that prices are informed by the pricing in a group of comparator countries. This was the initial intent when SEP was first introduced (Department of Health, 2014) but it hasn't materialised as the draft regulations are still under review. Disclosure agreements with manufacturing companies need to be strengthened to ensure information on manufacturing and logistics-related costs as well as volumes of medicine produced are made available to the Pricing Committee (Wadee *et al*., 2020).

Considering NHI introduction, there is a need for provision of a strategic purchasing framework for medicines for all beneficiaries which allows for redistribution of health resources leading to equitable access to allow health needs of the South African population to be met while keeping the markets viable for medicine manufacturers. The biggest challenge remains that the balance between affordability of medicines and viability of the markets must be reached, failing which some suppliers may withdraw from the SA market if their profits aren't viable (Bodhania, 2007).

While South Africa has made strides in increasing drug affordability, issues remain in balancing affordability and commercial viability. Addressing these difficulties requires governments, healthcare stakeholders, and the pharmaceutical sector to work together to assure long-term access to important pharmaceuticals for all segments of the population. Additional research and policy actions are required to accomplish these objectives and ensure equitable healthcare access in South Africa.

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APPENDIX A: ATC CODES FOR ANALYSIS

The below table shows the groups of medicines that were included and excluded from the analysis based on the inclusion and exclusion criteria applied. As the analysis was done at ATC2 level, distinction was made of which ATC4 groups were analysed.

Disease	**ATC2 group**	**ATC4 Code included in analysis**	**ATC4 Code included in analysis**
Diabetes	A10 (Sulphonamides, Biguanides, DPP IV inhibitors	A10BA	A10BG
		A10BB	A10BX
		A10BD	
		A10BK	
		A10BH	
Hypertension	C01 (Cardiac glycosides, Anti-arrhythmics, cardiac stimulants, vasodilators, cardiac preparations. C02 (antiadrenergics, arteriolar smooth muscle agents).		ALL CO1 AND C02
	C03 (Diuretics)	C03AA	C03BA
		C03CA	C03DA
	C07 (B-blockers)	C07AB	C07AA
		C07AG	C07DA
	C08 (Calcium channel blockers)	C08CA	C08DA
		C08GA	C08DB
	C09(ACE-inhibitors, ARBs)	C09CA	C09BA
		C09CO	
		C09DA	
		C09DB	
		C09AA	
		C09DX	
HIV	J05 (Antivirals)	J05AG	J05AB
		J05AR	J05AF
			J05AH
			J05AP
			J05AE
			J05AX

APPENDIX B: PLAGIARISM DECLARATION

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

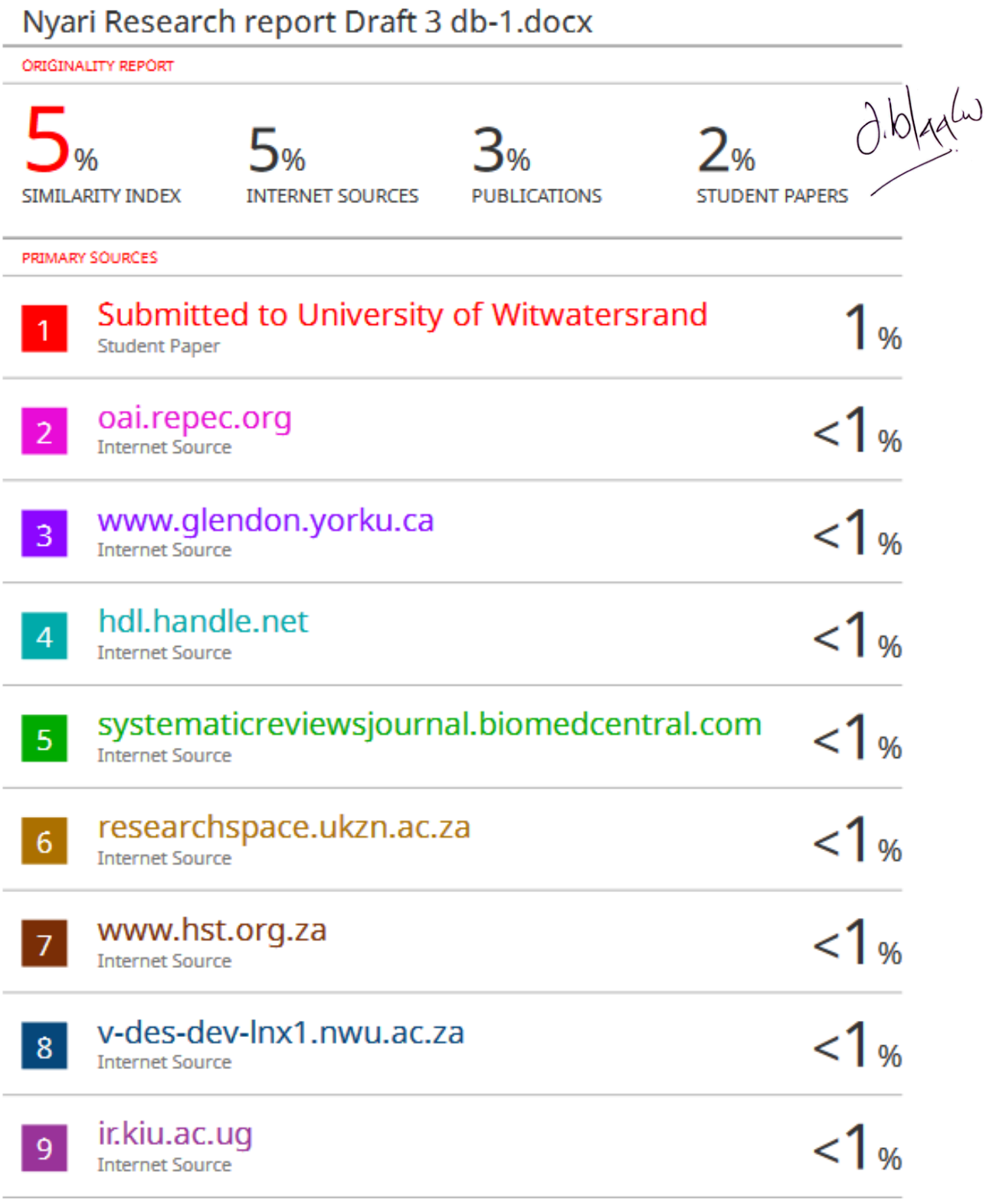
I NYARADZAI MATANYAIRE (Student number: 2373970) am a student registered for the degree of MASTER OF PUBLIC HEALTH (HEALTH ECONOMICS) in the academic year 2023.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: N MATS Date: 25/03/2024

APPENDIX C: TURNITIN REPORT



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APPENDIX D: ETHICS WAIVER CERTIFICATE

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Innovation)

17/05/2023

Ref: W-CBP-230517-01

TO WHOM IT MAY CONCERN

Waiver: This certifies that the following research does not require clearance from the Human Research Ethics Committee (Medical)

Investigator: Ms N Matanyaire
Student No. (if appropriate): 2373970
Staff No. (if appropriate):

Supervisor: Dr D Blaauw

School: Public Health
Department:
Centre for Health Policy
Medical School
University

Project title: *Variation in prices of medicines used in the management of HIV, Type 2 Diabetes Mellitus and hypertension in South Africa's private sector, 2022*

Reason: Review of information in the public domain
No human participants will be involved in the study

Dr CB Penny
Chairperson: Human Research Ethics Committee (Medical)

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