Retail pharmacy prescription medicines availability, prices, and affordability in Eswatini

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DECLARATION

In fulfilment of the requirements of the coursework degree of Master of Pharmacy, in the Discipline of Pharmacy, University of KwaZulu-Natal, Durban, South Africa, I, Garikai Shambira declare as follows:

i. That the work described in this thesis has not been submitted to UKZN or other tertiary institution for purposes of obtaining an academic qualification, whether by myself or any other party.

ii. The research reported in this dissertation, except where referenced, is my original work.

iii. This dissertation does not contain other person's text, tables, data, graphs or other information, unless specifically acknowledged as being sourced from other persons.

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PREFACE

This is a mini dissertation comprising of 50% research project component. The University of KwaZulu-Natal CR13 (c) directs that a dissertation "*may comprise one or more papers of which the student is the prime author, published or in press in peer-reviewed journals approved by the relevant college academic affairs board or in manuscripts written in a paper format, accompanied by introductory and concluding integrative material*". As such a standalone methodology is not required, as it forms part of the submitted paper/manuscript chapter. The outline of each chapter is presented at the end of Chapter 1.

ACKNOWLEDGEMENTS

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ABBREVIATIONS AND ACRONYMS

ANOVA – Analysis of variance

BREC – Biomedical Research Ethics Committee

CDE – Catastrophic Drug Expenditure

EML – Essential Medicines List

GDP – Gross Domestic Product

HAI – Health Action International

LPG – Lowest price generic

MPR – Median Price Ratio

MRP – Medicines Reference Price

MSH – Management Sciences for Health

NCD – Non-Communicable Disease

OB - Originator brand

SA – South Africa

SEP – Single Exit Price

SNPP – Swaziland National Pharmaceutical Policy

UK – United Kingdom

UKZN - University of Kwa-Zulu-Natal

USA – United States of America

USD – United States Dollar

VAT – Value Added Tax

WHO – World Health Organisation

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ABSTRACT

Background: The low availability of medicines in public health outlets coupled with unaffordable prices in the private sector can be a major barrier to medicines' access. Patients in Eswatini may be forced to buy medicines from the private sector due to the chronic medicines shortages in Eswatini public health facilities. The extent to which they can afford to do so is unknown.

Aim: To determine the availability, prices paid by patients and affordability of medicines, in the retail pharmacies in Eswatini and to compare the results regionally.

Setting: Retail pharmacy sector in the 4 administrative regions of Eswatini.

Methods: Data on availability, prices and affordability to patients for two products namely the originator brand (OB) and the lowest-priced generic equivalent (LPG) for 50 medicines were collected using the standardised World Health Organization/ Health Action International methodology. The data collection was conducted in 32 retail pharmacies in the 4 regions of Eswatini. Prices for each medicine were compared with South Africa.

Results: The overall mean availability of all medicines in selected retail pharmacy outlets was (38.5%; SD=20.4%) for OBs and (80.9%; SD=19.0%) for LPGs. The overall median price ratio (MPR) in the surveyed pharmacies was 18.61 for the OBs and 4.67 for LPGs. Most standard treatments with LPGs cost less than a day's wage whilst OB's cost more than a day's wages. The differences between Eswatini and South African prices were statistically significant.

Conclusion: There is a need to develop medicines pricing policies and price monitoring tools in the whole pharmaceutical chain in Eswatini to measure and monitor availability, affordability, and accessibility of medicines to the general populace.

Chapter 1: Introduction

1.1 Background

The price of medicines is a major contributing factor to lack of access to medicines in different countries.[1] Unavailability and/or low availability of essential medicines in the public health outlets may become a major barrier to medicines' access especially when coupled with high unaffordable prices in the private sector. [2] There is significant under-use of costly medicines in populations that do not have any medical insurance, and thus even the smallest price changes in drugs will impact adherence significantly among the poor.[3] It is thus imperative that prices in the private sector be affordable to ensure equity access. [3,4]

Medicines expenditure constitutes between 20% and 60% of health expenditure in low and middle-income nations compared to just 18% in European nations. In developing countries, only a mere 10% has health insurance and the rest buy medication through out-of-pocket payments, thus making medication the largest family expenditure item after food. [5]

Nobrega et al.[6] assert that the lack of medicines pricing legislation in the private sector and poor distribution of essential medicines in the public facilities negatively affect accessibility and burden consumers with out-of-pocket expenses. Patients in Eswatini may be forced to buy medicines from the private sector due to the chronic medicines shortages in Eswatini public health facilities.[7] The extent to which they can afford to do so is unknown.

The World Health Organisation/Health Action International (WHO/HAI) has set a benchmark of 80% medicine availability as high to ensure the supply of essential medicines. [8] Although generic medicines are way cheaper than the innovator brands, they are still relatively unaffordable in many parts of developing countries. [9]

Cross national differences in pharmaceutical prices are of great importance as they help governments to come up with appropriate domestic pricing policies.[10] However as Mhlanga et al [7] highlighted, there is a need to have reliable evidence on medicines' prices in order to ascertain the type of challenges in a country before deciding on solutions that will ensure availability of essential medicines at the lowest price to the consumer.

There is currently no price regulation of pharmaceuticals in Eswatini,[7] although the Medicines and Related Substances Act of 2016, Section 54 makes provision for the Minister of Health, on

the recommendation of the Authority to prescribe a pricing system for all medicines and scheduled substances.[11]

Availability, pricing and affordability surveys have been used to determine the extent of price differentiation and affordability in many countries.[10,12,13,14] Thus, for Eswatini, the WHO/HAI medicine price survey was used to identify medicine pricing and affordability in the Kingdom of Eswatini so as to provide policy makers and all stakeholders with evidence to draft policies that may improve availability, affordability and accessibility of medicines.

The aim of this study was to investigate the availability, affordability and prices that people pay for medicines in different parts of Eswatini. In addition, this study sought to ascertain how the medicines' prices in Eswatini compared to the prices of the same medicines in South Africa. Eswatini does not have any pharmaceutical manufacturing companies and depends on South Africa for most of their medications especially in the private market. The few medical aids operating in Eswatini are managed by South African administrators and their reimbursement schemes are extrapolated from the South African standards. It was thus important to compare Eswatini pricing to South Africa.

1.2 Research problem

There has been reported low availability of essential medicines in public health outlets [7] and patients may be forced to buy these medicines from the private pharmacy sector. The extent to which they can afford to do so is unknown. The research then sought to investigate the availability, affordability and prices that people pay for medicines in different parts of Eswatini.

1.3 The objectives of the study

The cross-sectional study investigated the availability, affordability and prices that people pay for medicines in different parts of the Kingdom of Eswatini for 50 medicines (14 from the global core list and 36 supplementary medicines). Data were collected from selected retail pharmacies in all the four administrative regions of the Kingdom of Eswatini. The study was designed:

i.   To determine the availability and prices that people pay for the key medicines in the retail pharmacies in the Kingdom of Eswatini.

ii.   To determine if the prices and availability of the key medicines varied in different parts of the country.

iii. To determine the affordability of medicines for the ordinary people,

iv. To ascertain how the medicines' prices in the Kingdom of Eswatini compared to the prices of the same medicines in South Africa.

1.4 Research questions:

i. What is the availability of key medicines and what prices do people pay for these medicines in the retail pharmacy sector in Eswatini?

ii. Do prices and availability of the key medicines vary in different parts of the country?

iii. How affordable are the key medicines for the ordinary people?

iv. How do medicines' prices in Eswatini compare to the prices of the same medicines in South Africa?

1.5 Hypothesis

There is anecdotal evidence that patient medicines prices and availability may vary with regional location. We hypothesized that medicines prices and availability would vary with location in Eswatini. **Study area and general methodology**

Study design

A quantitative cross-sectional descriptive study design was employed in this study.

Setting

The Kingdom of Eswatini is a small country, at just over 17000 km² and a population of just over a million people. The country is divided into 4 regions: Hhohho (North West), Manzini (central), Lubombo (East) and Shiselweni (South). An analysis of patient prices for 50 pre-determined medicines (14 from global core list and 36 supplementary medicines) was conducted in 32 retail pharmacies in the 4 administrative regions of Eswatini using the WHO/HAI Standard Methodology.[15]

Study Population and Sampling Strategy

A list of pharmacies was obtained from the office of the Deputy Director of Pharmaceutical Services in the Ministry of Health of the 60 registered retail pharmacies in Eswatini at the time of the study; with 14 geographically situated in Hhohho, 30 in Manzini, 10 in Lubombo and 6

in the Shisweleni region. Stratified sampling was used to group the pharmacies. The primary criterion was the region of location for the pharmacy.

A total number of 32 pharmacies were included in the study. Disproportionate stratified sampling was used to ensure that the sample was representative of the Eswatini retail pharmacy population. The sample comprised 12 pharmacies from Manzini, 8 from Hhohho, 6 from Lubombo and 6 from Shiselweni. Simple random sampling was used to select the pharmacies to use in each region. To analyze the effect of the size of the city/town on prescription prices; pharmacies were categorized as from either city or town/rural area.

Data Collection

Data collection took place between 15 June 2020 and 13 August 2020. The researcher collected the data. Data on price, availability and affordability to patient were collected for two products, namely the originator brand (OB) and the lowest price generic (LPG) using the standardised WHO/HAI methodology,[15] for 50 essential medicines (14 from the global core list and 36 selected based on local relevance).[16] The following specific data were collected using the WHO/HAI workbook, during visits to **"retail pharmacy outlets"**,

1. the name of pharmacy, administrative region where located, and whether it was in a city or town/rural area.
2. Brand/Product name and manufacturer of the lowest priced generic found at the site.
3. Availability of the Originator brand and the lowest priced generic.
4. Pack size and price of the pack found for the originator brand and the lowest priced generic.
5. Any other comments regarding a given product.

During the retail pharmacy visits, data was recorded on hard copy medicine prices data collection forms. The data collector made sure the data collection forms were complete and legible before leaving an outlet.

Data collection forms were reviewed every day after completion of the field work to ensure data quality. The data was then entered from the hard copy forms into the electronic survey workbook, and the double entry program was run, and any mistakes corrected. Any questionable data identified after running data checker, was investigated, and corrected.

Data Analysis

Data were entered in the pre-programed WHO/HAI Microsoft Excel Workbook.[17] The workbook automatically generated analysis of the data entered once complete giving summary tables of percentage availability and Median Price Ratios (MPR). Median local prices were expressed as ratios to international reference prices, using the formula.

Medicine Price Ratio (MPR) = <u>median local unit price</u>

International reference unit price

Management Sciences for Health (MSH)'s 2015 prices were used as the default source of international reference prices (IRP's). The IRP's used are prices offered to international not-for profit agencies for purchase of generics.[18]

The availability of medicines was determined as a percentage of outlets where medicine was found on the day of data collection. Mean availability of the 50 medicines was also reported. The differences in average percentage availability of OBs and LPGs determined if there was any variance in the availability of the two product types. To describe availability, the following ranges were used as reference, [8]

1. < 30% extremely low
2. 30% - 49% low
3. 50% - 80% fairly high
4. > 80% high.

The MPR pharmacy prices for each drug was compared across region categories using analysis of variance (ANOVA). The MPR pharmacy prices for each drug were compared between the two categories of location size using t-test. The lowest and maximum prices in Eswatini were compared to the lowest and highest permissible retail prices in South Africa (based on current dispensing fee guide in South Africa at the time),[19,20] and the differences were expressed as percentage price difference for similar products and were analysed using the t-test for statistical significance.

Affordability was calculated as the number of wage days that the lowest paid government worker needed to spend to pay for treatment and was based on the median local price of a medicine prescribed at a standard dose. [15] All analysis were carried out using SPSS version 27.

1.6 Layout of thesis

Chapter 1

The introductory chapter elaborates on the significance of this study. The background and research problem are highlighted and the objectives, research questions and hypothesis for the study are discussed. The chapter concludes by describing the study area and the general methodology that was employed to meet the objectives.

Chapter 2

The literature review chapter explores and discusses the general principles, foundations and implications of medicines' prices on availability and affordability of medicines to patients. Methods employed by policy makers to achieve price control and containment are also discussed. The chapter explains the current state of affairs with regards to medicines prices in Eswatini and South Africa. It concludes by discussing global studies that have employed the WHO/HAI methodology and their findings.

Chapter 3

This chapter presents the paper that was submitted to the African Journal of Primary Health Care and Family Medicine, as per the journal stipulated format and limitations in terms of graphs, tables and word count.

Chapter 4

The synthesis of the thesis is discussed in this chapter. Conclusions drawn from the primary research data are outlined in this chapter and the proposed recommendations are also discussed. Further research areas are highlighted and the chapter concludes by discussing the extent to which the study answered the research questions.

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Chapter 2: Literature review

2.1 Introduction

Although medicines are crucial in the healthcare system, they are generally not affordable to people globally. It is well documented in literature that price is a major barrier to access.[1] Prohibitive pricing is one of the major barriers to essential medicines access.[2] There is significant under-use of costly medicines in populations that do not have any medical insurance, and thus even the smallest price changes in drugs will impact adherence significantly among the poor.[3]

More than 30% of world population does not have reliable access to essential medicines. In some of the poorest countries in Asia and Africa the proportion is as high as 50%.[4] The price of drugs is a major contributing factor to lack of access in different countries.[5] Unavailability and/or low availability of essential medicines in the public health outlets may become a major barrier to medicines' access, especially when coupled with high unaffordable prices in the private sector.[6] It is thus imperative that prices in the private sector be affordable to ensure equitable access. [7,8]

Medicines' expenditure constitutes between 20% and 60% of health expenditure in low and middle-income nations compared to just 18% in European nations. In developing countries, only a mere 10% has health insurance and the rest buy medication through out-of-pocket payments, thus making medication the largest family expenditure item after food. [9]

Different policy options are available to governments to regulate pharmaceutical pricing from free-pricing systems, price-regulated systems, price differentiation, price competition and discounts, to tendering procedures. [10] Different schemes are used globally to regulate drug prices; for example, France and Italy utilise drug price controls to directly manage the drug prices. In Germany and Japan prices are indirectly controlled via reimbursement under social insurance schemes. The National Pharmaceutical Price Authority in Britain monitors price by regulating the profits that companies make on branded prescription medicines' sales. [11] It is widely believed that the drug prices are generally higher in countries with less stringent price regulation (like the UK) or no regulation at all (the US) as compared to countries with strict price regulation.[12]

The market share of innovator brands reduces significantly with the introduction of generics after the expiration of patent protection and the competition between the generic options lower

the prices of the branded products further.[12] Free-pricing systems may lower the medicines' prices when optimum conditions are created; and as much as regulation in price-controlled systems may reduce the prices of both generics and brands, it may become a barrier to incentives to lowering prices below the listed ones.[10]

Studies in the United States in price variability with other commodities besides pharmaceuticals, found that the poorer individuals usually find themselves paying more for similar goods and services as compared to their richer counterparts. [13] Grocery stores in poorer locations are usually smaller and more expensive than in the wealthier suburbs, mainly because of the existence of large chain stores in the more affluent areas and independents in the poorer areas. [13, 14] Not much is known about price regulation or affordability in low- and middle-income countries, especially across the African region.

2.2 The Eswatini Experience

The Kingdom of Eswatini has a Gross Domestic Product (GDP) per capita income of USD 3073 and is classified as a lower middle-income country. More than 60% of the population are living below the upper poverty line of USD 8.21 per capita per month. [15] There is currently no price regulation of pharmaceuticals in Eswatini,[16] although the Medicines and Related Substances Act of 2016, Section 54 makes provision for the Minister of Health, on the recommendation of the Authority to prescribe a pricing system for all medicines and scheduled substances.[17] Mhlanga et al.[16] highlighted the importance of reliable evidence on medicines' prices in ascertaining the type of challenges in a system, before deciding on solutions to ensure availability of essential medicines at the lowest possible price to the consumer.

Prices for prescription medicines are a significant obstacle to appropriate medicine use. [18] It is not easy to find reliable medicines prices' information in developing countries, [19] including in Eswatini. The World Health Organisation/Health Action International (WHO/HAI) has set a benchmark of 80% medicine availability to ensure the supply of essential medicines. [20] Although generic medicines are way cheaper than the innovator brands, they are still relatively unaffordable in many parts of developing countries. [21]

The current Eswatini Medicines and Related Substances Act provides for the establishment of a medicines regulatory authority, whilst the Pharmacy bill provides for the establishment of pharmacy council, however both are not in existence.[22] All prescription medicines (defined as any medicine on a valid doctor's prescription), attract Value Added Tax (VAT) at zero percent

and where there is no prescription VAT at 15% is levied.[17] Cross national differences in pharmaceutical prices are of great importance as they help governments to come up with appropriate domestic pricing policies.[23]

2.3 Medicines' Pricing in South Africa

South Africa, as Eswatini's neighbour, is considered as an upper middle-income country, and has introduced price controls for medicines. The Single Exit Price (SEP) mechanism lists the price that a medicine can be sold by a manufacturer to an end-dispenser. The South African Medicines and Related Substances Act (as amended) regulates the maximum additional dispensing fee that can be charged by people licenced to dispense as well as retail pharmacists, based on a tier-structure directly tied to the SEP. All retail medicines attract VAT at 15%. [24] The Act has a provision that prohibits the use of bonuses, rebates or any incentives in the supply of medicines, to avoid undermining the SEP. [25]

A study in South Africa investigated 50 medicines using the WHO/HAI methodology and the Interrupted Time-Series (ITS) model showed a significant decrease in medicines' prices immediately after implementing the Single Exit Price (SEP) in 2004. [26]

2.4 Pricing Surveys using the WHO/HAI methodology

Pricing surveys have been used to determine the extent of price differentiation and affordability in countries. A survey conducted in Peru using the WHO/HAI Medicines Prices and Availability survey did not find any significant differences in overall availability or prices of the medicines under study by retail location. [15]

Another study looked at the undiscounted prices for both innovator brand and the lowest priced generic for 25 essential medicines from 17 private pharmacies in Shaanxi province, Western China. It noted that generics were more available as compared to innovator brands and prices varied across different discount programs. The study concluded that price transparency of pharmaceuticals helps consumers in the identification of potential savings. [27]

An African study that used the standardized WHO/HAI methodology to measure medicines availability, prices and affordability in both public and private sectors was conducted from March 2012 to April 2013 in Sudan. The availability was generally low in both sectors with less than 10% for originator brands and less than 50% for the generics, and considerable price

differences noted between low priced generics (LPGs) and originator brands (OBs) of medicines. [22]

A cross-sectional study on 50 essential medicines' availability, prices and affordability was carried out in both private and public sectors in Malawi, using the standard WHO/HAI methodology. The availability of medicines was highest in the private retail pharmacy sector (71.1%), followed by 62.9% in Christian Health Association of Malawi facilities and private clinics had the least availability at 57.5%. It was noted that the cost of one course for more than half of the medicines under study exceeded the statutory minimum daily wage rendering them unaffordable to the biggest part of the population. [28]

Electronic questionnaires were used to carry out a study to assess the retail pricing, availability and affordability of medicines in private health facilities in low-income settlements within Nairobi County between September and December 2016. The availability of the indicator medicines varied amongst the different facilities ranging from 2% to 76%, whilst the retail prices were generally higher than IRPs. Although the different regions comprise people of similar social standing, price variations were noted amongst the different regions and this has a direct effect on accessibility of medicines. [29]

Guan et al.[30] findings highlighted the challenges associated with regional disparity and inequality between rural and urban areas in mainland China in the delivery of essential medicines. [31]

Thus, for Eswatini, the WHO/HAI medicine price survey was used to identify medicine pricing and affordability in the Kingdom of Eswatini so as to provide policy makers and all stakeholders with evidence to draft policies that may improve availability, affordability and accessibility of medicines.

The aim of this study was to investigate the availability, affordability and prices that people pay for medicines in different parts of Eswatini. In addition, this study sought to ascertain how the medicines' prices in Eswatini compared to the prices of the same medicines in South Africa and internationally.

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Chapter 3. Submitted Paper

This article has been submitted to African Journal of Primary Health Care and Family Medicine. See the submission acknowledgment email as proof (Appendix A).

This chapter presents the submitted paper as per the journal stipulated format https://phcfm.org/index.php/phcfm/pages/view/submission-guidelines#part_1 and limitations in terms of graphs, tables and word count. Written permission to conduct the study was sought from and granted by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, (BREC/00001237/2020 and Appendix B). See also The Kingdom of Eswatini Ministry of Health permission letter (Appendix C). See too the data collection sheet and informed consent documents (Appendix D). GS was responsible for proposal development, data collection and analyses with the assistance of a statistician and the write up. FS served as supervisor.

Title: Retail pharmacy prescription medicines availability, prices, and affordability in Eswatini

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Abstract

Background: The low availability of medicines in public health outlets coupled with unaffordable prices in the private sector can be a major barrier to medicines' access. Patients in Eswatini may be forced to buy medicines from the private sector due to the chronic medicines shortages in Eswatini public health facilities. The extent to which they can afford to do so is unknown.

Aim: To determine the availability, prices paid by patients and affordability of medicines, in the retail pharmacies in Eswatini and to compare the results regionally.

Setting: Retail pharmacy sector in the four administrative regions of Eswatini.

Methods: Data on availability, prices and affordability to patients for two products namely the originator brand (OB) and the lowest-priced generic equivalent (LPG) for 50 medicines were collected using the standardised World Health Organization/ Health Action International methodology. The data collection was conducted in 32 retail pharmacies in the 4 regions of Eswatini by the researcher. Prices for each medicine were compared with South Africa.

Results: The overall mean availability of all medicines in selected retail pharmacy outlets was (38.5%; SD=20.4%) for OBs and (80.9%; SD=19.0%) for LPGs. The overall MPR in the surveyed pharmacies was 18.61 for the OBs and 4.67 for LPGs. Most standard treatments with LPGs cost less than a day's wage whilst OB's cost more than a day's wages. Prices were higher in Eswatini and the differences between Eswatini and South African prices were statistically significant.

Conclusion: There is a need to develop drug pricing policies and price monitoring tools in the whole pharmaceutical chain in Eswatini to measure and monitor availability, affordability, and accessibility of medicines to the general populace.

Introduction

Although medicines are crucial in the healthcare system, they are generally not affordable to people globally. It is well documented in literature that price is a major barrier to access.[1] Prohibitive pricing is one of the major barriers to essential medicines access.[2] There is significant under-use of costly medicines in populations that do not have any medical insurance, and thus even the smallest price changes in drugs will impact adherence significantly among the poor.[3]

More than 30% of world population does not have reliable access to essential medicines. In some of the poorest countries in Asia and Africa the proportion is as high as 50%.[4] The price of drugs is a major contributing factor to lack of access in different countries.[5] Unavailability and/or low availability of essential medicines in the public health outlets may become a major barrier to medicines' access, especially when coupled with high unaffordable prices in the private sector.[6] It is thus imperative that prices in the private sector be affordable to ensure equity access. [7,8]

Medicines expenditure constitutes between 20% and 60% of health expenditure in low and middle-income nations compared to just 18% in European nations. In developing countries, only a mere 10% has health insurance and the rest buy medication through out-of-pocket payments, thus making medication the largest family expenditure item after food. [9]

Different policy options are available to governments to regulate pharmaceutical pricing from free-pricing systems, price-regulated systems, price differentiation, price competition and discounts, to tendering procedures. [10] Different schemes are used globally to regulate drug prices; for example, France and Italy utilise drug price controls to directly manage the drug prices. In Germany and Japan prices are indirectly controlled via reimbursement under social Insurance schemes. The National Pharmaceutical Price Authority in Britain monitors price by regulating the profits that companies make on branded prescription medicines' sales. [11] It is widely believed that the drug prices are generally higher in countries with less stringent price regulation (like the UK) or no regulation at all (the US) as compared to countries with strict price regulation.[12]

The market share of innovator brands reduces significantly after the introduction of generics after the expiration of patent protection and the competition between the generic options lower

the prices of the branded products further.[12] Free-pricing systems may lower the medicines' prices when optimum conditions are created; and as much as regulation in price-controlled systems may reduce the prices of both generics and brands, it may become a barrier to incentives to lowering prices below the listed ones.[10]

Studies in the United States in price variability with other commodities besides pharmaceuticals, found that the poorer individuals usually find themselves paying more for similar goods and services as compared to their richer counterparts. [13] The grocery stores in poorer locations are usually smaller and more expensive than in the wealthier suburbs, mainly because of the existence of large chain stores in the more affluent areas and independents in the poorer areas. [13,14] Not much is known about price regulation or affordability in low and middle income countries, especially across the African region.

The Kingdom of Eswatini has a Gross Domestic Product (GDP) per capita income of USD 3073 and is classified as a lower middle-income country. More than 60% of the population are living below the upper poverty line of USD 8.21 per capita per month. [15] There is currently no price regulation of pharmaceuticals in Eswatini,[16] although the Medicines and Related Substances Act of 2016, Section 54 makes provision for the Minister of Health, on the recommendation of the Authority to prescribe a pricing system for all medicines and scheduled substances.[17] Mhlanga et al.[16] highlighted the importance of reliable evidence on medicines' prices in ascertaining the type of challenges in a system, before deciding on solutions to ensure availability of essential medicines at the lowest possible price to the consumer.

Prices for prescription medicines are a significant obstacle to appropriate medicine use. [18] It is not easy to find reliable medicines prices' information in developing countries, [19] including in Eswatini. The World Health Organisation/Health Action International (WHO/HAI) has set a benchmark of 80% medicine availability to ensure the supply of essential medicines. [20] Although generic medicines are way cheaper than the innovator brands, they are still relatively unaffordable in many parts of developing countries. [21]

The current Eswatini Medicines and Related Substances Act provides for the establishment of a medicines regulatory authority, whilst the Pharmacy bill provides for the establishment of pharmacy council, however both are not in existence.[22] All prescription medicines (defined as any medicine on a valid doctor's prescription), attract Value Added Tax (VAT) at zero percent and where there is no prescription VAT at 15% is levied.[17] Cross national differences in

pharmaceutical prices are of great importance as they help governments to come up with appropriate domestic pricing policies.[23]

South Africa, as Eswatini's neighbour, is considered as an upper middle-income country, and has introduced price controls for medicines. The Single Exit Price (SEP) mechanism lists the price that a medicine can be sold by a manufacturer to an end-dispenser. The South African Medicines and Related Substances Act (as amended) regulates the maximum additional dispensing fee that can be charged by people licenced to dispense as well as retail pharmacists, based on a tier-structure directly tied to the SEP. All retail medicines attract VAT at 15%. [24] The Act has a provision that prohibits the use of bonuses, rebates or any incentives in the supply of medicines, to avoid undermining the SEP. [25]

Pricing surveys have been used to determine the extent of price differentiation and affordability in countries. A survey conducted in Peru using the WHO/HAI Medicines Prices and Availability survey did not find any significant differences in overall availability or prices of the medicines under study by retail location. [15]

Another study looked at the undiscounted prices for both innovator brand and the lowest priced generic for 25 essential medicines from 17 private pharmacies in Shaanxi province, Western China. It noted that generics were more available as compared to innovator brands and prices varied across different discount programs. The study concluded that price transparency of pharmaceuticals helps consumers in the identification of potential savings. [26]

An African study that used the standardized WHO/HAI methodology to measure medicines availability, prices and affordability in both public and private sectors was conducted from March 2012 to April 2013 in Sudan. The availability was generally low in both sectors with less than 10% for originator brands and less than 50% for the generics, and considerable price differences noted between low priced generics (LPGs) and originator brands (OBs) of medicines. [22]

A cross-sectional study on 50 essential medicines' availability, prices and affordability was carried out in both private and public sectors in Malawi, using the standard WHO/HAI methodology. The availability of medicines was highest in the private retail pharmacy sector (71.1%), followed by 62.9% in Christian Health Association of Malawi facilities and private clinics had the least availability at 57.5%. It was noted that the cost of one course for more than

half of the medicines under study exceeded the statutory minimum daily wage rendering them unaffordable to the biggest part of the population. [27]

Electronic questionnaires were used to carry out a study to assess the retail pricing, availability and affordability of medicines in private health facilities in low-income settlements within Nairobi County between September and December 2016. The availability of the indicator medicines varied amongst the different facilities ranging from 2% to 76%, whilst the retail prices were generally higher than IRPs. Although the different regions comprise people of similar social standing, price variations were noted amongst the different regions and this has a direct effect on accessibility of medicines. [28]

Guan et al.[31] findings highlighted the challenges associated with regional disparity and inequality between rural and urban areas in mainland China in the delivery of essential medicines. [29]

Thus, for Eswatini, the WHO/HAI medicine price survey was used to identify medicine pricing and affordability in the Kingdom of Eswatini so as to provide policy makers and all stakeholders with evidence to draft policies that may improve availability, affordability and accessibility of medicines.

The aim of this study was to investigate the availability, affordability and prices that people pay for medicines from retail pharmacies in different parts of Eswatini. In addition, this study sought to ascertain how the medicines' prices in Eswatini compared to the prices of the same medicines in South Africa.

Research methods and design

Study design

A quantitative cross-sectional descriptive study design was employed in this study.

Setting

The Kingdom of Eswatini is a very small country, at just over 17000 km² and a population of just over a million people. The country is divided into 4 regions: Hhohho (North West), Manzini (central), Lubombo (East) and Shiselweni (South). An analysis of patient prices for 50 pre-determined medicines (14 from global core list and 36 supplementary medicines) was

conducted in 32 retail pharmacies in the 4 administrative regions of Eswatini using the WHO/HAI Standard Methodology.

Study Population and Sampling Strategy

A list of pharmacies was obtained from the office of the Deputy Director of Pharmaceutical Services in the Ministry of Health of the 60 registered retail pharmacies in Eswatini at the time of the study; with 14 geographically situated in Hhohho, 30 in Manzini, 10 in Lubombo and 6 in the Shisweleni region. Stratified sampling was used to group the pharmacies. The primary criterion was the region of location for the pharmacy.

A total number of 32 pharmacies were included in the study. Disproportionate stratified sampling was used to ensure that the sample was representative of the Eswatini retail pharmacy population. The sample comprised 12 pharmacies from Manzini, 8 from Hhohho, 6 from Lubombo and 6 from Shiselweni. Simple random sampling was used to select the pharmacies to use in each region. To analyze the effect of the size of the city/town on prescription prices; pharmacies were categorized as from either city or town/rural area.

Data Collection

Data collection took place between 15 June 2020 and 13 August 2020. The researcher collected the data from the pharmacies. Data on price, availability and affordability to patient were collected for two products, namely the originator brand (OB) and the lowest price generic (LPG) using the standardised WHO/HAI methodology.[30] The following specific data was collected for 50 essential medicines as per the WHO listing (14 from the Global Core List and 36 selected based on local relevance), [31]using the WHO/HAI workbook,[32] during visits to **"retail pharmacy outlets"**,

1. the name of pharmacy, administrative region where located, and whether it was in a city or town/rural area.
2. Brand/Product name and manufacturer of the lowest priced generic found at the site.
3. Availability of the Originator brand and the lowest priced generic.
4. Pack size and price of the pack found for the originator brand and the lowest priced generic.
5. Any other comments regarding a given product.

During the retail pharmacy visits, data were recorded on hard copy medicine prices data collection forms. The data collector made sure the data collection forms were complete and legible before leaving an outlet.

Data collection forms were reviewed every day after completion of the field work to ensure data quality. The data were then entered from the hard copy forms into the electronic survey workbook, and the double entry program was run, and any mistakes corrected. Any questionable data identified after running data checker, was investigated, and corrected.

Data Analysis

Data was entered in the pre-programed WHO/HAI Microsoft Excel Workbook.[32]   The workbook automatically generated analysis of the data entered once complete giving summary tables of percentage availability and Median Price Ratios (MPR). Median local prices were expressed as ratios to international reference prices, using the formula.[30]

Medicine Price Ratio (MPR) = median local unit price

International reference unit price

Management Sciences for Health (MSH)'s 2015 prices were used as the default source of international reference prices (IRP's). The IRP's used are prices offered to international not-for profit agencies for purchase of generics.[33]

The availability of medicines was determined as a percentage of outlets where medicine was found on the day of data collection. Mean availability of the 50 medicines was also reported. The differences in average percentage availability of OBs and LPGs determined if there was any variance in the availability of the two product types. To describe availability, the following ranges were used as reference, [19]

5. < 30% extremely low
6. 30% - 49% low
7. 50% - 80% fairly high
8. > 80% high.

The MPR pharmacy prices for each drug was compared across region categories using analysis of variance (ANOVA). The MPR pharmacy prices for each drug were compared between the two categories of location size using t-test. The lowest and maximum prices in Eswatini were compared to the lowest and highest permissible retail prices in South Africa (based on current

dispensing fee guide in South Africa at the time),[34, 35] and the differences were expressed as percentage price difference for similar products and were analysed using the t-test for statistical significance.

Affordability was calculated as the number of wage days that the lowest paid government worker needed to spend to pay for treatment and was based on the median local price of a medicine prescribed at a standard dose.[30] All analysis was carried out using SPSS version 27.

Results

Medicines Availability on the day of data collection

The overall mean availability of all medicines in the surveyed retail pharmacy outlets was (38.5%;SD=20.4%) for the Originator Brands (OBs) and (80.9%;SD=19.0%) for the Lowest Price Generics (LPGs). Table 1 highlights the mean availability of the different classes of medicines in the different regions.

Although availability data only refers to the day of data collection, the availability of OBs was generally low in all the surveyed pharmacies with only Hhohho region recording more than 50% availability (56.1%), whilst Manzini had 42.3% availability, 28.5% for Shiselweni and then Lubombo with 23.6% availability. ANOVA results showed there were significant differences between the regions in terms of OBs availability ($F_{3,123}$ =15.236, $p < 0.001$). A post-hoc test (Bonferroni correction) showed that Hhohho had significantly higher OBs availability than Manzini, Shiselweni and Lubombo regions ($p < 0.001$). The difference between Manzini and Lubombo ($p = 0.170$), Manzini and Shiselweni ($p = 1$) and between Lubombo and Shiselweni ($p = 1$) were not statistically significant.

The mean availability of LPGs was fairly high in Lubombo and Shiselweni and high in Manzini and Hhohho, with the highest availability of 83.3% recorded in Manzini, followed by 82.4% in the Hhohho region, then Shiselweni with 79.6% and lastly Lubombo region with an availability of 76.2%. The differences were not statistically different ($p < 0.001$).

The overall mean availability of OBs in the surveyed outlets varied from 0% for medicines like simvastatin and glibenclamide to 88.5% for metformin. The higher mean availability of the LPGs was evident with 30 out of the 50 surveyed medicines recording more than 90% availability and 6 medicines with 100% availability.

Results showed that the pharmacies located within cities had a higher OBs mean availability (x = 54.3% , SD = 24.6%) as compared to the outlets situated in towns and rural areas (x = 28.6%, SD = 19.4%).The mean difference (25.7%) between the two locations was statistically significant (t = 10.26 (32); p = 0.001).

The availability of LPGs was high in the city and fairly high in the town located pharmacies, with pharmacies in the cities registering 87.4% availability and the outlets in towns and rural areas recording 76.5% availability. Results showed that this difference was statistically significant: t = 4.658 (48), p = 0.001.

TABLE 1: Mean availability of selected product groups in the different regions.

	Mean Availability Manzini (%)	Mean Availability Hhohho (%)	Mean Availability Shiselweni (%)	Mean Availability Lubombo (%)	Overall Mean Availability Eswatini (%)	n
All						50
LPGS	83.3%	82.4%	79.6%	76.2%	80.9%	
OBs	42.3%	56.1%	28.5%	23.6%	38.6%	
Medicine Type						
Anti-infectives						8
LPGs	85.7%	87.5%	88.9%	71.4%	86.7%	
OBs	37.5%	39.6%	23.3%	13.3%	30.7%	
NCD Medicines						42
LPGs	82.9%	81.1%	83.3%	76.4%	82.3%	
OBs	41.9%	21.4%	29.2%	21.4%	38.5%	
Essential Medicines						38
On EML						
LPGs	86.7%	88.9%	84.2%	80.2%	85.1%	
OBs	37.6%	57.2%	18.4%	25.6%	38.3%	
Not on EML						12
LPGs	72.9%	69.8%	65.3%	62.5%	69.0%	
OBs	40.2%	49.0%	26.7%	19.4%	40.0%	
Sample List						
Global Core						14
LPGs	89.3%	91.1%	88.1%	88.1%	89.2%	
OBs	41.7%	48.8%	35.0%	30.0%	40.0%	
Supplementary						36
LPGs	81.0%	78.9%	76.2%	71.4%	77.7%	
OBs	42.6%	58.8%	26.2%	22.0%	38.0%	

OB, originator brand; LPG, lowest-priced generic equivalent; NCD, non-communicable diseases; EML, essential medicines list.

The overall availability of all the different groups analysed was generally high for the LPGs and low for the OBs. The global core medicines had the highest LPGs mean availability (89.2%;SD=9.0%), followed by anti-infectives at 86.7%, then EML medicines with 85.1% mean availability, followed by 82.3% for the NCD medicines and then 77.7% overall mean availability for the supplementary medicines (Table 1). The differences between the different regions in terms of availability of LPGs of the different classes were not statistically significant.

A similar trend was observed with respect to availability of the different medicines' groups in both cities and smaller towns and the rural areas.

Consolidated Private Retail Sector Patient Price Ratios

Of the 50 medicines surveyed in the 26 outlets, price ratios were calculated for 33 originator brands (OBs) and 48 lowest price generics (where medicines were found in 4 or more outlets). Overall, the Median Price Ratio (MPR) was 18.60 for the OBs whilst the MPR for the LPGs for Eswatini retail outlets was 4.51. The 25th and 75th percentile MPR for innovator brands were 3.91 and 36.75 respectively, with an MPR range of 132.58 (0.70-133.28) and for the lowest price generics, they were 1.98 and 10.36 respectively, with 0.23 as the minimum MPR and 60.72 as the maximum MPR.

Regional Patient Prices Comparison

Overall patient prices in Shiselweni were approximately 4% and 8% more than patient prices in Manzini region, whilst the Lubombo prices were approximately 42% and 9% more in comparison to Manzini for innovator brands and lowest price generics, respectively. The overall MPR patient prices in Shiselweni were approximately 7% cheaper than the prices in Hhohho for the LPGs. ANOVA results showed there was no significant difference between the regions in terms of LPGs prices ($F_{3,160} = .448$, $p < 0.719$).

Table 2. Eswatini MPRs comparison by location.

Medicine Name (LPG)	Median Price Ratio (MPR)					
	Manzini (n=10)	Hhohho (n=6)	Shiselweni (n=5)	Lubombo (n=5)	Town/Rural (n = 15)	City (n = 11)
Acyclovir 200mg cap/tab	5.79	5.66	5 33	5.02	5.53	5.6
Amitriptyline 25mg cap/tab	9.98	11.07	9 27	12.47	10.00	10.79
Amlodipine 5mg cap/tab	11.68	11.68	10.29	13.99	11.69	11.67
Amoxicillin 500mg cap/tab	2.26	2.10	2.63	2 58	2.49	2.01
Amoxicillin + clavulanic acid 125+31.25mg susp	0.23	0.21	0 20	0 30	0.26	0.22
Anhydrous Theophylline 200mg cap/tab	3.85	-	3 19	3.73	3.63	3.85
Atenolol 50mg cap/tab	8.00	6.71	12.08	4 20	7.88	8.11
Atorvastatin 20mg cap/tab	0.97	0.92	0 99	1 37	1.09	0.87
Azithromycin 500mg cap/tab	13.00	14.52	10.13	15.59	13.3	14.22
Beclomethasone 100mcg/dose Inh	1.63	1.55	1 51	1 55	1.5	1.59
Bisoprolol 5mg cap/tab	1.55	1.78	1 54	2.01	1.67	1.57
Budesonide 0.5mg/ml Neb susp	59.44	62.40	-	-	61.27	60.72
Captopril 25mg cap/tab	1.27	1.10	1.46	1 56	1.46	1.22
Carbamazepine 200mg cap/tab	10.48	10.95	10.68	11.92	11.1	10.71
Carvedilol 12.5mg cap/tab	1.31	1.31	1 31	1.43	1.32	1.31
Ceftriaxone injection 1 g/vial	6.49	5.78	8 17	8 17	8.17	5.77
Cetirizine 10mg cap/tab	14.77	16.97	14.98	17.75	16.62	15.06
Ciprofloxacin 500mg cap/tab	6.51	6.89	7.47	7.85	7.46	6.7
Co-trimoxazole suspension 8+40mg/5ml susp	2.12	1.90	2 36	2 39	2.3	1.87
Diazepam 5mg cap/tab	2.22	1.00	-	-	6.58	1.12

Diclofenac 50mg cap/tab	6.51	7.09	9 57	9 57	9.57	6.64
Enalapril 20mg cap/tab	12.30	14.55	9.45	16.96	12.33	12.54
Fluoxetine 20mg cap/tab	2.12	3.63	3 33	3 58	3.41	3.27
Fluticasone/Salmeterol 25/250mg Inh	10.16	11.01	-	10.80	10.8	11.01
Furosemide 40mg cap/tab	2.12	9.38	6 59	7.69	6.59	4.33
Glibenclamide 5mg cap/tab	4.69	4.60	4 14	6.05	4.47	4.47
Gliclazide 80mg cap/tab	1.84	1.90	1.76	1.77	1.76	2.01
Hydrochlorothiazide 25mg cap/tab	6.56	9.05	8.04	8.74	8.74	6.4
Hydrochlorothiazide/Losartan 12.5/50mg cap/tab	1.78	1.79	-	-	1.6	1.79
Irbesatan 150mg cap/tab	10.40	10.61	9 92	11.04	10.83	10.21
Loratidine 10mg cap/tab	6.20	7.13	5 97	6 53	6.15	7.09
Losartan 10mg cap/tab	1.93	2.13	1.72	2 22	1.92	2.07
Metformin 500mg cap/tab	2.55	2.41	2 25	2 22	2.39	2.34
Methyldopa 250mg cap/tab	2.57	2.65	2 39	2.66	2.66	2.47
Montelukast 5mg cap/tab	6.61	7.07	7 14	7 25	7.14	7.03
Nifedipine Retard 20mg cap/tab	4.80	4.64	4.41	5 19	4.55	4.57
Omeprazole 20mg cap/tab	3.18	31.48	14.26	14.26	14.26	20.45
Paracetamol suspension 24mg/ml susp	1.67	1.69	2.04	2 21	2.05	1.68
Phenytoin 100mg cap/tab	4.94	4.99	5 20	5.84	5.52	4.98
Propranolol 40mg cap/tab	3.57	3.02	3.45	4 16	3.83	3.42
Risperidone 2mg cap/tab	57.91	62.09	50.40	-	54.41	60.59
Salbutamol inhaler 100mcg/dose	1.57	1.58	1 35	1.65	1.46	1.55
Salbutamol syrup 2mg/5ml	2.40	2.55	2.46	2.63	2.58	2.51
Simvastatin 20mg cap/tab	1.79	1.86	1 58	1.70	1.68	1.86
Sodium Valproate 200mg cap/tab	3.67	4.16	3.67	3 37	3.55	4.08
Spironolactone 25mg cap/tab	3.06	3.22	2.84	2 98	2.98	3.11
Tamsulosin 0.4mg cap/tab	10.60	11.13	10.72	10.81	10.76	10.72

mg, milligrams per dosage form; cap/tab, capsules or tablets as a dosage form; mcg/dose, micrograms per dose of medicine.

A few of the lowest price generics had large price differentials across the different regions. The LPG omeprazole 20mg cap/tab was sold to patients at 3.18MPR in Manzini, but was available at more than 4 times that price in Lubombo and Shiselweni regions, and in the Hhohho region the patients had to part with almost 10 times the Manzini price. The LPG furosemide was available at 2.12 MPR in Manzini, required more than 3 times this in Lubombo and Shiselweni and was available at 9.38 MPR in the Hhohho region. Atenolol 50mg, diclofenac 50mg and fluoxetine 20mg also showed large price differentials across the regions.

Overall patient prices in the cities were 3% more and 5% less than patient prices in the smaller towns for innovator brands and lowest generic equivalents, respectively. The LPG diazepam 5mg was available to patients at 1.12 MPR to patients in the cities whilst it was sold at 6.58MPR in the smaller towns.

OBs price ratios were only analysed for Hhohho and Manzini regions as the other two regions did not have significant OBs availability for any meaningful comparison. Overall patient prices in Manzini were approximately 3% and 1% more than patient prices in the Hhohho region for innovator brands and lowest generic equivalents, respectively. Results showed that the difference between Manzini and Hhohho OBs medicines prices was not statistically significant: $t = 1.432 (22)$, $p = 0.166$.

Comparison of retail prescription drug prices in the Kingdom of Eswatini and South Africa

Of the 32 OB's that were found in more than four (4) outlets in Eswatini only 2 products, diclofenac 50mg cap/tab and amlodipine 5mg cap/tab had their highest prices equal to the maximum permissible South African patient price, whilst 8 products had their Eswatini highest prices lower than the maximum permissible South African patient prices and the rest had Eswatini highest prices that were more than the maximum permissible South African patient prices. The differences were statistically significant: t = 3.10 (31), p = 0.004. Only one product, carvedilol 12.5mg cap/tab, had its lowest Eswatini unit price lower than the cheapest South African patient price, whilst the lowest prices for all the other OB's were higher than the lowest prices in South Africa of the same products. The differences were statistically significant: t = 2.549 (32), p = 0.14.Table 3. Comparison of Eswatini and South Africa's highest and lowest OBs prescription prices.

Medicine name	Eswatini highest unit price (E)	S.A maximum permissible unit price (E)	Price difference (%) Eswatini relative to S.A	Lowest unit price– Eswatini (E)	S.A lowest unit price (E)	% price difference
Salbutamol inhaler 100mcg/dose	1.91	0.72	+62%	0.51	0.41	+20%
Sodium Valproate 200mg cap/tab	13.27	6.45	+51%	5.72	4.69	+18%
Hydrochlorothiazide/Losartan 12.5/50mg cap/tab	14.68	7.80	+47%	6.09	4.85	+20%
Human insulin 30/70 isophane 100iu/ml vial	77.14	49.25	+36%	41.11	33.88	+18%
Risperidone 2mg cap/tab	55.40	35.44	+36%	35.94	27.52	+23%
Carbamazepine 200mg cap/tab	9.67	6.98	+28%	6.66	4.58	+31%
Bisoprolol 5mg cap/tab	9.29	7.18	+23%	5.12	4.40	+14%
Fluticasone/Salmeterol 25/250mg Inh	17.51	15.27	+13%	14.55	11.67	+20%
Montelukast 5mg cap/tab	25.99	23.06	+11%	19.86	16.78	+16%
Omeprazole 20mg cap/tab	36.37	32.77	+10%	31.24	25.05	+20%
Fluoxetine 20mg cap/tab	21.73	19.61	+10%	17.53	14.02	+20%
Metformin 500mg cap/tab	1.49	1.36	+9%	0.86	0.70	+19%
Phenytoin 100mg cap/tab	4.82	4.44	+8%	3.61	2.97	+18%
Spironolactone 25mg cap/tab	2.84	2.63	+7%	1.84	1.52	+17%
Tamsulosin 0.4mg cap/tab	18.78	17.38	+7%	14.01	12.12	+13%
Atorvastatin 20mg cap/tab	21.20	19.77	+7%	15.25	14.15	+7%
Irbesatan 150mg cap/tab	18.47	17.51	+5%	12.55	11.92	+5%
Ciprofloxacin 500mg cap/tab	33.00	32.41	+2%	24.73	21.07	+15%
Losartan 10mg cap/tab	7.11	7.02	+1%	5.02	4.28	+15%
Budesonide 0.5mg/ml Neb susp	28.77	28.48	+1%	24.63	20.23	+18%
Enalapril 20mg cap/tab	6.78	6.72	+1%	4.87	3.97	+18%
Diclofenac 50mg cap/tab	6.06	6.04	0%	4.08	3.35	+18%
Amlodipine 5mg cap/tab	11.28	11.30	0%	9.25	7.38	+20%
Furosemide 40mg cap/tab	9.03	9.16	-1%	6.65	4.87	+27%
Azithromycin 500mg cap/tab	107.29	109.53	-2%	85.58	71.32	+17%
Atenolol 50mg cap/tab	13.21	13.53	-2%	11.25	9.00	+20%
Nifedipine Retard 20mg cap/tab	14.82	15.54	-5%	14.28	11.90	+17%
Loratidine 10mg cap/tab	5.98	6.69	-12%	2.61	2.00	+23%
Carvedilol 12.5mg cap/tab	9.15	10.50	-15%	6.66	6.80	-2%
Amoxicillin + clavulanic acid 125+31.25mg susp	2.05	2.38	-16%	1.66	1.48	+11%
Cetirizine 10mg cap/tab	9.19	10.80	-18%	8.59	7.02	+18%

mg, milligrams per dosage form; cap/tab, capsules or tablets as a dosage form; mcg/dose, micrograms per dose of medicine.

Of the 48 LPGs analysed one product, tamsulosin had its Eswatini lowest price equal to South Africa's lowest generic patient price, 26 products' Eswatini lowest prices were higher than

South Africa's lowest prices and 18 products had their lowest prices lower than corresponding South African lowest generic prices for the same molecules. The lowest prices of Simvastatin 20mg and Omeprazole 20mg were more than 300% lower than the lowest generic patient prices in South Africa. The lowest and highest LPGs prices for South Africa were calculated using the Medicines Reference Prices (MRPs) from the Mediscor platform.[34]

Of all the LPGs that were analysed, only 11 products had Eswatini highest prices lower than the South African maximum permissible patient prices in the retail pharmacies and the other 37 products had highest prices higher than the highest generic patient prices for similar molecules in South Africa. The difference in the prices was statistically significant: $t = 2.549$ (47), $p = 0.014$.

Treatment affordability

The LPGs for the most common anti-infectives were generally affordable in all the regions, with an adult 7-days' course of amoxycillin, a paediatric 7-days' course of cotrimoxazole and a paediatric 7-days course of amoxycillin + clavulanic acid, all requiring less than a day's wages of the lowest paid government unskilled worker to purchase them. The OB for amoxycillin & clavulanic acid, however required 2.28 days' wages in Manzini and 2.13 days' wages in the Hhohho region. A single dose of 1g azithromycin for the treatment of Chlamydial infections was unaffordable for both LPGs and OBs in all the regions, save for Shiselweni region where purchasing the LPG course required only 0.94 days' wages of the lowest paid unskilled government worker.

A standard one-month treatment course for benign prostate hypertrophy (BPH) with tamsulosin 0.4mg once daily was unaffordable in all the four regions for both the LPGs and OBs. The lowest paid unskilled government worker needed to work for 3 days to afford the LPG and 5.98 days to be able to buy the OB in Manzini region.

Management of depression with fluoxetine 20mg once daily, was affordable for the LPGs in all the regions requiring 0.56 days' worth of wages of the lowest paid government unskilled worker Manzini, 0.88 days' wages in Shiselweni, 0.95 days in Lubombo and 0.96 days in the Hhohho region (table 2). The OB was only available in Hhohho and required the lowest paid unskilled government employee to work 7.16 days to afford to purchase a course for one (1) month.

The first line LPGs anti-hypertensives (hydrochlorothiazide, captopril and atenolol) were affordable in all the four (4) regions of Eswatini requiring less than a day's wage to purchase a

course, with hydrochlorothiazide being the most affordable, requiring only under 0.25 day's wages of the lowest paid unskilled government employee to purchase it. The second line and third line anti-hypertensives were generally unaffordable, requiring more than a day's wages for both the OBs and LPGs, apart from the LPGs for enalapril 20mg in Manzini (0.86 days) and Shiselweni (0.66 days).

Table 4. Affordability of selected LPG medicines

Medicine	Number of days' wages needed to purchase a course of treatment			
	Manzini	Hhohho	Shiselweni	Lubombo
Amoxicillin 500mg cap/tab	0.29	0.27	0.34	0.33
Azithromycin 500mg cap/tab	1.20	1.35	0.94	1.45
Beclomethasone 100mcg/dose Inh	0.84	0.80	0.78	0.80
Carbamazepine 200mg cap/tab	2.38	2.48	2.42	2.70
Enalapril 20mg cap/tab	0.86	1.02	0.66	1.19
Fluoxetine 20mg cap/tab	0.56	0.96	0.88	0.95
Fluticasone/Salmeterol 25/250mg/dose Inh	5.94	6.44	-	6.32
Glibenclamide 5mg cap/tab	0.33	0.32	0.29	0.42
Gliclazide 80mg cap/tab	1.10	1.14	1.05	1.06
Human Insulin 100iu/ml Inj	5.20	5.36	-	7.37
Hydrochlorothiazide 25mg cap/tab	0.17	0.24	0.21	0.23
Ibersatan 150mg cap/tab	1.89	1.93	1.80	2.00
Losartan 50mg cap/tab	1.36	1.50	1.22	1.57
Metformin 500mg cap/tab	0.47	0.44	0.41	0.41
Methyldopa 500mg cap/tab	1.53	1.58	1.42	1.59
Montelukast 5mg cap/tab	3.40	3.63	3.67	3.73
Nifedipine SR 20mg cap/tab	1.20	1.16	1.10	1.29
Omeprazole 20mg cap/tab	0.74	2.72	1.23	1.23
Salbutamol 100mcg/dose Inh	0.18	0.18	0.16	0.19
Sodium valproate 200mg cap/tab	3.13	3.55	3.13	2.87
Tamsulosin 0.4mg cap/tab	.93	3.08	2.97	2.99

The three anti-epileptic medicines surveyed required more than a day's wages to buy a course for one month, save for the LPGs for phenytoin 100mg tablets which required 0.94 days' wages in Manzini and 0.95 days' wages in the Hhohho region. To afford a course of sodium valproate for a month, the lowest paid government worker had to work for 4.52 days for the OB and 3.55 days for the LPG. A similar trend was observed with carbamazepine as well, with the most affordable OB requiring 4.19 days' wages whilst the most affordable LPG required 2.38 days' wages to purchase a course.

A course of salbutamol inhaler required less than 0.2 days' wages for the LPGs and just under 0.5 days' wages for the OB in all the regions where stock was available. Less than a single day's wages were adequate to purchase a month's supply of the LPGs of beclomethasone 100mg inhaler in all the regions surveyed. Management of asthma with montelukast 5mg once daily was unaffordable for both LPGs and OBs (requiring more than 3 days wages for the LPGs and just under 8 days wages for the OBs), as was fluticasone/salmeterol 25/250mcg which required about 6 days wages for the LPGs and more than 10 days wages to purchase a monthly course of the OBs .

The first line of management for diabetes mellitus-2 (DM II) was affordable for both the OBs and LPGs in all the four regions of Eswatini, with a monthly course of 60 tablets of glibenclamide 5mg requiring less than 0.5 days' wages to purchase. It is worth noting that less than 0.8 days' wages were required to purchase a course of either the OB or LPGs of metformin 500mg in the four regions. Gliclazide was less affordable and required more than the equivalent of the lowest paid unskilled government worker's single day wage to purchase a course for one month of the LPGs. No LPG was found for human insulin (30% regular/70% isophane) in all the surveyed areas and the OB required 5.20 days' wages in Manzini, 5.36 days' wages in Hhohho and 7.37 days' wages in the Lubombo region.

Table 5. Affordability of treatments for a family with multiple conditions (consolidated retail pharmacy sector – Eswatini)

Condition	Treatment	Type	Median Treatment Price (Emalangeni)	Days' wages
Hypertension	Enalapril 20mg od * 30 days	LPG	74.66	0.9
		OB	164.93	1.9
Diabetes Mellitus II	Metformin 500mg twice daily * 30 days	LPG	36.60	0.4
		OB	60.47	0.7
Respiratory Infection (Child)	Amoxicillin + Clavulanic acid 125/31.25mg 3 times daily * 7 days	LPG	60.40	0.7
		OB	187.58	2.2
Total		**LPG**	**171.66**	**2.0**
		OB	**412.98**	**4.8**

OB, originator brand; LPG, lowest-priced generic equivalent.

Table 5 illustrates the affordability of a 3-drug regimen when originator brands and lowest price generics when purchased from the retail pharmacy sector in Eswatini. The lowest paid government worker would have to work 2 days to afford the LPG regimen and in case the LPGs are not available, he will have to work for 4.8 days to be able to afford the OBs.

Discussion

The study showed that the overall availability of the LPG medicines in all the regions was higher than the recommended minimum availability benchmark set by World Health Organisation/Health Action International, of 80%.[20] It can be deduced from the results that there is promotion of generics' dispensing as compared to the branded products in all the regions. The more affluent settlements are in Hhohho and Manzini regions, and the availability of OBs was comparably higher in these 2 regions.

The overall availability of LPGs was not different in all the regions, however the pharmacies located in cities had higher availability than the ones in smaller towns and rural areas for both LPGs and OBs. It is commendable that the availability of LPGs on the Essential Medicines List (EML) was more than 90% in all regions, and as such in the event of medicines being unavailable at government hospitals, patients can access medications at retail pharmacies.

It was quite interesting to note that the LPGs' prices were comparable in all the 4 regions and the differences reflected were not statistically significant. Although there is currently no price regulation administered by the government, [36] the market forces 'regulate' the medicines' prices in the Eswatini pharmaceuticals market.

A careful analysis of the molecules that had large differentials e.g. omeprazole 20mg showed that the overseas parallel generic imports were available at a significantly lower price to the patients as compared to similar generic molecules that were sourced regionally. The clients in the more affluent locations are generally brand-sensitive as compared to patients in the rural settings, where outlets can afford to keep the most affordable non-branded import generics. There is need for the authorities to ascertain that these lowly priced molecules also meet the stipulated quality standards.

The study showed that generally the OBs patient prices were higher in Eswatini when compared to prices of the same prescription molecules in South Africa, and this is not a deviation from the expected as literature suggests medicines prices in regulated environments are generally lower than in countries with no price regulation.[23] Eswatini procures their OBs from South Africa where pricing is regulated and as such the best/lowest cost to the retail outlets for these would be at the SEP price and as such it's expected that the retailing prices will be higher than SEP in the Eswatini outlets. Eswatini prescription medicines' prices have VAT at 0%,[3] whereas in South Africa all medicines attract VAT at 15%, if the VAT regulation in Eswatini would

change from 0% to the standard 15% VAT,[24] the Eswatini prescription medicines' will become more expensive to the end users.

The Eswatini market is not limited to the South African generic molecules only as they also have access to parallel import generics from overseas which were found to be generally cheaper than the South African equivalent molecules. The difference in the GDP per Capita per month between South Africa and Eswatini needs to be considered, [8] as a small price difference may turn out to be huge with respect to affordability in the Eswatini context.

Most first line treatment regimens for NCD's were generally affordable, requiring less than a day's wages. It is worth noting that more than 60% of Eswatini's population lives below the upper poverty line of USD 8.21 per capita per month and as such,[8] treatment regimens calculated as affordable may still be way out of the range for the general populace.[16] There is usually more than one family member requiring chronic medications, and even though the individual courses may be affordable , the combined regimens will be unaffordable. Anti-epileptic medications and most second line management regimes required more than a day's wages hence unavailability at the public hospitals could lead to patients defaulting their treatments.

Limitations

Affordability was calculated based on the daily wage of the lowest paid unskilled government worker, but a large portion of the labour force is not employed by the government and the minimum wages are way lower than the salary of the lowest paid government worker– thus the data may not be a true reflection of affordability in Eswatini.

Availability refers to the day of data collection at each facility and might not indicate average availability over time. Availability and prices data were collected during level 2 lockdown (due to the COVID-19 pandemic) when supply chains were disrupted and hence these findings may not be a true reflection of the availability throughout the year(Eswatini depends entirely on imports as there is no manufacturing of any pharmaceuticals that takes place in the kingdom).

Recommendations

Future research should focus on comprehensive national surveys in all public and private entities to determine medicines prices, including from the wholesalers. Price components

throughout the entire pharmaceutical supply chain should be studied. Focus on these will assist in developing policies that will work towards improving affordability and availability.

Conclusion

Drug-pricing control by the government is one of the factors responsible for lower retail prices in South Africa. The concept of 'free market economy' in Eswatini may not be enough to regulate the prices of medicines. There is need to develop drug pricing policies that govern the whole supply chain,[16] however for that to happen all the necessary data on the current pricing structure in the whole pharmaceutical supply chain Eswatini should be gathered. The Medicines and Related Substances Act of 2016 makes provision for prescription of a pricing system for medicines in Eswatini. [17]

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Chapter 4: Synthesis, Conclusion and Recommendations

4.1 Synthesis

Prices for prescription medicines are a significant obstacle to appropriate medicine use.[1] It is not easy to find reliable medicines prices' information in developing countries, [2] including in Eswatini.

Kheder et al. [3] affirm that cross national differences in pharmaceutical prices are of great importance as they help governments to come up with appropriate domestic pricing policies. However as Mhlanga et al. [4] highlighted, there is a need to have reliable evidence on medicines' prices in order to ascertain the type of challenges in a country before deciding on solutions that will ensure availability of essential medicines at the lowest price to the consumer.

Pricing surveys have been used to determine the extent of price differentiation and affordability in many countries.[5,6,7,8] Thus, for Eswatini, the WHO/HAI medicine price survey was used to identify medicine pricing and affordability in the Kingdom of Eswatini so as to provide policy makers and all stakeholders with evidence to draft policies that may improve availability, affordability and accessibility of medicines.

The aim of this study was to investigate the availability, affordability and prices that people pay for medicines from retail pharmacies in different parts of Eswatini. In addition, this study sought to ascertain how the medicines' prices in Eswatini compared to the prices of the same medicines in South Africa.

The study revealed that the overall mean availability of all medicines in the surveyed retail pharmacy outlets was (38.5%; SD=20.4%) for OBs and (80.9%; SD=19.0%) for LPGs. The overall median MPR in the surveyed pharmacies was 18.61 for the OBs and 4.67 for LPGs. Most standard treatments with LPGs cost less than a day's wage whilst for OB's cost more than a day's wages. The differences between Eswatini and South African prices were statistically significant.

4.2 Conclusions

Overall, the availability of the surveyed medicines was fairly high in Lubombo and Shiselweni regions and high in Manzini and Hhohho; many generic options were available for most of the medicines, supporting one of the objectives of the Swaziland National Pharmaceutical Policy

(SNPP) to encourage generics prescription and dispensing as well as substitution and thus the only barrier to access to medicines would be the cost.

Medicines' pricing control by the government is one of the factors responsible for lower retail prices in South Africa. .Market forces alone may not be enough to regulate medicines' pricing in the Kingdom of Eswatini. There is need to develop drug pricing policies that govern the whole supply chain.[16]All the necessary data on the current pricing structure in the whole pharmaceutical supply chain should be gathered. The medicines and Related Substances Act of Eswatini of 2016 makes provision for prescription of a pricing system for medicines in Eswatini. [17]

4.3 Recommendations

Future research should focus on comprehensive national surveys in all public and private entities to determine medicines prices, including from the wholesalers. Price components throughout the entire pharmaceutical supply chain should be studied. Focus on these will assist in developing policies that will work towards improving affordability and availability.

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Appendix A – Proof of submission

Appendix B – BREC approval

23 April 2020

Mr Garikai Shambira (216050413)
School of Health Sciences
Westville

Dear Mr Shambira

Protocol reference number: BREC/00001237/2020
Project title: Prescription Medicines Prices in the Retail Pharmacy Sector in the Kingdom of Eswatini: Are people paying more in Certain Locations?
Degree Purposes: Masters
(Sub-study of BCA480/19)

EXPEDITED APPLICATION: APPROVAL LETTER

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application.

The conditions have been met and the study is given full ethics approval and may begin as from 23 April 2020. Please ensure that outstanding site permissions are obtained and forwarded to BREC for approval before commencing research at a site.

This approval is subject to national and UKZN lockdown regulations and the general BREC circular emailed by the Research Office on 23rd March 2020 and repeatedly since.

This approval is valid for one year from 23 April 2020. To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be noted by a full Committee at its next meeting taking place on 12 May 2020.

Yours sincerely

Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

Appendix C – The Kingdom of Eswatini Ministry of health permission letter

THE KINGDOM OF Eswatini

Date: 27th February 2020

Mr Garikai Shambira
Masters Student -UKZN
Eswatini

Dear Sir/Madam

RE: PERMISSION TO CONDUCT A STUDY ENTITLED – PRESCRIPTION MEDICINE PRICES IN THE RETAIL PHARMACY SECTOR IN THE KINGDOM OF ESWATINI: ARE PEOPLE PAYING MORE IN CERTAIN LOCATIONS?

The Ministry of Health hereby grants you permission to conduct a study in the retail pharmacy sector of the Kingdom of Eswatini entitled: "Prescription medicine prices in the retail pharmacy sector in the Kingdom of Eswatini: are people paying more in certain location?" as a Master student at University of Kwazulu Natal in the period March to August 2020.

The Ministry of Health strongly encourages research and mandates researchers to stick to guidelines set by the National Health Research Review Board (NHRRB) that grants and monitor approvals to conduct studies in the health sector and all guidelines set as per the University of KwaZulu-Natal approval. Researchers in the field of pharmaceuticals are encouraged to share the research protocol with the Pharmaceutical Services in the Ministry of Health and to disseminate the research finding with Pharmaceutical Services in the Ministry.

Kind regards

Fortunate Bhembe
Deputy Director Pharmaceutical Services
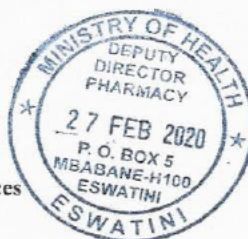
Appendix D – Data collection tool and informed consent letters

UKZN BIOMEDICAL RESEARCH ETHICS COMMITTEE

APPLICATION FOR ETHICS APPROVAL
For research with human participants (Biomedical)

INFORMED CONSENT RESOURCE TEMPLATE

<u>Information Sheet and Consent to Participate in Research</u>

Date: 01 February 2020

Dear Pharmacy Owner/Manager

My name is Garikai Shambira, a Master's in Pharmacy (Pharmacoeconomics) student at the University of Kwazulu-Natal (UKZN). My contact details are as follows: Phone number: +268-76488283 and e-mail address: gs141081@gmail.com.

You are being invited to consider participating in a study that involves research on Pharmaceutical Prices in the retail pharmacy sector in the Kingdom of Eswatini. The aim and purpose of this research is to determine the availability, affordability and the prices patients pay for 50 medicines, in the retail pharmacy sector in the Kingdom of Eswatini. The study will compare retail prices in the Kingdom of Eswatini, South Africa and Internationally. The study is expected to enroll 25 pharmacies: 10 from Manzini region, 6 from Hhohho region, 5 from Lubombo and 4 from Shiselweni region.

It will involve collection of specific data on availability and prices using the WHO/HAI workbook, during the visits to outlets. Data on price to patient, availability to patient will be collected. Data will be collected for two products, namely the originator brand (OB) and the lowest-priced generic (LPG). The following data will be collected using the WHO/HAI workbook, by the researcher during visits to **"retail pharmacy outlets"**;

6. The name of pharmacy, administrative region where located, and whether it is in a large city/town, small town or rural area.
7. Brand/Product name and manufacturer of the lowest priced generic found at the site.

8. Availability of the Originator brand and the lowest priced generic.
9. Pack size and price of the pack found for the originator brand and the lowest priced generic.
10. Any other comments regarding a given product.

During retail pharmacy outlet visits, data will be recorded on hard copy Medicine Prices Data Collection forms; and when less than 50% of medicines are available at a given outlet, the data collector will visit a back-up facility and reconduct the survey. The data collector will make sure the data collection forms are complete and legible before leaving an outlet.

We hope that the study will help in understanding the contribution of the current medicines costs (to the patient) to medicines access and to inform policy makers and all stakeholders when selecting options that will improve availability, affordability and accessibility of medicines in the Kingdom of Eswatini.

This study has been ethically reviewed and approved by the UKZN Biomedical research Ethics Committee (approval number_____).

In the event of any problems or concerns/questions you may contact the researcher at;

Consultation Room # 1
Corner Plaza Wellness Wing, Ezulwini
Box 3318, Manzini, M300
Eswatini Kingdom
Tel+ 268-76488283 or +268- 76025013
Email: gs141081@gmail.com

or the UKZN Biomedical Research Ethics Committee, contact details as follows:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus
Govan Mbeki Building
Private   Bag   X   54001
Durban
4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2604769 - Fax: 27 31 2604609

Email: BREC@ukzn.ac.za

Your participation in this research is entirely voluntary, it is your choice to participate or not. You may change your mind later and stop participating even if you agreed earlier and you will not incur any penalty. If the researcher fails to get at least 50% of the medicines under study in your facility, the researcher may terminate the participant from the study. No expenses will be borne by your outlet if you opt to participate in this research.

The information that will be collected from this research will be kept confidential. Information about the pharmacy that will be collected during the research will be put away and no one except the researcher will have access to it. Any information about your pharmacy will be assigned a random number instead of the pharmacy name and anonymized. Only the researcher will know the number of your pharmacy and will lock access to the identity. It will not be shared with or given to anyone except to Professor Fatima Suleman, who is the research Supervisor.

Data from the hard copies of the medicines prices collection forms will be entered on anonymized computer files soon after data collection, and these files will be password protected and only accessible to the researcher, research supervisor and the Biomedical Research Ethics Administration if need be, but noone else. Measures will be put in place The hard copies will be stored under lock and key in the researcher's office and only him will have access to them.

CONSENT

I   have been informed about the study entitled 'Prescription Medicines' Prices in the retail pharmacy sector in the Kingdom of Eswatini: Are people paying more in certain Locations?' by Garikai Shambira.

I understand the purpose and procedures of the study will involve collection of specific data on availability and prices using the WHO/HAI workbook, during the visits to outlets. Data on price to patient, availability to patient will be collected. Data will be collected for two products, namely the

originator brand (OB) and the lowest-priced generic (LPG). The following data will be collected using the WHO/HAI workbook, by the researcher during visits to **"retail pharmacy outlets"**;

1. The name of pharmacy, administrative region where located, and whether it is in a large city/town, small town or rural area.
2. Brand/Product name and manufacturer of the lowest priced generic found at the site.
3. Availability of the Originator brand and the lowest priced generic.
4. Pack size and price of the pack found for the originator brand and the lowest priced generic.
5. Any other comments regarding a given product.

I have been given an opportunity to answer questions about the study and have had answers to my satisfaction.

I declare that my participation in this study is entirely voluntary and that I may withdraw at any time without incurring any penalties. I will not bear any expenses by participating in this research.

If I have any further questions/concerns or queries related to the study I understand that I may contact the researcher at:

Garikai Shambira
Consultation Room # 1
Corner Plaza Wellness Wing, Ezulwini
Box 3318, Manzini, M300
Eswatini Kingdom
Tel+ 268-76488283 or +268- 76025013
Email: gs141081@gmail.com

If I have any questions or concerns about my rights as a study participant, or if I am concerned about an aspect of the study or the researchers then I may contact:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus
Govan Mbeki Building

Private Bag X 54001

Durban

4000

KwaZulu-Natal, SOUTH AFRICA

Tel: 27 31 2604769 - Fax: 27 31 2604609

Email: BREC@ukzn.ac.za

_____   _____

Signature of Participant   Date

_____   _____

Signature of Witness   Date

Appendix E – Afr J Prm Health Care Fam Med. Format

Cover Letter

The format of the compulsory cover letter forms part of your submission. Kindly download and complete, in English, the provided **cover letter**.

Anyone that has made a significant contribution to the research and the paper must be listed as an author in your cover letter. Contributions that fall short of meeting the criteria as stipulated in our policy should rather be mentioned in the 'Acknowledgements' section of the manuscript. Read our **authorship** guidelines and **author contribution** statement policies.

Original Research Articles

An original research article presents innovative research within the focus and scope of the journal, according to a clear and well-structured format. Detailed instructions are given below on the structure and contents required. The introduction should argue for the social and scientific value of the research and end with the aim and objectives of the study. Any conceptual or theoretical framework can also be included in the introduction. The methods section should be structured according to the following sub-headings: study design, setting, study population and sampling strategy, intervention (if appropriate), data collection, and data analysis. *Occasionally a different structure may be required, for example, in quality improvement or participatory action research*. The methods should be followed by a section on ethical considerations. After this, the results are presented. The article should end with a discussion section that summarises the key findings, and then discusses these findings, the strengths and limitations of the study, and any implications or recommendations. This should be followed by a conclusion, acknowledgements and references sections.

Word limit	3500-7000 words (excluding the structured abstract and references)
Structured abstract	250 words to cover a Background, Aim, Setting, Methods, Results and Conclusion
References	60 or less
Tables/Figures	no more than 7 Tables/Figure
Ethical statement	should be included in the manuscript
Compulsory supplementary file	ethical clearance letter/certificate
Language	only manuscripts presented in English or French will be considered