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The Economic Burden, Patients' Well-being, and Social Determinants Related to Diabetes in South Africa

By

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(HLLASS001)

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Declaration

I, Assegid Getahun Hellebo, hereby declare that The Economic Burden, Patients' Well-being, and Social Determinants Related to Diabetes in South Africa thesis is based is my original work (except where acknowledgements indicate otherwise) and neither the whole work nor a part of it has been, is being, or is to be submitted for another degree purpose in this or any other university.

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Title: The Economic Burden, Patients' Well-being, and Social Determinants Related to Diabetes in South Africa
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Abstract

Background: The health systems in Sub-Saharan Africa (SSA) are confronted by a growing prevalence of diabetes mellitus, with an estimated 24 million adults affected in 2021, a number expected to more than double by 2045. This rise in diabetes not only increases the risk of premature death, but also significantly reduces the quality of life and work productivity. South Africa is leading the diabetes epidemic in SSA, with the incidence rate increasing both in urban and rural settings, equally affecting both genders. While diabetes imposes high levels of health, financial and economic burdens, there is a dearth of studies focusing on identifying and analysing the factors that predict or influence a patient's well-being and quantifying productivity loss in relation to diabetes, particularly in SSA.

Objectives: This thesis aims to evaluate the economic and well-being burden of diabetes in South Africa, focusing on productivity impacts, associated social determinants on patient outcomes and predictors of quality of life. The specific objectives are: firstly, to use population life table modelling to estimate the impact of type 2 diabetes (T2D) on the South African population, particularly in terms of productivity-adjusted life of years (PALYs) metric; secondly, to review and synthesise information regarding the costs and cost-effectiveness of managing T2D in SSA to enhance awareness, optimise resource allocation, and support evidence-based decision-making; thirdly, to investigate the role of social determinants of health (SDoH) in diabetes self-care management practices, emphasising the importance of maintaining optimal glycemic control; and lastly, to assess health-related quality of life (HRQoL) and associated factors among people with diabetes in South Africa; lastly, to develop locally relevant utility score valuations for more accurate economic evaluations and healthcare decision-making in South Africa.

Methods: The thesis combined diverse methodological approaches to investigate the impact of T2D in South Africa. Life table modelling was used to simulate the health trajectory of individuals aged 20 to 65 with T2D, comparing cohorts with and without diabetes in terms of

excess deaths, years of life lost (YLL), and PALYs. These simulations included adjustments for variables like Gross Domestic Product (GDP), productivity indices, labour force dropout, and mortality risks, using data from the International Diabetes Federation (IDF), Statistics South Africa (Stats SA), and other sources, with the World Health Organisation (WHO) 3% annual discount rate for YLL and PALYs applied. For the second objective, a comprehensive systematic literature review, encompassing databases like PubMed-Medline and Google Scholar from 2010 to 2022, analysed the economic aspects of T2D management. Costs were normalised to 2023 US dollars, considering inflation and exchange rates. The third and fourth objectives utilised cross-sectional data of 539 people living with diabetes (PLWD) from urban and rural primary healthcare (PHC) facilities in Western Cape, South Africa. The third objective focused on assessing HRQoL using the EuroQol-3 Dimensions Questionnaire (EQ-5D-3L). The EQ-5D-3L responses were meticulously converted into a unified summary index score employing the UK time trade-off value set. HRQoL was assessed using the ordinal logistic regression. Lastly, the fourth objective explored the influence of SDoH on people with diabetes. Self-care management and adherence to recommended activities were measured, ranging from '0' (never) to '7' (daily adherence). The study employed binary and multinomial logistic regression analyses to investigate the interplay between SDoH, self-management, self-care management and self-care guidelines.

Results: In 2019, T2D affected 9.5% of the working-age population in South Africa, totalling 3.2 million individuals. Projections indicate that T2D will lead to 669,427 excess deaths, a loss of 6.2 million years of life (9.3%), and 13 million productivity-adjusted life years (PALYs, 30.6%) by the retirement age of this cohort. Economically, T2D's impact is significant, with the loss of PALYs estimated at US$223 billion or US$69,875 per person, based on 2019's GDP per full-time employee. In the systematic review, most studies assessed costs from the provider perspective (direct and outpatient costs) and reported T2D costs as enormous in SSA. The annual cost ranged from $337.50 for basic medical care of uncomplicated T2D to $2330.74 total provider cost per patient. The highest burden was among individuals in the low-income quantile. Furthermore, analysis utilising cross-sectional data of 539 participants older than 18 years receiving care from rural and urban clinics in the Western Cape, South Africa, revealed that healthcare utilisation was inversely related to diabetes self-care scores, indicating that patients with less frequent healthcare visits tended to have higher self-care scores. SDoH factors such as urban residency, education level, and obesity status were significant

determinants of self-care guidelines. Specifically, urban residency (AOR=0.50; 95%CI= 0.29, 0.88; p=0.03), secondary education (AOR=1.13; 95%CI= 1.02, 2.03; p=0.05), and being obese (AOR=0.43; 95%CI= 0.19, 1.00; p=0.03) were associated with varying levels of self-care. Additionally, food insecurity and long travel distances to healthcare facilities negatively impacted self-care adherence, while having a stable house was positively associated with higher self-care management. Regarding HRQoL, the study's participants had a mean utility score of 0.85. Males reported higher HRQoL compared to females (AOR=1.64; 95%CI= 0.96, 2.80; p= 0.07), and urban residents had lower HRQoL than rural (AOR= 0.41; 95%CI= 0.27, 0.63; p<0.01). Having at least primary education (AOR= 0.53; 95%CI= 0.36, 0.79; p<0.01) is associated with lower HRQoL, while higher AUDIT score correlated with increased HRQoL (AOR= 1.89; 95%CI= 1.13, 3.18; p= 0.02). Factors like higher self-efficacy and severe mental health issues were significantly associated with HRQoL, with the latter predicting very low HRQoL (AOR= 18.31; 95%CI= 2.21, 152.08; p= 0.01). Other factors, including body mass index (BMI), marital status, housing stability, and food security, showed no significant impact on HRQoL.

Conclusions: This series of studies emphasises the multifaceted impact of diabetes in South Africa, spanning public health, economics, individual well-being, and Social Determinants of Health. The findings call for a multi-pronged strategy encompassing prevention, effective management, and a broader socio-economic approach to tackle the diabetes epidemic. By addressing these areas, it is possible to mitigate the escalating impact of diabetes in South Africa and improve overall health outcomes for individuals living with this chronic condition.

Acknowledgements

I first heard about Health Economics in 2015 when I visited Professor Mulugeta Dinbabo at his office at the University of the Western Cape, seeking advice as I felt clueless after graduating with my Honours degree in Economics, which included a mini-thesis aspect in stock market development and industrial output in SA. During our conversation, he said, “Why don’t you pursue Health Economics at the University of Cape Town? I trust you have the result.” His gentle recommendation planted the seed of curiosity in my mind, urging me to explore the idea, which led me to discover the expansive and enriching environment of the Health Economics Unit (HEU).

Having read a few brochures online, I then visited the HEU in person. My initial impression was, 'Why does it look like someone’s house?' Little did I know what awaited me inside. As I stepped into the HEU, I entered an open office where I encountered Dr John Ataguba (currently a professor). Unbeknown to me, he would significantly inspire my career path. He warmly encouraged me to pursue the degree and suggested I apply for the Master's in Health Economics program. His welcoming demeanour and expert guidance gave me the support I needed to embark on this new journey, illuminating the path ahead. In the process, I have been fortunate to be taught by Professor Diane McIntyre and guided by a community of dedicated individuals whose unwavering commitment to excellence has fuelled my passion for research and learning. Dr Lucy Cunnama, Professor Susan Cleary, and Professor Edina Sinanovic supported me throughout my journey. I met Dr Amarech Obse in the midst of COVID-19, and whenever I faced challenges or all seemed unachievable, I would walk to her office or make a telephone call, and she would calmly ask, "Then what is your plan?" before she guides me to towards the right direction or methodology. Thank you for your unwavering support.

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Preface

This thesis is presented in fulfilment of the requirements for the degree of Doctor of Philosophy in the School of Public Health, Faculty of Health Sciences, University of Cape Town. The work on which this thesis is based is original research and has not, in whole or in part, been submitted for another degree at this or any other university. The contents of this thesis are entirely the work of the candidate, or in the case of multi-authored published papers, constitutes work for which the candidate was the lead author.

This thesis includes published manuscripts, as per general provision 6.7 in the General Rules for the Degree of Doctor of Philosophy (PhD) of the University of Cape Town. I confirm that I have been granted permission by the University of Cape Town's Doctoral Degrees Board (on 02/02/2024) to include the following publications in my PhD thesis, and where co-authorships are involved, my co-authors have agreed that I may include the publications. The following manuscripts (one published, two under review and one prepared for submission) are included in the thesis and are presented as self-contained chapters in the following order:

1. Hellebo A, Kenge AP, Alaba, O. Costs and Cost-Effectiveness of Type 2 Diabetes Management in Sub-Saharan Africa: A Systematic Review. Health Economics Reviews: 418f11a3-e309-4fe8-9291-55b80fd891ec.
2. Hellebo A, Kengne AP, Ademi Z, Alaba O. The Burden of Type 2 Diabetes on the Productivity and Economy in Sub-Saharan Africa: A Life Table Modelling Analysis from a South African Perspective. Pharmacoeconomics. 2024 Jan 24. Doi: 10.1007/s40273-024-01353-3.
3. Hellebo A, Kenge AP, Obse A, Levitt N, Myers B, Cleary S, Alaba, O. Social Determinants of Health and Diabetes Self-Care Management in South Africa. BMC Public Health: 68b4473a-e5e8-4145-b75c-eaa75fabd72c (Under review for publication).
4. Hellebo A, Kenge AP, Obse A, Levitt N, Myers B, Cleary S, Alaba, O. Health-Related Quality of Life and Its Predictors Among Individuals with Diabetes. The Case of the Western Cape, South Africa. Elsevier SSM-Health Systems (Upcoming submission for publication).

The contribution of the candidate to each manuscript is outlined at the start of each chapter (Chapters Three to six). The candidate was the lead and corresponding author on all manuscripts, prepared the datasets for analysis, and drafted all versions of the manuscripts. All co-authors reviewed and approved the submitted manuscripts and the candidate reviewed co-author comments and integrated them into the manuscripts prior to submission.

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List of Tables

List of Figures

List of Acronyms and Abbreviations

ADA……….American Diabetes Association
AMR……….Annual Mortality Rates
AOR………..Adjusted odds ratio
AUDIT...……Alcohol Use Disorders Identification Test
BMI................Body Mass Index
CEA………....Cost-effectiveness analysis
CVDs.............Cardiovascular diseases
DSMQ............Diabetes Self-Management Questionnaire
DALYs............Disability-adjusted Life Years
ECI…………..Economic Complexity Index
EQ-5D.............EuroQol 5D
EQ-5D-3L…...EuroQol-3 Dimensions
GDP.................Gross Domestic Product
HREC...............Health Science's Human Research Ethics Committee
HRQoL……….Health-related quality of life
HIV………..…Human Immunodeficiency Virus
HP2020………Healthy People 2020
HP2030...….... Healthy People 2030
ICER…………Incremental cost-cost-effectiveness ratio
ICN...................International Council of Nurses
IDF………..…International Diabetes Federation
LHIs………….Leading Health Indicators
LMICs……..…Low- and middle-income countries
NDoH……..….National Department of Health
NHI………..…National Health Insurance
NPHW……..…Non-professional health workers
OOP…………. Out-of-pocket
PALYs……….Productivity-Adjusted Life Years
PICOS…..……Population, Intervention, Comparison, Outcomes and Study
PLWD…...……People living with the disease
PRISMA…..…Preferred Reporting Items for Systematic Reviews and Meta-Analyses
MIND………..Project of mental illness in chronic disease care
QALYs……….Quality-Adjusted Life Years
SAMRC………South African Medical Research Council
SES……...……Socio-economic Status
SDoH…...…….Social Determinants of Health
SAGE...……….Study on global AGEing and adult health
SEMDSA……..Society of Endocrinology, Metabolism and Diabetes of South Africa
SF-36………….Short Form-36
SMS……....….Short Message Service

SSA……........…Sub-Saharan Africa
Stata SA……...Statistics South Africa
RR………...….Relative Risk
T1D…….…….Type 1 diabetes
T2D…….…….Type 2 Diabetes
TTO…………Time Trade-Off
UN……………United Nations
US$..................United States Dollar
VAS………….Visual Analogue Scale
WCDoH…........Western Cape Department of Health
WHO…..…….World Health Organization
WTP…………Willingness to pay
YLL…….........Years of Life Lost
YLL$_d$ ………..Lived in the labour force
ZAR……........South African Rand

Table of Contents

1. Chapter One: Introduction and Overview

1.1 Outline of the Thesis

This first section (**Chapter One**) introduces diabetes mellitus, including its types, effects, and global prevalence trends, before narrowing down to the specific context of sub-Saharan Africa (SSA). It also discusses the various health burdens associated with this disease, such as macrovascular and microvascular complications, and reviews existing diabetes management programs. This section further situates the research within the demographic, economic, and healthcare landscape of South Africa, providing a rationale for the study and outlining its aims and objectives. **Chapter Two** provides a literature review examining the economic and well-being burdens of diabetes, including social determinants. The subsequent four results chapters; C**hapters Three to Six**, present a systematic review and analyses focusing on the costs and cost-effectiveness of diabetes management, the impact of diabetes on productivity and the economy, health-related quality of life among individuals with diabetes and its predictors, and the social determinants of health associated with self-care management in South Africa. The thesis concludes in **Chapter Seven** with a discussion and summary of findings, highlighting key messages, the generalisability and limitations of the research. The references and appendices sections are also included at the end of the dissertation.

1.2 What is Diabetes?

Diabetes mellitus is a multifactorial disease caused by the combined effect of genetic predisposition and environmental factors [1-4]. It manifests as high blood sugar levels due to a combination of insufficient insulin production by the pancreas and impaired insulin action, whereby the body is unable to utilise the insulin produced effectively [5-8]. Diabetes is potentially preventable, and appropriate management can halt or delay its complications once diagnosed [9]. However, it remains the most undiagnosed form of non-communicable disease (NCD) due to factors such as its asymptomatic nature in its early stages, lack of public awareness, and limited access to healthcare in many regions [9, 10]. As a result, it wreaks havoc, particularly when healthcare systems are not aligned and consistently functioning [11, 12].

1.2.1 Types of Diabetes

There are two main types of diabetes- type 1 (T1D) and type 2 (T2D) [13]. Type 1 diabetes tends to occur mostly in children or adolescents, while T2D is usually common in adults, although it has increasingly been reported in adolescents [3, 5, 14]. The remainder of the cases include gestational diabetes and other specific types [13]. Generally, diabetes can be classified into the following four categories:

a) Type 1 diabetes is characterised by absolute insulin deficiency and requires daily administration of insulin injections for the rest of the patient's life [3]. Rapid onset in childhood or adolescence, requiring lifelong insulin therapy, involves autoimmune destruction of pancreatic β-cells, with genetic predisposition and environmental factors playing significant roles [3,15]. Currently, neither the cause nor the means to prevent it are fully known, and it accounts for 5% to 10% of all cases of diabetes [15].
b) Type 2 diabetes is characterised by insulin resistance and relative insulin deficiency. Gradual onset, often starting with prediabetes, is the most generic form and accounts for 90% to 95% of all global cases of diabetes [16, 17]. It involves the progressive β-cell dysfunction that exacerbates hyperglycaemia over time, often influenced by genetic factors, obesity, a sedentary lifestyle, and age [17].
c) Gestational diabetes occurs for the first time during pregnancy and generally resolves after delivery due to hormonal changes that cause insulin resistance, with risk factors including obesity, family history, and previous gestational diabetes [10]. Besides being a reason for the increased risk of complications during pregnancy and delivery, gestational diabetes is the risk factor for future T2D among mothers and children [10, 16].
d) Other types of diabetes, such as neonatal diabetes and maturity-onset diabetes of the youth caused by monogenic diabetes syndromes and drug- or chemical-induced diabetes of the adults caused by treatments, infections, pancreatic disease or after surgery account for 1% of 5% of all diagnosed cases [17, 18].

Diabetes and related complications are potentially preventable through adequate risk factor control, early detection, and timely treatment. Individual awareness regarding the risk factors, such as family history and genetics, coupled with controlling lifestyle factors, especially by improving diet and exercise regimen, can reduce the risk of diabetes [13, 19]. Often, people living with diabetes (PLWD) do not realise the seriousness of their health status at the earliest, and delayed diagnosis results in numerous health problems [20, 21]. Type 1 diabetes is manageable with insulin injections, alongside a healthy diet and regular physical exercise, all of which can significantly improve the quality of life for individuals with this condition. [7, 22]. It is important to recognise that these lifestyle changes, including adhering to a carefully planned diet, engaging in regular physical activity, and conducting regular blood glucose monitoring, are crucial for managing both Type 1 and Type 2 diabetes [20]. However, managing T2D often requires a more intricate approach that goes beyond standard medication and lifestyle changes. This includes personalised nutrition plans, specific weight management strategies, comprehensive psychosocial support, in-depth education and self-management training, meticulous comorbidity management, and utilisation of advanced medication regimens [16]

1.3 Trends and Prevalence of Diabetes

1.3.1 Global Trend and Prevalence of Diabetes

To date, in defiance of efforts made, diabetes prevalence continues to rise globally, with an estimated 537 million adults (20-79 years) living with a diabetes condition in 2021 [25], compared to 422 million adults in 2014 and 108 million in 1980 [24, 27]. It is further projected to rise to 643 million by 2030 and 783 million by 2045 [25]. The age-standardized global prevalence doubled from 4.3% to 9.0% in the adult population (20-79 years) between 1980 and 2014 [24, 26], which reached 10.5% in 2021 [25]. Approximately 80% of individuals with diabetes reside in LMICs, and its economic and financial burden is anticipated to escalate significantly globally, disproportionately impacting LMICs and the most vulnerable populations in high-income countries [27, 28].

Further analysis showed that the distribution of prevalent diabetes population varies by country [25, 28]. Countries with the highest number of people with diabetes (in millions) in the world, ranked accordingly, are China (141), followed by India (74), Pakistan (33), the United States of America (32), Indonesia (19), Brazil (16), and Mexico (14) [25]. Europe has witnessed an increase in diabetes prevalence, although at a slower rate compared to Africa and other global regions [28 - 30]. Notably, the United Kingdom (UK) stands out, reporting a more than twofold increase over the past two decades, with 3.7 million individuals aged 17 or older currently identified as living with the disease [29]. Literature attributed the increase in the number of

PLWD globally to risk factors such as population growth and ageing, a rise in age-specific prevalence rates, and, most importantly, an interlinkage of the risk factors [29, 30].

1.3.2 Trends and Prevalence of Diabetes in Sub-Saharan Africa

During the 1980s and 1990s, diabetes prevalence in SSA was relatively low, often perceived as a disease predominantly affecting affluent individuals [24, 31]. However, over the last forty years, there has been a steady increase in the age-standardized prevalence of diabetes, which reached 8.9% in 2014 [32]. Additional meta-analysis of prevalence studies highlighted that among those aged 55 and above, the diabetes prevalence was 13.7% [33]. The adult diabetic population, which stood at 24 million in 2021, is projected to escalate by 134% by 2045 compared to a global average increase of 51% [34, 35]. According to recent estimates, unless action is taken, the total number of individuals living with diabetes in SSA is projected to reach 55 million by 2045 [36]. However, the region has little advocacy and promotion of awareness of diabetes management, which has a negative impact on the government's ability to supply care for diabetes complications [37, 38]. The situation of undiagnosed diabetes in the region is high, with an estimated 54% of diabetes cases not identified [39]. This issue is particularly acute in SSA, where it is reported that three-quarters of diabetic individuals are within the working-age bracket of 20 to 65 years [40].

This sharp escalation is of diabetes in SSA driven by an ageing population and a rapidly expanding working-age demographic within the region [41, 42]. It was evidenced that lifestyles, imported dairy practices, and globalisation are the root causes [43, 44]. These factors, combined with urbanisation and changes in dietary habits influenced by globalisation, have significantly contributed to the rising incidence of diabetes in the region, indicating a shift from traditional to more sedentary lifestyles and Western dietary patterns [45]. Over the past decade, the diabetes epidemic has become generalised in most populations in SSA, where it remains a significant public health challenge [46, 47]. However, the healthcare expenditure in 2019 for PLWD was still less than 1% of the total global spending for diabetes [27].

According to findings from the NCD-Risk Africa working group that analysed pooled data from 76 surveys (182,000 participants) from 32 countries between 1980 and 2014, Africa's Northern and Southern regions had higher diabetes prevalence estimates than the global average [32]. On the one hand, the age-standardized prevalence ranged from 4.2% to 16% for an east-central African country, Burundi, in 2014 [32].

1.3.3 Trends and Prevalence of Diabetes in South Africa

There is an increasing prevalence of diabetes in South Africa, presenting a notable public health concern, placing the country as the second highest in the prevalence of PLWD in SSA [48]. According to IDF estimates, the prevalence of diabetes at the population level has witnessed a significant increase, soaring from 4.5% in 2010 to 11.3% in 2021. [25]. However, a Systematic Review and Meta-Analysis indicated a higher pooled prevalence of T2D in individuals 25 years and older, ranging around 15.25% (11.07–19.95%) [49]. This figure surpasses the IDF's estimate of 5.4%, possibly attributed to the exclusion of participants under 25 years in their study. Nonetheless, this trend is further underscored by the fact that in 2021, approximately 4.2 million people aged 20 to 79 were living with diabetes in South Africa, with half of these cases remaining untreated or undiagnosed [39, 48]. This is particularly worrisome as individuals with pre-diabetes are at a heightened risk of developing type 2 diabetes [50]. This concern persists, even considering a study utilising South African Demographic Health Survey data, which revealed that 67% of both males and females were identified as pre-diabetic [47]. This resulted from rapid demographic, economic, and socio-cultural transformations following the advent of democracy, which have significantly influenced this increase in diabetes prevalence [51]. These shifts have led to changes in environmental and social stressors, dietary habits, and physical activity patterns, contributing to a notable epidemiological transition [43, 47]. This transition is marked by increasing levels of obesity and a rise in cardiovascular disease prevalence over the past quarter-century [51]. In South Africa, 69% of women and 39% of men are overweight or obese [52]. Obesity significantly contributes to the T2D epidemic, with excess body weight estimated to be a factor in 87% of T2D cases in the country [53]. Ongoing data trends also show a dramatic increase in both urban and rural settings, affecting both genders equally, driven by rapid urbanisation and changes in diets and levels [43, 54]. The IDF projects a steep increase in diabetes cases in South Africa, with potential numbers reaching 7.4 million by 2045 [25].

1.4 Diabetes Related-Health Burdens

1.4.1 Effects of Uncontrolled Diabetes

Although blood sugar testing for the early detection and diagnosis of diabetes is a relatively low-cost procedure, especially when compared to the high financial burden of treating advanced diabetic complications, it is concerning that globally, one in two adults with diabetes remains undiagnosed [55]. Inadequate management of blood sugar levels in individuals with diabetes significantly increases the risk of both acute and chronic complications, the former presenting immediate health threats and the latter leading to long-term detrimental effects on various organ systems. [56]. Diabetic ketoacidosis and hyperglycaemic hyperosmolar coma are the two common life-threatening types of acute metabolic complications [57].

1.4.2 Macrovascular Complications of Diabetes

Diabetes places a significant burden on patients due to its complications, with an increased total cost of disease management by 250% compared to those without complications [58, 59]. Increased risk of hospitalisation in PLWD is attributable to macrovascular complications refer to cardiovascular diseases, including cerebrovascular, coronary heart, and peripheral arterial diseases [16, 60]. In general, the risk of macrovascular complications amongst the populations with diabetes is two to four times higher than those without diabetes [2, 60]. Some studies indicate that in developed nations, macrovascular complications affect approximately 16% of individuals with diabetes [30, 61]. In developing countries, this figure is notably higher, impacting up to 26% of the diabetic population [62]. Concurrent management of diabetes and hypertension, which afflicts up to 75% of these patients, is essential due to the increased risk of early morbidity and mortality associated with these conditions [63, 64].

1.4.3 Microvascular Complications of Diabetes

Microvascular complications of diabetes are those long-term complications that affect small blood vessels [20, 65]. The risk of microvascular complications is 10 to 20 times higher among PLWD compared to those without [30, 60]. The main types of microvascular complications are: *(I) Diabetic retinopathy,* a serious complication characterised by damage to the retina of the eye, affects over one-third of individuals with diabetes and is implicated in 80% of blindness cases among these patients [53]. This condition can progress to vision loss at any stage of diabetes progression [66]. *(II) Diabetic neuropathy* is a highly prevalent and debilitating consequence of diabetes that causes nerve fibre damage, with prevalence rates varying widely from 9.6% to 88.7% across different populations globally [67]. This variation reflects differences in diagnostic criteria, study populations, and diabetes duration, complicating accurate prevalence estimation. *(III) Diabetic nephropathy* is a critical complication where diabetes precipitates a progressive deterioration of kidney function, where the disease process initiates scarring within the kidneys, leading to impaired fluid and salt regulation, culminating in increased pressure [68]. The prevalence of diabetic nephropathy is estimated to affect 25% to 40% of individuals with diabetes [69]. As diabetes progresses, it inflicts damage on the microvasculature, causing blood vessel walls to become rigid and malfunction, playing a pivotal role in the escalation of hypertension, which can further accelerate the journey towards kidney failure and, ultimately, end-stage renal disease [68, 69].

1.5 Standard Diabetes Management Plans/Programmes

Diabetes management programmes are structured approaches designed to help individuals living with diabetes effectively manage their condition. These plans typically involve a combination of medical treatment, lifestyle modifications, and regular monitoring [70]. Key components include blood sugar monitoring, a balanced diet, regular physical activity, and patient medication adherence, generally known as self-care management [70, 71]. These often entail seeking knowledge about the disease, skills for daily diabetes management, and strategies to prevent complications [71]. The goal is to maintain blood glucose levels within a target range, reducing the risk of long-term complications and enhancing the overall quality of life. Such programmes and planning are costly and require significant investments and individual efforts to maintain blood sugar under the recommended levels [72]. The effectiveness of diabetes management depends on patients checking their blood sugar levels and consistently undertaking the recommended routine self-care. Studies indicated that high levels of self-care and medication adherence increase the effectiveness of treatment and lead to better patient outcomes [73, 74]. It is crucial for improving self-care and medication adherence, which increases the effectiveness of treatment and leads to better health outcomes [73, 74].

1.6 Research Setting

1.6.1 Demographic and Economic Features of South Africa

South Africa is a middle-income country with abundant natural resources that attract foreign direct investment [75]. The country's population estimate for 2019 was 58.56 million, with 12 million living in extreme poverty [76]. Structural challenges and sluggish economic growth have hindered efforts to alleviate poverty, a situation further exacerbated by the recent COVID-19 pandemic [77]. High levels of poverty imply a substantial burden of healthcare expenditure for the government, with the National Department of Health (NDoH) holding overall responsibility for 84% of the population. [78]. In addition, the prevalence of unemployment, poverty, and inequality in South Africa has been accelerated in recent years by sluggish economic growth, slowing from 0.4% in 2016 to 0.2% in 2019 [79]. While the high unemployment rate persists, the government is adamant about improving and implementing strategies to stimulate job creation and economic diversification [80]. However, the country continues to face structural challenges (i.e., shortage of skills, frequent stoppages of work because of strikes and a decrease in global competitiveness), which, in turn, constrain economic growth [81]. As a result, the current government faces increased pressure from the listed challenges, while the economic outlook is also expected to remain slow [79].

The 2021 World Bank overview of South Africa concludes and emphasises the existence of the world's highest and most persistent inequality rates, with a consumption Gini coefficient of 0.63, which not only signifies one of the highest levels of inequality worldwide but also underscores its deep-rooted and persistent nature in the nation's economic framework [75]. The country’s high inequality is perpetuated by a well-documented history of exclusion of marginalised communities and a pattern of economic growth that has been insufficient in creating jobs [78, 82]. These factors collectively contribute to limited access to healthcare services and lower awareness of healthy lifestyle practices among the population, exacerbating the risk of disease outbreaks [81].

1.6.2 Health System Context and Structure of South Africa

South Africa has a two-tiered and highly unequal healthcare system [83, 84]. The legacy of Apartheid has left South Africa with an inequitable health system, with the minority having disproportionate access to health services, leading to a situation where preventable diseases of poverty persist in low-income communities [85, 86]. Almost 80% of the population depends entirely on the public sector for health services, while heavily subsidised private healthcare and inpatient care are available for only 16% [78]. The private sector is primarily funded through individual contributions to medical aid schemes or health insurance and serves a few population groups which can afford to pay the premium [78].

The public health system carries an inevitable financial burden; hence, inefficient and inadequate care has been provided for the majority of the population, specifically people experiencing poverty, who are exempt from service payments or user fees when seeking care in the public sector [83]. The public sector is underfunded, while most South Africans cannot afford the exorbitant cost of private care. According to Statistics South Africa (Stats SA), the public sector utilises 12% of the total government budget, more than the 5% recommended by the World Health Organization (WHO) [87].

South Africa has 4200 public sector facilities, with an estimated 28% of the population accessing private primary healthcare (PHC) facilities [88]. Given this landscape of healthcare accessibility, where a significant portion of the population relies on PHC facilities, the South African parliament's recent passage of the National Health Insurance (NHI) bill represents a pivotal step towards restructuring the nation’s healthcare system [89]. The NHI proposal is to provide universal healthcare by purchasing services from health professionals through an NHI Fund and providing care for all [90]. Despite the ongoing efforts and high government expenditure, South Africa has poor health outcomes, replicating greater inequality within healthcare compared to other middle-income countries [80]. According to the NHI bill, services would be delivered at private and public facilities to curb unequal health outcomes and related challenges [89]. However, numerous unanswered questions regarding the operational details and concerns about securing the required funds have led to significant uncertainties about the effective implementation of this scheme [91]. In this regard, evidence is needed on how the current healthcare financing system ensures fairness in financing [83]. Thus, it is vital to address the burden and implications of diabetes adequately and effectively in South Africa in the context of proposals for NHI.

1.6.3 Healthcare Provision Challenges in South Africa

When the democratic government took over from the apartheid regime in 1994, the health system had massive challenges, many of which still persevere [83, 85]. One of the challenges identified is the fragmentation in the medical schemes market and the absence of a universal system where access to and use of health services is not dependent on income but on the need for care [83]. Some have argued that these challenges are an outcome of post-1994 macroeconomic policies which focused on promoting economic growth rather than redistribution, which added to the persistence of economic disparities among racial groups and residential areas (urban or rural, formal or informal) [85]. The public health system, which caters for healthcare for the majority of the population, was transformed into an integrated and comprehensive system; however, failures in leadership and weak management of resources resulted in the inadequate implementation of some potential policies [51, 85]. Crucial aspects of primary healthcare are mostly not in place in public hospitals, and a considerable number of human resources (health professionals) face crises in the health system. According to the International Council of Nurses (ICN), it is also believed that a shortage of crucial medical personnel hinders the quality of the public sector healthcare provision [92]. In South Africa, the primary care reengineering initiative integrates non-professional health workers (NPHW) into delivering health services for chronic conditions, aiming to establish their role more firmly within the healthcare framework [93]. The evidence further suggests that NPHWs can be as effective as their qualified counterparts in administering lifestyle interventions to prevent diabetes, highlighting the potential for broader implementation of NPHW-led programs in diabetes care [94, 95].

On the other hand, a decade ago, WHO set healthcare expenditure standards under the umbrella of the Commission on Macroeconomics and Health's estimates of healthcare resource requirements [96]. South Africa, with the highest total per capita healthcare spending in Africa [97], has a relatively adequate per capita healthcare spending to provide more than the basic level of care for everyone in South Africa. The average estimate of WHO was $237 for 2007 and $259 for 2015 for scaling up priority health interventions in middle-income SSA countries [96]. South Africa exceeded the estimated average required by the WHO in 2006, as the per capita healthcare spending was $425 [97]. Looking at the monetary terms, one could expect a well-equipped and sophisticated healthcare system in the country, yet it has been shown that private and higher-level public health services are skewed toward the rich [78, 83]. Contemporary evidence also indicates the major challenge where those with the greatest need for healthcare services benefit less than those with relatively less need [98, 99].

1.7 Rationale for the Study

Non-communicable diseases (NCDs), including diabetes, are increasingly prevalent in LMICs including those in SSA, mainly due to ageing populations and lifestyle challenges [45]. Factors such as obesity, pollution, unhealthy diets, physical inactivity, alcohol abuse, and smoking have escalated the NCD burden in regions already grappling with infectious diseases [5]. By 2030, NCDs are projected to account for three-quarters of the disease burden in middle-income countries [100]. Additionally, there is a complex interplay of risk factors, disease management, and health outcomes between communicable diseases (CDs) and NCDs [14]. For instance, tobacco use is a risk factor for both tuberculosis and chronic obstructive pulmonary disease, while HIV and diabetes are linked to chronic kidney disease [14]. This multifaceted health challenge exacerbates the morbidity and mortality associated with NCDs, such as diabetes in LMICs and SSA, straining healthcare systems and impacting economic stability [46].

South Africa is experiencing a diabetes epidemic as the country goes though the epidemiological transition [101]. The healthcare system is increasingly burdened by the escalating costs and prevalence of diabetes, a major NCD [102], accounting for 51.3% of all deaths, while CVDs are responsible for 38.4% of deaths in South Africa [103]. Diabetes is a leading cause of mortality in the country, ranked the second deadliest disease of the ten leading underlying causes of death, and responsible for 6% of the total deaths in the country [44]. The year 2018 saw significant diabetes-related complications, including 12,614 cases of blindness, 3,311 amputations, 11,037 strokes, and 8,672 cases of ischemic heart disease [104]. For a country with a high number of adult and working-age populations, this represents a substantial number of losses to the economy, with more economically dynamic South Africans projected to succumb prematurely to diabetes-related death each year [105]. The economic impact of diabetes is substantial, with the public health sector bearing a significant portion of direct healthcare costs [106, 107]. The high prevalence of diabetes-related complications exacerbates this financial strain and requires extensive medical care and management [108]. The high costs associated with managing diabetes and other complications are exerting additional strain on South Africa's economy, particularly as the public health sector bears a significant portion of these healthcare costs [109]. Particularly because the burden of diabetes extends beyond healthcare costs to include loss of productivity due to disability and premature death, further impacting the economy [110].

Diabetes significantly impacts economically productive adults in South Africa, not only restricting individuals' functional capacity and satisfaction but also adversely affecting their health-related quality of life (HRQoL) [111]. The complications of diabetes in the working-age population often lead to disability [112], emphasising the persistent and far-reaching economic repercussions of the disease. This impact extends beyond the health system, undermining the health of the workforce and leading to substantial productivity losses extending beyond the health system, undermining the health of the workforce and leading to substantial productivity losses [100]. Consequently, the national economy suffers due to decreased remuneration, reduced tax revenue, and diminished Gross Domestic Product (GDP)

[113]. The epidemic is intensified by Social Determinants of Health (SDoH) that play a significant role in shaping health outcomes and disparities hindering adherence to diabetes care [114]. Socioeconomic status, education, and healthcare access are key factors influencing the management of the disease in PLWD [82]. Particularly in lower socioeconomic communities, limited access to healthcare and education impedes proper diabetes care, affecting HRQoL [115].

A comprehensive health system restructuring focused on enhancing PHC for early detection and management, improving access to care in underserved communities, and emphasising patient education for effective self-management is essential [43]. While South Africa has made strides in diabetes management, surpassing some of the initial targets set forth in the National Strategic Plan for NCDs (2022-2027), there remains a necessity for more rigorous objectives [114]. The next step is to aim beyond current achievements by enhancing diabetes awareness, increasing intervention rates for those with elevated blood glucose levels, and improving control rates among treated individuals to reflect a truly ambitious and comprehensive approach to diabetes management in line with evolving healthcare standards [116]. To ensure better health outcomes and sustainability within South Africa's unique healthcare landscape, yet there is a need for robust implementation of evidence-based strategies and strengthening of the healthcare system [117].

The rationale for this thesis is the urgent need for comprehensive research on the burden of diabetes, particularly focusing on its social aspects and economic impact. A deeper understanding of how diabetes management at the individual level incurs economic costs and how social and environmental factors influence crucial practices for blood sugar control once diagnosed is required. Additionally, exploring the overall impact of diabetes on the well-being of the South African population is vital. This knowledge is envisaged to inform evidence-based interventions, mitigation strategies, and preventive measures, considering the full scope of diabetes's effects on the economy and society. Such insights are especially critical as the South African health system undergoes significant transformations, including a shift towards primary healthcare and the planned implementation of the NHI.

1.8 Overall Aim

This thesis aims to evaluate the economic and well-being burden of diabetes in South Africa, focusing on productivity impacts, associated Social Determinants on patient outcomes and predictors of quality of life.

1.9 Specific Objectives

The specific objectives are to:

1. systematically review the costs and cost-effectiveness of type 2 diabetes management in Sub-Saharan Africa.
2. quantify the burden of type 2 diabetes on the productivity and economy in South Africa through a life table microsimulation modelling to:
    - quantify excess mortality
    - estimate Years of Life Lost (YLL) and
    - assess the extent of Productivity-Adjusted Life Years (PALYs) lost among the working-age (20 to 65 years) South Africans living with diabetes.
3. assess the predictors of health-related quality of life (HRQoL) and time trade-off utility (TTO) values among people with diabetes in South Africa.
4. investigate Social Determinants of Health (SDoH) associated with diabetes self-care management and adherence in South Africa.

1.10 Ethical Considerations

This doctoral study utilised secondary data from Statistics South Africa, IDF, and Project MIND trial. Particularly, the Project MIND trial obtained ethical clearance from the South African Medical Research Council (SAMRC) (EC 004–2/2015), the University of Cape Town (089/2015), and Oxford University (OxTREC 2–17). The Western Cape Department of Health (WCDoH) also approved this study (WC2016_RP6_9).

The Project MIND participants consented to the trial; this extends to utilising the data for this thesis. In addition, all data was anonymised and acquired in a Stata format with no individual identifying information included. Therefore, this doctoral research did not pose any risk to the participants and/or those involved in the trial. Additionally, the Faculty of Health Science's Human Research Ethics Committee (HREC) at the University of Cape Town (UCT) thoroughly reviewed the PhD proposal of the current study and granted ethical approval, as indicated by HREC reference number 646/2022 (***UCT approval letter found in Appendix 3***).

1.11 Summary of the Methodology Used

This section briefly outlines the analytical methodology utilised to address the thesis's overall aim and specific objectives, and a further summary is presented in ***Table 1***. For Chapter Three, the PhD Candidate engaged with the Vital Statistics Department at Statistics South Africa (Stats SA) to obtain mortality data, labour reports for 2019, and population data stratified by age group and gender. A comprehensive literature review was conducted to compensate for the absence of locally specific utility scores for quantifying Quality-Adjusted Life Years (QALYs). For diabetes-related information and prevalence data, the candidate reached out to the IDF due to the absence of a local repository. This approach ensured the acquisition of relevant and up-to-date data for the study. The PhD candidate developed a Microsoft Excel-based simulation model to integrate and analyse this data. This model facilitated the microsimulation, assuming no diabetes, analysis of excess deaths among the diabetic population and the calculation of Years of YLL and PALYs.

The comprehensive systematic literature review was undertaken to assess the costs and cost-effectiveness of managing T2D diabetes in SSA, analysis found in Chapter Four. Guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework, a comprehensive literature search was conducted across multiple databases, focusing on Type 2 Diabetes (T2D) management costs and effectiveness in SSA. Inclusion criteria were based on the population, intervention, comparison, outcomes and study (PICOS) framework, with studies selected for relevance to T2D in African contexts. Data extraction followed the Cochrane Handbook guidelines, using Microsoft Excel for organisation and analysis. Key variables included population characteristics, intervention details, and outcome measures like QALYs and DALYs. Costs were adjusted for inflation and exchange rates to ensure consistency and comparability.

In Chapter Five, the study utilised data from Project MIND, an acronym for strengthening South Africa's health system through integrating treatment for mental illness into chronic disease care [118]. A trial integrating mental illness treatment into chronic disease care in Western Cape, South Africa. The trial encompassed 24 clinics, 15 urban and nine rural, enrolling 1,200 participants aged 18 years and above with HIV and/or diabetes in 2017 [118]. These clinics were specifically chosen for their capacity to treat a significant number of people with HIV and diabetes and were required to be co-located within PHC facilities. Given that HIV and diabetes services are typically provided in separate, vertically organised units within the same PHC facility, this selection criterion is considered to minimise the likelihood of introducing selection bias into the trial. For this sub-study, baseline data from 539 participants diagnosed exclusively with diabetes were analysed. The methodology involved cross-tabulating key SDoH variables against self-care management and binary logistic regression to examine associations with self-care scales. Additionally, multinomial logistic regression assessed factors influencing self-care adherence categories. A comprehensive analysis of diabetes self-care guidelines and their determinants was conducted using Stata® software version 17.

For Chapter Six, the Project MIND data of 539 participants was utilised. To overcome the absence of South Africa-specific utility value sets, the PhD candidate created new sets stratified by 5-year age groups and gender. The Time Trade-Off (TTO) method was used to estimate South African TTO utility scores for PLWD in South Africa. The predictors of Health-Related Quality of Life (HRQoL), adjusting for age and gender, were also identified using Stata software version 17. The HRQoL utilities were categorised into four ordinal levels (Low, Moderate, High, and Perfect) based on TTO scores. Ordinal logistic regression, suitable for the ordered HRQoL variable, analysed the proportional odds of HRQoL categories. Additionally, logistic regression examined factors influencing the 95th percentile of TTO utility scores, creating a dichotomous dependent variable for participants with very low TTO utility values (HRQoL below 0.64).

Table 1: The relationship of analytical methods to specific PhD research objectives.

Study Component	Specific Objectives	Analytical Method	Main Outcomes	Publication status
Life Table Modelling Analysis	To estimate the impact of T2D on the South African population, focusing on PALYs.	Life table modelling to simulate health trajectories and compare cohorts with and without diabetes. Adjustments for GDP, productivity indices, labour force dropout, and mortality risks.	Excess deaths, years of life lost (YLL), and PALYs metrics for individuals aged 20-65 with T2D.	Published in Pharmacoeconomics
Systematic Literature Review	To review and synthesise information on the costs and cost-effectiveness of managing T2D in SSA.	Comprehensive literature review from 2010 to 2022, costs adjusted to 2023 US dollars.	Economic aspects of T2D management in SSA, including cost-effectiveness and resource allocation insights.	Protocol registered on PROSPERO, currently under review by Health Economics Reviews
Cross-Sectional Data Analysis ***SDoH Assessment***	To investigate SDoH factors associated with diabetes self-care management practices.	Analysis of cross-sectional data from 539 individuals with diabetes receiving care in urban and rural PHC facilities. Binary logistic and multinominal regression analyses were utilized.	Influence of SDoH on diabetes self-care management and adherence levels among participants.	Under review by BMC Public Health
Cross-Sectional Data Analysis ***HRQoL Assessment***	To assess factors associated with HRQoL in South Africans with diabetes and develop utility value sets.	Analysis of cross-sectional data from 539 individuals with diabetes to assess HRQoL. Conversion of EQ-5D-3L responses into a unified summary index score using the UK TTO value set. Binary and ordinal logistic regression analyses were utilized.	Factors associated with HRQoL in individuals with diabetes and locally relevant utility value set development.	Under review by Elsevier SSM-Health Systems

2. Chapter Two: Literature Review

This section reviews the literature on productivity-adjusted life of years (PALYs), social determinants of health (SDoH) and the health-related quality of life (HRQoL) associate with diabetes at the population level. It also reflects on the emerging debate behind the relationship between SDoH and diabetes care and self-management at the individual level.

2.1 Economic Burden of Diabetes

2.1.1 Financial Burden of Managing Type 2 Diabetes

The burden of T2D extends beyond the substantial clinical consequences to significant economic implications for individuals, households, healthcare systems, and nations [108 - 120]. The cost of illness (COI) studies offer a comprehensive analysis of this impact, considering both direct medical costs and indirect costs such as productivity losses and familial care-related expenditures [30, 74, 121]. Direct medical expenses, which encompass hospital admissions, ongoing pharmaceutical treatments, and the persistent nature of chronic disease management, constitute a significant portion of these costs [122, 123]. These costs are further necessitated by the critical need to control blood glucose levels and prevent the onset of acute events and long-term complications, which, if unmanaged, can lead to more intensive and costly interventions [72, 124]. Indirect costs amplify this burden, including travel expenses to clinics and hospitals, often distant from patients' homes, which can be substantial [73]. These are particularly consequential in a region where a substantial workforce demographic is affected, undermining economic stability [37]. Additionally, the costs of T2D are further fuelled by systemic issues such as insufficient health insurance coverage leading to high out-of-pocket (OOP) expenditures for patients and inadequacies in healthcare infrastructure that inflate care delivery costs [91, 99]. In tandem, these factors contribute significantly to the financial toll of T2D, with studies using the human capital approach identifying permanent disability due to T2D as the primary contributor to indirect costs [122, 125].

In SSA, the strain of T2D is notably pronounced, not only due to inadequate healthcare infrastructure and rising lifestyle-related incidence rates but also because of significant financial costs, driven by complications and comorbidities [8, 72, 106]. The impact of T2D in SSA is further complicated by weak health systems, limited access to care, and the risk of catastrophic health expenditures due to high OOP payments [46]. These expenditures often exceed 50% of total health costs, driving financial catastrophes underlined by the inability to pay and the lack of prepayment mechanisms for financial risk pooling [126, 127]. The financial burden in SSA ranges from $337.50 for basic medical care of uncomplicated T2D to $2330.74 for the total provider cost per patient [128]. Cost-effectiveness studies in SSA have furthered the understanding of the burden of T2D management strategies [130, 131]. For instance, the adaptation of a private-sector T2D management programme to the South African public sector revealed an increased annual per capita cost from $774.23 to $932.42, yet the intervention was deemed cost-effective with an Incremental Cost-Effectiveness Ratio (ICER) of $1309.25 per QALY gained [132]. In SSA, where the minimum wage often falls below adequate living standards, the financial burden of diabetes management can represent a significant portion of an individual's income, exacerbating economic disparities and healthcare access inequalities [133, 134].

A comprehensive systematic review was conducted to delve into the intricacies of the financial burden of T2D care. Chapter Three extensively presents the detailed findings and discussions of this review.

2.1.2 Productivity Burden of Type 2 Diabetes

Assessing the health burden within a society is a pivotal component of health economic evaluations, which aims to determine the most efficient allocation of resources by systematically evaluating the cost-effectiveness of various interventions [135]. As described by Drummond in 2005, these evaluations involve a meticulous approach to contrasting the costs and outcomes of different health strategies [136]. The valuation of these strategies is methodologically complex due to the multifaceted nature of the disease and its treatment, requiring the consideration of diverse factors such as long-term cost savings, prevention of mortality, and the impact on quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs) [137]. These evaluations are also required to account for varying disease progressions, treatment responses, and the economic context of the healthcare system, all of which add layers of methodological intricacy [135]. Each metric offers valuable data to guide the distribution of healthcare resources and the selection of necessary interventions. Disability-adjusted life years measure disease burden and resulting disability within populations, quantifying the divergence from an ideal state of population health by accounting for reduced life expectancy and years lost to disability and premature mortality [138]. It also measures the gap between a population's health and hypothetical ideal health achievement and further measures the gap by measuring reduced life expectancy, years lost to disability and disease burden [117]. Similarly, QALYs capture the aggregate impact of health interventions on mortality and morbidity across different health states that individuals may experience under treatment versus no-treatment scenarios [139]. In summary, QALYs and DALYs quantify the cost and consequences based on the effect of interventions and the disease burden in a population, respectively [139, 140]. However, these two models do not adjust years of life lived for productivity loss attributable to diseases [119].

The societal perspective of economic evaluations requires the inclusion of productivity costs when performing economic evaluations [2, 138]. Previously validated tools quantified productivity loss at work, including the Health and Labour Questionnaire, Work Limitations Questionnaire, and Work Productivity and Activity Impairment Questionnaire [141, 142]. These tools provide evidence for a given study sample over a short period of time; however, they do not outline productivity loss at a population level or over a working lifetime [143]. The productivity-adjusted life of years model is proposed as a new measure of disease burden that addresses this knowledge gap [123, 144]. The PALYs model further estimates costs that are useful in providing a policy impetus for change in practice, including time spent with reduced work productivity or a productive day missed at work because of ill health, for which the QALYs and DALYs do not account [119, 145]. Additionally, it measures the essential, significant, and primarily undiscovered full portion of the costs of the burden of diseases [144].

Integrating the PALYs model into healthcare evaluations provides a novel approach for governments to understand better and address the wider economic impacts of diseases [119, 145]. This model is particularly relevant as there is a global gap in knowledge regarding productivity loss from both health systems and patient perspectives. Productivity encompasses both paid and unpaid work, and its reduction is a crucial economic concern [146]. Production costs arise from the loss and replacement of individuals who are unable to work due to illness, disability, or premature death [147, 148]. The health of an individual significantly influences their work capacity, with poor health often leading to absenteeism (time off work) or presenteeism (working at reduced capacity), thereby contributing to notable productivity losses [121, 149, 150]. These losses can further be caused by a lack of investment in preventive healthcare or effective treatment options, leading to broader societal and economic consequences [73]. The burden of chronic illness extends beyond health implications, exerting a profound economic impact on individuals, societies, and health systems [59]. These diseases cost economies millions of dollars annually due to increased direct medical expenses, premature mortality, and intangible costs such as diminished Health-Related Quality of Life (HRQoL) and productivity losses, including absenteeism and presenteeism [123]. Diabetes is one such disease with a high burden not only tied to the medical care costs but also the profound indirect costs resulting from lost income, disability, and premature mortality [111, 115].

Growing evidence shows that diabetes-related economic costs drive a severe, expanding strain on population productivity [151]. The costs impose a substantial economic burden on patients and their immediate families [73]. The combined effects of these burdens negatively affect a country's economic growth, labour market competitiveness, and tax revenue, potentially triggering fiscal pressure, poor health outcomes, and increased poverty [152]. As a result, health systems around the world are struggling to meet the burden of T2D care, and the financial burden has reached an estimated $760 billion, with 4.2 million deaths recorded in 2019[25].

A critical aspect of this PALYs burden of diabetes is highlighted by only six studies that exist in five countries globally, conducted in Australia [151, 153], Bangladesh [149], China [113], Germany [154], and the United States of America [121]. The findings indicate that there has been a significant productivity loss attributable to T2D in the nations, which extended beyond the individual, impacting employers and national economies through diminished earnings, reduced tax revenues, and a consequent contraction in GDP. However, the global scope of research into this domain remains limited, with notable gaps, particularly in the context of SSA. ***Table 2*** summarises the existing global studies, explicitly highlighting the absence of research from SSA, thereby reinforcing the novelty and significance of this current study.

Table 2: Global literature on the productivity loss attributed to T2D.

Author/s & study title	Aim/Objective	Target group	Study design/methods	Summary of the findings
Hird et al. (2019). The impact of diabetes on productivity in China [113].	To estimate the impact of T2D on Mortality, years of life lost, and productivity-adjusted life years (PALYs) lost within the population.	Working age (20-49 years in women and 20-59 years in men) until retirement age (50 years for women and 60 years for men).	Life table modelling was used with simulated follow-up of those with T2D in the Chinese population.	Approximately 4.1 million additional deaths are estimated, resulting in the loss of an extra 22.7 million YLL and 75.8 million PALYs. On average, individuals with T2D experienced a loss of 1.3 PALYs, translating to a total GDP loss of Chinese ¥17.4 trillion (US$2.6 trillion). This corresponds to a mean economic impact of ¥307,925 (US$45,959) per person, based on the GDP per full-time worker in 2017.
Magaliano et al. (2018). The productivity burden of diabetes at a population level in Australia [151].	To estimate the lifetime and population impact of T2D on productivity using the novel measure of PALYs lost to T2D.	Working age 20-65 years.	Life table modelling. Simulated follow-up until 69 years	T2D resulted in a 3% decrease in the total years of life lived by the cohort, equivalent to a reduction of 190,219 years. Additionally, T2D led to a reduction of 11.6% and 10.5% in PALYs among men and women, respectively. The most significant impact was observed in the age group of 20-24 years.

American Diabetes Association. (2018). Economic costs of diabetes in the USA in 2017 [155].	To estimate the economic burden of diagnosed T2D by quantifying the additional health resource usage and lost productivity associated with the disease.	The population-level study, using the commercially Insured population data.	The Cost of Diabetes Model employed a prevalence-based methodology that incorporated the demographics of the U.S. population in 2017, T2D prevalence rates, epidemiological data, healthcare costs, and economic data.	In 2017, the estimated cost of diagnosed T2D amounted to US$90 billion in reduced productivity. This economic impact encompasses various indirect costs, including increased absenteeism (US$3.3 billion), diminished on-the-job productivity (US$26.9 billion) within the employed population, productivity loss for individuals not in the labour force (US$2.3 billion), incapacity to perform job duties due to illness-induced disability (US$37.5 billion), and the productivity lost due to 277,000 premature deaths associated with T2D (US$19.9 billion).
Afroz et al. (2020). The impact of diabetes on the productivity and economy of Bangladesh [149].	To estimate the impact of T2D in terms of Mortality, years of life lost (YLL), and PALY loss.	Working age 20-59 years.	A life table model was constructed with the simulated follow-up to 60 years (retirement age).	T2D was responsible for an estimated 813,807 excess deaths, resulting in a loss of 4 million YLL and 9.2 million PALYs. This equates to 0.7 YLL and 1.6 PALYs lost per person. The overall loss in PALYs corresponds to a total GDP impact of US$97.4 billion, equivalent to US$16,987 per person.

Menon et al. (2021). Productivity Benefits of Preventing T2D in Australia: A 10-Year Analysis [153].	To estimate the potential increase in productivity that could result from preventing T2D over the next decade.	Working age 20-69 years over the Period from 2020 to 2029.	Dynamic life table simulation model was constructed by assuming currently expected trends in the incidence of T2D, then repeated assuming the incidence was reduced.	Australians of working age are projected to live a total of 140 million years of life and contribute 87 million PALYs, contributing AUD 18.0 trillion to the country's GDP. A 10% reduction in the incidence of T2D would yield a gain of 2,510 PALYs and AUD 532 million (US$400 million) in GDP.
Tonnies et al. (2021). Productivity-adjusted life years lost due to type 2 diabetes in Germany in 2020 and 2040 [154].	To estimate productive life years lost associated with T2D on the individual and population level in Germany in 2020 and 2040 while accounting for future trends in mortality.	Working age (20-69 years) in Germany in 2020 and 2040.	In estimating PALYs lost, the study aggregated productivity losses arising from surplus mortality and reductions in labour force participation, presenteeism, and absenteeism, contributing to years of productivity loss. The projection utilised input data sourced from meta-analyses, representative population-based studies, and population projections to account for future trends in mortality.	In 2020, individuals with T2D, on average, experienced a loss of 2.6 PALYs compared to those without diabetes. Within this, 0.4 years were attributed to YLL, and 2.3 years were attributed to lost productivity. Women and younger age groups were anticipated to face a more substantial PALY loss than men and older age groups. The study estimated that the 4.6 million people with prevalent T2D in 2020 would collectively lose 12.06 million PALYs (1.62 million due to YLL and 10.44 million due to lost productivity). Looking ahead to 2040, individual-level PALY losses are projected to slightly decrease due to a reduction in YLL. However, the anticipated increase in the number of people with T2D to 5.45 million is expected to elevate population-wide PALY losses to 15.39 million.

The SSA region is home to a billion people, half of whom will be 25 years old by 2050 [75]. The World Bank Economists projected massive human capital gain from investments in young people if efficiently handled [156]. Researchers previously voiced out that, to maximise developmental prospects, countries in the region must focus and invest in alleviating poverty, creating new jobs, and improving education and health [124]. This agreed with the WHO Commission on Macroeconomics and Health, demonstrating the two-way causal relationship between health and economic development [96]. This two-way recognition by WHO stressed health investments to reduce the burden of preventable diseases, stimulate economic growth, and raise a society's ability to invest in public health [152]. Type 2 Diabetes prevalence is notably high in working-age populations, with younger individuals facing a more pronounced burden due to longer disease duration and increased risk of chronic complications [153]. This is because diabetes-related morbidity can lead to reduced workforce participation and productivity, and the younger populations are hindered from performing to their full potential [154, 157]. For instance, diabetes is expected to cost the South African public healthcare system over 35.1 billion South African Rands (ZAR) (equivalent to $2.5 billion) by 2030 [53]. This is merely the financial cost (i.e., direct medical costs), but diabetes complications impose a substantial economic burden on society through lost productivity, premature mortality, and intangible costs in the form of reduced HRQoL [155, 158]. Productivity loss (PALYs) accrued from a combination of premature mortality and morbidity is enormous but unknown to date [59, 119].

One significant factor is that T2D notably reduces workforce participation and productivity, particularly among younger populations. This occurs because the disease's long-term impacts prevent these individuals from achieving their full potential [113]. To date, the published literature addressing the T2D burden is based only on the 'direct' costs of diabetes relating to healthcare expenditure in SSA. It did not incorporate 'indirect' costs, which are diabetes-related productivity losses, particularly lacking evidence from SSA [108].

2.2 Well-Being Burden of Diabetes

Well-being is a multifaceted concept that encompasses the experience of health, happiness, and prosperity, blending mental and physical health for a more comprehensive approach to disease prevention and health promotion [158, 159]. It entails a broad spectrum of life aspects, including an individual's sense of purpose, stress management abilities, and HRQoL[159]. As a conceptual construct, HRQoL involves various dimensions of an individual's life, capturing their perceptions and experiences of physical, emotional, and social well-being [160]. The World Health Organization [161] defines it as a construct that includes cognitive aspects, such as satisfaction with life, and emotional elements, like feelings of happiness. Existing literature describes HRQoL as a complex and multidimensional concept that cannot be shaped by one particular determinant, but rather by multiple determinants including medical predictors (i.e., types and duration of diabetes, treatment routine, level of glycaemic control, and state of complications): demographic predictors (i.e., age, gender, education level) and attitudinal predictors (i.e., self-efficacy, locus of control and social support) [159, 162, 163]. The core domains assessed by HRQoL also feed the WHO's full definition that health is not the absence of disease but the presence of physical, mental, and social well-being [164, 165].

As a multidimensional concept, HRQoL is extensively utilised to assess the influence of health status on one's overall quality of life [166]. It encompasses a wide array of domains relating to health status, including the physical and emotional aspects of well-being and the social facets [167] These include mobility, pain/discomfort, self-care, anxiety/depression, and usual activities domains, with five dimensions and three levels of severity, culminating in 243 unique health states in particular [165, 168]. HRQoL integrates the cognitive dimension of satisfaction, reflecting an individual's appraisal of their life circumstances, and the emotional dimension of happiness, indicating their affective state [162] As detailed by Palamenghi et al. (2020), this comprehensive approach underscores the importance of considering subjective and objective factors in evaluating health outcomes and interventions [167, 168].

Measuring HRQoL often involves interviewing or appraising questionnaires of an individual's self-reported feelings, behaviour, and attitude [169]. However, existing studies that utilised HRQoL measurements in PLWD have revealed lack of homogeneity across studies [169]. Further studies recommended that the HRQoL scores converted into TTO utility scores offer insights into how individuals value their quality of life in relation to the challenges posed by their condition [170, 171]. When used in conjunction with standard HRQoL measures, whether generic or diabetes-specific, TTO scores enrich the assessment by quantifying the trade-offs individuals are willing to make due to the impact of diabetes [171]. This integrated approach offers a more comprehensive view of the HRQoL outcomes for people living with diabetes, capturing their subjective experiences and their valuation of different health states [172].

Diabetes is a demanding disease affecting a person's ability to function and satisfaction, negatively affecting HRQoL [173]. Studies from SSA show that PLWD have a diminished quality of life compared to people with no chronic illness [111, 115] Because they confront a continuous awareness of their condition, markedly affecting their everyday existence [72, 111]. The rigours of managing blood sugar levels, adhering to specialised diets, and maintaining medication schedules disrupt normal routines, resulting in significant psychological and social challenges [29, 174]. Additionally, the ever-present risk of complications triggered by diabetes further restricts individuals' functional abilities and satisfaction in life, adversely impacting their HRQoL [111, 175]. This constant management and the associated health risks differentiate the experiences of PLWD from those without the condition, often leading to a life that diverges from what is considered 'normal [120, 176].

Diabetes-related complications often lead to emotional distress and financial strain, potentially causing patients to experience social isolation due to health-related lifestyle limitations [124]. Subsequently, the HRQoL among PLWD becomes worse as complications begin to coexist [175]. Major diabetes complications, among others that lower the HRQoL, are coronary artery disease, renal failure, blindness, kidney failure, and sexual dysfunction [174]. It is also clear that obesity, hypertension, depression, and arthritis are also common factors that further deteriorate a life of people with diabetes [9, 58, 177]. Amputations of lower limbs are more prevalent in PLWD than in those without, imposing enormous physical disabilities and psychological impacts [65, 174, 178]. Non-traumatic amputations (such as an arm or leg) are also very prevalent among PLWD, accounting for 50% to 70% [179]. Consequently, investigating disease-specific predictors of HRQoL among people with diabetes is crucial for understanding how to effectively manage and mitigate the impacts of the condition on patients' overall well-being [175, 180]. Predictably, numerous demographic and psychosocial factors influence patients' quality of life, and WHO strongly recommends that HRQoL measures be used to guide and evaluate treatment interventions [174, 175, 180].

2.2.1 Predictors of Health-Related Quality of Life (HRQoL)

Health-related quality of Life is associated with several demographic and socio-economic factors [181]. Some of these crucial factors are age, gender, place of residence (urban and rural sites), level of education, marital status, employment status and income, duration of diabetes and comorbidities [168, 169]. Research on HRQoL in people with diabetes has identified a spectrum of predictors that play a crucial role, such as sociodemographic and economic factors, alongside clinical variables like body mass index (BMI [56, 163, 182]. The impact of diabetes on HRQoL is further modulated by lifestyle choices and mental health scores, underlining the interplay between physical health and psychological well-being [94]. Additionally, educational status, comorbidities, and chronic complications are critical in shaping HRQoL outcomes for PLWD [181, 183]. Odili et al. (2008) comprehensively reviewed the conceptual and practical aspects of assessing HRQoL in diabetes [111]. The study summarised the HRQoL domains consist of at least mental health or emotional well-being (i.e., depressive symptoms and positive affect); functional status (i.e., whether a patient can manage a household, use the telephone, or dress independently); social engagement (i.e., involvement with others, engagement in activities); and symptom states (i.e., pain, shortness of breath and fatigue). These domains measure a person's well-being, possibly impaired by diabetes-related diseases [184]. In addition to the above crucial theories, the WHO guidelines for treating T2D highlight that one of the goals is to improve HRQoL in PLWD [161]. In the exploration of HRQoL among people with diabetes, further studies from various regions provided comprehensive insights into the determinants influencing HRQoL.

A Korean study utilized the EuroQol 5D (EQ-5D) and Short Form-36 (SF-36) surveys, employing a linear mixed model for analysis [185]. This research identified significant determinants of HRQoL in 2012, including gender, age, education, BMI, and specific complications like atrial fibrillation and retinopathy. A subsequent Korean study a decade later corroborated these findings [186]. Moving to East China, a study employing the EQ-5D scale further agreed that variables such as age, gender, regional economic development, education level, and marital status played crucial roles in shaping the HRQoL of individuals with diabetes [187]. In Germany, a longitudinal assessment of HRQoL in elderly diabetics, utilising the SF-12 and multiple regression analyses, highlighted insulin therapy, glycated haemoglobin levels, and diabetes-related complications as key predictors of HRQoL over time [188]. Similarly, a cross-sectional investigation in Kuwait, employing the SF-12 and Diabetes Self-Management Questionnaire (DSMQ), revealed that self-management practices, gender, and diabetic complications significantly impacted HRQoL [188]. Although deployed the WHO Quality of Life-BREF, a Saudi Arabian research utilising multilevel linear regression identified gender, age, and educational level as significant determinants of HRQoL [189].

A comprehensive meta-analysis of behavioural interventions in LMICs demonstrated a positive impact on the HRQoL of people with T2D [190]. Despite the limited scope of previous reviews, this analysis, including studies published from 2000 to 2022, indicated moderate evidence that health behaviour interventions significantly enhance HRQoL [190]. Contrarily, a meta-analysis of studies from SSA synthesised HRQoL data and associated factors, reporting that age was significantly associated with negative impacts on various domains of the WHO-QoL-BREF as the duration of living with diabetes increased [191].

Examining HRQoL among PLWD in Nigeria, a study utilising the SF-36 tool found a significant decline, particularly in those with foot ulcers [195]. This emphasized the profound impact that specific diabetes-related complications, such as foot ulcers, can have on patients' quality of life [192]. In Ethiopia, an assessment of HRQoL through the EQ-5D-5L and EQ-VAS instruments, using linear regression, revealed how clinical and medication-related variables influenced HRQoL [192]. Similarly, research from Botswana, gathering sociodemographic and clinical data using a structured questionnaire, identified crucial factors correlating with HRQoL through logistic regression [193]. These findings aligned with the Nigerian study, emphasising the multidimensional impacts on people with diabetes' lives [192].

The outpatient focus of both the Ugandan [194] and South African [192] HRQoL studies provide complementary perspectives on how patient characteristics and medical conditions affect HRQoL in real-world clinical settings. This aligns with the findings from another South African study using data from the Wave 1 Study on global AGEing and adult health (SAGE), which also reported an association between diabetes, lower quality of life, and more significant disability influenced by sociodemographic factors, health behaviours, and comorbidities [180].

The aforementioned studies conducted in various global regions collectively highlight the intricate interplay of medical, demographic, and socio-economic factors in shaping HRQoL among PLWD [195, 196]. Often, appropriate management is used to enhance HRQoL, emphasising the importance of empowering patients with practical self-care strategies to control diabetes and prevent complications [20, 22, 69, 137]. However, most of the studies focused on the impact of demographic variables on HRQoL and thus overlooked the significant role of individuals' perceptions of their health, mental health scores, and self-efficacy [118]. It was documented that almost half of the PLWD frequently face mental health issues, such as anxiety and depression among PLWD, which is a critical factor influencing HRQoL [165, 197].

The co-occurrence of mental health conditions such as anxiety and depression among PLWD significantly impacts HRQoL, necessitating integrating a broad spectrum of predictors in diabetes management plans—encompassing sociodemographic, economic, BMI and lifestyle factors [198]. The SSA systematic review of 2021 uncovered five studies conducted in Ethiopia, four in Nigeria, and two in South Africa pertaining to influencers of HRQoL among PLWD [191]. Additionally, one study per country was found in Botswana, Ghana, Mauritius, Swaziland, and Uganda, respectively. Given the limited diverse and holistic evidence on HRQoL necessary for creating effective interventions to improve HRQoL in SSA, a region grappling with the growing diabetes epidemic, there is a high need for comprehensive research and data synthesis. Particularly, amid the current diabetes epidemic, the available evidence in South Africa lacks holistic and compressive analysis from all domains (i.e., mental health or emotional well-being, demographic predictors, and attitudinal predictors), particularly from the low socio-economic communities. The current research's innovation lies in its comprehensive inclusion of these psychological, mental health, and self-efficacy factors, aspects previously underrepresented in similar studies, thereby providing a more holistic understanding of the determinants of HRQoL in people with diabetes.

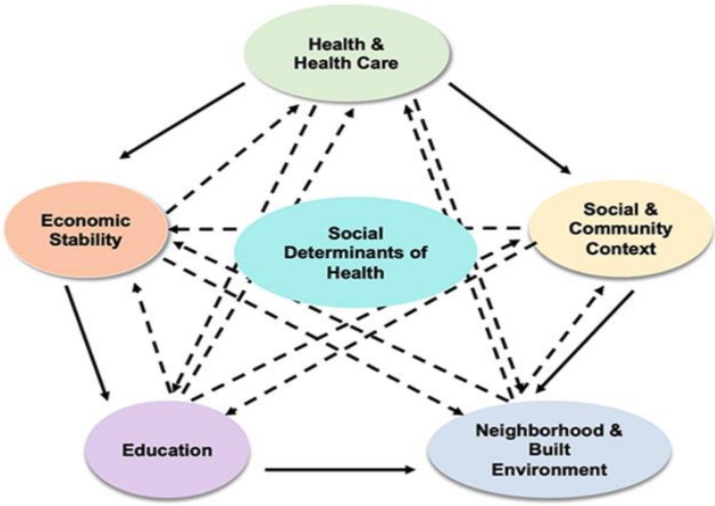
2.3 Social Determinants of Health (SDoH)

Social determinants of health (SDoH) are the conditions in which people are born, grow, live, work, and age in our communities [199]. These circumstances are shaped by the distribution of money, power, and resources, which are mostly responsible for health inequities and unfair and avoidable differences in health status between communities and individuals [199, 200]. The United States Centers for Disease Control and Prevention further characterised SDoH as economic and social situations that influence the health of people and communities [175]. SDoH is also believed to be directly linked to health equity, where there are no remediable differences among groups of people; thus, every person can achieve their best health [201]. Some of the key SDoH include SES, the neighbourhood and physical environment, the food environment, healthcare, social cohesion and social capital [167]. Life-course vulnerability based on the length of time spent living in resource-deprived environments defined by poverty, lack of quality education, or lack of healthcare significantly impacts disparities in diabetes risk, diagnosis, and outcomes [167]. These aspects can be improved by changing relevant policies because these determinants are often a result of unequal social and economic systems. Most LMICs lack such policies to mitigate NCDs, and the SDoH are the primary contributor to unfair and avoidable differences in health status, particularly the increasing risk of disease complications [202].

Healthy People (HP2020 and HP2030) represents a collaborative effort, functioning as a data-driven initiative with a 10-year target period, which is instrumental in guiding health promotion and disease prevention strategies to improve health outcomes across various populations [203]. It focuses on achieving health equity—the highest level of health for all individuals—through collaborative, data-driven approaches [203, 204]. These approaches entail implementing evidence-based policies and interventions that target the SDoH and aim to reduce health disparities [205]. Its Leading Health Indicators (LHIs) are central to the Healthy People initiative[1]—representing a subset of objectives selected for their significance to national health issues and challenges [204]. Leading Health Indicators prioritise upstream measures, such as environmental factors affecting health, and are regularly updated and disseminated by Healthy People [203, 205]. This ongoing data management is intended to fuel public health efforts that address urgent health concerns, thus improving the nation's overall health and well-being [206]. This framework sets five overarching goals for the decade, crucial in directing health promotion and disease prevention strategies [206], presented in ***Figure 1***. The figure shows specific factors of SDoH, such as education, economic stability, social context, living neighbourhood and health and healthcare [207]. Aimed at achieving health equity, creating environments conducive to health, promoting healthy development and engaging leadership and the public in multi-sectoral actions for health improvement [203]. By focusing on high-priority health issues and leveraging upstream measures, the framework aims to stimulate activities that address pressing public health challenges [208]. As such, Healthy People HP2030 represents a comprehensive strategy for enhancing the nation's health, emphasising the importance of addressing SDoH and advancing health equity to tackle existing health disparities [205, 208].

[1] Primarily supported by the U.S. Department of Health and Human Services, along with other federal agencies like the CDC and NIH.

Figure 1: The five domains of social determinants of health (SDOH)



Source: Healthy People 2023 *[207]*

The recent advancements in HP 2030 have been specifically designed to deepen the understanding of SDoH and to develop evidence-based resources and tools that support interventions at state and local levels, as highlighted by the US Department of Health and Human Services [204, 209]. Research has consistently indicated that these social determinants are fundamental in driving inequities in health outcomes, significantly influencing the likelihood of developing diabetes, the effectiveness of diabetes self-management, and the prevalence of related complications [210]. For instance, the diabetes LHI within HP 2030 has shifted its focus from the prevalence of the condition to its incidence, while the LHI for adolescent cigarette smoking has broadened its scope to encompass all forms of tobacco use [210].

2.3.1 Social Determinants of Health and Diabetes

In diabetes, understanding and mitigating the impact of SDoH calls for attention due to disease prevalence, economic costs, and the disproportionate population burden it causes [211, 212, 152]. The American Diabetes Association (ADA) published a scientific statement on socio-ecological determinants of pre-diabetes and diabetes almost a decade ago [213]. There is ongoing progress toward the objective of comprehending and enhancing health prospects for populations with diabetes by tackling SDoH, especially in countries where diabetes prevalence is high [214].

In the context of diabetes management, the HP2030 framework emphasises a holistic approach that addresses both individual and environmental factors influencing health outcomes [209]. This approach focuses on what affects PLWD's access to healthcare, ensuring they have the necessary services for regular monitoring and medication management [215]. It also underscores the importance of addressing the SDoH, such as SES, education, and access to nutritious food, significantly impacting diabetes management and outcomes [216]. By integrating interventions that target these broader determinants along with individual healthcare needs, HP2030 aims to reduce health disparities in diabetes care and improve overall health outcomes for people living with diabetes [215, 216].

Social determinants of health have multidimensional factors that include SES (i.e., education, income, occupation, debt, medical bills), neighbourhood and physical environment (i.e., safety, housing, build environment, toxic environmental exposures), food environment (i.e., food security, food access, food availability), healthcare (access, affordability, availability, quality), social context (i.e., social cohesion, social support, social capital, diabetes knowledge) [78, 200]. These determinants intricately interact to influence health outcomes—lower SES, income, and educational attainment are particularly associated with suboptimal chronic disease self-care management and reduced rates of healthcare utilisation [180, 211]. In addition, studies have suggested that diabetes knowledge, social support and neighbourhood and physical environment play a vital role in the adequacy of healthcare and diabetes self-management among PLWD [78, 205].

2.3.2 Social Determinants of Diabetes Self-Care Management and Adherence

The WHO labels diabetes self-management and adherence as pivotal in effectively treating diabetes [217]. Diabetes self-care management, measured using the scale based on the summary of the diabetes self-care activities scale [180], which is adherence to the self-management regimen, encompasses diet, medication, and exercise, is connected to periodontal well-being in PLWD [218]. The Diabetes Self-Care Activities Scale (DSCAS) score is derived by summing the frequency of self-care activities reported over the past week in key self-management regimens [218]. Each area's total score is obtained by adding the number of days the participant engaged in specific activities, providing a quantitative measure of their diabetes self-management [219].

A study by Vest et al. (2013) [220] targeting a low-income urban population in Buffalo, New York, revealed that access to social capital was pivotal in bolstering self-efficacy in diabetes self-management. The same study revealed that social support networks, the doctor-patient relationship, and the patient-healthcare system relationship were crucial in facilitating or impeding successful self-management. Patients' low-income status, inadequate insurance, and mistrust in the medical system emerged as barriers to effective management, suggesting that leveraging social capital from multiple spheres could enhance diabetes care [220].

A study by Tinoco et al. (2020) [221] in Mexico City, a multicomponent integrated care program for diabetes care, revealed the significant role of social and other health determinants in managing T2D. The study's before-and-after design showcased the program's effectiveness in improving glycemic control and health-related quality of life. Education level, baseline diabetes knowledge, and self-care scores were significant predictors of glycemic control improvement [221].

A study in Ethiopia by Gurmu et al. (2018) [222] focusing on adult diabetes patients in public hospitals, identified several factors associated with self-care guidelines. This cross-sectional study involving PLWD reported that higher diabetes knowledge, self-efficacy, and social support were pivotal in predicting good self-care guidelines [222]. Another study by Timm et al. (2020) [223] encompassing rural Uganda, urban South Africa, and disadvantaged suburbs in Sweden, assessed self-management determinants from an implementation perspective. Data from interviews, focus group discussions, and observations suggested that patient-provider interactions, health service delivery, and community initiatives could facilitate self-management.

A study by Stephani et al. (2018) [224] in SSA reviewed self-management behaviours among individuals with type 2 diabetes, pointing out a concerning trend of poor self-management. The analysis of 43 studies underscored the rarity of self-monitoring glucose levels, low physical activity frequency, and moderate adherence to dietary and medication recommendations [224]. Notably, economic instability significantly impedes practical diabetes self-care management and adherence [212, 225]. Limited financial resources can restrict access to healthcare, essential medications, and monitoring equipment, leading to poor blood glucose control [226]. Additionally, the high cost of nutritious foods often forces those with economic constraints to opt for less healthy options, adversely affecting diabetes management [226]. Consequently, individuals facing economic challenges may deprioritise long-term diabetes care due to immediate financial needs, exacerbating self-care management difficulties [104]. As a result, psychological stress induced by financial hardship may further deteriorate health behaviours and medication adherence [227].

Educational programs tailored for diabetes self-management have been shown to significantly enhance knowledge, self-care behaviours, and self-efficacy. These programs emphasise fundamental self-care activities such as balanced eating, physical exercise, medication adherence, foot care, and psychological adjustment [228]. However, the effectiveness of these programs varies significantly across different economic contexts. In high-income countries, where resources and infrastructure are more robust, educational interventions substantially improve diabetes self-management and outcomes. Conversely, in low-income settings, the efficacy of these programs is often restricted by limitations in infrastructure and resource availability.

Additionally, demographic influences on adherence to diabetes health education have been observed, with females exhibiting higher adherence rates than their male counterparts [211, 224]. The fear of hypoglycaemia also significantly affects adherence, highlighting the importance of incorporating psychological considerations into self-management strategies [229]. Support from friends and family can positively impact diabetes self-care behaviours, such as timely glucose check-ups, increased physical activity, and dietary control [229].

Further research from developed countries provides evidence about the crucial determinants of diabetes self-management and healthcare access, highlighting an unequal distribution of these predictors based on location, specifically between urban and rural areas [211]. Such predictors impacting self-care management and healthcare usage further impact glycaemic control and blood pressure to varying degrees [163, 230]. Despite the physician's recommendation that PLWD engage in diabetes-related self-care, which is critical to successfully managing the disease and attending routine and more frequent medical visits with physicians [59, 124, 155].

Although a focus on SDoH remains high on the health agenda globally, South Africa, where diabetes is one of the leading causes of death, has little evidence regarding SDoH in relation to the diabetes burden [231]. This exemplifies stark social inequities, which translate into a high burden of premature mortality and marked health inequities among PLWD in the country [232]. The government's dedication to prioritising PHC with an emphasis on SDoH was formally ratified in the Health Act (61 of 2003) [233]. Nonetheless, implementing these initiatives has encountered substantial challenges, primarily due to diverse stakeholders' lack of political and policy commitments [234, 235]. Addressing these social determinants is believed to be a cornerstone of the NDoH's PHC Re-engineering Strategy [114, 233].

More research has been recommended to characterise better the direct impact of SDoH on health outcomes in diabetes, particularly among adults from low socioeconomic settings in treatment [211, 230]. Diabetes care, including taking a frequent dose of medications and fulfilling therapeutic recommendations, is complex, and contributing factors extend beyond objectively measured financial resources [111, 236]. Particularly, unaffordability is one of the primary reasons why patients fail to adhere to therapeutic recommendations, and this burden is especially concerning among PLWD from disadvantaged backgrounds [41, 237]. To mitigate the current soaring costs and the increased prevalence of diabetes, there is an urgent need to establish a better understanding of the factors that influence health behaviours among PLWD in South Africa. The incumbent will add to the literature by assessing some of these SDoH factors affecting PLWD to provide researchers and public health professionals with better aid for individuals with diabetes to acquire the best health outcomes in South Africa.

2.4 Conclusion and Research Gaps

Considering the structured literature review presented, it is apparent that there are substantial research gaps concerning diabetes prevention measures and the disease burden, particularly among low-income communities. These gaps underscore the need for targeted studies that address the socioeconomic disparities in diabetes care and outcomes. Furthermore, there is a lack of comprehensive data on the effectiveness of community-based interventions and their long-term impact on reducing the incidence of diabetes. Questions remain unanswered regarding the optimal integration of prevention strategies into existing healthcare frameworks in a cost-effective and culturally sensitive manner. Additional research is necessary to fully understand the complex interplay between diabetes management and social determinants of health and how these factors collectively influence the sustainability of health improvements within economically disadvantaged populations.

In light of the identified knowledge gaps, this research aims to assess whether SDoH influences self-care and/or adherence, what the predictors of HRQoL are, how much it costs to manage

T2D in SSA and whether it is cost-effective as well as the productivity burden of T2D in PLWD and the South African Economy (in terms of GDP).

3. Chapter Three: Costs and Cost-Effectiveness of Type 2 Diabetes Management in Sub-Saharan Africa: A Systematic Review

3.1 Context of the Study

This chapter includes a systematic review that forms the primary focus of this project. It comprehensively examines the costs and cost-effectiveness of T2D management in SSA. This review synthesises findings from prior studies, highlighting existing gaps and offering recommendations for accurately assessing the financial burden of T2D management in SSA. The analysis encompassed patient-level costs, healthcare expenditures, and resource utilisation in T2D management. The systematic search was conducted across multiple databases, including PubMed-Medline, Africa Wide Information, Web of Science, Cochrane Library, CINHAL, and Scopus, focusing on studies conducted in SSA in both English and French.

The review uncovered substantial direct annual costs, with a notable concentration of studies from Nigeria. Prior to this review, there was a lack of synthesised evidence on the costs and effectiveness of managing T2D in SSA. Furthermore, the review identified a predominant use of the healthcare system perspective in SSA studies, primarily relying on cross-sectional facility-level data and healthcare provision for cost-related information. Most of these studies employed a total medical cost approach, capturing a significant portion of the costs of PLWD.

A critical methodological challenge identified was the perspective of the study. More than half of the reviewed studies adopted a provider perspective, leading to a potential underestimation of the total societal costs associated with T2D management. Only a few studies addressed costs from a societal perspective, highlighting a significant gap in the literature. Additionally, the review found that cost-effectiveness studies of T2D interventions in SSA exhibited considerable methodological differences and limitations. This review seeks to consolidate information on the costs associated with T2D in SSA and to identify methodological gaps in the existing research.

The systematic review reveals significant direct and indirect costs associated with Type 2 Diabetes management in Sub-Saharan Africa, emphasising the economic impact of insufficient cost-effective strategies. These findings underscore the necessity of incorporating productivity loss metrics into economic evaluations. By showing that existing studies often neglect broader economic impacts, such as increased absenteeism and reduced work capacity, the review justifies the thesis objective to integrate productivity assessments, providing a fuller picture of diabetes' economic burden.

The review identifies a critical gap in cost-effectiveness studies of Type 2 Diabetes management: the neglect of Social Determinants of Health (SDoH) that significantly influence outcomes and costs. This oversight highlights the need for interventions that are both medically effective and culturally and contextually tailored, which can improve adherence and quality of life. By linking these findings to the thesis objective to explore SDoH impacts, the review supports the development of more comprehensive and effective diabetes management strategies in Sub-Saharan Africa.

This manuscript was submitted to Health Economics Reviews. It fulfils the objective 1.) To systematically review the costs and cost-effectiveness of type 2 diabetes management in sub-Saharan Africa. It is presented in the format it has been submitted for this thesis. Assegid Hellebo is the first author, with supervisory input from Andre Pascal Kengne and Olufunke Alaba.

3.2 Abstract

Background: Type 2 Diabetes (T2D) is rapidly increasing in Sub-Saharan Africa (SSA), with related health and financial implications. Knowledge of the costs and cost-effectiveness of managing diabetes is needed to increase awareness, improve resource allocation and enhance the use of evidence-based decision-making. Accordingly, this study sought to synthesise and critically review evidence on the costs and cost-effectiveness of managing T2D in Sub-Saharan Africa (SSA).

Methods: Multiple databases, including PubMed-Medline, Africa Wide Information, Web of Science, Cochrane Library, Africa-wide Information, CINHAL, Scopus, and Google Scholar, were published between January 2010 and December 2022. Costs were reported in 2023 United States dollars (US$), and inflation and exchange rates were accounted for. PROSPERO registration number- CRD42022300580.

Results: The search yielded 4137 unique abstracts, and 19 studies were included for review, most originating from Nigeria. Most studies assessed costs from the provider perspective

(direct and outpatient costs) and reported T2D costs as enormous in SSA. The annual cost ranges from US$337.50 for basic medical care of uncomplicated T2D to US$2330.74 total provider cost per patient. The highest burden was among individuals in the low-income quantile. Only five dealt with the cost-effectiveness aspect of economic evaluation, with most being modelling and simulation studies. T2D management programs can be cost-effective, but the evidence is not definitive.

Conclusions: This review identified a significant variation and heterogeneity in T2D cost studies in SSA, emphasising a need for standardisation and addressing data collection challenges for improved analysis. The existing cost-effectiveness evidence is limited and inconclusive. Rigorous studies are needed in SSA to assist decision-makers in setting priorities and allocating resources for T2D management.

3.3 Introduction

Diabetes mellitus is a leading public health challenge worldwide (1,2). Once regarded as a disease of affluence, it has become a significant and growing health challenge in low- and middle-income countries (LMICs) (3,4). The term diabetes was new and rarely mentioned by public health experts in the African region in the 1980s and 1990s. However, in 2021, it was one of the leading causes of non-communicable disease (NCD) deaths, contributing to 416,000 deaths in sub-Saharan Africa (SSA) (3). An astonishingly high number of diabetes-related deaths occurs among economically productive adults below the age of 60 years (4,5). The International Diabetes Federation (IDF) estimates that the number of individuals living with diabetes in the SSA region will be 55 million in 2045 from 24 million in 2021 (5).

Around 60% of individuals with diabetes in SSA remain undiagnosed, making it a notable characteristic of the disease in the region (6), underscoring the need for improved screening and diagnostic efforts to ensure timely detection and proper management. Among the countries located in SSA, more than 50% of working-age adults with diabetes live in South Africa, Nigeria, the Democratic Republic of Congo, and the Federal Republic of Ethiopia, which are the region's most prominent countries (5,7). The increase in diabetes figures and linked morbidities and mortality impose an immense financial burden on households, healthcare systems and the states (7,8). According to the IDF, the SSA region's healthcare expenditure due to diabetes was 3.4 billion in 2015 and is estimated to reach 5.5 billion in 2040 (3,5).

Diabetes is potentially preventable; appropriate management can halt or delay related complications. Diabetes is a notorious disease, difficult to control, with only 50% of the patients reaching their treatment goals (11,12). To curb the reported low self-management, individual patient-level, clinician, or organisation-targeted interventions are recommended to improve care delivery, check-up rates and glycaemic management among PLWD (5,11,12). The World Health Organisation (WHO) guidelines recommend managing the disease at its early stage (13). Such management often involves an improved diet, taking medications and monitoring blood glucose. The intended primary outcome is to manage blood glucose levels and reduce risk factors levels, including body mass index (BMI) and blood pressure (BP), to avoid further complications and early death (11,12,13).

Managing T2D often carries a high burden of direct (medical and non-medical) and indirect costs. Costs are resources incurred by providing or attaining healthcare goods and services to maintain or implement a person or population health programme (14). The direct medical costs include hospital stays, laboratory tests, and doctor visits. At the same time, non-medical costs also include travel for treatment and care for loved ones taking care of the patient (15). The indirect costs include lost productivity for the people involved in the patient's care and work absenteeism (16,17). On the other hand, cost-effectiveness is one branch of economic evaluation that examines the costs and health outcomes of one or more interventions (15,16). While comparing two interventions/programmes, intervention/programme 'A' is considered cost-effective if the cost per unit effectiveness for 'A' is less than that of intervention/programme 'B'. The cost-effectiveness of interventions may also be measured using a threshold or benchmark of a region/country per the gross domestic product (GDP) per capita (16). Numerous past studies have used the cost-effectiveness thresholds established by the Commission on Macroeconomics and Health (16). This is the cost per averted disability-adjusted life years (DALY) of less than three and less than one times the country's GDP per capita for cost-effective and highly cost-effective interventions, respectively (16, 17). Such health outcomes are measured through a difference in the quality of life (QoL), DALYs, quality-adjusted life years (QALYs) and return on investment (ROI) (17, 23).

T2D demands continuous clinical care and management, which consumes significant healthcare resources (23, 26). For a region where resources are constrained, and health financing heavily depends on out-of-pocket payments, the authorities battle with the costs of managing diabetes (8). Therefore, conducting economic evaluation research in SSA is crucial to raising awareness and potentially improving resource allocations. Thus, this study aimed to synthesise available evidence on the costs and cost-effectiveness of managing T2D and its complications in SSA. This systematic review was conducted to (i) provide costs of T2D management in SSA and (ii) assess whether lifestyle interventions for T2D management are cost-effective in SSA or not. PROSPERO registration number- CRD42022300580.

3.4 Materials and Methods

3.4.1 Searches and Search Strategies

The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guided the literature search for this study (18) in the following databases: Medline via PubMed, Africa Wide Information, Web of Science, Cochrane Library, Africa Wide Information, CINHAL, Scopus, and Google Scholar. Key terminologies were carefully chosen to acquire all the pertinent information, which an experienced university librarian verified. Searches were conducted between December 2022 and March 2023. The search terminologies and strategies were based on the study's target population, interventions, control and outcomes (PICOS). A summary of the search strategies, including the search terms is found in ***Appendix 1***.

3.4.2 Inclusion Criteria

When undertaking the literature review, PICOS was used to guide eligibility criteria, where the relevant elements were used to decide on the inclusion and exclusion measures (18). Searches were restricted to English and French language literature; all the search results were imported from all the databases and merged them. Duplicates were removed using Rayyan software (47). The abstracts were screened if it was unclear whether the study was relevant to the research question based on the study title alone. The last step involved examining the eligibility of the studies by reviewing them to decide if the inclusion criteria were satisfied. The first author drafted the review, which was further reviewed and examined by an independent reviewer, with a third consulted when there was a lack of consensus regarding the inclusion/exclusion of the studies.

Studies were included that covered at least one African nation, offered original research findings on T2D costs and cost-effectiveness, and were published in peer-reviewed journals.

They were included if the participants/population consisted of PLWD and/or their caregivers. Because this is the most generic form of diabetes affecting SSA, and it is highly prevalent owing to high rates of obesity and rapid urbanisation (10,19). Given the high prevalence, it was sought that it is suitable to compare the costs and cost-effectiveness of managing T2D, providing and receiving usual care or taking part in other interventions.

The study outcomes were the cost-effectiveness of T2D interventions and their consecutive study designs. Incremental costs per unit of benefits assessed the effectiveness of the intervention. Some of the units of benefits consisted of the cost of an intervention per QALYs, improved health-related quality of life (HRQoL), and DALYs.

3.4.3 Exclusion Criteria

The following studies were excluded based on predetermined criteria: studies unrelated to T2D management, qualitative studies or reviews, studies with incomplete or insufficient data on costs or cost-effectiveness, duplicate or overlapping studies, grey literature, academic theses, studies with full context not located and studies conducted outside of SSA.

3.4.4 Data Extraction

The latest Cochrane Handbook guided data extraction for systematic reviews of interventions (20). Using an Excel spreadsheet, essential information from each study, including population size, characteristics of the participants, data collection methods, study perspective, study country, duration of the intervention, active and maintenance phases, details of intervention procedures, glycated haemoglobin (HbA1c), blood pressure (BP) outcomes and outcome measurements (QALYs, DALYs) were extracted.

Costs were adjusted for inflation if the study was undertaken before the year 2023. The exchange rates were then applied when the cost studies for which the exchange rate for the United States Dollar ($) was not reported at the time of costing. At the same time, the average exchange rate was used for the costing period based on the Forex (FX) currency converter [22] for studies in which the exchange rates were not reported. The local currencies were converted into United States dollars ($). Costs were further converted in their original costing year and local currency to 1$ after being first adjusted for inflation to generate costs in 2023. When a research study was done over two years, from November 2009 to January 2010, the costing year was presumptively treated as the year the study ended (i.e., 2010).

This systematic review consisted of narrative synthesis evidence based on the following frameworks. (I) how the intervention/programme functions, why and whom it was intended for, (II) synthesising the outcomes of the relevant and included studies, and (III) ascertaining links among and between them.

3.5 Results

3.5.1 Results of the Search

A total of 4137 unique abstracts were screened, and 19 studies were included: 14 studies investigated the cost of T2D management, and five performed cost-effectiveness analysis (CEA), as illustrated in ***Figure 2***. Out of 19 studies, 12 were from the provider's perspective, while five were undertaken from the patient's perspective. A further detailed summary of the methods used, costs and cost-effectiveness outcomes of the included studies are outlined in ***Table 1***.

Figure 2: PRISMA flow chart of the search strategy and study selection process.

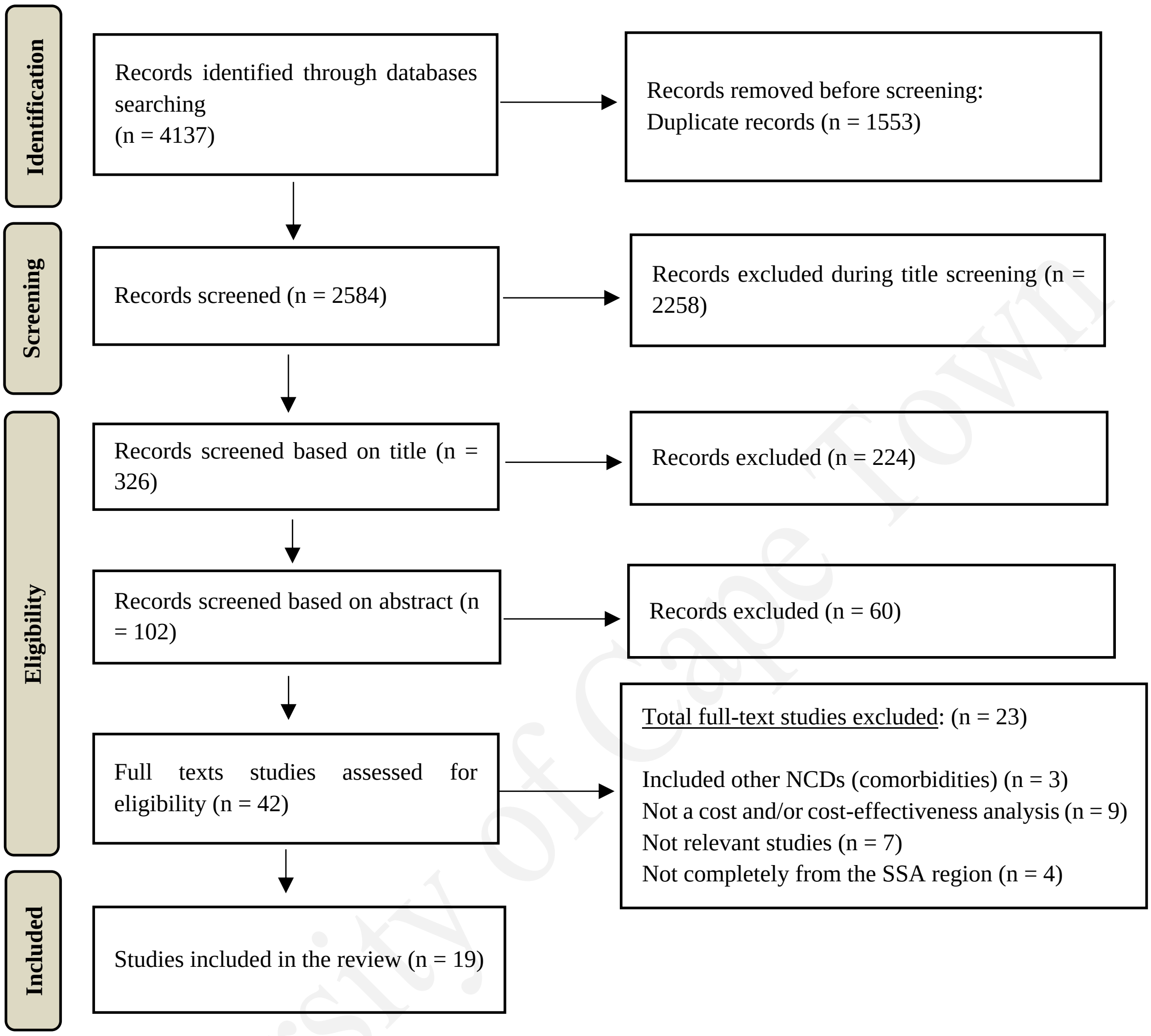


Table 1: Summary of the methods used, costs and cost-effectiveness outcomes of the included (n=19) studies.

Author/s and Year	Country	Study design and/or study method	Target population and/or sample size	Duration/ analytical time horizon	Comparator	Intervention type and/or cost items	Intervention effectiveness outcome/s	Perspective	Cost in 2023 US$ and unit of cost	ICER, $/QALYs or unit cost (in 2023 US$)
Abduganiyu & Fola (*2014*) [23]	Nigeria	Retrospective review of sampled 120 case notes. Cost of illness computation	T2D patients attended the University Teaching Hospital (UMTH) clinic (n=96)	One year	None	The direct cost of T2D management	Not reported	Provider	US$799.24 per annum/patient	Not reported
		Cost analysis to determine which antidiabetic option is a lower-cost choice.	(n=1200)	One year	Branded (innovator products that were considered generic) and the equivalent used	Mean cost per defined daily dosage (DDD) antidiabetic therapy in a tertiary healthcare institution	Not reported	Patients	0.32 per generic DDD vs. US$0.50 per branded DDD	Not reported
Abide et al. (2013) [24]	Nigeria	A randomised controlled study, activity-based costing	T2D patients who were on hypoglycaemic therapy (n= 220)	One year	Usual care	Pharmaceutical care	Not reported	Patients	Not reported	US$742/annum per QALY gained
Fadare et al. (2015) [25]	Nigeria	A cross-sectional study carried out using the eight-item Morisky Medication Adherence Scale (MMAS-8)	T2D patients who had been on medication for at least six months attending the medical outpatients' diabetes clinic (n=129)	Three months	None	Assessing direct cost and the level of adherence to antidiabetic drugs among outpatients in a teaching hospital	Not reported	Patients	US$55.35 per month/patient	Not reported

Ipingbemi & Erhun (2015) [26]	Nigeria	Retrospective study using case files	T2D patients attending secondary healthcare facility (n=52)	One year	None	Direct and indirect costs of diabetes	Not reported	Patients	US$508.37 per annum/patient	Not reported
Ipingbemi et al (2021) [27]	Nigeria	A quasi-experimental study	T2D patients attending the endocrinology outpatient clinics in two-tertiary facilities (n=201)	One year	The control group continued to receive the usual care	The direct cost of disease management is for pharmacist-led educational intervention to resolve adherence discrepancies.	Significant reduction in the HbA1c and systolic blood pressure as well as improvement in weekly physical activity	Patients	US$333.0 ± US$118.4 per annum/patient	Not reported
Okoronkwo et al. (2015) [28]	Nigeria	Cross-sectional descriptive survey	T2D patients aged between 31 and 65 years managed at a tertiary health institution (n=308)	One year	None	Direct cost borne by patients	Not reported	Patients	US$502.63 per annum/patient	Not reported
Suleiman and Oloyede (2005) [29]	Nigeria	Retrospective, random selection. Cost of illness	Patients with type 2 diabetes (n=33)	One year	None	Direct outpatient costs	Not reported	Provider	US$477.52 per annum/patient	Not reported
Alouki et al. (2017) [30]	Mali	Cross-sectional study participants were randomly selected from registries.	T2D patients attending three public hospitals, pharmacies, private clinics and private pharmacies (n=500)	One year	Costs for basic medical care of uncomplicated diabetes	Costs for basic medical care of complicated chronic diabetes	Not reported	Patients	Median annual expenditure is US$337.5 per patient with complications while US$249.2 without complications.	Not reported
Bermudez-Tamayo et al. (2017) [31]	Mali	Observational retrospective case-control	Randomly selected participants from diabetes registries (n=500)	Three months	Those with no diabetes (n=500)	Direct and indirect costs (productivity losses by patients and caregivers and absenteeism)	Not reported	Societal	US$346.01 for three months/patient	Not reported

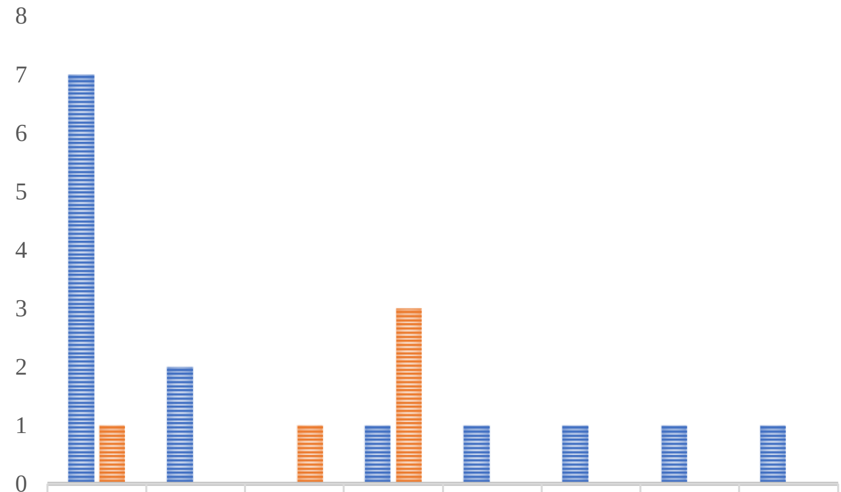
Masis et al. (2022) [32]	Kenya	A retrospective cost analysis combining micro- and gross costings	Uncomplicated T2D patients (n=331)	One year	None	Direct and indirect medical costs of outpatient treatment	Not reported	Provider	US$46.86/ (visit consultation, RBS test, HbA1c test and the annual pharmacotherapy regimens)	Not reported
Obakiro et al. (2021) [33]	Uganda	Retrospective, cross-sectional	Diabetes patients attending the outpatient medical clinic (n=2612)	One year	None	Outpatient medical clinic costs	Not reported	Patients	US$12.59 Cost/patient/prescription	Not reported
Quaye et al. (2015) [34]	Ghana	Descriptive cross-sectional, random selection	Patients with type 2 diabetes (n=304)	One year	None	Case management carried out in clinics	Not reported	Provider	US$498.40 per annum/patient	Not reported
Wargny et al. (2018) [35]	Senegal	A controlled open clinical trial with a randomised time allocation of the intervention	People with T2D accessing mDiabetes programme residing in northwest and south of Dakar centres (n=186)	Six months	None	Sending daily Short Message Service (SMS) for three months	HbAc1 decreased over the three months after having stopped in both centres	Provider	US$3.80 per 3 months/campaign patients	Not reported
Erzae et al. (2019) [36]	South Africa	Bottom-up (person-based) using cost of illness (COI) approach	T2D patients who were diagnosed, treated and controlled in 2018 (n=55,000)	One year	Estimated direct medical costs for basic chronic treatment	Actual expenditures of diabetic patients	Not reported	Provider	US$986.6 per annum/patient	Not reported
Opperman & De Klerk (2021) [37]	South Africa	Retrospective Review	T2D patients served by medical schemes (n= 2111)	Two years	None	Total cost of diabetes (direct and indirect)	Not reported	Provider	US$2330.74 per annum/patient	Not reported

Bekele et al. (2021) [38]	Ethiopia	Markov model for T2DM disease progression with five health states	Population with controlled T2D with one of the second-line treatments (hypothetical age above 40, lifetime)	One year	Only metformin	Saxagliptin plus glibenclamide as a second-line therapy added to metformin	Metformin was more costly and less effective than metformin plus glibenclamide	Provider	US$367/unit cost/annum/patient	US$2727/DALY Averted
Juarez -Garcia et al. (2012) [39]	South Africa	Lifetime simulation model	Patients with T2D (n=585)	One year	Sulphonylureas plus Metformin	Saxagliptin plus Metformin	Low incidence of hypoglycaemia and reduction in complications in cohort in intervention	Provider	Not reported	US$6294.13/ QALY gained. Per patient per lifetime
Mash et al. (2015) [40]	South Africa	A randomised controlled trial. Markov micro-simulation model	Uninsured people with T2D attending 17 selected community health centers in Cape Town metropolitan area (n=710)	One year	No intervention (n=860)	Group education program	Reduction of blood pressure (systolic by 4.65 mmHg & diastolic by 3.30/mmHg	Provider	Not reported	US$2363.40/ICER/ QALY gained
Volmink et al. (2014) [41]	South Africa	Probabilistic modelling utilised for incremental cost-effectiveness ratio analysis	Secondary data used in the model design with total participants (n=8176)	One year	Public sector practice clinical model based on the 2002 SEMDSA guidelines	CEA adapting a private sector diabetes management programme to the public sector	Not reported	Provider	Annual per capita cost of the intervention model was US$932.42, while the comparator was US$774.23, a cost increase of 20.3%	US$1309.25/ICER/ QALY gained

3.5.2 Characteristics of Included Studies

The number of publications and the importance of diabetes management increased over time, with 18 out of the 19 (95%) studies undertaken in recent years (2013-2022). However, only one study from Nigeria, which assessed the cost of illness from patients' perspective, was older than a decade, 2005 (39) (***Figures 3***).

Figure 2: Number of T2D costs and cost-effectiveness studies by country in SSA.



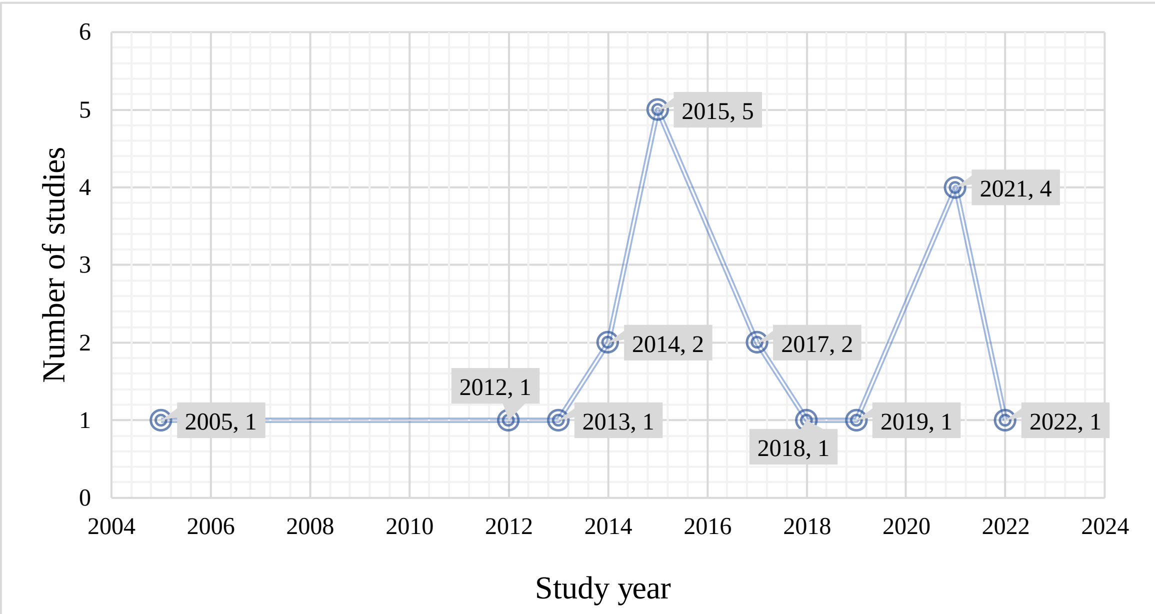
	Nigeria	Mali	Ethiopia	South Africa	Kenya	Uganda	Ghana	Senegal
Cost Analysis	7	2		1	1	1	1	1
Cost-effectiveness Analysis	1		1	3				

The systematic review included various study designs, such as retrospective reviews of case notes, cost analysis, randomised controlled studies, cross-sectional studies, Markov models, bottom-up approaches, quasi-experimental studies, and lifetime simulation models. The studies aimed to assess the cost of illness, determine cost-effective options, evaluate disease progression, measure medication adherence, and analyse cost-effectiveness ratios.

The study population included patients attending specific clinics, registered patients, patients on particular therapies, patients from public and private healthcare facilities (outpatient and inpatient), patients with controlled diabetes, uninsured individuals, patients with uncomplicated diabetes, and patients managed by medical schemes.

The sample sizes range from 33 to 55,000 participants with a median sample size of 605, and in some cases, secondary data with a total of 8,176 participants were used for modelling purposes. Some included studies did not report sex and age proportions, while the modelling and simulation studies assessed the lifetime burden. The proportion of women in the included studies was 68.6%, with a mean age of 27 years, while it was 30 for male participants. Out of 46 countries found in the SSA region, this topic was only researched in eight countries, which are Nigeria [8], South Africa [4], Mali [2], Ghana [1], Senegal [1], Ethiopia [1], Kenya [1], and Uganda [1] (***Figure 4***).

Figure 3: Number of T2D costs and cost-effectiveness studies by year of publication in SSA.



While 15 studies specifically discussed the cost of T2D, only five out of the 19 studies performed cost-effectiveness analysis, with an outcome indicator being QALYs gained and DALYs averted. Health priority areas were often from the provider's perspective [n=13 studies], followed by patients' perspectives [n=7], and societal level [n=1] costing research. Most cost studies evaluated activities related to direct and indirect medical costs, outpatient medical costs, and referral case management of T2D. The cost-effectiveness of saxagliptin plus metformin and saxagliptin plus glibenclamide as a second-line therapy added to metformin and group education program intervention were assessed in Ethiopia and South Africa, respectively (27, 32, 33). One study assessed the cost-effectiveness of pharmaceutical care intervention versus usual care (UC) in managing T2D in Nigeria (24).

3.5.3 Cost Outcomes

Most provider perspective studies costed the direct annual cost to T2D management (23, 29, 34, 36, 37, 38), with two studies investigating the direct and indirect cost of T2D management in SSA (26, 32). A study conducted at a clinic in Nigeria illuminated the financial landscape, revealing an annual direct cost of T2D management at a substantial US$799.24 per patient per annum (23). In the same study, medications and diagnostic/monitoring tests accounted for 80% of the financial cost. Similarly, a cross-sectional study in Ghana unveiled an average annual cost of US$498.40 per patient per annum for case management interventions, with the cost of medications accounting for 71% of the financial cost (34). South Africa further contributed to this discourse, estimating direct medical costs for controlled T2D patients at US$986.6 annually for direct medical costs for essential chronic treatment (36), while another study focusing on people with T2D served by medical schemes reported an even higher average annual cost per patient, amounting to US$2330.74 (37). In Nigeria, the direct cost of controlled T2D management was US$477.52 per annum per patient (29), while it was US$367 in Ethiopia (38). A retrospective assessment of patients attending a secondary healthcare facility explored both direct and indirect diabetes costs and reported an annual cost of US$508.37 per patient in Nigeria (26). However, a study that used a similar perspective from Kenya among patients with uncontrolled T2D reported US$46.86 per visit, which included consultation, different tests, and annual pharmacotherapy regimens (32).

There were noticeable financial burden differences among the three studies that undertook the patient perspective cost of T2D management. In Nigeria, patients paid a substantial direct cost burden of $502.63 per annum (28), while in Mali, annual costs range from US$249.2 for uncomplicated diabetes to $337.5 for complicated chronic diabetes care (30). Overall, in the pharmacist lead educational interventions group, the mean direct costs of T2D management per patient increased from US$221 to US$225 (6-month post-baseline), a total of 446 per annum (27). These interventions aimed to resolve adherence discrepancies and enhance physical activity, ultimately reducing HbA1c and systolic blood pressure. In contrast, Mali's approach focused on comparing costs based on the presence of complications, emphasising the financial challenges that arise when diabetes-related health issues escalate.

Four studies reported the cost of programmes and interventions to improve T2D management (23,25, 33, 36). Across Senegal, Nigeria, and Uganda, various diabetes care programs and cost analyses provided insights into the effectiveness of interventions and the financial burdens on patients. In Senegal, the mDiabetes program employing short message services (SMS) messages demonstrated a cost-effective means of reducing HbA1c over three months at US$3.80 per patient (36). In Nigeria, a patient-focused cost analysis at a clinic showcased the economic advantage of generic antidiabetic medications, saving US$0.32 per daily dosage compared to branded options (23). Nigeria's teaching hospital also reported a monthly direct cost of US$55.35 per patient for outpatient diabetes care, emphasising the financial implications for patients (25). Conversely, Uganda’s retrospective study revealed a significant financial strain, with individuals incurring US$12.60 per visit for outpatient clinic care (33).

Two societal perspective studies from Mali assessed the T2D management costs (30, 31). One study reported that the median direct costs for primary medical care among individuals with uncomplicated diabetes amount to US$249.2 per patient, while those with chronic complicated diabetes bear a higher burden at US$337.5 per patient (30). Another study in the same country reported an average cost of US$1384 annually, encompassing both direct and indirect perspectives (31). In the cost analysis, direct medical costs encompassed various healthcare services like inpatient stays, doctor visits, laboratory tests, and medications. Direct non-medical costs included travel expenses for treatment and caregivers' payments. Indirect costs accounted for productivity losses due to patients' and caregivers' inability to work and absenteeism (31). Including direct non-medical costs, inpatient costs, and lost productivity due to patients' and caregivers' inability to work and absenteeism significantly increases the overall T2D management costs, highlighting the substantial financial burden (31). Furthermore, a societal perspective study shed light on patients' significant financial and economic challenges and broader societal implications.

3.5.4 Cost-effectiveness Outcomes

Five studies assessed the cost-effectiveness of T2D in terms of cost incurred per QALYs gained or DALYs averted (24, 38, 39, 40, 41). Activity-based costing study that used an acceptability curve for cost-effectiveness and reported that the pharmaceutical care intervention was more cost-effective than usual T2D care per patient annually in Nigeria, with a cost (US$742/QALY gained) threshold (24). A structured group education program performed in South Africa by mid-level trained healthcare workers at community health centres for T2D management was reported as cost-effective (US$2363.40/ICER/QALY gained) from the provider perspective (40). In addition, using secondary data, another study reported that adopting a private sector (capitation intervention group) T2D management programme to the South African public sector was also cost-effective (US$1309.25/ICER/QALY gained) (41). This probabilistic modelling with an ICER/QALY gained significantly below the Willingness-to-Pay threshold in South Africa (41). A life simulation study over a patient's lifetime projected the cost-effectiveness of adding saxagliptin to metformin as a second-line therapy and reported potential improvements in QALYs at an extra cost of US$6294/QALY gained per lifetime in South Africa (39). However, saxagliptin was not deemed cost-effective, costing US$2727/DALY averted as a second-line therapy for inadequately controlled T2D alongside metformin monotherapy, considering Ethiopia's GDP per capita per DALY averted threshold (US$953) based on the recommended cost-effectiveness threshold of 50% of the country's per capita GDP for DALY averted and willingness-to-pay (38). This study found that using metformin in isolation incurred higher costs and yielded inferior outcomes than using metformin and glibenclamide (38).

3.6 Discussion

This systematic review identified 19 peer-reviewed studies published until March 2023, with information on cost and cost-effectiveness outcomes related to managing T2D, which yielded several key findings in SSA. The studies uncovered substantial direct annual costs, with studies from Nigeria constituting almost half of the included cost of T2D management studies.

From the provider perspective, T2D management cost in SSA averaged US$680 per patient per annum; medication costs accounted for up to 74% of the financial burden (36, 38). At the same time, the patient perspective costs averaged US$380 (28, 30). From a patient's perspective, outpatient clinic visits cost an average wide disparity among countries, averaging US$34 per patient (25, 33). Pharmacist-led educational interventions and mDiabetes program, employing SMS messages, were effective on T2D and improved health outcomes at lower costs (27, 36). Societal perspective studies were undertaken in Mali, and unaffordable T2D management costs were reported according to the country's GDP per capita. (31). A pharmaceutical care intervention in Nigeria was reported cost-effective (24), while structured group education program intervention and private sector T2D management programmes were reported cost-effective in South Africa (40, 41). Evidence was inconsistent concerning saxagliptin with metformin as second-line therapy in South Africa, demonstrating potential improvements in QALYs; however, it did not meet the threshold for cost-effectiveness (39). In contrast, combining Metformin with Glibenclamide as second-line therapy was considered cost-effective, compared with the standard of care in Ethiopia, costing less than half the amount compared to the cost in South Africa (38, 39). The studies highlighted the importance of considering both the clinical effectiveness and the economic context when assessing the cost-effectiveness of different treatments for T2D.

This cost and cost-effectiveness of managing T2D in the SSA study synthesised significant challenges that warrant careful consideration. Most included studies focused on direct and indirect costs associated with T2D management. The cost of medications dominated as a significant total direct cost item of T2D management in SSA (23,33,34). This supports the previous cost of illness analysis of the T2D study of the LMICs, which reported that the expense of medications drove the direct (6, 44). There has been a call for urgent intervention to reduce the cost of medications used for T2D management and its comorbidities; with little attention given, this burden continues to affect populations in SSA (24). For example, 94.3% of the study participants could not afford medications in Uganda (33), which underscores a significant healthcare accessibility and affordability issue, potentially leading to adverse health outcomes due to the inability to access essential medications. Similarly, in Nigeria, the patient-borne costs for follow-up care in tertiary-level hospitals were more than three times higher than the country's minimum wage of US$125 per month (25), which can deter individuals from seeking timely medical attention, potentially resulting in delayed diagnoses and inadequate treatment. With the rising prevalence of T2D, such direct costs will only grow if current care regimes are unchanged, and tracing undiagnosed cases is improved in SSA.

The studies in this review underscore the significant societal financial distress caused by managing T2D in SSA. Notably, the annual cost of T2D illness, which can reach up to 88% of the annual per capita income (23), exemplifies the substantial economic strain on individuals and families dealing with T2D. Furthermore, the case study of Mali serves as a stark reminder of the complex financial dimensions surrounding T2D management, with annual societal costs surpassing twice the country's GDP per capita (31). Available evidence also suggests that individuals with diabetes incurred costs nearly four times higher than those without (31), exceeding comparisons in developed nations. Comprehensive approaches are crucial, including government-led initiatives such as free or subsidised T2D management programs and proactive preventive advocacy campaigns (40). Additionally, promoting awareness about the benefits of health insurance schemes is essential in mitigating the financial burden, particularly in low-income countries. Ultimately, the affordability of diabetes treatment remains a pressing concern, necessitating innovative strategies to ensure equitable access to care for vulnerable populations in SSA.

The high out-of-pocket healthcare expenditure rate has previously been reported in the SSA region (8), and T2D complications management can only worsen this burden. Evidence from this review highlighted the urgency to promote programmes/interventions to mitigate this strain. One such evidence came from Nigeria, which reported that all socio-economic status groups suffered catastrophic expenditure, but the poorest quartile had the highest incidence (28). Exorbitated by the escalating costs correlated with the late diagnosis of T2D and the concurrent increase in healthcare burden, T2D raises a compelling imperative for the health sector in SSA to strategically address these issues and alleviate the resultant fiscal pressure (44). Addressing such challenges demands a multifaceted approach, prioritising diabetes prevention strategies tailored to specific settings, early screening measures, and effective management to delay and mitigate complications in SSA.

Where assessed, T2D management programmes/interventions in SSA presented as cost-effective in selective settings (24, 40, 39, 41). Saxagliptin, compared with glibenclamide as a second-line therapy added to metformin and structured group education programs led by pharmacists, was found cost-effective and important to manage T2D to improve glycemic control and reduce the occurrence of hypoglycemic events compared to standard care (39, 40). However, the importance of factoring in per-capita income when determining second-line therapy options in SSA countries was highlighted, at least in the lower-income countries perspective (38). Given the SSA economic status, whereby more than half of the countries are categorised as lower-income, it is also crucial to consider the Willingness-to-Pay threshold (WTP) (17, 45). One distinct decision the authors undertook during the study in Ethiopia was to use a new recommendation from the literature and use 50% of a country's GDP per capita as a reference (38). This recommendation aligns with the existing call for treatment decisions that align with the economic realities of the populations in SSA, ensuring equitable access to effective interventions (45). In addition, incorporating the patient perspective into the CEA and explicitly considering affordability (WTP) would introduce supplementary perspectives for decision-makers (44, 45). This resonates with a comprehensive approach of the WHO and its call to integrate diabetes management with social determinants of health (SDH) (16), which is the situations surrounding the patients (46).

In the absence of a sufficient patient perspective CEA, one available study emphasised the significance of evidence-based and contextually relevant interventions in addressing the complexities of T2D management regarding clinical outcomes and economic considerations (38). Integrating T2D care into primary healthcare settings was highlighted as a pragmatic approach to ensuring affordable services and better outcomes would be a pillar of long-term response to T2D was also supported (32, 40). Coupled with the development of mHealth interventions, leveraging the high penetration of mobile phones in LMICs presents a promising avenue for reducing diabetes-related complications and improving the overall management of T2D (35). These highlights agree with the well-established call that addressing the economic burden of diabetes in SSA requires collaborative efforts, informed policies, and innovative solutions to mitigate the financial strain on individuals, families, and healthcare systems (46). In addition, a recommendation to initiate trial collaborations between private and public sectors has been made to facilitate precise economic assessments and qualitative evaluation of programs (41). This proposition considers the disparities in data within the public health sector in SSA. In summary, the imperative lies in implementing T2D interventions that balance cost-effectiveness and resonance with the specific economic benchmarks of the countries in the SSA region.

3.7 Methodological Issues and Limitations

On the issue of the study perspective, a significant methodological challenge emerged. More than half the studies took a provider perspective. Evidence on the total societal cost of managing the disease is lacking; thus, the aggregate costs associated with disease management are most likely underestimated. About 60% of the studies in this review took a provider or health service perspective, another aspect that appeared to be a crucial methodological challenge. In contrast, only one country has evidence that addresses cost from a societal perspective. Neglecting inclusive costs faced by all parties, given the nature of T2D, may lead to underreporting the actual costs and the full burden of the disease. Thus, there is a critical need for robust T2D cost data, its burden on healthcare budgets, individuals and families, and the country's GDP to aid the discussion. This calls for the countries in the SSA region to work towards acquiring more rigorously performed cost and cost-effectiveness evidence to make fully informed decisions. For instance, 42% of the 19 included costs of T2D studies were from one West African country, Nigeria. This shows a need for more diverse and robust scientific evidence regarding the cost of T2D in the SSA region.

Another study limitation is the direct comparison of diabetes management costs between private and public sectors. Given that the private sector is regulated under prescribed minimum benefits, ensuring comprehensive diabetes coverage, its cost data is structured and may not accurately reflect the more varied and resource-constrained environment of the public sector, which serves a much larger and diverse population. Therefore, while the private sector's data provides valuable insights into potential efficiencies and standards, these findings should be used with caution when applying them to the public sector. Differences in delivery models, funding mechanisms, and patient demographics make it challenging to generalise findings across these sectors without careful consideration of the context-specific factors that significantly influence health service delivery and associated costs.

The cost-effectiveness studies of T2D interventions revealed distinct methodological differences and limitations. Firstly, there is a significant variation in cost metrics employed, with some studies focusing on cost per QALY gained (24, 39), ICER/QALY (40, 41), or cost per DALY averted (38), rendering direct comparisons challenging. Secondly, the studies span different geographic regions, encompassing Nigeria, South Africa, and Ethiopia, each characterised by unique healthcare systems, economic contexts, and healthcare cost structures, potentially limiting the generalizability of their findings to others. Thirdly, there is a disparity in the perspectives considered, with some studies examining cost-effectiveness from a provider viewpoint, such as healthcare system costs, while others adopted a patient perspective, considering out-of-pocket expenses. Fourthly, the reliance on primary data collection versus secondary data sources introduces variability in data quality and accuracy, potentially impacting the reliability of the cost-effectiveness analyses (CEA). Lastly, differences in modelling approaches and the use of distinct thresholds and WTP values contribute to variations in the conclusions drawn regarding the cost-effectiveness of T2D interventions across these diverse settings. These methodological disparities underline the importance of considering the specific context and methodology when interpreting and applying the findings of these studies to inform decision-making in T2D management.

3.8 Conclusions and Policy Implications

The impact of substantial costs of T2D is felt universally in SSA, affecting individuals across various socio-economic strata, with the most significant effect observed among the poorest quartiles (46). Urgent attention is required to tackle the expenses associated with diabetes treatment and its accompanying health issues. The endeavour to alleviate the catastrophic expenditures of diabetes encompasses policy deliberations, mainly focusing on the most financially disadvantaged sections of the population. Policy interventions need to alleviate the patient's financial burden and enhance access to essential medicines. Thus, policies should focus on reducing the burden of diabetes on individuals and affordable diabetes medications and management in general. This holds particular significance for nations aiming for universal healthcare, such as those in the SSA region. Moreover, ongoing contributions from these countries, like the randomised controlled trial and Markov micro-simulation model conducted in South Africa, provide valuable insights into cost-effectiveness and incremental ratios, benefiting the broader SSA context.

3.9 References

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4. Chapter Four: The Burden of Diabetes on the Productivity and Economy in Sub-Saharan Africa. A Life Table Modelling Analysis from a South African Perspective.

4.1 Context of the Study

Type 2 Diabetes (T2D), a chronic and costly disease, presents a significant public health challenge in developing countries. This challenge stems from its rapidly growing prevalence, associated complications, and the necessity for sustained care. T2D burdens individuals, families, societies, and national economies considerably. Although the economic impact of T2D is documented in the literature, most studies focus on high-income countries, leaving a notable gap in the context of SSA. Only six studies address this issue globally, underscoring a significant shortfall in current research.

In low- and middle-income countries, the few studies examining the burden of diabetes in SSA show wide methodological variations, largely influenced by data availability, which in turn affects cost estimate accuracy and generalisability. Comparing results across different countries is further complicated by economic factors such as fluctuating exchange rates and varying purchasing power parities.

This study aims to address the gap in knowledge about the economic impact of T2D in SSA, with a specific focus on South Africa, where T2D is increasingly burdening the economy. However, research on accurately estimating productivity loss due to T2D and its contributing factors remains scarce. This study employs PALYs, an innovative and validated approach for evaluating health outcomes and the effect of diseases like diabetes on population-level productivity. The study's strengths include gender and age stratification integration, which enhances data analysis precision and provides crucial insights for targeted healthcare interventions, ultimately aiming to improve public health outcomes.

The findings highlight the growing strain on healthcare systems and the amplification of productivity loss, underscoring the urgent need for preventive strategies. The complex task of quantifying lifetime productivity loss in individuals with T2D involves numerous variables. This research underscores the necessity of evaluating anticipated missed production opportunities to aid informed decision-making in public health resource allocation. The outcomes of this novel study will help public health policymakers and the general populace in South Africa, and potentially SSA regions, understand the current economic burden of T2D. Given the fact that understanding is crucial for making informed decisions about healthcare benefits, focusing on disease control, and developing initiatives to enhance the health of those living with T2D.

This manuscript was published in Pharmacoeconomics in 2024 and was to fulfil objective 2.) To quantify the burden of type 2 diabetes on the productivity and economy in South Africa through a life table microsimulation modelling to quantify excess mortality, estimate Years of Life Lost (YLL) and assess the extent of Productivity-Adjusted Life Years (PALYs) lost among the working-age (20 - 65 years) South Africans living with diabetes. Formal permission for print and electronic copy reuse was obtained by the publisher Springer Nature (under a license number: CC BY-NC 4.0). Assegid Hellebo is the first author, with supervisory input from Andre Pascal Kengne and Olufunke Alaba. The citation is [238]:

> *Hellebo A, Kengne AP, Ademi Z, Alaba O. The Burden of Type 2 Diabetes on the Productivity and Economy in Sub-Saharan Africa: A Life Table Modelling Analysis from a South African Perspective. Pharmacoeconomics. 2024 Jan 24. Doi: 10.1007/s40273-024-01353-3.*

4.2 Abstract

Background and Aim: The prevalence of type 2 diabetes (T2D) is rapidly increasing in sub-Saharan Africa (SSA). T2D increases the risk of premature death and reduces the quality of life and work productivity. This population life table modelling analysis evaluated the impact of T2D in terms of productivity-adjusted life years (PALYs) on the South African working-age population.

Research Design and Methods: Life table modelling was employed to simulate the follow-up of individuals aged 20 to 65 with T2D in South Africa (SA). Two life table models were developed to simulate health outcomes for a SA cohort with and without diabetes. The difference in the number of deaths, years of life lost (YLL), and PALYs lost between the two cohorts represented the burden of diabetes. Scenarios were simulated in which the proportions of gross domestic productivity (GDP), productivity indices, labour force dropout, and mortality risk trends were adjusted to lower and upper uncertainty bounds. Data was sourced from the

International Diabetes Federation, Statistics SA, and both publicly available and published sources. The WHO standard annual discount rate of 3% was utilised for YLL and PALYs.

Results: In 2019, an estimated 9.5% (7.68% men and 11.37% women) or 3.2 million total working-age people had T2D in SA. Simulated follow-up until retirement predicted 669 427 excess mortalities, a loss of 6.2 million years of life (9.3%) and 13 million PALYs (30.6%) in SA. On average, this resulted in 3.1 PALYs lost per person. Based on the GDP per full-time employee in 2019, the PALYs loss equated to US$223 billion, or US$69 875 per person.

Conclusions: This study emphasises the significant impact of T2D on society and the economy. Relatively modest enhancements in T2D prevention and treatment management could lead to substantial economic benefits in SA.

Keywords: South Africa, Diabetes, T2D, Gross Domestic Product, Productivity loss, Years of life lost, PALYs, Productivity Adjusted Life Years

4.3 Introduction

Type 2 Diabetes (T2D) is a chronic disease characterised by chronic hyperglycaemia resulting from variable combinations of defective insulin secretion and/or action [1]. It poses significant public health challenges that substantially impact society [1,2]. Recent data indicate that over one-third of diabetes-related deaths occur in those under 60, adversely affecting labour force participation and diminishing the productivity of affected workers [2].

Africa, currently home to one billion people, is projected to reach 2.4 billion by 2050, with more than half of the population expected to be under the age of 25, as per United Nations forecasts [3] [156] [156] [156][156]. The World Bank Economists further projected massive human capital gain from investments in young people if efficiently handled [4]. It has been suggested that to maximise developmental prospects, countries in the region should focus on alleviating poverty, creating new jobs, and improving education and health [5]. The World Health Organisation (WHO) Commission on Macroeconomics and Health further highlighted the two-way causal relationship between health and economic development [6]. This two-way recognition by WHO stresses investments in health to reduce the burden of preventable diseases, stimulate economic growth, and increase a society's ability to invest in public health

[4,7]. At the same time, the severity of diseases can also affect individuals' productivity and cause premature death [8].

Sub-Saharan Africa (SSA) region is known to have a heavy burden of non-communicable diseases (NCDs) [9]. South Africa (SA) is undergoing an epidemiological transition led by rapid urbanisation, changes in diets and physical activity levels, and population ageing [9,10]. The country faces an epidemic of NCDs, including type 2 diabetes T2D [11,12]. The 10th Edition of the IDF (International Diabetes Federation) reports that 4.2 million adults in SA aged 20 to 79 years are living with T2D [13]. At 11.3%, SA has one of the highest rates of T2D prevalence in the SSA region [13,14]. One study projected the financial cost (i.e., direct medical costs) of diagnosed T2D to the South African public healthcare system to reach over ZAR35.1 billion, equivalent to US$2.5 billion by 2030 [15]. However, according to IDF, diabetes-related health expenditures in SA reached US$1700 per person in 2021, contributing to 96 000 deaths, with an estimated total ZAR109 billion, equivalent to US$7.2 billion in health expenditures for that year [16]. The loss in productivity, stemming from a combination of premature mortality, morbidity leading to workforce dropouts, and notably, reductions in effective performance while at work (known as presenteeism), is substantial [17,18].

Economic theory assesses productivity as output, a function of capital and labour input [17,19]. Neglecting this productivity aspect and the related costs during economic evaluations implies that these costs are zero [17,19]. Studies on societal costs suggest that cost-effectiveness analyses incorporate the total resource implications of mortality changes [20,22]. This includes evaluating the productivity of individuals on a scale from entirely unproductive (0) to fully productive (1) in relation to their health conditions and taking into account the segment of productivity impairment [19,21].

A population-level study assessing productivity loss due to diabetes in China concluded that T2D significantly contributes to the loss of Productivity-Adjusted Life Years (PALYs), resulting in a total loss of US$2.6 trillion in GDP due to reduced productivity, with an average of $45 959 lost per person in 2017 [19]. Diabetes-associated complications resulted in an approximate loss of $89.9 billion in the United States in 2017, including absenteeism (US$3.3 billion), presenteeism (US$26.9 billion), diabetes-related decreased labour force participation (US$37.5 billion) and premature deaths (US$19.9 billion) [20]. Such estimates of productivity loss are essential to encompass the broader economic impact of T2D and provide evidence for investing in its prevention and disease management.

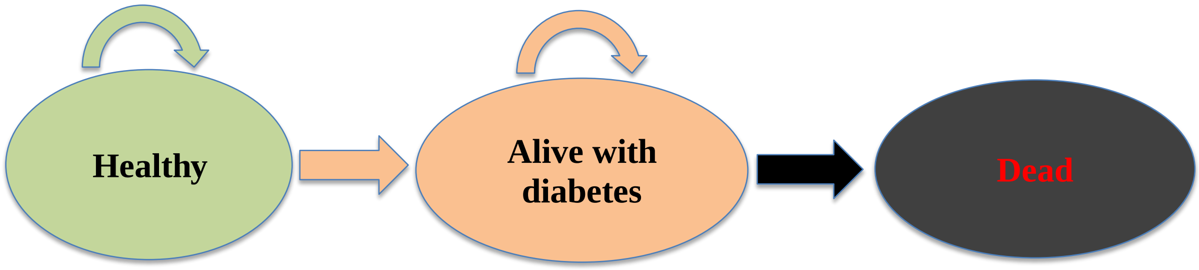
In SA, the burden of T2D presents significant challenges, especially in the context of the proposed National Health Insurance. A deeper understanding of T2D-related productivity loss is critical, not just locally but globally, and is particularly pressing in SSA. However, there is a notable lack of comprehensive data on the impact of T2D on productivity, especially among the working-age population. This gap includes limited insights into the disease's contribution to excess mortality, YLL, and PALYs lost. The study aimed to fill this crucial gap by providing detailed evidence on the extent of productivity loss due to T2D in SA. Such evidence is vital to inform effective, scalable interventions in resource-constrained settings, responding to an urgent call by researchers for data-driven strategies to manage the growing T2D epidemic.

4.4 Methods

This study created a lifetable modelling approach with a single-year cycle length and estimated the health and productivity burden of T2D in working-age South Africans. Life table modelling in combination with decision analysis were utilised to simulate the follow-up of the T2D cohort.

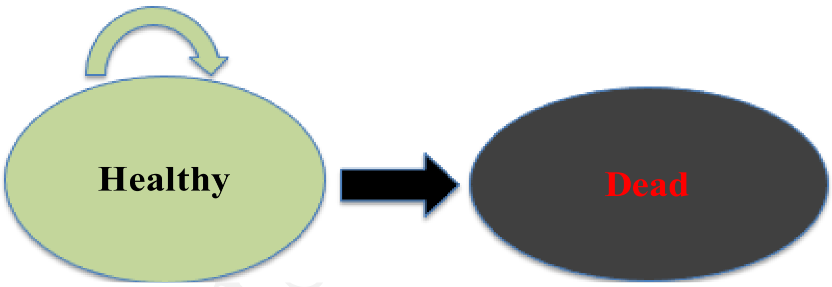
The study specifically focused on T2D due to its prevalence, healthcare costs, and impact on the burden of labour productivity [18-22]. A life table modelling was used to project the health outcomes of the working-age population in South Africa. The model was developed in the Microsoft Excel version 2021. Two models were constructed within Excel: ***Model 1*** simulated a cohort with T2D, and ***Model* 2** re-simulated the same cohort under the hypothetical absence of T2D. Model is depicted in the ***Figure 5***, notably, the life-table models did not account for transitions between non-diabetic and diabetic states or the possibility of T2D recovery. Instead, the stidy relied on baseline prevalence data and population demographics to simulate cohort progression to mortality transitions, omitting changes between diabetic and healthy states.

Figure 4: Model description for cohort with T2D, including two health states.



By contrasting these cohorts—one with T2D, presented in ***Figure 5***, and the other hypothetically without T2D, presented in ***Figure 6***—the impact of T2D was quantified on life years lived and workforce productivity. First, the difference in the total excess mortality and YLL between the two models in labour force participation reflected the impact of diabetes-related productivity loss in labour dropout—accounting for the shortfall in labour force participation in those with T2D compared to those without [16-18]. Secondly, the PALY metric, which depends on productivity indices and YLL, was calculated [17].

Figure 5: Model description for cohort without T2D (hypothetically).



Data were derived both from publicly available databases and published sources. Population labour force data from Statistics South Africa (Stats SA)) was used for 2019 [23], ***Appendix 2***. The 5-year age group and sex-stratified data of working-age population prevalence and annual mortality rate (AMR) were obtained from the IDF Atlas 10th Edition, the vital statistics department in Statistics SA, respectively [11,13,23]. All monetary values were converted from South African Rands (ZAR) to United States dollars (US$) using the 2019 average exchange rate of ZAR14.4496 to US$1 to allow comparability with other populations [24].

4.4.1 Type 2 Diabetes (T2D) Prevalence

Five-year age group and sex-stratified T2D prevalence data for the SA population were obtained from the 2021 IDF Atlas [12]. This data then was applied to the midpoint of each age band to estimate single-year age prevalence rates. Two distinct scenarios were established in separate sheets: ***Model 1***, using the actual T2D prevalence from IDF data, and ***Model 2***, assuming zero T2D prevalence. These data points were extrapolated over time, incorporating demographic shifts. The method used life-table models to simulate the cohort's progression to mortality transitions based on the existing prevalence data and population demographics, as detailed in ***Appendix 2***. This approach enabled us to assess the impact of the presence and absence of T2D on the South African population.

4.4.2 Annual Mortality Rates (AMR)

The 5-year age- and sex bands mortality rates for the SA population in 2019 were obtained from Stats SA [10,30]. Mortality rates attributed to individuals with and without T2D were analysed based on age, sex, and T2D prevalence. In the current context of T2D, the IDF Atlas 2021 method of age-related estimation of T2D mortality in conjunction with age was utilised.

This study applied the average annual proportional reduction in adult mortality for the past decade in SA of 1.8% per year data obtained from the WHO progressively across the model time horizon to project temporal risk trends in population mortality [25]. AMR was used, assuming that death occurs halfway through the cycle. Information regarding the burden of mortality and excess deaths related to diabetes is often limited and unreliable, especially in low and middle-income countries (LMICs). This is also the case for estimates in SA, which have primarily relied on death certificate data from the Department of Home Affairs submitted to Stats SA. However, death certificate data alone may not account for the complex nature of deaths influenced by multiple causes. Formulas used to calculate AMR for individuals with and without T2D, categorised by age group and sex, are found in ***Appendix 2.***

All-cause mortality associated with T2D was sourced from a study conducted within the Asia Pacific population [19]. The decision to utilise data from the Asia Pacific region was driven by the lack of comprehensive, specific mortality risk data related to T2D in the South African population and the cultural similarity between the two populations [26,38]. Through the process, the excess deaths caused by T2D and the YLL were quantified. The YLL is a metric that quantifies the effects of premature death by estimating the years a person would have lived had they not died early [17-19]. This calculation is derived by subtracting the age at death from a predetermined life expectancy value, known as the standard life expectancy (SLE). Hence, the formula for YLL is expressed as the difference between the years of life lived in the 'T2D cohort' assuming no T2D and the years lived in the T2D cohort. The model estimation included the SLE and the age at which the person died. In SA, at birth in 2019, men had a lower life expectancy of 64 years, while women had a higher life expectancy of 70 years [27].

4.4.3 Productivity Indices

Productivity indices signify a productivity index that can be calculated by dividing an output index by an index of hours worked [17,28]. While the productivity index for T2D patients is expected to be less than 1, in those without diabetes, it was assumed to be 1 (fully productive).

a) **Absenteeism-** the number of lost workdays in a year owing to diabetes, commonly represented as a percentage of the total number of working days in a year [21]. Both women and men of all age groups in SSA were estimated to miss 8.6 days on average [22].

b) **Presenteeism-** self-assessed productivity loss indicator while at work, is expressed as a percentage of total productivity. Data estimated by the 'Global Economic Burden of Diabetes' in adults aged 20–79 years for SSA indicate that 1.0% of women and 0.6% of men experienced a decrease in production due to presenteeism related to T2D [22].

To determine the PALYs for the T2D cohort, the time period that the cohort spent in the workforce was multiplied by a productivity index. The index was determined based on estimates of absenteeism and presenteeism related to diabetes. This process is similar to multiplying the years of life lived by a measure of utility to calculate QALYs [29]. Thus,

c) **PALYs** = ([1]productivity index)([2]each year lived in the labour force (YLL_d) by T2D cohort)

[1]absenteeism and presenteeism caused by T2D-related impairment

[2]((YLL_d)(labour force participation rate of SA))

There were 250 calendar working days in 2019 in SA. This study estimated the combined productivity shortfall related to diabetes, including absenteeism and presenteeism, which was 4.44% in women (T2Da productivity index of 0.9556) and 4.04% in men (with a productivity index of 0.9596), with the formulas employed for estimation found in ***Appendix 2***. On the other hand, the productivity index among individuals without T2D was assumed to be 1 (fully productive) for simplicity of calculations.

4.4.4 Labour Force Participation

The 5-year age sex-stratified population-level employment was obtained from the Labour Department of Stats SA [27]. This data was used to quantify the inability to work and early retirement among people with T2D compared to those without T2D. The labour force participation was quantified using a full-time equivalent (FTE) employment rate. The FTE considers the total hours worked by individuals in a given age group relative to the complete standard full-time working hours, thus adjusting the proportion of employed individuals in that group. In the general population of SA, the lowest labour force participation rates were observed in the 60—64 age group, with 4.68% for males and 5.78% for females. Conversely, the highest participation rate was in the 25 to 29 age brackets for males at 16% and in the 20 to 24 age bracket for females at 15.4% (***Table 4***) [23].

Diabetes-related labour force dropout was expressed as a difference in labour force participation rates, varying from 7.0% in females and 5.2% in males aged 20-29 years with T2D to 12.8% in females and 8.3% in males over 40 years [21]. These relative reductions were applied to 2019 sex- and age-group-specific SA labour force participation rates to derive the participation rates in those with and without T2D. The decline in labour force participation is often triggered by an inability to work and early retirement among individuals with T2D compared to individuals without, accounting for absenteeism and presenteeism [17].

4.4.5 Gross Domestic Product (GDP)

The data on GDP per capita in SA were sourced from the World Bank and stood at ZAR96 584.38 (US$6 684.04) in 2019 [30]. The projected temporal trends in GDP growth rate of 1.6% for 2019 were obtained from the OECD Compendium [31]. In this study, it was assumed that the economic value of each PALY corresponded to the annual GDP per effective full-time (EFT) worker, based on a constant GDP per EFT worker of US$6 684.04 [30]. This calculation reflects the potential GDP loss incurred when a worker drops out of the workforce due to T2D and does not reflect the actual annual earnings of an EFT worker. Furthermore, this does not account for the indirect costs incurred by the worker when forced out of the workforce due to diabetes, which is currently under investigation in this study for the year 2019. The GDP per EFT worker was held constant throughout the model time horizon.

4.4.6 Sensitivity and Scenario Analysis

To assess the robustness of the model used, deterministic sensitivity analyses was conducted. These analyses examined the impact of uncertainties in diabetes-related mortality risk, productivity indices, economic data inputs, and potential PALYs lost due to T2D. The upper and lower 95% confidence intervals around the risk ratios of T2D to were incorporated estimate the bounds for all-cause mortality risk associated with T2D. Additionally, uncertainty limits around productivity indices were assessed by varying absenteeism, presenteeism, and labour force dropout estimates by 25%. Scenario analyses were also conducted to explore the effects of different model assumptions. These included scenarios where the mortality risk doubled from the population's average annual reduction in mortality risk of 1.8% to 3.6% per year [25], maintaining 2019 mortality risks over the model's time horizon, and varying trends in GDP per worker by either doubling the average annual GDP growth rate from 1.6% to 3.2% or keeping it constant throughout the model [30]. Lastly, the effect of applying a 5% discount rate, in contrast to the standard WHO annual discount rate of 3% [32] was explored, to evaluate its impact on the findings.

4.5 Results

4.5.1 Type 2 Diabetes (T2D) Prevalence

Working-age individuals living with T2D in SA accounted for 9.5% of the total working-age population (7.7% for men and 11.4% for women), equivalent to 3.2 million aged 20 to 65 years in SA in 2019 ***(Table 4)***. Further details regarding people (men and women) living with T2D aged between 20 and 65 and the data sources are found in ***Appendix 2.***

Table 3: Age and Sex-Specific Prevalence of T2D Among the Working-Age Population in South Africa, 2019 [12,23].

	Male				Female			
5-year age group	**Working-age men population**	**Prevalence as a proportion of the population**	**Prevalence of T2D**	**Number of men with T2D**	**Working-age female population**	**Prevalence as a proportion of the population**	**Prevalence of T2D**	**Number of women with T2D**
20-24	2 620 000	0.16	0,02	44 802	2 602 000	0.15	0,02	45 275
25-29	2 646 000	0.16	0,03	72 765	2 565 000	0.15	0,03	81 311
30-34	2 502 000	0.15	0,04	105 584	2 375 000	0.14	0,05	128 013
35-39	2 247 000	0.14	0,06	139 763	2 186 000	0.13	0,09	186 903
40-44	1 940 000	0.12	0,09	170 138	1 901 000	0.11	0,13	240 286
45-49	1 605 000	0.09	0,12	189 872	1 742 000	0.10	0.17	303 805
50-54	1 192 000	0.07	0,15	182 376	1 358 000	0,08	0.23	305 414
55-59	999 000	0.06	0,19	189 510	1 209 000	0,07	0.27	329 090
60-64	773 000	0.05	0,23	174 621	977 000	0,06	0.31	302 870
Total SA working-age population	**16 524 000**	**1.00**	**0,10**	**1 695 730**	**16 915 000**	**1,00**	**0.14**	**2 436 512**
Calculated	**Weighted average % prevalence among men = 7.7%**				**Weighted average % prevalence among women = 11.4%**			

**The figures in Table 1 for the working-age population and the number of men and women with T2D were derived and estimated using Stats SA [23] and IDF Atlas 10th Edition data [12]. The prevalence of T2D was rounded to the nearest decimal during the calculation process. In addition, Stats SA rounded the working-age population figures to the nearest thousand prior to providing this data. Therefore, the final figures in the table may not precisely correspond to what may be found elsewhere*.

4.5.2 Quantifying Excess Death and Years of Life Lost (YLL) to Diabetes

The lifetable model, detailing the follow-up of the current working-age SA population until retirement, is presented in ***Table 5***. The projected number of deaths in individuals with T2D compared to those without diabetes was 669 427. The male cohort is estimated to have 315 558 excess deaths, and the female cohort 353 839. Additionally, ***Table 5*** indicates an estimated 6.2 million YLL would be lost due to T2D over the model time horizon. This translates to 1.9 years of life lost per person during their working lifetime, with a higher impact observed among men (2.5 years) compared to women (1.6 years).

Table 4: Excess mortality and YLL across the working-age lifespan of South Africans with T2D, as modelled in a life table.

	Age-group	Deaths in cohort with T2D	Deaths in ' T2D cohort' assuming no T2D	Excess deaths in the T2D cohort	Years of a life lived in the cohort T2D	Years of life lived in ' T2D cohort' assuming no T2D	Years of life lost (YLL)	% YLL
Male	20 - 24	39 481	26 669	12 811	818 434	994 707	176 272	9,7
	25 - 29	63 596	42 951	20 645	1 199 734	1 486 743	287 009	10,7
	30 - 34	91 621	61 812	29 809	1 553 934	1 942 945	389 011	11,1
	35 - 39	130 259	100 416	29 843	1 825 616	2 399 293	573 676	13,6
	40 - 44	142 211	95 155	47 056	1 872 240	2 419 721	547 481	12,8
	45 - 49	152 943	101 263	51 680	1 740 431	2 247 855	507 424	12,7
	50 - 54	137 028	89 014	48 014	1 334 309	1 695 222	360 913	11,9
	55 - 59	122 793	77 122	45 672	1 018 758	1 241 237	222 480	9,8
	60 - 64	73 649	43 592	30 058	524 553	587 858	63 305	5,7
	Total	**953 583**	**637 995**	**315 588**	**11 888 009**	**15 015 580**	**3 127 571**	**11,6**
Female	20 - 24	36 127	25 528	10 599	875 870	1 011 196	135 326	7,2
	25 - 29	64 331	45 553	18 778	1 436 104	1 665 959	229 856	7,4
	30 - 34	99 962	70 939	29 024	2 032 290	2 400 257	367 966	8,3
	35 - 39	140 654	99 172	41 481	2 690 648	3 166 190	475 542	8,1
	40 - 44	178 221	126 876	51 345	2 908 951	3 468 046	559 096	8,8
	45 - 49	214 106	152 356	61 750	3 082 415	3 653 896	571 481	8,5
	50 - 54	196 811	139 561	57 249	2 479 268	2 889 103	409 834	7,6
	55 - 59	176 977	124 405	52 572	1 944 207	2 191 612	247 405	6,0
	60 - 64	100 439	69 397	31 042	967 377	1 031 733	64 357	3,2
	Total	**1 207 627**	**853 788**	**353 839**	**18 417 130**	**21 477 992**	**3 060 862**	**7,7**
	Total	**2 161 210**	**1 491 783**	**669 427**	**30 305 139**	**36 493 572**	**6 188 433**	**9,3**

Years of life lived were estimated using life tables that incorporated a half-cycle correction and were subjected to an annual discount rate of 3%.

4.5.3 Evaluating Productivity Adjusted Life of Years (PALYs) lost to diabetes

An estimated 13 million PALYs were lost among the working-age cohort living with T2D in South Africa over their working lifetimes, with 4.4 million lost in men and 8.7 million in women. This represents 30.6% of PALYs lost for the total cohort (22.5% for men and 37.5% for women), as detailed in ***Table 6***. This equates to a loss of 3.1 PALYs per individual (2.6 for men and 3.6 for women). The present study used the human capital approach, whereby GDP is an oft-reported economic metric, similar to data on workforce participation [33]. Using the measure of GDP per person employed, which reflects labour productivity as the economic output generated by each employed individual, the calculation is based on dividing South Africa's GDP by the total number of people employed. Assuming a constant GDP per EFT employee of ZAR248 472 (US$17 136) per annum [31], this results in an estimated productivity loss due to diabetes in South Africa of ZAR3.2 trillion (US$223 billion) in GDP, as shown in ***Table 7***. This equates to ZAR1 009 693 (US$ 69 875) per person with T2D over the working lifetime in SA.

Table 5: PALYs Lost During the Working Lifespan of South Africans with T2D, as simulated in the Life Table.

	Age-group	PALYs lived in the cohort with T2D	PALYs lived in a 'T2D cohort' assuming no T2D	PALYs lost	% PALYs lost	PALYs lost per person
Male	20 - 24	551 552	800 938	249 386	18,4	5,6
	25 - 29	867 610	1 270 424	402 814	18,8	5,5
	30 - 34	1 132 816	1 696 472	563 656	19,9	5,3
	35 - 39	1 294 704	2 059 286	764 582	22,8	5,5
	40 - 44	1 283 750	2 031 111	747 362	22,5	4,4
	45 - 49	1 104 374	1 798 688	694 314	23,9	3,7
	50 - 54	732 940	1 235 261	502 321	25,5	2,8
	55 - 59	416 213	742 241	326 028	28,1	1,7
	60 - 64	132 236	245 927	113 691	30,1	0,7
	Total	**7 516 194**	**11 880 348**	**4 364 154**	**22,5**	**2,6**
Female	20 - 24	453 533	799 055	345 522	27,6	7,6
	25 - 29	758 888	1 401 595	642 707	29,7	7,9
	30 - 34	1 056 567	2 022 282	965 715	31,4	7,5
	35 - 39	1 352 203	2 634 259	1 282 056	32,2	6,9
	40 - 44	1 320 087	2 791 222	1 471 135	35,8	6,1
	45 - 49	1 192 387	2 768 206	1 575 818	39,8	5,2
	50 - 54	720 462	1 938 969	1 218 507	45,8	4,0
	55 - 59	324 585	1 156 821	832 236	56,2	2,5
	60 - 64	42 725	363 660	320 935	79,0	1,1
	Total	**7 221 438**	**15 876 069**	**8 654 631**	**37,5**	**3,6**
	Total	**13 737 632**	**27 256 417**	**13 018 785**	**30,6**	**3,1**

Estimation of PALYs was modelled in life tables and subject to an annual discount rate of 3%

4.1.1 Sensitivity and Scenario Analyses

***Table 7** illustrates the sensitivity and scenario analyses performed by altering one input variable while holding all other model inputs constant (Ceteris paribus) as done elsewhere [20,22].*

Table 6: Sensitivity and Scenario Analyses for Evaluating Uncertainty of Key Data Inputs.

	Sensitivity and Scenario Analysis	**PALYs lost owning to T2D**	**% in PALYs lost compared to the base**	**GDP lost from the Economy (US$ billion)**	**GDP lost per person T2D (US$)**
	Base scenario details	13 018 785		223	69 875
a)	Annual discount rate increased from 3% to 5% (Scenario analysis)	10 658 726	-18%	182	57 208
a)	Annual discount rate halved from 3% to 1.5% (Scenario analysis)	15 419 232	18%	264	82 759
b)	The annual GDP growth rate was doubled to 3.2% (Sensitivity analysis)			230	72 259
b)	No temporal trend in GDP (Sensitivity analysis)			219	68 644
c)	25% increase in absenteeism and presenteeism (productivity indices upper uncertainty bound) (Sensitivity analysis)	13 297 870	2,14%	227	71 373
c)	25% reduction in absenteeism and presenteeism (productivity indices lower uncertainty bound) (Sensitivity analysis)	12 739 699	-2,14%	218	68 377
d)	25% increase in labour force dropout (upper uncertainty bound) (Sensitivity analysis)	14 791 455	14%	236	74 022
d)	25% reduction in labour force dropout (lower uncertainty bound) (Sensitivity analysis)	11 234 029	-14%	211	66 151
e)	The temporal trend in population mortality risk doubled from 1.8% to 3.6% annually (Scenario analysis)			287	85 016
e)	No temporal trend in population mortality risk per year (Scenario analysis)			165	56 869
f)	Upper uncertainty bound of all-cause mortality risk associated with T2D (Sensitivity analysis)	13 565 269	4,2%	239	74 999
f)	Lower uncertainty bound of all-cause mortality risk associated with T2D (Sensitivity analysis)	12 317 845	-5,4%	211	60 827

Analyses were performed by altering one input simultaneously while holding all other model inputs constant.

In sensitivity analyses, a 25% increase in labour force dropout, representing the upper uncertainty bounds of the 95% confidence interval (CI), led to an additional 14.8 million PALYs lost (a 14% increase). Conversely, with a 25% decrease in dropout and the lower uncertainty bound, the estimate of PALYs lost was reduced to 11.2 million, reflecting a 14%

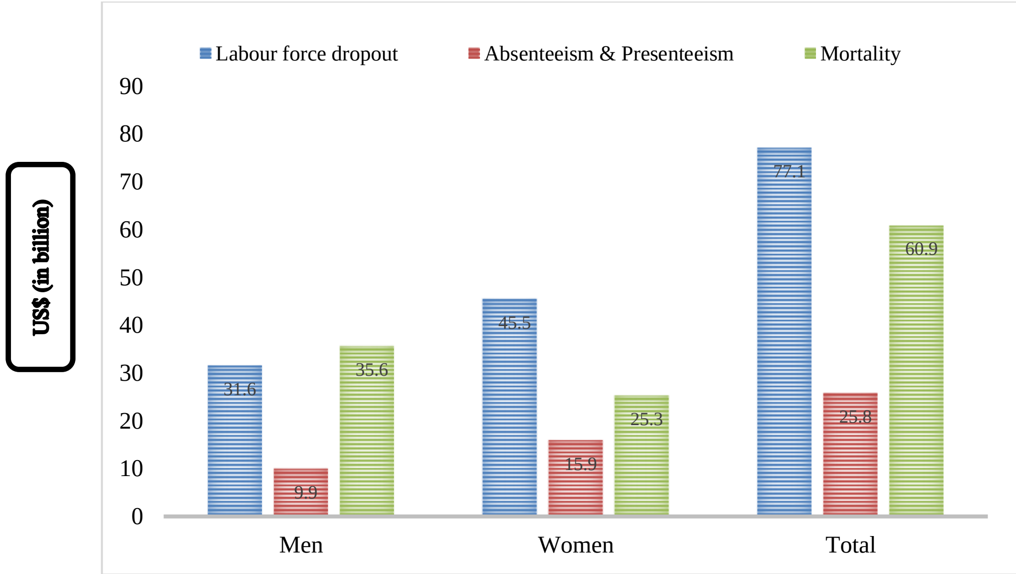
decrease. This highlights the significant effects on workforce productivity from early retirement, which was used as a proxy for T2D-related complications.

In the scenario analyses, altering mortality risk and economic growth rates further illustrated the sensitivity of the model to external economic factors. When the temporal trend in population mortality risk was doubled from 1.8% to 3.6% annually, PALYs lost increased to 287 000, as opposed to 165 000 PLAYs lost without mortality trend.

Adjusting for the upper and lower uncertainty bounds in absenteeism and presenteeism, PALYs lost due to T2D fluctuated by ±2.14% from the base case. Similarly, varying the all-cause mortality risk associated with T2D resulted in a 4.2% increase and a 5.4% decrease in PALYs lost. Economically, doubling the annual GDP growth rate from 1.6% to 3.2% escalated the estimated economic impact of T2D-related productivity loss to US$230 billion. Conversely, maintaining 2019 GDP levels throughout the model's timeline reduced the estimated loss to US$219 billion. Adjusting the annual discount rate to 5% and 1.5% varied the PALYs lost by -18.1% and +18.4%, respectively.

Figure 7 shows that labour force dropout and mortality account for the majority of productivity loss at 47.1% and 37.2%, respectively. Absenteeism and presenteeism contributed 15.8% of the loss. Cost-wise, labour force dropout leads with US$77.1 billion, followed by mortality at US$60.9 billion and absenteeism and presenteeism at US$25.8 billion. PALYs lost are higher among men (21.7%) than women (15.4%) for mortality, while dropout and absenteeism rates are higher for women, at 27.8% and 9.7%, respectively, versus men's 19.3% and 6%.

Figure 6: Economic impact of reduced productivity due to T2D-related absenteeism, presenteeism, premature mortality, and labour force dropout in the South African working population.



4.6 Discussion

This study underscores the substantial burden of T2D, resulting in reduced years of life and productivity for the working-age population in SA. Through the simulated follow-up of the T2D population, hypothetically considering a scenario with 'no T2D' and following until the retirement age of 65, it was estimated that there would be 669,427 excess deaths, a loss of 6.2 million life years (9.3%), and 13 million PALYs (30.6%) in SA.

Decreased productivity is commonly associated with various factors, including missed workdays due to absenteeism, reduced workforce participation due to disability caused by disease, and the premature loss of working years due to diabetes-related mortality during an individual's working lifetime [18, 20, 35]. Hence, PALYs are a novel and well-tested approach to measuring health outcomes and the population-level impact of disease (such as diabetes) on productivity [17,33].

The findings of this study are consistent with prior research conducted in Bangladesh [21] and China [19], utilising a similar modelling approach. The study underscores the significant impact of T2D on YLL, particularly noticeable among younger individuals. This phenomenon is attributed to the cumulative losses linked to early-onset T2D among younger age groups.

The results from the lifetable model estimated the loss of 13 million PALYs among those with T2D, or 3.1 PALYs lost per person, over the working lifetime. The per-person PALYs loss in SA was higher than the previously reported outcomes from China [19], Australia [33] and Bangladesh [21], with 1.3, 1.6 and 1.4, respectively, with further details found **in online ESM *Table 3***. In SA, the retirement age is 65 for both genders. However, when compared to patients in China, SA patients experienced higher productivity loss. Men in SA faced a five-year greater loss, while women incurred a 15-year higher loss than their Chinese counterparts. This discrepancy stems from differences in the working-age population structure; in China, it ranges from 20 to 59 years for men and 20 to 49 years for women [19]. Moreover, the prevalence of T2D-related YLL in SA is more than twice that of Australia, reflecting elevated mortality risk and labour force dropout in SA compared to Australia [33]. It is crucial to note that the Australian PALY study did not discount its results. While these findings offer valuable insights for comparison, it's important to acknowledge the potential influence of unaccounted variables on the overall data interpretation. However, the model structure in both studies is similar. Furthermore, with its higher Economic Complexity Index (ECI) and higher per capita income, SA experiences more significant losses in its population than Bangladesh, which has a lower ECI and lower per-capital income [33].

In terms of absolute numbers, men experienced greater PALYs lost compared to women, primarily due to higher labour-force participation among men (64.9%) than women (54.3%) in SA [39]. However, the relative decrease in productivity caused by T2D was more pronounced in women (37.5%) compared to men (12.25%), primarily attributable to a higher rate of labour force dropouts (70.8% in women versus 40.3% in men).

Furthermore, the lost productivity was estimated of ZAR 3.2 trillion (US$223 billion) in GDP. This translates to an average of ZAR 1 009 693 (US$ 69 875) per person with T2D over their working lifetime. At the same time, T2D prevalence (9.5%) is significantly higher in SA compared to other populous countries, such as Nigeria, with a 4.3% rate [34]. Spending on the prevention of T2D strategy was further estimated, since it can generate financial gains by enhancing work productivity and decreasing the direct costs of T2D treatment and management. Considering that T2D is not entirely preventable, if an intervention could prevent 10% of diabetes cases, the break-even investment would amount to US$6,627 per working-age individual, making it a cost-saving initiative. This estimation is derived solely from the perspective of saved productivity, making it a conservative figure. Additional economic benefits are likely, especially from the savings in direct costs associated with diabetes management [15]. Therefore, framing the allocation of resources towards T2D prevention should be considered an investment, not an expenditure.

The present study's strength lies in its use of gender and age stratification, which sharpens the precision of the data analysis. This approach enables more accurate identification of the impact of diabetes across different demographics. To address uncertainties in the model, sensitivity and scenario analyses were conducted, ensuring a comprehensive and robust examination of the impact of diabetes on productivity. The life table model proved more sensitive to variations in labour force dropout (±13.7%) than fluctuations in productivity indices (absenteeism and presenteeism) by 25%, which had a minimal effect on the estimates of PALYs (±2.14%). Notably, the life table model did not consider individuals in the SA population with T2D who remain undiagnosed or unaware of their condition (52.4% are estimated to have T2D but undiagnosed) [41]. Consequently, the findings may underestimate the impact of T2D on work productivity, as it can still affect those with undiagnosed T2D. Additionally, it was assumed that projections for temporal trends in mortality and GDP growth rates would remain constant throughout the model's time horizon for simplification and practicality. However, GDP growth was considered in the scenario analysis.

4.7 Limitations

In adhering to the two-model approach—one representing a cohort with T2D and the other without—the study acknowledges a fundamental limitation: the sole transition probability considered is towards death, excluding other potential transitions such as onset or remission from T2D. This simplification, while streamlining the model, may not fully capture the dynamic nature of diabetes progression and its varied impacts on different population segments. Secondly, the productivity-indices predictions for different age groups was not classified because the required data on absenteeism and presenteeism was lacking.

Due to the unavailability of data from Stats SA on the division of the labour force into full- and part-time based on disease status, all labour force participants were treated as full-time employed in both the T2D and simulated cohorts. Consequently, this study did not account for the impact of T2D on unpaid work (caregiving, child-rearing, household, and community roles), potentially missing a proportion of the overall impact. The life table model was used to simulate the progress of the current cohort of South Africans with known T2D but could not account for those who had undiagnosed T2D at the time of data extraction. Finally, it was assumed that the economic value of one PALY is equivalent to that of annual GDP per employee, as done elsewhere [19,21,33]. It was also acknowledged that these assumptions and limitations could lead to unaccounted costs, thus underestimating the burden.

Furthermore, the influence of diabetes-related comorbidities, such as a high prevalence of obesity and hypertension among SA populations [40], on productivity loss could not be disentangled from these projections. This limitation stems from the need for more data. It was further assumed that work pertains to paid employment, presuming that the entire population worked full-time, and the study did not account for unpaid and part-time workers. Despite these limitations, it is improbable that the study's core findings and conclusions would be substantially altered.

In addition, Stats SA, the national statistical service provider, and Diabetes South Africa, the T2D Association of SA, did not have T2D prevalence data—citing that the Department of Health does not mandate them to keep T2D statistics. In addition to the lack of a local country depository for confirmed T2D or prevalence, the IDF indicated that the quality and number of data sources examining the prevalence of T2D in adults was very low. Second, the relative risk (RR) and utility scores were extrapolated with predictions using the Asia Pacific region and Ethiopian studies, respectively, without available data from SA. Utilising real-time data would significantly enhance the accuracy, generalisability, and reproducibility of the evidence. Consequently, it is paramount for SA to prioritise the collection and analysis of diabetes-related data. This focus will enable more precise and relevant analyses in future research.

4.8 Conclusion

Type 2 Diabetes is a major contributor to mortality and morbidity in SA. This study brings new insights from the South African context, specifically focusing on health, well-being, and productivity losses associated with T2D. This research also elucidates that quantifying the lifetime earnings lost due to T2D is a complex endeavour influenced by various factors. It emphasises the need for enhanced allocation of public health resources through informed decision-making, particularly by assessing projected lost production opportunities. In light of these findings, the importance of viewing prevention, treatment, and efficient management of T2D should not merely be seen as healthcare expenditures but as valuable investments. This perspective is crucial for shaping strategies that effectively address the broader economic implications of this disease in SA. This study calls for adequate interventions to control and mitigate the burden of T2D in SA.

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5. Chapter Five: Health-Related Quality of Life and Its Predictors Among Individuals With Diabetes. The Case of the Western Cape, South Africa

5.1 Context of the Study

In this study, the primary aim is to assess the overall impact of diabetes on HRQoL and to explore the specific predictors that contribute to either positive or negative outcomes in this context. The investigation is particularly significant in South Africa, a region where research on this topic in LMICs is scarce. While substantial research has been conducted in developed countries regarding the predictors and impact of HRQoL among PLWD, such studies are notably limited in LMICs, including South Africa. Amid the diabetes epidemic, this gap in the literature necessitates a focused study in the South African setting. This research aims to evaluate HRQoL, its predictors, and health state utility values using the TTO method, specifically in South Africa.

This pioneering study is the first in South Africa to report age and gender-stratified utility values, which are crucial for quantifying QALYs and PALYs and conducting economic evaluations tailored to specific demographic segments. The study also addresses the gap in the assessment of HRQoL among PLWD from both urban and rural primary healthcare settings in SSA, including South Africa. By incorporating both physical and mental health components, the study provides essential insights for crafting interventions aimed at improving HRQoL among PLWD.

Understanding the predictors of HRQoL in PLWD is vital. This study highlights how factors such as gender, receiving care from urban clinics, education level, and mental health significantly influence HRQoL among this demographic. Such insights are invaluable for healthcare providers, policymakers, and other stakeholders in developing targeted interventions and support mechanisms to enhance HRQoL and the overall well-being of PLWD in South Africa. The findings emphasise the importance of considering psychological well-being and self-efficacy alongside clinical treatment to improve the quality of life in individuals with diabetes. This research not only contributes to the global literature on diabetes but also offers critical evidence for future studies to understand the nuanced impacts of various factors on health outcomes in the context of diabetes.

This manuscript was submitted to is under review by SSM- Health Systems. It fulfils the objective 4.) To assess the predictors of health-related quality of life (HRQoL) and time trade-off utility (TTO) values among people with diabetes in South Africa. It is presented in the format it has been submitted for this thesis. Assegid Hellebo is the first author and with supervisory input from co-authors in particular Andre Pascal Kengne, Amarech Obse and Olufunke Alaba.

5.2 Abstract

Objectives: The purpose of the present study was to address the gap in understanding the factors that influence Health-Related Quality of Life (HRQoL) in people with diabetes in South Africa. It also aimed to develop South Africa-specific utility value sets, crucial for accurate Quality-Adjusted Life Year estimations, thereby improving local economic evaluations and healthcare decision-making.

Methods: The study utilised data from Project MIND, a cluster randomised controlled trail, collected in 2017 and evaluated the HRQoL in PLWD from 15 urban and nine rural primary healthcare facilities in Western Cape, South Africa. Data was analysed using the EuroQol-5 Dimension Questionnaire (EQ-5D-3L), with responses translated into a single summary crosswalk index score using the UK time trade-off value set. The predictors were assessed using ordinal logistic regression analysis by Stata software version 17.

***Results*:** In this study, 539 PLWD, with a mean age of 54 years, predominately female (76%), unemployed (70%), attained only primary school (88%). The mean utility score was 0.85 (standard deviation of 0.11). Males reported higher HRQoL than females (AOR=1.64, p= 0.07). Participants who received care from urban clinics had lower HRQoL compared to their rural counterparts (AOR= 0.41, p<0.01). Primary education was associated with reduced HRQoL (AOR= 0.53, p<0.01). Conversely, higher alcohol consumption was associated with increased HRQoL (AOR= 1.89, p= 0.02). Higher self-efficacy was associated with better HRQoL, whereas severe mental health scores predicted very low HRQoL (AOR= 18.31, p= 0.01), alongside food insecurity and urban living. BMI, marital status, housing stability, and food security showed no significant impact with HRQoL.

Conclusions: The outcome of this study highlights the multifaceted nature of HRQoL among PLWD in South Africa. Factors like gender, urban residency, education level, and mental health significantly influence HRQoL. The findings underscore the importance of addressing psychological well-being and self-efficacy beyond clinical treatment to enhance HRQoL in people with diabetes.

5.3 Introduction

Diabetes is increasingly recognised as a significant health challenge in low and middle-income countries (LMICs), accounting for nearly 80% of diabetes-related deaths globally [1-3]. Within the Sub-Saharan Africa (SSA) region, South Africa stands out as a particularly affected country, with rising prevalence primarily attributed to lifestyle changes, shifts in dietary habits and physical inactivity [2]. These factors have been extensively cited as primary drivers behind the growing incidence of diabetes, leading to a substantial impact on individuals' health-related quality of life (HRQoL) [2,3]. The concept of HRQoL is inherently multidimensional, encapsulating various domains of health status such as physical, emotional, and social well-being and satisfaction [1,2]. HRQoL is a pivotal measure in evaluating the impact of preventable diseases like diabetes on individual health [3]. It is shaped by a range of factors, including medical aspects (types and duration of diabetes, treatment approaches, glycemic control, and complications), as well as demographic and attitudinal elements [5].

The EuroQol-5 Dimensions and 3 Levels (EQ-5D-3L) system assesses HRQoL using methods like Discrete Choice Experiments (DCE), Standard Gamble (SG), Visual Analogue Scale (VAS) and/or Time Trade-Off (TTO) to determine health state utilities for economic evaluations [3,4]. However, VAS faces criticism for subjectivity and limited comparability. The SG method encounters challenges in cognitive complexity, bias, and ethical concerns, while DCE experiences difficulty in complex choices, impacting reliability and necessitating careful design and interpretation [4,5]. Conversely, TTO is generally regarded as more robust, yielding theoretically substantiated utility values by incorporating dimensions of time and mandating trade-offs between life quality and quantity [5]. Unlike the alternative methods, TTO allows respondents to choose between living a shorter period in perfect health or a longer period in a less desirable health state, deriving utility values that reflect perceived quality of life. TTO is also instrumental in generating quality-adjusted life years (QALYs), enriching cost-utility analyses and facilitating cross-intervention comparability [5]. Specifically, QALYs amalgamate life expectancy and varying health states into a singular utility score, ranging from 1 (indicating full health) to 0 (representing death), primarily derived through methodologies such as TTO [5,6]. In this context, TTO is a proxy for Health-Related Quality of Life (HRQoL). It has been widely applied to assess the quality of life among patients with Non-Communicable Diseases (NCDs), providing a comprehensive measure of their health status [4,5,41].

Literature advocates for assessing HRQoL in individuals with diabetes for economic evaluations and comprehensive health improvement and identified it as a key predictor of morbidity and mortality [6,7]. HRQoL serves as a pivotal outcome metric embodying the ultimate objectives of healthcare interventions, aligning closely with the World Health Organisation's (WHO) comprehensive definition of health, which includes physical, mental, and social well-being [7]. For individuals with diabetes, a chronic condition requiring a comprehensive regimen that includes dietary monitoring, exercise, blood glucose checks, and medication schedules, the impact on various aspects of daily life and personal well-being is notably tangible [8,9]. The associated frequent physician visits and the looming threat of potential complications often compound the psychological burden for people with diabetes, an issue substantiated by its observed association with morbidity and mortality [10,11]. Literature indicates that the HRQoL is notably compromised in those suffering from diabetes-related complications compared to those without [12-14]. Reinforcing the importance of HRQoL, the WHO's 2012 guidelines for diabetes management underscore its utility as an outcome measure to gauge the overall health and monitor the population-level impact of the disease [7, 10].

Recommendations have been issued to identify and address predictive factors that adversely influence HRQoL in individuals with diabetes [14-16]. These factors span demographic, socioeconomic, and clinical variables, including age, gender, residential setting, education level, marital status, employment, and income [12, 18]. Clinical determinants such as body mass index (BMI) (i.e., obesity), disease duration, severity, and comorbidities, as well as self-care guidelines, have been scrutinised for their impact on HRQoL [14-20]. Comorbid conditions further complicate disease management, thereby adversely affecting overall well-being. In addition, hazardous or harmful levels of consumption of alcohol, tobacco, and drugs have been documented to adversely affect HRQoL in individuals with diabetes, leading to poor glycemic control, augmented health complications, and reduced overall well-being [23,24].

Furthermore, the frequent co-occurrence of anxiety and psychological depression (mental health issues) among people with diabetes has been identified as a significant determinant of compromised HRQoL [25]. Elevated anxiety symptoms can worsen life stress, further deteriorating HRQoL in this population [25,26]. On the other hand, patients' self-efficiency, health status, and satisfaction are intricate and impactful. Enhanced self-efficacy was linked to more significant health satisfaction in people with diabetes, as they confidently manage their condition for improved disease control [26]. This boosts emotional well-being, reduces anxiety, and enhances HRQoL [27,28]. A cyclical pattern emerges where higher self-efficacy heightens health satisfaction, positively impacting HRQoL. Low self-efficacy conversely diminishes both, underscoring the need for interventions that reinforce self-efficacy and positive health perceptions to elevate well-being among people with diabetes [27-29].

Considerable research has assessed the predictors and impact of HRQoL among people with diabetes in developed countries [15]; such studies are scarce in LMICs, including South Africa. A 2021 systematic review of the SSA region revealed only two studies from South Africa addressing this issue [30]. Studies published in 2016 and 2018 focused on HRQoL among individuals with Type 2 diabetes, documenting key factors related to disease control, severity, and demographics. They also explored the interplay between diabetes, HRQoL, and disability among the older adult population in South Africa [31].

Amid the diabetes epidemic, South Africa faces a critical need for comprehensive research. This study seeks to address a notable gap in the existing literature, as there has been a lack of investigation into predictive factors such as mental health and self-efficacy in relation to HRQoL within the country. The study aimed to evaluate HRQoL, its predictors, and health state utility values using the TTO method in the South African context.

5.4 Methods

5.4.1 Study Data, Participants and Sampling Procedures

This study employed a cross-sectional design, utilising baseline (2017) data from the Project MIND trial, a cluster-randomised controlled trial of adult patients (n=1340) with either HIV or diabetes and receiving antiretroviral therapy or diabetes medication in the Western Cape, South Africa [19]. Data for the current study (n=539) for diabetes-only patients was extracted from

Computer-Assisted Personal Interviews (CAPI), focusing on HRQoL among adults in fifteen urban and nine rural primary healthcare sites [20]. People with diabetes aged 18 and above were screened and evaluated using the EQ-5D-3L instrument to assess general health and daily life [20].

Specifically, respondents were selected from a list of healthcare centers that included community clinics and regional hospitals. In urban areas, patients were sampled from facilities such as the Cape Town City Health Clinic and the Groote Schuur Hospital. In rural districts, participants were drawn from the George Regional Hospital and the Knysna Community Health Centre, among others.

The selection process and purposeful sampling involved collaborating with healthcare providers who assisted in identifying patients according to the study criteria. This process ensured that the sample was representative of the broader population receiving treatment for these conditions in both types of settings. Patients were approached during their visit to these centers, and after explaining the purpose and nature of the study, informed consent was obtained from those who agreed to participate.

Further details about the parent study, Project MIIND trial, integrating psychological treatment into chronic disease care in the Western Cape, South Africa, can be found in the relevant publication [19].

5.5 Analysis and Measures

5.5.1 Outcome Variable

The dependent variable, HRQoL, comprises mobility, pain/discomfort, self-care, anxiety/depression, and usual activities domains, with five dimensions and three levels of severity, culminating in 243 unique health states [42]. Domain scores were derived by calculating the mean score of the items within each specific domain. These domain scores reflect different aspects of HRQoL, with a higher domain score indicating a superior level of functioning or well-being in that domain [42]. The overall TTO utility score was categorised into four levels: Low (<0.681), Moderate (>0.681&<0.835), High (>0.835& <1) and Perfect (=1) as reported elsewhere [53,54], representing a composite measure of HRQoL, integrating these domain scores.

5.5.2 Predictors of HRQoL and Operational Definitions

i. Sociodemographic and Economic

These factors represent a spectrum of socioeconomic variables that influence overall well-being and health perception [31]. Specifically, age, gender, marital status, educational level, predicted monthly household income, employment status, residential location, food security, and stable[2] living conditions [35]. While age was treated as continuous, the remaining variables were recoded as binary.

ii. Body Mass Index (BMI)

BMI assesses whether an individual's weight is appropriate for height [32]. It was determined through the division of weight by the square of height. Subsequently, BMI was categorised into three groups in the present study using the WHO classification: recoded as normal weight (BMI <25), overweight (BMI 25-30), and obese (BMI $\geq$ 30 kg/m^2) [36].

iii. Lifestyle

This domain included toxic environmental exposures and lifestyle factors, assessed through patient reported alcohol consumption, cigarette and illicit drug use [26]. Binary alcohol consumption variable was evaluated using the Alcohol Use Disorders Identification Test (AUDIT) cut-off score of 8, where scores below 8 signified low-risk drinking and scores of 8 or above indicated hazardous or harmful drinking. Smoking and illicit drug use were also binary, either 'yes' or 'no.' Due to the lack of variation, as 98% of participants reported 'no' to illicit drug use, it was excluded from the analysis.

iv. Mental Health Score

Participants in Project MIND were specifically selected for their diagnosis of diabetes and associated comorbidities such as depression or harmful alcohol use; it is pertinent to note that depression is highly prevalent among individuals with diabetes in South Africa. Existing studies indicate a prevalence rate of 46.6%, suggesting that nearly half of the diabetic

[2]refer to residential housing that meets certain structural and legal standards. This includes living in permanent buildings that are safe and secure, having reliable access to essential utilities like electricity, water, and sanitation, and holding legal rights to the property to prevent arbitrary eviction.

population experiences depression [33]. Given the substantial prevalence of psychological distress, including psychological distress, measured using K10 in the past 30 days as a predicting factor for assessing HRQoL is highly relevant. In Project MIND, psychological distress was assessed using the K10 ten-item questionnaire about emotional states, each with a five-level response scale [27]. The aggregate scores ranged from a minimum value of 50. In the current study, mental health (K10) score was re-coded as low (<20), moderate (20-30) and severe (>30).

v. Self-Efficiency Scale

General self-efficacy was used to measure people with diabetes' perceived capability to manage various situations related to diabetes care, overall well-being, and satisfaction with health status [34]. This construct was quantified using a generalised self-efficacy scale that ranged from 1 to 40, re-coded as low (<25), moderate (20-30) and high (>30).

5.6 Statistical Analysis

The TTO technique is a well-established method for deriving utility values, essential for calculating QALYs in health economic evaluations. Given the absence of a national TTO survey in South Africa, Great Britain's (UK) TTO value set was used as a proxy for deriving health utility scores [40]. The TTO method carried out in the UK was used since it was often applied in Asia Pacific countries' studies to assess HRQoL [43,46].

This study employed a TTO method to assess participants' willingness to trade length of life for quality of life across different health states. The EQ-5D-3L responses were transcribed into predefined numerical health state codes, wherein each digit represents a level of impairment in a specific health dimension. For example, code '11111' would signify full health, while code '33333' would denote severe problems across all dimensions. These numerical codes were then matched with TTO utilities, quantifying the HRQoL for each participant. TTO utilities are bounded from 1 (indicating optimal health) to 0 (representing a health state equivalent to death). Negative values are conceivable for health states worse than death (WTD). The below formula calculates TTO utility (*U*) using *t*, the years in complete health. It transforms the health state codes into utility values to measure HRQoL based on individual EQ-5D-3L responses as presented below;

a. For conventional health states, TTO or better than dead **(BTD):** ***U = t/10***

b. For health states considered **WTD:** ***U = (t - 10)/10***

The constant 10, which signifies a baseline of 10 years in perfect health, is utilised in conjunction with the lead-time TTO method. This approach is commonly used among direct techniques because of its greater comparability with the method used to develop the EQ-5D scoring algorithm [41]. Secondly, a significant gap identified in this study is the absence of South Africa-specific utility value sets stratified by age group and gender. This lack of detailed, localised data challenges precise health economic evaluations within South Africa. To address this, the methodology involved the creation of new utility value sets that are stratified by 5-year age group and gender, specifically tailored to the South African population, thereby filling a critical gap in the existing health economic data. Using Stata 17, comprehensive health state valuation analyses were conducted. This included estimating TTO utilities and identifying predictors of HRQoL, with adjustments made for age and gender. All predictors were included in a single adjusted model to ensure comprehensive analysis drawn from existing evidence.

The dependent variable, HRQoL, was categorised into four ordinal levels: Low ($\leq$0.681), Moderate (>0.681&<0.835), High ($\geq$0.835& <1) and Perfect (=1) using the TTO utility score. Ordinal logistic regression is particularly suitable for this analysis due to the ordered nature of the HRQoL variable presented in ***Equation 1***.

$$\text{Logit}(P(Y \leq j|X)) = \ln\left(\frac{P(Y\leq j|X)}{P(Y>j|X)}\right) = \alpha_j - (\beta_1 X_1 + \beta_2 X_2 + ... + \beta_p X_p) \quad \text{………..…..(1)}$$

Logit($P(Y\leq j|X)$) denotes the proportional odds of the dependent variable Y being in category j or lower, given the independent variable X. while αj is the threshold (or intercept) for category j. There are $J-1$ thresholds; as the last category, J is the reference. $\beta 1, \beta 2, ..., \beta p$ are the coefficients for the independent variables $X1$, $X2$,..., Xp and $Y\leq j|X$) is the cumulative probability of the dependent variable Y being in category j or lower, given the independent variables X. The logistic regression was further employed to examine the factors influencing the 95th percentile of the TTO utility score. A dichotomous dependent variable was created to distinguish participants with low TTO utility values (HRQoL) below 0.64, recoded as '1' otherwise '0' assessed using ***Equation 2***.

$$\log\left(\frac{P}{1-P}\right) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_n X_n \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots..(2)$$

Here, p is the probability of falling into the 95th percentile, and X_1, $X_2, \ldots,$ *and* X_n are the predictors. The $\beta_1, \beta_2, \ldots, \beta_n$ are log odds quantifying the impact of each predictor.

5.7 Results

5.7.1 Sociodemographic, Economic, Clinical and Lifestyle Characteristics Results

Table 8 describes the sociodemographic and other characteristics of the analytical sample of 539 participants. Among participants, 21.4% were aged 55 to 59 years, while only 0.7% were in the 25 to 29 age group, with an average participant age of 54 years and a 10.8 standard deviation. A higher proportion were women (73.6%). Half of the participants were married or cohabiting, and a significant portion resided in rural areas (36.9%). Regarding education and employment, only 11% completed high school education, while 88.7% had some high school and completed primary education.

The majority of the participants were unemployed (70.1%), with lower-limit and upper-limit average monthly income proportions of 46.1% and 18.2%, respectively. Nearly a quarter of the participants (24.7%) reported being food insecure, and 15.2% did not have stable living conditions. A notable proportion engaged in hazardous or harmful alcohol consumption (26.3%) and smoking (24.3%), but illicit drug use was low (1.3%). The BMI score data indicated that most participants were overweight (58.8%) or obese (31.5%), 29.3% experienced severe stress levels, and 29.9% reported a low self-efficacy scale. The mean score for generalised self-efficacy among the participants was 27.8, with scores ranging from 10 to 36.

5.7.2 Descriptive Statistics of The HRQoL Domains Results

Table 7: Sociodemographic, economic, clinical and Lifestyle characteristics of the participants (n=539)

Independent variables	Description	n =539	
		n	%
Gender	Overall	539	100
	Male	128	26.4
	Female	411	73.6
Age[a]	Age in years	54 ($\bar{x}$)	10.8 (*sd*)
5 year age group	≤29	11	2.0
	30-34	18	3.4
	35-39	16	3.0
	40-44	47	8.8
	45-49	77	14.3
	50-54	83	15.5
	55-59	115	21.4
	60-64	78	14.5
	65-69	65	12.1
	≥70	29	5.4
Marital Status	Married/cohabiting	272	50.5
Study site	Rural	199	36.9
Education level	Secondary education completed Others (some secondary education school, and completed primary school)	61 478	11.3 88.7
Employment status	Unemployed Employed	378 161	70.1 29.9
Predicted monthly income (ZAR)[a,b]	Mean Lower-limit Upper-limit	1799 ($\bar{x}$) 1029 2903	524 (*sd*) 46.1 18.2
Food security	Insecure	133	24.7
Stable housing/living	No	82	15.2
AUDIT score	Hazardous/Harmful	142	26.3
Smoking	Yes	131	24.3
Drug use	Yes	7	1.3
BMI score categories	Normal (< 25 kg/m^2) Overweight (25-30 kg/m^2) Obese (BMI>30 kg/m^2)	79 290 170	15.9 58.8 31.5
Mental health (K10 score)	Low distress Moderate distress Severe distress	177 204 158	32.8 37.9 29.3
Self-efficacy scale	Low Moderate High	161 187 191	29.9 34.7 35.4
Perceived health score[a]	Numerical perceived health rating	76.7 ($\bar{x}$)	24.3 (*sd*)

[a]Mean and standard deviation were reported; [b]Mean, minimum and maximum reported; $\bar{x}$ = mean; sd = standard deviation

Table 8 summarises key descriptive statistics regarding the HRQoL domain scores. It shows that the mobility, self-care, and usual activities domains exhibit lower mean scores and lesser variability, as indicated by their standard deviations, than the pain and anxiety domains. This trend, as evidenced by the statistical measures presented in ***Table 9,*** suggests a heightened level of reported impairment within the Pain and Anxiety domains compared to others. The narrow confidence intervals associated with each domain underscore a high level of precision in estimating their respective mean scores, thereby enhancing the reliability of the observed patterns.

Table 8: HRQoL domain score of the participants (n=539)

HRQoL Domain	Sample size (n)	Mean ±SD	95% CI
Mobility	539	1.20 ± 0.40	1.16 – 1.23
Self-care	539	1.09 ± 0.30	1.07 – 1.12
Usual activities	539	1.16 ± 0.38	1.13 – 1.19
Pain	539	1.54 ± 0.57	1.49 – 1.59
Anxiety	539	1.56± 0.64	1.51- 1.62

5.1.1 HRQoL utility scores, stratified by gender and 5-year age group

The analysis noted limited observations within the 18 to 29-year-old age group.

Table 9: Gender and age-stratified HRQoL utility scores among people with diabetes in the Western Cape, South Africa (n = 539)

5 year age group	Male (mean± SD)	Female (mean ± SD)
≤29	0.95 ± 0.54	0.93 ± 0.68
30-34	0.96 ± 0.05	0.86 ± 0.09
35-39	0.87 ± 0.01	0.90 ± 0.08
40-44	0.89 ± 0.08	0.87 ± 0.11
45-49	0.88 ± 0.11	0.85 ± 0.12
50-54	0.85 ± 0.13	0.82 ± 0.11
55-59	0.88 ± 0.11	0.83 ± 0.11
60-64	0.88 ± 0.10	0.83 ± 0.12
65-69	0.84 ± 0.11	0.83 ± 0.11
70+	0.86 ± 0.12	0.87 ± 0.14

To enhance the statistical robustness of the TTO utility values, particularly in estimating HRQoL utility scores stratified by gender and 5-year age groups, all ages up to 29 were consolidated into a single category.

This approach was intended to strengthen the power of the analysis and ensure a more reliable interpretation of HRQoL variations across different age demographics. The data presented in ***Table 10*** showed similar trends across different age groups, such as 55 to 69 among females. Males consistently reported higher HRQoL than females in the same age brackets. For instance, in the 30-34 age group, males had a mean TTO utility of 0.96, while females reported 0.87. This pattern of higher HRQoL in males was observed across various age groups, with the most significant differences noted in younger demographics, particularly those below 29 years.

5.7.3 Predictors Associated with the HRQoL Utility Scores: The Ordinal Logistic Regression

Table 10: Predictors of HRQoL utility scores among people with diabetes in the Western Cape, South Africa, (n = 539).

Predicting variables of HRQoL	AOR (p-Value)	95% Confidence Interval
Age	0.98*	0.96 – 1.00
Male	1.64*	0.96 – 2.80
Married	1.01	0.69 – 1.49
Urban	0.41***	0.27 – 0.63
Stable Housing	1.13	0.67 – 1.90
Food Insecurity	1.04	0.67 – 1.62
Household Income	1.00	0.99 – 1.00
Primary Education	0.53***	0.36 – 0.79
Alcohol Consumption	1.89**	1.13 – 3.18
Smoking	0.95	0.59 – 1.53
BMI Score Categories		
Overweight	1.42	0.79 – 2.54
Obese	1.19	0.63 – 2.25
Self-Efficacy Scale		
Moderate	1.52*	0.97 – 2.40
High	2.04***	1.29 – 3.21
Mental Health Score		
Moderate	0.34***	0.21 – 0.55
Severe	0.16***	0.09 – 0.27

Significance level 1%, 5%**, 10% ****

Given the ordinal nature of these categorised TTO scores, ordinal logistic regression was employed for analysis. The mean EQ-5D-3L utility score was 0.85, with a standard deviation of 0.11.

The HRQoL index scores ranged from 0.53 to 0.98. The study population had a relatively high quality of life, given that the TTO HRQoL index ranges from -1 to 1, with higher scores denoting better health states. However, in the 95th percentile, 27 patients (6%) reported HRQoL scores $\leq$ 0.681, indicating very low overall health and well-being perception among this subgroup. As presented in ***Table 11***, male participants were more likely to report higher HRQoL compared to females (AOR) of 1.64 (p = 0.07). Those receiving care from urban clinics reported lower HRQoL compared to their rural counterparts, as indicated by an AOR of 0.41 (p<0.01).

Individuals with only primary education had lower odds of higher HRQoL compared to those with completed secondary education (AOR = 0.53, p<0.01). Surprisingly, a higher AUDIT score was positively associated with HRQoL (AOR = 1.89, p = 0.02).

Crucially, psychological aspects played a significant role. Higher self-efficacy was positively associated with higher HRQoL; individuals with moderate and high self-efficacy had AORs of 1.52 (p = 0.07) and 2.04 (p<0.01), respectively, compared to those with low self-efficacy. Additionally, mental health status was a strong predictor; those with moderate and severe mental health scores were significantly less likely to report higher HRQoL, with AORs of 0.34 (p<0.01) and 0.16 (p<0.01), respectively. BMI categories, marital status, housing stability, and food security showed no statistically significant association with HRQoL.

5.7.4 Predictors of Very Low HRQoL Utility Scores: The 95th Percentile

About 6% (27 patients) were in the bottom 95th percentile of TTO scores, with utility values ≤0.681. Presented in ***Table 5***, using the logistic regression model, food insecurity significantly increased the likelihood of reporting very low HRQoL (AOR= 2.70, CI: 1.15 - 6.34, p= 0.02). Urban also emerged as a relevant factor, with patients receiving care from clinics in urban areas showing increased odds of very low HRQoL (AOR= 3.68, CI: 0.97 - 13.95, p= 0.05). An educational level further influenced HRQoL, as those with only primary education were more likely to report very low HRQoL (AOR= 2.83, CI: 1.17 - 6.81, p= 0.02), indicating the importance of educational resources in effective diabetes care. The results present two surprising findings regarding the factors influencing HRQoL. Firstly, smokers were unexpectedly less likely to report very low HRQoL, as indicated by an adjusted odds ratio (AOR) of 0.14 (CI: 0.03 - 0.75, p= 0.02). Secondly, overweight individuals showed significantly lower odds of reporting very low HRQoL compared to those with normal weight, with an AOR of 0.20 (CI: 0.05 - 0.73, p= 0.01). Most importantly, severe mental health scores were strongly associated with an increased likelihood of very low HRQoL (AOR= 18.31, CI: 2.21-152.08, p= 0.01), highlighting the profound impact of mental health on the quality of life in people with diabetes.

Table 11: Predictors of very low HRQoL utility scores among the participants (n = 539)

Predicting variables of very low HRQoL	**AOR (p-Value)**	**95% Confidence Interval**
Age	1.02	0.98 – 1.07
Male	1.01	0.31 – 3.31
Married	2.02	0.83 – 4.88
Urban	3.68**)	0.97 – 13.95
Stable Housing	0.48	0.16 – 1.47
Food Insecurity	2.70**	1.15 – 6.34
Household Income	1.00	0.99 – 1.00
Primary Education	2.83**	1.17 – 6.81
AUDIT score	0.29	0.06 – 1.47
Smoking	0.14**	0.03 – 0.75
BMI Score Categories		
Overweight	0.20**	0.05 – 0.73
Obese	0.30*	0.08 – 1.20
Self-Efficacy Scale		
Moderate	0.72	0.26 – 2.01
High	0.85	0.32 – 2.30
Mental Health Score		
Moderate	4.41	0.51 – 37.82
Severe	18.31***	2.21 – 152.08

*The regression model was adjusted for Age, Male, Married, Urban, Stable Housing, Food Insecurity, Household Income, Primary Education, AUDIT score, Smoking, BMI Score Categories, Self-Efficacy Scale and Mental Health Score. Significance level 1%***, 5%**, 10% **

5.8 Discussion

This study critically analysed HRQoL among people with diabetes in South Africa, integrating the complex interplay of predicting factors such as socioeconomic factors, education, household stability, and lifestyle. Despite a generally high mean EQ-5D-3L utility score of 0.85 across 539 participants, a significant subgroup of 27 participants (6%) reported HRQoL scores indicative of very low ($\leq$0.681) health outcomes. The findings suggest key predictors of HRQoL, with urban residency, primary education level, and lifestyle factors such as alcohol consumption and smoking. Remarkably, those with severe mental health issues experienced very low HRQoL, 18 times higher than those with common distress, underscoring the profound and substantial impact of psychological well-being on overall health.

The findings of the present study, similar to studies from Bangladesh, the Netherlands, and England, indicate that anxiety/depression and pain/discomfort are significant health concerns [44] in the South African diabetic population. The highest utility value less than perfect health in South Africa was for the 11112 states of 0.8534, aligning closely with international values such as Ethiopia (0.94) [45], Indonesia 0.92) [48], England (0.95) [46], and China (0.95) [47], while being higher than Bangladesh (0.62) [43].

Analysis revealed multifaceted factors influencing health-HRQoL among South African people with diabetes. The gender disparity observed, with males reporting higher HRQoL, aligns with existing literature suggesting varying health management practices and perceptions between genders [43,44]. Urban residency, negatively associated with HRQoL, highlights the unique challenges of urban living, potentially tied to lifestyle stressors or toxic environmental factors found in developing countries [49,52]. These health challenges prevalent in urban settings are known to affect HRQoL adversely. Another study from China reported no significant difference in HRQoL between urban and rural participants, suggesting that the impact of urban living on HRQoL can vary greatly depending on specific regional and cultural contexts [187].

The counterintuitive finding of alcohol consumption and a positive correlation with HRQoL aligns with another South African study that reported the possibility that alcohol consumption may offer temporary relief from stress or anxiety, potentially influencing self-reported HRQoL, especially in short-term contexts [23]. Similarly, the adverse relationship between smoking and very low HRQoL contributes to the evidence base on smoking's negative impact on chronic diseases [23,24]. The study's most striking finding is the significant influence of mental health issues on HRQoL, markedly diminishing HRQoL, highlighting the critical need for integrating mental health support within diabetes care frameworks. Data show that in South Africa, the lifetime prevalence of any disorder is 30.3% [51], and about 46% of people with diabetes face mental health challenges [33].

Another intriguing aspect is the paradoxical relationship between higher self-efficacy and lower HRQoL. This counterintuitive result suggests that individuals with higher self-efficacy might have higher life quality standards, thus perceiving their HRQoL as lower when these standards are not met [26-29]. This finding adds a new dimension to understanding HRQoL in chronic diseases and calls for a deeper exploration of the role of self-efficacy in diabetes management.

The significant impact of higher BMI scores and urban residency on HRQoL among the subgroup (n=27) with very low scores suggests that for individuals already facing substantial quality-of-life challenges, the additional health and psychological burdens of being overweight or obese while residing in urban areas are more acutely felt. Household income and having a stable living situation are often considered important in health outcomes [31,35] and warrant further investigation into the underlying reasons and the interplay of other factors.

This pioneering study is the first in South Africa to report age- and gender-stratified utility values, which were previously lacking in quantifying QALYs and conducting economic evaluations tailored to specific demographic segments. By providing this critical data, this study offers valuable evidence for future studies aimed at understanding the nuanced impacts of age and gender on health impacts or outcomes. Secondly, not enough studies have assessed the HRQoL of people with diabetes using detailed data from urban and rural primary healthcare facilities and settings, including physical and mental health components of people with diabetes in SSA, including South Africa. Given the limited research availability and less exploration, this study furnishes crucial insights for tailoring interventions to bolster HRQoL among people with diabetes.

Improving access to healthcare in rural areas is essential to mitigate disparities in diabetes management between urban and rural communities. Enhancing diabetes education tailored to communities with lower educational levels and supporting economic stability through food security programs are critical to fostering effective diabetes self-care and management. Implementing these measures could help address the complex interplay of social determinants that influence health outcomes, ultimately leading to more equitable healthcare delivery across different population segments.

One notable limitation of this the data utilised is the lack of external validation for newly identified HRQoL predictors. While this study acts as a validation of previously known predictors within a South African context, thereby contributing to the robustness of existing models, the absence of external validation for new predictors means that their generalizability and applicability to other populations remain uncertain. Future research should focus on validating these new predictors in diverse cohorts to strengthen the overall findings and enhance the reliability of health-related quality of life models.

In acknowledging the limitations of the study, the potential introduction of cultural or societal biases by applying UK TTO values is recognised, which may not fully capture the health state preferences of the South African population. While collection of South African-based data to derive utility sets that are more representative of the domestic population's health state preferences are crucial, the study's strengths lie in incorporating a comprehensive set of theoretically relevant and clinically interpretable predictors, thus providing valuable insights into the multifaceted predictors of HRQoL.

5.9 Conclusion

The investigation into HRQoL among South African people with diabetes has revealed pivotal factors such as gender, urban residency, education, and mental health as significant predictors. The study highlights the necessity for diabetes management strategies that encompass these determinants to enhance patient outcomes. It also calls for further research to develop locally nuanced utility sets, ensuring that future health economic assessments are tailored to the unique South African context. These insights pave the way for more personalised and effective healthcare interventions, ultimately improving the quality of life for individuals with diabetes in South Africa.

5.10 References

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6. Chapter Six: Social Determinants of Health and Diabetes Self-Care Management in South Africa

6.1 Context of the Study

The escalating prevalence of diabetes in South Africa and its substantial economic costs and disproportionate burden on specific population segments underscores the critical need to understand and address the impact of SDOH on diabetes management and health outcomes. This study explores the association between SDOH and diabetes self-care management practices, employing a comprehensive 5-domain SDOH framework developed by the Healthy People 2020 (HP2020) initiative. By investigating various domains, including demographic status, economic factors, education, lifestyle, and healthcare, the study aims to understand self-care management and determinants of adherence among individuals with diabetes.

Addressing SDoH remains prominent on the universal healthcare agenda and is in line with the goals and priorities outlined by the WHO. However, South Africa has stark social inequities, translating into a high burden of health inequities and premature deaths among people with diabetes. Consolidating these research directions was needed to provide a comprehensive roadmap for future studies to deepen the understanding and improve diabetes care strategies.

The associations between SDOH and diabetes self-care management in the South African context highlight the necessity for a more holistic understanding and approach to interventions. The analysis carries significant implications for future intervention strategies and policy frameworks. It provides a foundation for understanding the complex determinants of diabetes self-care management in South Africa, a country experiencing a rising prevalence of diabetes. The findings emphasise the crucial role of socio-demographic factors in diabetes self-care, suggesting that interventions should consider these variables to enhance self-care guidelines among individuals with diabetes. A comprehensive approach, as outlined in this study, may pave the way for more robust, tailored interventions to improve self-care management and overall health outcomes for individuals with diabetes in South Africa.

This manuscript was submitted to BMC Public Health. It fulfils the objective 3.) To investigate Social Determinants of Health (SDoH) associated with diabetes self-care management and adherence in South Africa. It is presented in its submitted format within this thesis. Assegid

Hellebo is the first author, with supervisory input from co-authors, particularly Andre Pascal Kengne, Olufunke Alaba, Amarech Obse and Susan Cleary.

6.2 Abstract

Objective: Diabetes is an incapacitating condition affecting millions of people in South Africa. Maintaining optimal glycaemic control is crucial in preventing diabetes complications, highlighting the importance of diabetes self-care. This study examined how Social Determinants of Health (SDoH) are associated with self-care management practices in individuals with diabetes in South Africa using the framework developed by the Healthy People 2020 initiative.

Methods: This study utilised cross-sectional Project Mind baseline data collected in 2017. Self-care management was coded on a scale from '0' (never) to '7' (daily adherence). For analysis, this scale was dichotomised into two categories: low self-care (scores 0-5) and high self-care (scores 6-7). Furthermore, adherence with these daily self-care activities was categorised into three levels: no adherence, partial adherence (inconsistent or partial adherence to activities), and full adherence (consistent adherence to all self-care activities).

Results: The analytical sample (n=539) was predominantly female (76%), with a mean age of 54 years, urban residents (60%), unemployed (70%), and attained secondary education (11.3%). In determining the attainment of a higher scale of self-care, age (AOR=1.02, CI=[0.99,1.05]) and secondary education (AOR=1.13, CI=[1.02, 2.03]) were associated with an increase in the scale of self-care. Conversely, urban residency (AOR=0.50, CI=[0.29,0.88]) and being obese (AOR=0.43, CI=[0.19,1.00]) were associated with a lower scale of self-care. Although not statistically robust, food insecurity decreased while being a woman and having a stable house showed an increased association. Travelling longer distances to access healthcare was positively associated with no adherence, and urban residency has a negative association with full adherence relative to partial adherence.

Conclusions: The associations between SDoH and diabetes self-care management within a South African context highlight the need for a more holistic understanding and approach to interventions. Future endeavours should examine these determinants more broadly and formulate integrative strategies to ameliorate diabetes self-care.

6.3 Introduction

Diabetes is a prevalent lifestyle-related disease that imposes substantial financial strains on healthcare systems worldwide. In 2021, the global cost of diabetes was approximately $966 billion, a figure that's expected to surge due to increasing prevalence and treatment expenses [1,2]. Within this global context, South Africa's diabetes-related health expenditure in the same year was estimated to be US$7.2 billion by the International Diabetes Federation (IDF) [2]. This significant national expense can be attributed to late diagnosis and inadequate self-care management, leading to increased comorbidities [2].

Self-care management, appropriate access to healthcare services, and regular consultations with healthcare providers about diabetes status are crucial in improving glycated haemoglobin (HbA1c) levels [3]. Evidence suggests that individuals with diabetes who exhibit a higher degree of self-care management tend to have fewer healthcare facility visits [4,5]. This is due to the fact that enhanced self-care practices lead to improved health outcomes, including reduced need for emergency services or care for complications [4]. This reduction can decrease the incidence of diabetes-related complications such as retinopathy, nephropathy, and neuropathy [4,5].

The literature has shown that Social Determinants of Health (SDoH) - the socioeconomic conditions in which individuals work, live, and age - play a substantial role in influencing health outcomes [6,7]. The United States Centers for Disease Control and Prevention (CDC) characterised SDoH as economic and social situations that influence the health of people and communities [7]. Some key SDoH domains include sociodemographic, economic, health and healthcare, lifestyle, and social capital [6,11]. These circumstances are shaped by the distribution of money, power, and resources, primarily responsible for health inequities and unfair and avoidable differences in health status between communities and individuals [7,13].

The socioeconomic domain is traditionally gauged by income, education, and occupation [9,12], yet factors like housing, healthcare accessibility, insurance coverage, residence area, lifestyle, and social capital also contribute to these evaluations [10,15]. Intertwined with life-course vulnerability from prolonged exposure to resource-deprived environments, these attributes significantly impact disparities in disease risk, diagnosis, and outcomes [11-14]. These aspects could be improved by changing relevant policies because the determinants are often a result of unequal social and economic statuses or systems. South Africa has policies for mitigating non-communicable diseases (NCDs) but lacks practical implementation. [19-21]. As a result, the SDoH remain the primary contributor to unfair and avoidable differences in health status, including the increased risk of diabetes and diabetes-related complications [20,22].

Addressing SDoH remains prominent on the universal healthcare agenda in line with the goals and priorities outlined by WHO [17]. However, South Africa has stark social inequities, translating into a high burden of health inequities and premature deaths among people with diabetes [19]. The country has one of the highest numbers of people with diabetes in SSA, with an estimated 4.2 million people with diabetes aged 20–79 years in 2021 [2]. The burden disproportionately affects the 'economically disadvantaged', leading to higher rates of morbidity and mortality due to limited access to healthcare, education, and necessary management resources [22,28]. Addressing social determinants is believed to be a cornerstone of the National Department of Health's Primary Healthcare (PHC) Re-engineering Strategy [21]. The government's commitment to prioritise PHC with its focus on SDoH was endorsed in the Health Act (61 of 2003). However, implementing it has been challenging because of a lack of political and policy commitments from various stakeholders within the government [21,22].

Although research has demonstrated the importance of SDoH in shaping health generally [4,28,29], evidence pertaining to diabetes often revolves around understanding its prevalence and clinical outcomes. In contrast, investigations into how various SDoH factors intersect with diabetes self-care management have been limited. This study aimed to elucidate the relationship between traditional and less frequently studied SDoH factors and their impact on diabetes self-care management and healthcare-seeking adherence behaviours. By doing so, it was sought to deepen the understanding of how various SDoH elements influence patient self-care management and adherence behaviours in diabetes care. This South African study employed a unique 5-domain SDoH framework developed by the Healthy People 2020 (HP2020) initiative, also known as the SDoH factors [49]. Using the HP2020 domains, such as demographic status, economic factors, education domains, lifestyle domains and healthcare domains, this study examined self-care management as well as determinants of adherence among individuals with diabetes.

6.4 Methods

6.4.1 Study Data, Design and Population

The data for this study were sourced from Project MIND, a clustered randomised controlled trial integrating psychological treatment into chronic disease care in the Western Cape, South Africa [27]. Conducted across 24 HIV and diabetes clinics in the Western Cape, it included 15 urban and nine rural facilities. In 2017, Project MIND enrolled 1340 participants aged 18 and above, receiving treatment for HIV and/or diabetes from selected clinics. For this sub-study, baseline data from 539 participants exclusively diagnosed with diabetes was utilised. Detailed methodology is available from Myers et al. (2018) [27].

6.4.2 Analysis and Measures

In this analysis, key independent variables and outcomes were first cross-tabulated against the dependent variable, self-care management, to observe initial patterns and relationships. Subsequently, binary logistic regression was applied to examine the association between the independent variables and self-care management scales categorised into low and high self-management. Multinomial logistic regression was utilised to explore the relationships between the independent variables and the different categories of self-care adherence (no, partial, and full).

6.4.3 Outcome Variables

i. ***Diabetes self-care management and adherence categories***

Diabetes self-care was measured with the Summary of Diabetes Self-care Activities Scale [30]. Participants were asked about their daily self-care activities over the last seven days using the following three domains: following a healthy eating plan, doing at least 30 minutes of physical activity, and checking their feet. Participants rated the extent to which they implemented the activity on a scale from 0 (not following the activity at all) to 7 (following the activity every day of the past week). To assess overall self-care, a dichotomous dependent variable was created, categorising self-care as 'Low' for those participants who scored between 0 and 5 in any of the domains, indicating less frequent or incomplete adherence, and 'High' for scores of 6 or 7 in all domains, reflecting consistent daily adherence to all three activities. The creation of a dichotomous dependent variable aligns with Agidew et al. (2021), who employed percentage-based adherence scores and found that self-care practices conducted with >75% adherence, equivalent to 6 or 7 days a week in the analysis, significantly improved diabetes outcomes [18]. Furthermore, self-care was additionally categorised into three adherence levels: 'No adherence' signifies no adherence to any activities, capturing a complete lack of engagement in self-care; 'Partial adherence ' indicates adherence to some but not all activities, reflecting varying degrees of engagement; and 'Full adherence' represents adherence to all three activities, denoting optimal self-care adherence.

Table 13: Definitions and Scoring Criteria for Self-Care and Adherence Categories

Domain	**Score = -1**	**Score > 0 & <= 5**	**Score >= 6**
Last seven days' health eating plan	Non-Adherent	Partially Adherent	Fully Adherent
Last seven days doing at least 30 minutes of physical activity	Non-Adherent	Partially Adherent	Fully Adherent
Last seven days checking one’s feet	Non-Adherent	Partially Adherent	Fully Adherent

Outcome Variable	**Definition**
Self-Care Score = 1 (High)	All domains scored 6 or above
Self-Care Score = 0 (Low)	Any domain scored below 6
Fully Adherent (Category 1)	All domains scored 6 or above
Non-Adherent (Category 3)	All domains scored -1
Partially Adherent (Category 2)	Any combination of scores not fitting into categories 1 or 3

6.4.4 Independent Variables

This study employed the socio-ecological framework from Healthy People 2020, which is designed to elucidate SDoH [44]. This framework aids in creating evidence-based resources and tools by systematically categorising SDoH into distinct domains [44], as explained below:

i. Demographic Domain

Differences in diabetes self-management behaviours based on age, gender, marital status, and study site (urban vs. rural) have been shown to be associated with differences in self-management [42]. These factors were investigated in the South African context.

ii. Economic Stability Domain

The household monthly average income, employment status, food security, and stable living conditions were considered due to their reported impact on diabetes self-care management [5, 33]. To quantify household income, interval regression was employed to transform categorical income bands into quantitative measures. Employment status was categorised into a binary variable, indicating either 'employed' or 'unemployed.' Similarly, food security and housing stability were each coded as binary variables. For these, a '1' represented the presence of food security and stable living conditions, while a '0' indicated the absence of these conditions.

iii. Education Domain

The level of education was evaluated to understand their relationship with self-care and health outcomes among individuals with diabetes. Education was assessed by the question, "What is the highest level of education you have passed?". It was recorded as binary: primary school and some secondary education '0' and completed high school and further studies '1'.

iv. Lifestyle Domain

This domain included lifestyle exposures (i.e., alcohol, tobacco, and illicit drug use). The impact these substances have on health is well documented [34]. In this domain, alcohol use was assessed using the Alcohol Use Disorders Identification Test (AUDIT). The categorisation included no drinking, low-risk drinking (<8), hazardous drinking (8-15), and harmful drinking (>16). However, due to small frequencies in the hazardous and harmful categories, data was consolidated into low-risk (<8) and harmful/hazardous drinking (>8). Individuals with an AUDIT score <8 were coded as low-risk, while those with a score >8 were classified as hazardous or harmful. Smoking and drug use were coded as 'no' and 'yes' for current smoking or illicit drug use. However, 98% of the study participants reported 'no' to drug use. Thus, the variable was dropped, given the absence of adequate variation.

v. Health and Healthcare Domains

The health domain comprises well-being, which is vital for managing diabetes, whereby obesity, defined as body mass index (BMI) > 30 kg/m^2, is a leading risk factor [35,36]. BMI data was recoded into three categories—normal ($BMI<25\ kg/m^2$), overweight ($25\leq BMI<30\ kg/m^2$), and obese ($BMI>30\ kg/m^2$). Once diagnosed with diabetes, effective management is crucial and necessitates accessing healthcare services for treatment and regular diabetes monitoring [41]. Travel time to the clinic, measured in continuous minutes and categorised for analysis, served as a proxy for healthcare access, with longer times indicating greater barriers to accessing medical services [41].

6.4.5 Statistical Analysis

This study employed a binary logistic regression for its primary analysis, presented in Equation 1, to assess the influence of SDoH on adherence to diabetes self-care. The dependent variable was recorded as a '0' for low and a '1' for high (>75%) adherence self-care practices..

$$\log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_n X_n, \quad \ldots\ldots\ldots\ldots\ldots\ldots(1)$$

The β coefficients represent the change in the log-odds of achieving higher self-care for a one-unit change in the predictor variables (X), holding other variables constant. While describing the dependent variable's log of odds in a binary logistic regression model, P is the probability of the event occurring (e.g., a higher scale of self-care management).

Furthermore, a secondary analysis assessed factors associated with different degrees of adherence to self-care using the multinomial logistic regression presented in Equation 2. The study data was categorised into three levels of adherence categories (no, partial and full adherence).

$$\text{Logit}(P(Y = j|X)) = \ln\left(\frac{P(Y=j|X)}{P(Y=J|X)}\right) = \beta_{0j} + \beta_{1j}X_1 + \beta_{2j}X_2 + \ldots + \beta_{pj}X_p \quad \ldots\ldots\ldots\ldots\ldots\ldots(2)$$

Where Logit(P(Y=j|X)) is the log-odds of outcome j relative to a reference category. β1j, β2j., and βpj are the coefficients to be estimated for outcome j. X1, X2., and Xp are the independent variables. P(Y=j|X) is the probability of the outcome j given the independent variables X.

6.5 Results

6.5.1 Demographic Characteristics

Table 13 describes the sociodemographic and other characteristics of the analytical sample (n=539). Gender (p=0.419) was not significantly associated with the variability of self-care management. Female participants accounted for 76% of the sample size, and the mean age was 54.3 ± 11 years. Half the participants were married or cohabiting, and 60% accessed treatment at an urban or peri-urban clinic. In terms of employment, 70% of the sample was unemployed, and 11.3% had achieved secondary and further education. The predicted lower average household monthly income limit in South African Rand (ZAR) was ZAR1029 (US$55.78), and an upper limit of ZAR2903 (US$157.35), with the predicted average monthly patient income of ZAR1799 (US$97.49). About 25% of the participants expressed some level of food insecurity. A stable living situation was absent for 15% of participants. Only 12% of the participants engaged in high levels of self-care by achieving a score of 6 or more out of a maximum of 7 on the self-care scale.

Further analysis that assessed the level of adherence to diabetes self-care indicated that 2% of the participants reported complete none-adherence, 86% were partially adherent, that is they only did some of the self-care activities (for example, six days of checking feet and 0 days of healthy eating or physical exercise or vice versa). On the other hand, 12% of participants reported being fully adherent to recommended practices. One-fourth of the participants reported smoking cigarettes, pipes, or chewing tobacco, while 26% of the participants reported harmful/hazardous alcohol use. Drug use was infrequent, reported by less than 2% of the participants. Among the participants, 59% were overweight, and 31% were obese (BMI>30). The Society of Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) guidelines recommend that individuals with diabetes undergo check-ups every three to six months [25]. However, the data revealed varying levels of adherence to this guideline.

Table 14: Descriptive characteristics of the analytic sample (n=539)

Variables	***Description***	***n***	***%***
Gender	Overall	539	100
	Male	128	26.4
	Female	411	73.6
Age[a]	Age in years	54 ($\bar{x}$)	10.8 (sd)
Marital status	Not married	267	49.5
Study site	Rural	199	36.9
Education level	Primary and some secondary school completed	478	88.7
	Secondary education completed	61	11.3
Employment Status	Unemployed	378	70.1
Predicted monthly income (ZAR)[b]	Mean	1799 ($\bar{x}$)	524 (sd)
	Lower limit	1029	46.1
	Upper limit	2903	18.2
Food security	Insecure	133	24.7
Stable living	No	82	15.2
Self-care scales	Low ($\leq$5 days out of 7)	476	88.3
	High ($\geq$ 6 days out of 7)	63	11.7
Self-care adherence categories	No adherence (0 of 7)	12	2.2
	Partial adherence (1-6 of 7)	463	85.9
	Full adherence (7 of 7)	64	11.9
AUDIT score	No/low risk	397	73.6
	Hazardous/Harmful	142	26.3
Smoking	None smoker	408	75.6
	Current smoke	131	24.3
Drug use	Yes	7	1.3
BMI score	Normal (BMI< 25 kg/m^2)	79	15.9
	Overweight (BMI25-30 kg/m^2)	290	58.8
	Obese (BMI>30 kg/m^2)	170	31.5

[a]Mean and standard deviation were reported; [b]Mean, minimum and maximum reported; sd= standard deviation; $\bar{x}$ = mean; CI=confidence interval

Table 14 illustrates participants' adherence to individual diabetes self-care practices, revealing varying levels of adherence to each practice. Adherence to a recommended daily eating plan was the least commonly implemented self-care strategy, with only 31% of participants being fully adherent to this guideline. Physical activity for at least 30 minutes daily was reported by 38% of the sample, while daily foot care was the most practised self-care activity, with 52% of participants reporting full adherence. Only 2% of participants demonstrated no adherence, almost 86% exhibited partial adherence, and about 12% achieved full adherence to diabetes self-care.

Table 15: Domain-wise distribution of self-care practices among participants, n=539

Self-care practices	***Lower scale (0 to 5)***		***Higher scale (6 and 7)***	
	n	***%***	***n***	***%***
Followed the recommended daily eating plan in the past 7 days	371	69	168	31
Engaged in at least 30 minutes of physical activity daily in the past 7 days	335	62	204	38
Checked feet daily in the past 7 days	260	48	279	52

6.5.2 SDoH and Self-care Management

The primary findings regarding the association between binary self-care management and predictor variables are outlined in ***Table 15***. Following this, a binary logistic regression analysis was conducted, revealing age, receiving care from clinics in urban settings, secondary and higher education, stable housing, and elevated BMI score as statistically significant predictors ($p < 5\%$) of self-care.

A one-year increase in age yielded an adjusted odds ratio (AOR) of 1.02 (95% CI = 0.99, 1.05; p = 0.04), suggesting a modest increase in the likelihood of higher self-care associated with an increase in age. Conversely, residing in areas served by clinics located in urban settings, particularly in townships, reduced the odds of higher self-care compared to individuals in rural areas, with an adjusted odds ratio (AOR) of 0.54 (95% CI = 0.30, 0.97; p = 0.03). Secondary and further education was linked to higher self-care odds compared to those who completed only primary school and had some high school, with an AOR of 1.13 (95%CI = 1.02, 2.03; p=0.05). For overweight individuals, the adjusted odds ratio (AOR) of 0.57 (95%CI = 0.28, 1.16) suggested a trend toward lower self-care. However, this result did not reach statistical significance at the conventional alpha level of 0.05, as indicated by the p-value of 0.1 and the confidence intervals spanning unity. Obese individuals, with an AOR of 0.41 (p=0.03, CI = [0.18, 0.95]), had decreased odds of higher self-care compared to those with normal weight. Other variables such as marital status, gender, food insecurity, household monthly income, AUDIT score and distance travelled to access health care at a diabetes clinic were not statistically significant.

Table 16: Logistic regression results for self-care management (n=539)

Independent variables	***AOR***	**95% Confidence Interval**
Age	1.02**	[0.99, 1.05]
Female	1.07	[0.52, 2.00]
Married	1.29	[0.73, 2.27]
Urban	0.54**	[0.30, 0.97]
Stable housing	2.2***	[0.78, 6.67]
Food insecurity	0.74	[0.36, 1.52]
Predicted monthly income	1.00	[0.99, 1.00]
Secondary education	1.13**	[1.02, 2.03]
AUDIT score	0.83	[0.42, 1.52]
BMI (overweight)	0.57*	[0.28, 1.16]
BMI (obese)	0.41**	[0.18, 0.95]
Travel time to clinic	1.00*	[0.99, 1.00]

The regression model was adjusted for Age, Female, Married, Urban, Stable Housing, Food Insecurity, Predicted Monthly Household Income, Secondary Education, AUDIT score, BMI Score, and Travel Time to Clinic as a proxy of distance travelled to access diabetes healthcare. Significance level Significance level 1%, 5%**, 10% ****

6.5.3 SDoH and Self-care Adherence

The multinomial logistic regressions in ***Table 16*** demonstrate significant associations between key social determinants and self-care adherence practices, with partial adherence serving as the reference category.

Table 17: Multinomial logistic regression results for self-care guidelines adherence, n=539

Independent variables	***AOR(*NA)***	***95% CI(NA)***	***AOR(**FA)***	***95% CI (FA)***
Age	0.96**	[0.90, 1.01]	1.01	[0.98, 1.04]
Female	0.25***	[0.06, 0.99]	1.03	[0.52, 2.03]
Urban	0.69	[0.19, 2.50]	0.55**	[0.32, 0.96]
Household income	1.00	[0.99, 1.00]	0.99	[0.99, 1.00]
High school completed	0.66	[0.13, 3.20]	0.13	[0.02, 1.03]

Stable House	0.18***	[0.05, 0.64]	2.24	[0.76, 6.54]
BMI (Overweight)	4.46	[0.43, 46.23]	0.57*	[0.28, 1.15]
BMI (Obese)	5.79	[0.47, 71.35]	0.40**	[0.17, 0.94]
Travel time to Clinic	0.94**	[0.88, 0.99]	0.99	[0.99, 1.00]

NA= no adherence; **FA= full adherence
NB: Partial adherence (PA) was the reference category
Significance level 1%, 5%**, 10% ****

Women demonstrated a decreased likelihood of non-adherence compared to men (AOR= 0.25; 95% CI= 0.06, 0.99; p= 0.04). Urban residents tended to be less fully compliant (AOR: 0.55; CI= 0.32, 0.97; p= 0.03), suggesting that urban living might pose challenges to consistent self-care. Stable housing emerged as a critical factor, significantly reducing the likelihood of no adherence (AOR: 0.18; CI= 0.04, 0.64; p= 0.01) and increasing the likelihood of full adherence (AOR: 2.24; CI= 0.77, 6.5; p=0.139), highlighting its role in facilitating better self-care. Obesity was associated with lower odds of full adherence (AOR: 0.40; CI= 0.17, 0.94; p=0.03). In addition, increased travel time to clinics, as a proxy to distance travelled to access diabetes care, was associated with small but significant reductions in the odds of non-adherence (AOR: 0.942; CI= 0.888, 0.999; p=0.04). This suggests that accessibility may play a role in influencing engagement in self-care practices.

6.6 Discussion

This study examined the influence of various SDoH factors, including socioeconomic status, education, household stability, lifestyle, and health and healthcare domains, on adherence to diabetes self-care guidelines. Among the findings, 88% of participants reported lower self-care scores (≤5 days), while 86% of participants reported partial adherence to self-care. Significant predictors included age, urban residence, primary education, and BMI. Notably, lower rates of self-care are associated with more diabetes complications and clinic visits, with 73% of those who missed diabetes clinic appointments in the last three months did not reschedule or attend in the previous three months. Furthermore, 60% of participants visited the diabetes clinic 2 to 3 times in the last 3 months, exceeding the SEMDSA recommendation of once every 3 or 6 months [25], while 86 of participants reported partial adherence with self-care. Several factors could contribute to this higher frequency of visits. Firstly, it may indicate a higher burden of diabetes complications or uncontrolled diabetes in this population, necessitating more frequent monitoring and adjustments in treatment [26]. Secondly, it could reflect a lack of access to or familiarity with self-management practices, leading to increased reliance on healthcare services

[30]. Additionally, socio-economic factors, such as limited access to medication or healthcare advice outside of a clinical setting, might compel patients to seek more frequent in-person consultations [30,26].

Analysis suggests slight improvements in self-care for older participants, possibly due to increased health awareness, access to care for other health conditions, and the longer duration of their diabetes. Longitudinal studies have also linked age to improved diabetes self-management and glycemic control [29,42]. Conversely, overweight and obese individuals in urban areas were less likely to report adherence to self-care guidelines, potentially attributed to physical constraints, comorbid conditions related to BMI, as well as the availability of resources and opportunities in urban townships for healthy eating and exercise [35]. The finding that urban residency significantly reduces the likelihood of higher self-care aligns with existing evidence suggesting that, despite typically having better access to healthcare resources and diabetes education [18], urban residents may face unique challenges that impact their engagement in self-management. While awareness of diabetes management is high, self-care is often impeded by stress, lack of access to fruits and vegetables, and environmental factors [40]. Urban challenges, particularly safety concerns and inadequate outdoor exercise spaces, hinder physical activity and healthy diet, a vital element of diabetes self-care [47].

Individuals with secondary-level education showed higher odds of effectively managing their condition. Lower educational attainment, often linked to limited health literacy and fewer resources for self-care, can be exacerbated by lower socioeconomic status. Conversely, higher literacy levels promote judgment and decision-making, encouraging adherence to self-care [6,31]. Considering these findings, policymakers should contemplate initiatives encompassing accessible health educational programs, informational materials, and community outreach efforts, specifically targeting individuals with lower educational attainment and socioeconomic status. These initiatives may enhance awareness and understanding of effective diabetes self-care management [6,31]

This study found that food insecurity is associated with lower self-care management in diabetes, but its impact is less pronounced. This aligns with the existing literature, noting a similar link between food insecurity and reduced diabetes self-care management [39]. Notably, monthly predicted household income did not show association with higher self-care management. This may be due to the predominantly low-income sample, with a 70%

unemployment rate and incomes below South Africa's minimum wage [22]. The study's unique characteristics, including high unemployment and pensioner rates, suggest that income may not be the primary determinant of higher adherence to diabetes self-care guidelines in this population.

Gender and marital status did not show an association with higher self-care management in this sample, contrary to some assumptions and existing literature [6] that emphasise their role in health outcomes. Additionally, despite the presence of hazardous drinkers and current smokers (25%), alcohol consumption and smoking did not significantly impact self-care behaviours in this demographic.

Regarding self-care adherence, women showed slightly higher adherence with self-care practices, which aligns with findings from a similar study in Egypt [47], suggesting a similar pattern across different cultural contexts. This gender-specific trend in self-care adherence may be influenced by the generally higher health awareness and engagement in preventive healthcare behaviours observed in females [44,45]. The correlation between urban residence and reduced adherence in the study may be linked to the challenges posed by urban lifestyles, which often include sedentary behaviours and increased consumption of unhealthy foods due to economic development [45,48]. These findings emphasise the importance of considering gender and urbanisation when developing targeted interventions to promote self-care practices.

Other studies align with the current findings, indicating a correlation between those who are able to access health care and those who are proactive in diabetes self-management [37,49]. These individuals, familiar with healthcare settings, may be more inclined to inquire about their diabetes care, thus enhancing their self-management practices. This finding supports the idea that promoting self-care is a cost-effective and beneficial strategy, in contrast to frequent healthcare facility visits that can impose considerable provider costs [40]. It underscores the importance of further research to uncover predictors of healthcare system navigation and its connection with diabetes self-management in this population. In addition, the varying significance of income across different analytical groups emphasises the need for methodological rigour and a comprehensive, empirically grounded approach to explain the complex interplay among socioeconomic factors, healthcare services access, and self-care management.

Frequent healthcare visits were associated with participants reporting suboptimal self-care, deviating from daily diabetes management practices. This pattern, imposing both direct and indirect costs on healthcare systems and patients [38,40], highlights the need for interventions aligned with the American Diabetes Association (ADA) and SEMDSA standards to mitigate complications. It also suggests the importance of healthcare providers tailoring their advice to patients' perceptions and circumstances for effective self-care [40,41]

This study identifies several key areas for further investigation to enhance understanding of diabetes self-care management. These include exploring the underlying factors such as healthcare access, cultural attitudes, and environmental influences, examining the impact of income and economic diversity on self-care practices, investigating the role of lifestyle factors in self-management, and understanding the reasons behind high clinic visit frequency.

This study has limitations, including not accounting for confounding variables like media exposure to diabetes information, family history, comorbidities, or traditional medicines. The assessment of self-care practices was confined to a 7-day period, not capturing long-term adherence impacts on glycemic control. Its cross-sectional nature restricts causal conclusions, and reliance on subjective self-care assessments may introduce recall and social desirability biases. Additionally, it is important to note that the analytical sample was part of a cluster randomised controlled trial (cRCT), where two arms received interventions for depression or alcohol use. Although these interventions were not administered at baseline, this sample may represent a lower mental health status compared to the average diabetic dependent on government health services, potentially influencing the study outcomes.

This study also acknowledges BMI's potential endogeneity but does not correct it due to the complexity of applying methods like instrumental variables within the constraints of cross-sectional data. This limitation necessitates a cautious interpretation of BMI's influence on diabetes self-care as associative, not causal, and underscores the need for further causally oriented research using more robust statistical techniques to clarify these effects.

The decision to recode the continuous TTO utility score into ordinal categories while enhancing interpretability and model suitability potentially limits the analysis by reducing the granularity of data. This transformation may obscure subtle but clinically important variations within the utility scores, which could be crucial for detailed econometric modelling and precise health outcome assessments. Future studies should consider incorporating methods that maintain the continuous nature of TTO scores to capture a more nuanced understanding of health utilities. Although initial explorations indicated a low risk of multicollinearity due to distinct categorical variables and a moderate number of predictors, the lack of formal multicollinearity testing in the reporting could impact the transparency and reliability of the findings. Formal testing in future studies will enhance the statistical robustness and credibility of the results. Reclassifying continuous self-care scores into 'Low' and 'High' categories simplifies analysis but may lead to a loss of detailed information, potentially obscuring nuanced differences in self-care practices. Future research should consider models that retain the continuous nature of the data to capture more comprehensive insights. Nevertheless, this analysis carries substantial implications for future intervention strategies and policy frameworks, providing a foundation for understanding the multifaceted determinants of diabetes self-care management in South Africa as diabetes prevalence continues to rise.

6.7 Conclusion

The investigation sheds light on the multifaceted nature of social determinants impacting diabetes self-care management, with varied adherence levels to diabetes self-care practices among participants. The findings highlight the importance of socio-demographic factors in diabetes self-care and suggest that interventions should consider these variables to improve self-care practices among individuals with diabetes. Future studies should delve deeper into these associations and broaden the investigative scope to encompass other socioeconomic and environmental determinants. Such a comprehensive approach may set the foundation for more robust, tailored interventions aiming to ameliorate a higher activity scale of self-care management and overall health outcomes for individuals with diabetes within the South African setting

6.8 References

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7. Chapter Seven: Discussion and Conclusion

7.1 Overview of the chapter

This section synthesises the comprehensive findings from the four core results chapters (three to six), which scrutinise the economic, well-being, and social determinants of the diabetes burden in South Africa. A discussion of the key research findings, strengths, and limitations of the thesis is presented in this chapter. Moreover, it underscores the unique contributions of this thesis to the existing body of knowledge and bridges existing gaps in the scholarship, while others signify pioneering analyses within the country and the broader Sub-Saharan Africa region.

7.2 Summary of the Thesis Findings

7.2.1 Aim of the Research

As described in Chapter One, section 1.8, the overall aim of this research was to evaluate the economic and social burden of diabetes in South Africa, focusing on productivity impacts, management costs and cost-effectiveness, and the influence of social determinants on patient outcomes and predictors of health-related quality of life.

7.2.2 Specific Objectives Were

1. To systematically review the costs and cost-effectiveness of type 2 diabetes management in sub-Saharan Africa.
2. To quantify the burden of type 2 diabetes on the productivity and economy in South Africa through a life table microsimulation modelling to a) quantify excess mortality, b) estimate Years of Life Lost (YLL), and c) assess the extent of Productivity-Adjusted Life Years (PALYs) lost among the working-age South Africans living with diabetes.
3. To assess the influence of Social Determinants of Health (SDoH) associated with diabetes self-care management and adherence in South Africa.
4. To assess the predictors of health-related quality of life (HRQoL) and time trade-off utility (TTO) values among people with diabetes in South Africa.

The aim and all the specific objectives were accomplished through four parent studies. This thesis reviewed and synthesised information regarding the costs and cost-effectiveness of managing T2D in SSA, with the aim of enhancing awareness, optimising resource allocation, and supporting evidence-based decision-making. It further evaluated the economic and social burden of diabetes in South Africa and utilised population life table modelling to estimate the impact of T2D on the South African population, specifically in terms of the novel PALYs metrics. Moreover, it investigated the role of SDoH in diabetes self-care management practices, emphasising the importance of maintaining optimal glycemic control. The TTO method was used to assess HRQoL in South Africans with diabetes due to its robustness and the theoretically substantiated utility values it yields by incorporating dimensions of time and mandating trade-offs between life quality and quantity.

7.2.3 Summary of the Chapter Contents

Based on the findings presented in Chapters three to Six of this thesis, the following findings were established:

Chapter Three- costs and Cost-effectiveness of Type 2 diabetes management in sub-Saharan Africa: A systematic review includes a paper currently under peer-review for publication. From an economic standpoint, the research presents a significant burden imposed by the management of T2D. With significant direct costs to both healthcare providers and patients, studies spotlight the stark disparity in the financial burden of diabetes care. Innovative care models like pharmacist-led interventions and mobile health (mDiabetes) programs have emerged as cost-effective solutions. Still, the cost-effectiveness (CEA) of different interventions varied widely, largely dependent on the economic context of each country within SSA. Notably, while some interventions were lauded for their economic prudence in specific settings, others failed to meet the threshold for being considered cost-effective, especially when analysed against the GDP per capita of countries in the region. The studies collectively paint a grim picture of the societal financial distress caused by T2D. In some instances, the annual cost of diabetes care approaches or exceeds 88% of the average annual income, laying bare the economic strain on individuals and families. This strain is exacerbated by the high OOP healthcare expenditure prevalent in SSA, a region already grappling with numerous economic challenges.

Chapter Four: burden of diabetes on the productivity and economy in Sub-Saharan Africa. A life table modelling analysis from a South African perspective includes a paper published in Pharmacoeconomics. This chapter found a profound burden of T2D management.

In 2019, the working-age population of South Africa was approximately 22.73 million people, accounting for about 38% of the total population. The loss of 13 million PALYs thus represents a significant impact, affecting nearly 57% of the working-age population in terms of lost productivity over their lifespan. This is substantial and highlights the profound economic and social implications of diabetes on the South African workforce. Furthermore, to put the GDP loss into perspective, South Africa's total annual GDP in 2019 was approximately USD 351 billion. The estimated GDP loss from the impact of Type 2 diabetes, as mentioned in the thesis, approximates USD 1.87 billion annually, accounting for about 0.53% of the annual GDP. This loss is significant, considering it represents a continuous drain on the nation's economic resources, affecting healthcare spending and reducing the country's overall economic productivity and growth potential.

Chapter Five- health-related quality of life and its predictors among individuals with diabetes. the case of the Western Cape, South Africa includes a paper currently under peer-review for publication. This chapter explored the multifaceted nature of HRQoL among people with diabetes. It reveals that HRQoL is influenced by a complex mix of factors including gender, lifestyle, socioeconomic status, and mental health. Key findings include males generally reporting higher HRQoL than females and urban residents having lower HRQoL compared to their rural counterparts. Education, particularly at the primary level, correlates with reduced HRQoL, and intriguingly, alcohol consumption shows a positive correlation with HRQoL. However, this does not infer a cause-and-effect relationship. Severe mental health issues emerge as a strong predictor of very low HRQoL (AOR= 18.31, p= 0.01). Conversely, traditional health indicators such as BMI, marital status, housing stability, and food security do not significantly impact HRQoL. This chapter underscores the importance of addressing mental health in addition to physical health in efforts to enhance HRQoL among people with diabetes.

Chapter Six- Social Determinants of Health and diabetes self-care Management in South Africa includes a paper currently under peer review for publication. This chapter, delving into the social determinants of diabetes (SDoH), provides insight into the complexity of diabetes self-care and adherence. Age, urban residency, and BMI were identified as key influencers of self-care guidelines, while the frequency of clinic visits emerges as a metric of healthcare system interaction. Intriguingly, the studies suggest that while increased awareness and healthcare access in urban settings could aid in diabetes management, the associated lifestyle and stressors might conversely impede effective self-care. The research also casts light on the interplay between socio-demographic factors and self-care guidelines, suggesting that targeted interventions need to be sensitive to these variables to improve diabetes self-management. This is particularly crucial given the rising prevalence of diabetes in the working-age population of South Africa, which not only affects individual productivity but also has broader implications for the nation's economy.

7.3 Discussion of the Thesis Findings

The research embodied in this thesis presents a holistic examination of the economic burden, patient well-being, and the social determinants related to diabetes in South Africa. The findings illuminate the substantial impact of T2D on individuals, healthcare systems, and the nation's economy, demonstrating a critical need for multifaceted interventions tailored to the unique socio-economic landscape of South Africa. The findings weave a narrative that underscores the pressing public health concern that diabetes represents in SSA and also highlights the complexities and challenges faced by PLWD and healthcare systems [239-241].

The economic implications are stark, with diabetes presenting a significant drain on resources that could otherwise contribute to national productivity and individual well-being. The thesis suggests an urgent redirection of focus towards preventive strategies, which hold the potential for cost savings through enhanced productivity and reduced direct treatment expenses [242]. Moreover, the research indicates that investing in diabetes prevention could yield substantial returns, mitigating the disease's impact on South Africa's GDP as proven to yield savings in Chinese population [113]. From a societal standpoint, the thesis reveals that diabetes imposes a disproportionate economic burden on individuals, particularly affecting the poorest segments of the population. This burden manifests not only in the direct costs associated with treatment but also in the broader socio-economic consequences of the disease [243, 244]. The studies collectively call for policy interventions that reduce patients' financial load, improve medication accessibility, and promote comprehensive health insurance schemes to cushion the blow of out-of-pocket expenditures for diabetes care [245-247].

The research findings reveal a high frequency of clinic visits among PLWD in South Africa, indicating a potential prevalence of complications in this population. Combined with the observed lack of alignment with international diabetes care guidelines, these results suggest inefficiencies in patient care that may potentially lead to increased costs for individuals as well as the health system [248]. Results from a systematic review suggest that cost-effective interventions, such as mHealth initiatives and pharmacist-led educational programs, which have shown efficacy in improving health outcomes in Senegal and Nigeria [249-251], could be beneficial. While these interventions were not directly studied in this thesis, the findings underscore the importance of exploring such cost-effective strategies for healthcare improvement in future research in the South African context.

A notable trend across the studies is the significance of mental health in managing diabetes [132, 252-256], of which this thesis is also in agreement. Mental health issues have a profound impact on HRQoL among PLWD, suggesting that mental health support should be an integral component of diabetes care frameworks. This underscores the need for a holistic approach to diabetes care that integrates mental health support within the larger framework of patient management.

The thesis advocates for a comprehensive strategy in addressing diabetes within South Africa, encompassing economic, societal, and healthcare reforms by extending beyond merely treating the medical symptoms of diabetes, also focusing on the social factors that impact patient health outcomes. By amalgamating insights from various studies, it lays down a strategic framework that could steer future research, policy formation, and healthcare initiatives. This integrated approach is crucial for improving patient outcomes and diminishing the economic and social impacts of diabetes in the SSA region at large.

This body of work paints a detailed picture of the diabetes situation in South Africa, underscoring the need for a coordinated policy approach. It suggests transitioning to a healthcare system that is not just reactive but also equitable and sustainable, aligning diabetes management strategies with the socio-economic context of the area. The synthesis of findings from these studies forms a solid base for holistic strategies designed to avert the diabetes burden and improve the quality of life for those affected, both within South Africa and in broader contexts.

In synthesis, these studies articulate the need for an integrated approach to diabetes management in SSA, one that factors in the economic, societal, and healthcare system challenges unique to the region. The findings point towards the necessity of policy interventions that ease the financial burden on patients, enhance access to essential medications, and foster preventive and early screening measures. Furthermore, they advocate for the incorporation of mental health support in diabetes care strategies, along with the promotion of health insurance schemes as a buffer against the financial hardships associated with diabetes care [257]. Because diabetes in South Africa is not merely a medical condition to be managed but a complex socio-economic issue that demands comprehensive strategies encompassing economic, social, and health system reforms [258, 259].

The integration of findings from these four studies provides a roadmap for addressing diabetes in South Africa and emphasises the need for multifaceted interventions to enhance patient outcomes and alleviate the economic burden on the healthcare system. The holistic summary of this thesis, thus, provides a consolidated foundation for future research and policy making aimed at mitigating the impact of diabetes in SSA and improving the quality of life for those affected.

7.4 Strengths and Limitations of the Thesis

The studies conducted in this thesis acknowledge some limitations in the methodological approaches and data sources. A significant constraint is the microsimulation two-model approach, which focuses exclusively on mortality transitions, potentially oversimplifying the dynamic nature of diabetes and its varied impact across populations. This approach may not fully account for transitions like the onset or remission from T2D, potentially not fully representing the disease's progression. A critical assumption in the economic analysis is equating the value of one PALY with the annual GDP per employee. While this assumption aligns with existing methodologies, it could lead to an underestimation of the economic burden of T2D, as it may not reflect the actual costs incurred by individuals and the broader economy.

Data gaps present another challenge, particularly in the analysis of productivity indices. The absence of detailed data on absenteeism and presenteeism, along with the assumption of full-time employment for all labour force participants, may lead to an underestimation of the impact of T2D on different forms of employment, including part-time and unpaid labour. In The absence of locally sourced, age- and gender-stratified diabetes prevalence data in South Africa necessitated reliance on extrapolated figures from the International Diabetes Federation. This approach, while practical, may present a limitation by potentially underrepresenting the true impact of diabetes within the country. Moreover, the predominance of a provider-centric perspective in over half of the studies reviewed potentially underrepresents the total societal cost of diabetes management. This skew towards the healthcare provider perspective may lead to an incomplete picture of the economic impact of T2D. In terms of HRQoL assessment, the study adapts UK TTO values due to the absence of local South African data. This adaptation could potentially introduce cultural or societal biases, as UK TTO values may not accurately reflect the health state preferences of the South African population.

Despite these limitations, in the realm of diabetes self-care management research, this thesis introduces a novel approach by focusing on adherence, an aspect often overlooked in existing literature. Rather than solely relying on patient-reported self-care practices, the thesis innovatively develops an adherence variable, distinguishing between no adherence (for none of the recommended activities), partial adherence (for some but not all activities, despite daily recommendations), and full adherence (for all activities daily). This method provides a nuanced understanding of the factors influencing various levels of adherence, offering valuable insights for policymaking in the context of social determinants of health. Additionally, in assessing HRQoL, the study adopts an innovative categorisation approach, differentiating quality of life into distinct levels: perfect, high, moderate, low, and very low. This categorisation allows for a closer examination of the predictors of HRQoL at each level, facilitating the design of targeted interventions suited to specific quality-of-life categories. By providing detailed data on the utility trade-offs within these HRQoL categories, the study contributes significantly to the understanding of quality-of-life determinants, aiding in the development of more effective healthcare strategies.

The thesis further contributes significantly to the field of the burden of diabetes research in South Africa. It provides valuable age and gender-stratified utility values, filling a crucial gap in the literature and offering essential data for quantifying QALYs and conducting economic evaluations tailored to specific demographic segments in South Africa. The use of PALYs as a metric offers an innovative perspective on the impact of diabetes, particularly concerning productivity losses. This approach extends the evaluation of the disease's burden beyond traditional metrics like DALYs and QALYs. This simulation and modelling significantly contributed to a knowledge gap regarding the impact of diabetes on productivity loss in South African adults, as well as provided evidence for the SSA region, thereby illuminating the economic ramifications of diabetes and offering a foundation for policy interventions aimed at mitigating these losses.

In addition, the study leveraged meticulously gathered Project MIND data from 24 distinct clinics (rural and urban), each offering diabetes care to PLWD in the Western Cape, South Africa. This diverse array of clinics, spanning various regions, ensured a comprehensive and nationally representative dataset. The findings thus contain enhanced credibility and applicability across South Africa, as these clinics collectively embody the country's demographic and healthcare diversity. The identification of key areas for further investigation in diabetes self-care management is another strength of the thesis. It underscores the importance of socio-demographic factors in self-care and adherence, highlighting the need for tailored interventions and policies to address SDoH. The comprehensive exploration of HRQoL among people with diabetes in South Africa, incorporating a wide range of predictors, provides substantial insights for future interventions to improve the life quality of people with diabetes. This depth in HRQoL analysis positions the study as a significant contributor to understanding the impact of diabetes in South Africa.

The collective evidence from these studies offers a robust foundation for future research, policy development, and healthcare interventions aimed at reducing the diabetes burden and enhancing the quality of life for those affected in South Africa and similar contexts.

7.5 Summary Contribution of the Thesis

The amalgamated results from the four independent studies underscore the interconnected hurdles of economic strain, societal burden, and healthcare system challenges unique to South Africa and, to a larger extent, the SSA region. In SSA, these challenges are often exacerbated by factors such as widespread poverty, socio-political instability, limited healthcare infrastructures, and high disease burden [260, 261]. These contexts are marked by a high prevalence of both communicable diseases like HIV/AIDS and malaria and non-communicable diseases such as diabetes [152, 262-264]. This double burden of disease further strains the already limited resources in these countries. Furthermore, socio-economic disparities and inequities in health access pose significant obstacles to effective diabetes management in these settings [80, 265, 266]. As such, the findings of this study not only contribute to a deeper understanding of the complex landscape of diabetes management in South Africa, but also provide valuable insights that may inform strategies to address similar challenges in the broader SSA region.

In the face of these challenges, the thesis emphasises the urgent need for affordable and preventive measures, heightened awareness, and improved self-care adherence in managing diabetes. Investment in these areas is highlighted not as an expense, but as a potential investment capable of significantly reducing the long-term economic and societal burden of diabetes. Furthermore, the systematic review encompassing 46 SSA countries serves to collate essential information and offer a holistic understanding of the costs and cost-effective interventions associated with managing T2D. This resource can guide policymakers in different countries to utilise these interventions in country-specific settings, depending on their willingness to pay and the GDP per capita.

The methodologies used in this research, especially the innovative and novel Life Table Modelling, provide valuable tools for SSA countries to inform decision-making. This novel method reveals the complex burden of diabetes, a growing concern in both urban and rural settings within SSA affecting working-age men and women [170, 267]. Recognising that self-care and adherence play crucial roles in mitigating further complications and comorbidities associated with diabetes, the study investigated the impact of social determinants, mental health, and psychological ability on these aspects. Importantly, it brought to light the need to consider mental health factors when making decisions about diabetes management, as well as the influence exerted by socioeconomic and lifestyle factors. The insights from this research contribute significantly to a more holistic understanding of the factors affecting diabetes self-care and adherence, offering valuable guidance for clinicians, researchers, and policymakers in shaping effective diabetes management strategies.

Another pivotal aspect of this research was the assessment of HRQoL among people with diabetes using the TTO method. This tool, widely favoured in health economics, is instrumental in generating QALYs, thereby enriching cost-utility analyses and facilitating cross-intervention comparability [170]. Importantly, this study marked the creation of the first-ever sex- and age-stratified utility score that is specific to the South African population, contributing a significant milestone in South African health economics. This study also contributed significant insights into the factors affecting the quality of life among people with diabetes, with TTO serving as a proxy for HRQoL, therefore, play a crucial role in shaping more nuanced, effective, and patient-centred approaches for diabetes care and management recommendations.

7.6 Conclusion of the Thesis

The findings of this thesis are pivotal for future policy formulation, providing a substantive basis for the development of targeted and cost-effective interventions and efficient policies. These insights are instrumental in guiding strategic planning and budget allocation to address the diabetes epidemic in South Africa effectively. The analysis not only underscores the multifaceted nature of the disease but also highlights the necessity for a holistic approach to mitigate its impact. This work serves as a crucial resource for policymakers, healthcare practitioners, and stakeholders to curtail the rising tide of diabetes and improve health outcomes in the region.

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9. Appendices

Appendix 1: Supplemental information linked to Chapter Three

Table 12: Detailed Search Strategies for the Listed Domains.

Medline via PubMed	#1 Search: (Diabetes Mellitus, Type 2[Mesh Terms]) OR (Type 2 Diabetes OR Diabetes Mellitus Type II OR Diabetes OR DMT2 OR Diabetes Mellitus Type 2) #2 (Weight Loss OR Weight Reduction Programs[MeSH Terms]) OR Dietary Education OR Dietary Intake OR Risk Factors OR Risk Reduction OR Risk Reduction Behaviour OR Community Networks OR Community Organization And Administration OR Health Promotion OR Alternative Subjects OR Life Style OR Lifestyle OR Intervention OR Interventions OR Patient Education OR Administration OR Population Surveillance OR Epidemiology OR Behaviour Education OR Behavior Education OR Behavioural Intervention OR Glucose Tolerance OR Fasting Glucose OR Glucose Homeostasis OR Behavioural Intervention OR Nutrition Education OR Lifestyle Intervention OR Nutritionist OR Registered Dietitian OR Registered Dietician OR Physical Activity OR Diabetes Prevention OR Diabetes Control OR Diabetes Management OR Therapy OR Preventive Intervention OR Weight Check OR Stress Management OR Alcohol Cessation OR Social Support OR Nicotine Reduction OR Cigarette Smoking OR Treatment OR Treatments OR Management OR Managements OR Medication OR Medications OR Drug OR Drugs OR metformin OR Life-therapy OR Surveillance OR Food Quality OR Patient Care Management OR Patient Care Planning OR Patient Care Team OR Comprehensive Health Care OR Self Care OR Patient Participation OR patient education OR Reminder Systems OR Information Systems OR Decision Support Systems OR Clinical OR Information Systems OR Decision Support Systems OR Decision Making OR Computer-Assisted OR Ambulatory Care Information Systems OR SMS Text OR Digital Messaging OR Text messaging OR Reminder OR comprehensive lifestyle intervention OR Adiposity OR Weight reduction Program OR Weight Loss OR Weight management OR Reduce Obesity OR Fat Reduction OR Psychological Stress OR Sleep Duration Medical Nutrition therapy OR Pharmacologic Therapy OR hyperglycemia OR Glucagon-like Peptide 1 Receptor OR GLP-1 OR Dual Glucagon-like Peptide 1 Receptor OR Dual GLP-1 OR Glucose-dependent Insulinotropic Polypeptide OR GIP OR Intensive Lifestyle Modification OR Exercise OR Aerobic Exercise OR Resistance Training OR Psychological Interventions OR Insulin Therapy OR Alcohol withdrawal #3 Search: (Costs And Cost Analysis[Mesh Terms]) OR (Cost OR Cost Effectiveness OR Cost-Effectiveness) OR Health Care Cost OR Health Facility Costs OR Health Expenditures OR Economic Aspects OR Economic Evaluation OR Numerical Data #4 Search: Africa South Of The Sahara [Mesh] OR Sub-Saharan Africa, Angola OR Benin OR Botswana OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR Cameroon OR Cameroun OR "Canary Islands" OR "Cape Verde" OR "Central Africa" OR "Central African Republic" OR Chad OR Comoros OR Congo OR "Cote d'Ivoire" OR "Democratic Republic Of Congo" OR Djibouti OR "Eastern Africa" OR Eritrea OR Eswatini OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR Guinea-Bissau OR "Ivory Coast" OR Jamahiriya OR Kenya OR Lesotho OR Liberia OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mayotte OR Mozambique OR Namibia OR Niger OR Nigeria OR Principe OR Reunion OR Rwanda OR "Sao Tome" OR Senegal OR Seychelles OR "Sierra Leone" OR "Saint Helena" OR Somalia OR "St Helena" OR "South Africa" OR "Southern Africa" OR Sudan OR Swaziland OR Tanzania OR Togo OR Uganda OR "Western Africa" OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe OR "South Africa" OR "Southern Africa" OR Sudan OR Swaziland OR Tanzania OR Togo OR Uganda OR "Western Africa" OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe #5 Search: ((((Diabetes Mellitus, Type 2[MeSH Terms]) OR (Type 2 Diabetes[Text Word] OR Diabetes Mellitus Type II[Text Word] OR Diabetes[Text Word] OR DMT2[Text Word] OR Diabetes Mellitus Type 2[Text Word])) AND ((Weight Loss OR Weight Reduction Programs[MeSH Terms]) OR (Dietary Education[Text Word] OR Dietary Intake[Text Word] OR Risk Factors[Text Word] OR Risk Reduction[Text Word] OR Risk Reduction Behaviour[Text Word] OR Community Networks[Text Word] OR Community Organization[Text Word] AND Administration[Text Word] OR Health Promotion[Text Word] OR Alternative Subjects[Text Word] OR Life Style[Text Word] OR Lifestyle[Text Word] OR Intervention[Text Word] OR

	Interventions[Text Word] OR Patient Education[Text Word] OR Population Surveillance[Text Word] OR Epidemiology[Text Word] OR Behaviour Education[Text Word] OR Behavior Education[Text Word] OR Behavioural Intervention[Text Word] OR Glucose Tolerance[Text Word] OR Fasting Glucose[Text Word] OR Glucose Homeostasis[Text Word] OR Nutrition Education[Text Word] OR Lifestyle Intervention[Text Word] OR Nutritionist[Text Word] OR Registered Dietitian[Text Word] OR Registered Dietician[Text Word] OR Physical Activity[Text Word] OR Diabetes Prevention[Text Word] OR Diabetes Control[Text Word] OR Diabetes Management[Text Word] OR Therapy[Text Word] OR Preventive Intervention[Text Word] OR Weight Check[Text Word] OR Stress Management[Text Word] OR Alcohol Cessation[Text Word] OR Social Support[Text Word] OR Nicotine Reduction[Text Word] OR Cigarette Smoking[Text Word] OR Treatment[Text Word] OR Treatments[Text Word] OR Management[Text Word] OR Managements[Text Word] OR Medication[Text Word] OR Medications[Text Word] OR Drug[Text Word] OR Drugs[Text Word] OR metformin[Text Word] OR Life-therapy[Text Word] OR Surveillance[Text Word] OR Food Quality[Text Word] OR Patient Care Management[Text Word] OR Patient Care Planning[Text Word] OR Patient Care Team[Text Word] OR Comprehensive Health Care[Text Word] OR Self Care[Text Word] OR Patient Participation[Text Word] OR patient education[Text Word] OR Reminder Systems[Text Word] OR Information Systems[Text Word] OR Decision Support Systems[Text Word] OR Clinical[Text Word] OR Decision Making[Text Word] OR Computer-Assisted[Text Word] OR Ambulatory Care Information Systems[Text Word] OR SMS Text[Text Word] OR Digital Messaging[Text Word] OR Text messaging[Text Word] OR Reminder[Text Word] OR comprehensive lifestyle intervention[Text Word] OR Adiposity[Text Word] OR Weight reduction Program[Text Word] OR Weight Loss[Text Word] OR Weight management[Text Word] OR Reduce Obesity[Text Word] OR Fat Reduction[Text Word] OR Psychological Stress[Text Word] OR Sleep Duration Medical Nutrition therapy[Text Word] OR Pharmacologic Therapy[Text Word] OR hyperglycemia[Text Word] OR Glucagon-like Peptide 1 Receptor[Text Word] OR GLP-1[Text Word] OR Dual Glucagon-like Peptide 1 Receptor[Text Word] OR Dual GLP-1[Text Word] OR Glucose-dependent Insulinotropic Polypeptide[Text Word] OR GIP[Text Word] OR Intensive Lifestyle Modification[Text Word] OR Exercise[Text Word] OR Aerobic Exercise[Text Word] OR Resistance Training[Text Word] OR Psychological Interventions[Text Word] OR Insulin Therapy[Text Word] OR Alcohol withdrawal[Text Word] OR OR[Text Word] OR OR[Text Word]))) AND ((Costs And Cost Analysis[MeSH Terms]) OR (Cost[Text Word] OR Cost Effectiveness[Text Word] OR Cost-Effectiveness[Text Word]) OR Health Care Cost[Text Word] OR Health Facility Costs[Text Word] OR Health Expenditures[Text Word] OR Economic Aspects[Text Word] OR Economic Evaluation[Text Word] OR Numerical Data[Text Word])) AND ((Africa South Of The Sahara[MeSH Terms]) OR (Sub-Saharan Africa, Angola[Text Word] OR Benin[Text Word] OR Botswana[Text Word] OR "Burkina Faso"[Text Word] OR Burundi[Text Word] OR "Cabo Verde"[Text Word] OR Cameroon[Text Word] OR Cameroun[Text Word] OR "Canary Islands"[Text Word] OR "Cape Verde"[Text Word] OR "Central Africa"[Text Word] OR "Central African Republic"[Text Word] OR Chad[Text Word] OR Comoros[Text Word] OR Congo[Text Word] OR "Cote d'Ivoire"[Text Word] OR "Democratic Republic Of Congo"[Text Word] OR Djibouti[Text Word] OR "Eastern Africa"[Text Word] OR Eritrea[Text Word] OR Eswatini[Text Word] OR Ethiopia[Text Word] OR Gabon[Text Word] OR Gambia[Text Word] OR Ghana[Text Word] OR Guinea[Text Word] OR Guinea-Bissau[Text Word] OR "Ivory Coast"[Text Word] OR Jamahiriya[Text Word] OR Kenya[Text Word] OR Lesotho[Text Word] OR Liberia[Text Word] OR Madagascar[Text Word] OR Malawi[Text Word] OR Mali[Text Word] OR Mauritania[Text Word] OR Mauritius[Text Word] OR Mayotte[Text Word] OR Mozambique[Text Word] OR Namibia[Text Word] OR Niger[Text Word] OR Nigeria[Text Word] OR Principe[Text Word] OR Reunion[Text Word] OR Rwanda[Text Word] OR "Sao Tome"[Text Word] OR Senegal[Text Word] OR Seychelles[Text Word] OR "Sierra Leone"[Text Word] OR "Saint Helena"[Text Word] OR Somalia[Text Word] OR "St Helena"[Text Word] OR "South Africa"[Text Word] OR "Southern Africa"[Text Word] OR Sudan[Text Word] OR Swaziland[Text Word] OR Tanzania[Text Word] OR Togo[Text Word] OR Uganda[Text Word] OR " Western Africa"[Text Word] OR "Western Sahara"[Text Word] OR Zaire[Text Word] OR Zambia[Text Word] OR Zimbabwe[Text Word]))OR " Western Africa" OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe)

Africa-Wide Information/ Web of Science/ Cochrane Library	S1- Diabetes Mellitus OR Type 2 OR Type 2 Diabetes OR Diabetes Mellitus Type II OR Diabetes OR DMT2 OR Diabetes Mellitus Type 2 S2- Dietary Education OR Dietary Intake OR Risk Factors OR Risk Reduction OR Risk Reduction Behaviour OR Community Networks OR Community Organization And Administration OR Health Promotion OR Alternative Subjects OR Life Style OR Lifestyle OR Intervention OR Interventions OR Patient Education OR Administration OR Population Surveillance OR Epidemiology OR Behaviour Education OR Behavior Education OR Behavioural Intervention OR Glucose Tolerance OR Fasting Glucose OR Glucose Homeostasis OR Behavioural Intervention OR Nutrition Education OR Lifestyle Intervention OR Nutritionist OR Registered Dietitian OR Registered Dietician OR Physical Activity OR Diabetes Prevention OR Diabetes Control OR Diabetes Management OR Therapy OR Preventive Intervention OR Weight Check OR Stress Management OR Alcohol Cessation OR Social Support OR Nicotine Reduction OR Cigarette Smoking OR Treatment OR Treatments OR Management OR Managements OR Medication OR Medications OR Drug OR Drugs OR metformin OR Life-therapy OR Surveillance OR Food Quality OR Patient Care Management OR Patient Care Planning OR Patient Care Team OR Comprehensive Health Care OR Self Care OR Patient Participation OR patient education OR Reminder Systems OR Information Systems OR Decision Support Systems OR Clinical OR Information Systems OR Decision Support Systems OR Decision Making OR Computer-Assisted OR Ambulatory Care Information Systems OR SMS Text OR Digital Messaging OR Text messaging OR Reminder OR comprehensive lifestyle intervention OR Adiposity OR Weight reduction Program OR Weight Loss OR Weight management OR Reduce Obesity OR Fat Reduction OR Psychological Stress OR Sleep Duration Medical Nutrition therapy OR Pharmacologic Therapy OR hyperglycemia OR Glucagon-like Peptide 1 Receptor OR GLP-1 OR Dual Glucagon-like Peptide 1 Receptor OR Dual GLP-1 OR Glucose-dependent Insulinotropic Polypeptide OR GIP OR Intensive Lifestyle Modification OR Exercise OR Aerobic Exercise OR Resistance Training OR Psychological Interventions OR Insulin Therapy OR Alcohol withdrawal S3- Costs and cost analysis OR Cost OR cost effectiveness OR cost-effectiveness OR Health care cost OR Health Facility Costs OR Health Expenditures OR Economic Aspects OR Economic evaluation S4- Africa South of the Sahara OR Sub-Saharan Africa, Angola OR Benin OR Botswana OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR Cameroon OR Cameroun OR "Canary Islands" OR "Cape Verde" OR "Central Africa" OR "Central African Republic" OR Chad OR Comoros OR Congo OR "Cote d'Ivoire" OR "Democratic Republic of Congo" OR Djibouti OR "Eastern Africa" OR Eritrea OR eSwatini OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR Guinea-Bissau OR "Ivory Coast" OR Jamahiriya OR Kenya OR Lesotho OR Liberia OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mayotte OR Mozambique OR Namibia OR Niger OR Nigeria OR Principe OR Reunion OR Rwanda OR "Sao Tome" OR Senegal OR Seychelles OR "Sierra Leone" OR "Saint Helena" OR Somalia OR "St Helena" OR "South Africa" OR "Southern Africa" OR Sudan OR Swaziland OR Tanzania OR Togo OR Uganda OR "Western Africa" OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe"South Africa" OR "Southern Africa" OR Sudan OR Swaziland OR Tanzania OR Togo OR Uganda OR "Western Africa" OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe S5- S1 AND S2 AND S3 AND S4

CINHAL	S1- (MH "Diabetes Mellitus, Type 2") S2- type 2 diabetes OR diabetes mellitus type II OR diabetes OR DMT2 OR diabetes mellitus type 2 S3- S1 OR S2 S4- Dietary Education OR Dietary Intake OR Risk Factors OR Risk Reduction OR Risk Reduction Behaviour OR Community Networks OR Community Organization And Administration OR Health Promotion OR Alternative Subjects OR Life Style OR Lifestyle OR Intervention OR Interventions OR Patient Education OR Administration OR Population Surveillance OR Epidemiology OR Behaviour Education OR Behavior Education OR Behavioural Intervention OR Glucose Tolerance OR Fasting Glucose OR Glucose Homeostasis OR Behavioural Intervention OR Nutrition Education OR Lifestyle Intervention OR Nutritionist OR Registered Dietitian OR Registered Dietician OR Physical Activity OR Diabetes Prevention OR Diabetes Control OR Diabetes Management OR Therapy OR Preventive Intervention OR Weight Check OR Stress Management OR Alcohol Cessation OR Social Support OR Nicotine Reduction OR Cigarette Smoking OR Treatment OR Treatments OR Management OR Managements OR Medication OR Medications OR Drug OR Drugs OR metformin OR Life-therapy OR Surveillance OR Food Quality OR Patient Care Management OR Patient Care Planning OR Patient Care Team OR Comprehensive Health Care OR Self Care OR Patient Participation OR patient education OR Reminder Systems OR Information Systems OR Decision Support Systems OR Clinical OR Information Systems OR Decision Support Systems OR Decision Making OR Computer-Assisted OR Ambulatory Care Information Systems OR SMS Text OR Digital Messaging OR Text messaging OR Reminder OR comprehensive lifestyle intervention OR Adiposity OR Weight reduction Program OR Weight Loss OR Weight management OR Reduce Obesity OR Fat Reduction OR Psychological Stress OR Sleep Duration Medical Nutrition therapy OR Pharmacologic Therapy OR hyperglycemia OR Glucagon-like Peptide 1 Receptor OR GLP-1 OR Dual Glucagon-like Peptide 1 Receptor OR Dual GLP-1 OR Glucose-dependent Insulinotropic Polypeptide OR GIP OR Intensive Lifestyle Modification OR Exercise OR Aerobic Exercise OR Resistance Training OR Psychological Interventions OR Insulin Therapy OR Alcohol withdrawal S5- (MH "Cost Benefit Analysis") OR (MH "Health Care Costs") OR (MH "Health Facility Costs") OR (MH "Costs and Cost Analysis") OR (MH "Economic Aspects of Illness") "Costs and Cost Analysis") OR (MH "Economic Aspects of Illness") S6- Costs and cost analysis OR Cost OR cost effectiveness OR cost-effectiveness OR Health care cost OR Health Facility Costs OR Health Expenditures OR Economic Aspects OR Economic evaluation S7- S5 OR S6 S8- Africa South of the Sahara OR Sub-Saharan Africa, Angola OR Benin OR Botswana OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR Cameroon OR Cameroun OR "Canary Islands" OR "Cape Verde" OR "Central Africa" OR "Central African Republic" OR Chad OR Comoros OR Congo OR "Cote d'Ivoire" OR "Democratic Republic of Congo" OR Djibouti OR "Eastern Africa" OR Eritrea OR eSwatini OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR Guinea-Bissau OR "Ivory Coast" OR Jamahiriya OR Kenya OR Lesotho OR Liberia OR Madagascar OR Malawi OR Mali OR Mauritania OR Mauritius OR Mayotte OR Mozambique OR Namibia OR Niger OR Nigeria OR Principe OR Reunion OR Rwanda OR "Sao Tome" OR Senegal OR Seychelles OR "Sierra Leone" OR "Saint Helena" OR Somalia OR "St Helena" OR "South Africa" OR "Southern Africa" OR Sudan OR Swaziland OR Tanzania OR Togo OR Uganda OR "Western Africa" OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe " OR "South Africa" OR "Southern Africa" OR Sudan OR Swaziland OR Tanzania OR Togo OR Uganda OR "Western Africa" OR "Western Sahara" OR Zaire OR Zambia OR Zimbabwe S9- S3 AND S4 AND S7 AND S8

Scopus	S1- "Diabetes mellitus" OR "type 2" OR "type 2 diabetes" OR "diabetes mellitus type II" OR "diabetes" OR "DMT2" OR "diabetes mellitus type 2" OR "DMT2" OR "diabetes mellitus type 2" S2- “Dietary Education” OR “Dietary Intake” OR “Risk Factors” OR “Risk Reduction” OR “Behavior” OR “Risk Reduction Behaviour” OR “Community Networks” OR “Community Organization and Administration” OR “Health Promotion” OR “Alternative Subjects” OR “Life-Style” OR “Lifestyle” OR “Intervention*” OR “Patient Education” OR “Administration” OR “Population Surveillance” OR “Epidemiology” OR “Behavioural Intervention” OR “Glucose Tolerance” OR “Fasting Glucose” OR “Glucose Homeostasis” OR “Nutrition Education” OR “Nutritionist” OR “Registered Dietitian” OR “Registered Dietician” OR “Physical Activity” OR “Diabetes Prevention” OR “Diabetes Control” OR “Diabetes Management” OR “Therapy” OR “Preventive Intervention” OR “Weight Check” OR “Stress Management” OR “Alcohol Cessation” OR “Social Support” OR “Smoking” OR “Treatment*” OR “Management*” OR “Medication*” OR “Drug*” OR “Metformin” OR “Life-Therapy” OR “Food Quality” OR “Patient Care Management” OR “Patient Care Planning” OR “Patient Care Team” OR “Comprehensive Health Care” OR “Self-Care” OR “Patient Participation” OR “Information System*” OR “Decision Support System*” OR “Clinical” OR “Decision Support Systems” OR “Decision Making” OR “Computer-Assisted” OR “Ambulatory Care Information System*” OR “SMS Text*” OR “Digital Messaging” OR “Text Messaging” OR “Reminder” OR “Comprehensive Lifestyle Intervention” OR “Adiposity” OR “Weight Reduction” OR “Weight Management” OR “Reduce Obesity” OR “Fat Reduction” OR “Psychological Stress” OR “Sleep Duration” OR “Medical Nutrition Therapy” OR “Pharmacologic Therapy” OR “Hyperglycemia” OR “Glucagon-Like Peptide 1 Receptor” OR “GLP-” OR “Dual Glucagon-Like Peptide 1 Receptor” OR “Dual GLP-1” OR “Glucose-Dependent Insulinotropic Polypeptide” OR “Gip” OR “Intensive Lifestyle Modification” OR “Exercise” OR “Aerobic Exercise” OR “Resistance Training” OR “Psychological Interventions” OR “Insulin Therapy” OR “Alcohol Withdrawal” OR “Weight Loss” S3- "Costs and cost analysis" OR "Cost" OR "cost-effectiveness" OR "cost-effectiveness" OR "Health care cost" OR "Health Facility Costs" OR "Health Expenditures" OR "Economic Aspects" OR "Economic evaluation" OR "Health Facility Costs" OR "Health Expenditures" OR "Economic Aspects" OR "Economic evaluation" S4- "Africa South of the Sahara" OR "Sub-Saharan Africa" OR "Angola" OR "Benin" OR "Botswana" OR "Burkina Faso" OR "Burundi" OR "Cabo Verde" OR "Cameroon" OR "Cameroun" OR "Canary Islands" OR "Cape Verde" OR "Central Africa" OR "Central African Republic" OR "Chad" OR "Comoros" OR "Congo" OR "Cote d'Ivoire" OR "Democratic Republic of Congo" OR "Djibouti" OR "Eastern Africa" OR "Eritrea" OR "eSwatini" OR "Ethiopia" OR "Gabon" OR "Gambia" OR "Ghana" OR "Guinea" OR "Guinea-Bissau" OR "Ivory Coast" OR "Jamahiriya" OR "Kenya" OR "Lesotho" OR "Liberia" OR "Madagascar" OR "Malawi" OR "Mali" OR "Mauritania" OR "Mauritius" OR "Mayotte" OR "Mozambique" OR "Namibia" OR "Niger" OR "Nigeria" OR "Principe" OR "Reunion" OR "Rwanda" OR "Sao Tome" OR "Senegal" OR "Seychelles" OR "Sierra Leone" OR "Saint Helena" OR "Somalia" OR "St Helena" OR "South Africa" OR "Southern Africa" OR "Sudan" OR "Swaziland" OR "Tanzania" OR "Togo" OR "Uganda" OR "Western Africa" OR "Western Sahara" OR "Zaire" OR "Zambia" OR "Zimbabwe"" OR "Mali" OR "Mauritania" OR "Mauritius" OR "Mayotte" OR "Mozambique" OR "Namibia" OR "Niger" OR "Nigeria" OR "Principe" OR "Reunion" OR "Rwanda" OR "Sao Tome" OR "Senegal" OR "Seychelles" OR "Sierra Leone" OR "Saint Helena" OR "Somalia" OR "St Helena" OR "South Africa" OR "Southern Africa" OR "Sudan" OR "Swaziland" OR "Tanzania" OR "Togo" OR "Uganda" OR "Western Africa" OR "Western Sahara" OR "Zaire" OR "Zambia" OR "Zimbabwe" S5- S1 AND S2 AND S3 AND S4
Google Scholar	S1- Type 2 diabetes mellitus AND lifestyle intervention AND (cost OR cost-effectiveness) AND Sub-Saharan Africa The first 100 search outcomes were reviewed.

Appendix 2: Supplementary information linked to Chapter Four

South African diabetes prevelence in 2021 (Source: IDF, 2023)		
Sex	Age-group	% of Prevalence
Female	20-24	0,0174
Male	20-24	0,0171
Female	25-29	0,0317
Male	25-29	0,0275
Female	30-34	0,0539
Male	30-34	0,0422
Female	35-39	0,0855
Male	35-39	0,0622
Female	40-44	0,1264
Male	40-44	0,0877
Female	45-49	0,1744
Male	45-49	0,1183
Female	50-54	0,2249
Male	50-54	0,1530
Female	55-59	0,2722
Male	55-59	0,1897
Female	60-64	0,3100
Male	60-64	0,2259

Table 13: 2019 South African labour force data for the national population.

Total number of employed men and women in 2019 (source: Stats SA, 2023)	
Age group	Labour force
20-24	2 371 000
25-29	3 686 000
30-34	3 779 000
35-39	3 543 000
40-44	3 089 000
45-49	2 613 000
50-54	1 816 000
55-59	1 279 000
60-64	483 000
Total	**22 659 000**

- ***Calculation of annual mortality rates (AMR) in those with and without T2D in the South African population by age group and sex was based on the following formula:***

MortNon-diabetes = MortTotal / (T2D Prevalence*RR+(1- T2D Prevalence))
The mortality rate for those with T2D were based on the following formula:
MortDiabetes = MortNon- T2D Prevalence *RR
Whereby:
MortTotal = total deaths in population/total population
MortDiabetes = mortality rate in those with T2D
MortNon-diabetes = mortality rate in those without T2D
RR=relative rate of all-cause mortality in those with T2D compared to those without T2D

- ***Calculation of the productivity index***

NB: There were 250 working days in South Africa in 2019.

Absenteeism = [(Total working days in SA in 2019 – number of days individuals are absent at work because of T2D)/ Total working days in SA in 2019]

Presenteeism = the percentage estimated by the Global Burden of Diabetes study or both genders.

Productivity shortfall= Absenteeism + Presenteeism

Table 14: Data and data sources used to measure the productivity loss burden of T2D.

Data input description for a life table model	Data sources
Labour force Participation	The labour market department within Statistics South Africa provided the estimated resident labour force participation statistics by sex and 5-year age groups for 2019 [7].
Prevalence of T2D among working-age populations stratified by sex and 5-year age groups in 2021	T2D national prevalence (%) for the year 2019 with [Confidence interval] (working age 20-65) stratified by 5-year age group and sex were obtained from the International Diabetes Federation (IDF) Atlas (10th Edition) [8].
Population mortality rates for the year 2019 stratified by sex and 5-year age groups	The Health and Vital Statistics department within Statistics South Africa published the Mortality and Causes of Death (MACOD) for the year 2019, obtained from the annual mortality rate (AMR) [7,9].
a) **T2D -related productivity:** b) **Absenteeism and presenteeism among working-age populations with T2D**	a) Productivity Adjusted Life Years (PALYs) lived by the T2D cohort; each year of life lived. The productivity indices are based on estimates by the American Diabetes Association (ADA) [3,9]. b) Each year lived by the T2D cohort in the labour force was multiplied by a productivity index calculated from evaluations of T2D-related presenteeism and absenteeism to estimate PALYs lived by the T2D cohort.
a) **The GDP and GDP per capita effective full-time (EFT) S.A. workers in 2019.** b) **Projected temporal trends in GDP growth rate for the year 2019**	a) The World Bank: World Development Indicators, 2019 [10]. b) Organisation for Economic Co-operation and Development (OECD) long-term GDP forecast data for 2019 was sourced [11].

Table 15: Age and sex stratified mortality rate estimation (with and without T2D).

5-year age group	Mortality rate in the total population	Mortality rate assuming no T2D	Mortality rate among people with T2D
Men			
20-24	0,003056	0,00285565	0,01459184
25-29	0,004651	0,00423956	0,01921374
30-34	0,005150	0,00456788	0,01836073
35-39	0,007257	0,00625904	0,02231351
40-44	0,008308	0,00698466	0,02208462
45-49	0,010393	0,00856411	0,02401660
50-54	0,014581	0,01187764	0,02954229
55-59	0,019942	0,01622869	0,03579993
60-64	0,027501	0,02261440	0,04424542
Women			
20-24	0,001840	0,00112715	0,00575953
25-29	0,003057	0,00199045	0,00902075
30-34	0,004605	0,00323426	0,01300020
35-39	0,005167	0,00388026	0,01383314
40-44	0,005738	0,00461599	0,01459518
45-49	0,006676	0,00563006	0,01578854
50-54	0,009261	0,00827290	0,02057650
55-59	0,011864	0,01092208	0,02409372
60-64	0,016700	0,01582576	0,03096335

Annual mortality rates (AMR) were Calculation in those with and without T2D population by age group and sex based on the following formula:

- $\text{Total deaths in population/total population} = \frac{\text{Total Mortality Rate}}{(\text{T2D prevalence}*\text{RR}+(1-\text{T2D Prevalence}))}$
    - Mortality rate in those with T2D = Mortality among non-T2D* RR

Relative rate of all-cause Mortality in those with T2D compared to those without T2D

Appendix material references

1. Hird, T. R., Zomer, E., Owen, A. et al. (2019). The impact of diabetes on productivity in China. Diabetologia.
2. Magliano, D.J., Martin, V.J. & Owen, A.J. et al. (2018). The Productivity Burden of Diabetes at a Population Level. Diabetes Care.
3. American Diabetes Association (ADA) (2018). Economic costs of diabetes in the U.S. in 2017. Diabetes Care.
4. Afroz, A., Hird, T.R. & Zomer, E. et al. The impact of diabetes on the productivity and economy of Bangladesh. BMJ Global Health.
5. Menon, K., Courten, B., & Liew, D. et al. 2021. Productivity Benefits of Preventing Type 2 Diabetes in Australia: A 10-Year Analysis. Diabetes Care.
6. Tönnies T, Hoyer A, Brinks R. Productivity-adjusted life years lost due to type 2 diabetes in Germany in 2020 and 2040. Diabetologia.
7. StatsSA. 2021. The South African labour market is more favourable to men than to women. South Africa.
8. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. International Diabetes Federation; Brussels, Belgium: 2021.
9. Bragg F, Holmes MV, Iona A, et al. (2017) Association between diabetes and cause-specific Mortality in rural and urban areas of China.
10. The Word Bank. (2019). GDP per capita (current US$) – South Africa.
11. Organisation for Economic Co-operation and Development (OECD) (2018) OECD Economic Outlook: Statistics and Projections: Long-term baseline projections, Real GDP long-term forecast (indicator). OECD Publishing, Paris.

Appendix 3: UCT PhD Ethical Approval (HREC 646/2022)

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/home/human-research-ethics

24 October 2022

HREC REF: 646/2022

Dr O Alaba
Division of Public Health & Family Medicine
Falmouth Building-FHS
Email: olufunke.alaba@uct.ac.za
Student: Hllas001@myuct.ac.za

Dear Dr Alaba

PROJECT TITLE: THE ECONOMIC BURDEN, WELL-BEING, AND SOCIAL DETERMINANTS OF DIABETES IN SOUTH AFRICA-
DOCTORATE CANDIDATE-MR ASSEGID HELLEBO

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 October 2023.

Please submit a progress form, using the standardised Annual Report Form (FHS016) if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Mr Assegid Hellebo will also be involved in this study.

Please quote the HREC REF 646/2022 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

Signed by candidate

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637. Institutional Review Board (IRB) number: IRB00001938 NHREC-registration number: REC-210208-007

HREC/ref 646.2022

Appendix 4: Co-authors’ Affiliations

Name	Affiliations	Email address
Olufunke Alaba	Health Economics Unit and Division, School of Public Health, Faculty of Health Sciences, University of Cape Town, Observatory, 7925 South Africa	olufunke.alaba@uct.ac.za
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Susan Cleary	Health Economics Unit and Division, School of Public Health, Faculty of Health Sciences, University of Cape Town, Observatory, 7925 South Africa	susan.cleary@uct.ac.za
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Appendix 5: Permissions for Inclusion of Publications in PhD Thesis

School of Public Health
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18 January 2024

Dear DDB Committee,

Permission to include publications in PhD thesis of Assegid Hellebo entitled: "Economic Burden, Patients' Well-being, and Social Determinants Related to Diabetes in South Africa."

I, Olufunke Alaba, the supervisor and co-author of the publications listed below, on behalf of myself and all co-authors, whom I have received their consent and permission via email, do hereby give Assegid Hellebo (Student number: HLLASS001) permission to include these publications in his PhD thesis. The status of each publication (published, under review and prepared for submission) is correct at the time of writing.

List of the Papers:

1. Hellebo A, Kenge AP, Ademi Z, Alaba O. The Burden of Type 2 Diabetes on the Productivity and Economy in Sub-Saharan Africa: A Life Table Modelling Analysis from a South African Perspective. Pharmacoeconomics: 10.1007/s40273-024-01353-3. (Accepted for publication).
2. Hellebo A, Kenge AP, Alaba, O. Costs and Cost-Effectiveness of Type 2 Diabetes Management in Sub-Saharan Africa: A Systematic Review. Health Economics Reviews: 418f11a3-e309-4fe8-9291-55b80fd891ec (Under-review for publication).
3. Hellebo A, Kenge AP, Obse A, Levitt N, Myers B, Cleary S, Alaba, O. Health-Related Quality of Life and Its Predictors Among Individuals With Diabetes. The Case of the Western Cape, South Africa. Elsevier SSM-Health Systems (Upcoming submission for publication).
4. Hellebo A, Kenge AP, Obse A, Levitt N, Myers B, Cleary S, Alaba, O. Social Determinants of Health and Diabetes Self-Care Management in South Africa. BMC Public Health: 68b4473a-e5e8-4145-b75c-eaa75fabd72c (Under-review for publication).

Yours sincerely,

Signed by candidate

Dr O. A. Alaba
Health Economics Unit
University of Cape Town

Our vision is to be an inclusive, engaged and research-intensive African university.

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enAble Institute

Faculty of Health Sciences

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Web research.curtin.edu.au/enable/

23 January 2024

Dear DDB Committee,

Permission to include publications in PhD thesis of Assegid Hellebo entitled: "Economic Burden, Patients' Well-being, and Social Determinants Related to Diabetes in South Africa."

I, Bronwyn Myers, the Principal Investigator of 'Project MIND', and co-author of the publications listed below, on behalf of myself and my team, do hereby give Assegid Hellebo (Student number: HLLASS001) permission to include these publications in his PhD thesis. The status of each publication (under review and prepared for submission) is correct at the time of writing.

List of Papers:

1. Hellebo A, Kenge AP, Obse A, Levitt N, Myers B, Cleary S, Alaba, O. Health-Related Quality of Life and Its Predictors Among Individuals With Diabetes. The Case of the Western Cape, South Africa. Elsevier SSM-Health Systems (Upcoming submission for publication).
2. Hellebo A, Kenge AP, Obse A, Levitt N, Myers B, Cleary S, Alaba, O. Social Determinants of Health and Diabetes Self-Care Management in South Africa. BMC Public Health: 68b4473a-e5e8-4145-b75c-eaa75fabd72c (Under-review for publication).

Yours sincerely,

Signed by candidate

Prof Bronwyn Myers
Director: Curtin enAble Institute, Curtin University
Chief Specialist Scientist: Mental Health, Alcohol, Substance Use and Tobacco Research Unit, South African Medical Research Council
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CDIA
CHRONIC DISEASE INITIATIVE FOR AFRICA

30th January 2024

The Chairperson
UCT DDB Committee,

Dear Chair

Re: Permission to include publications in a PhD thesis of Assegid Hellebo entitled: "Economic Burden, Patients' Well-being, and Social Determinants Related to Diabetes in South Africa."

I, Naomi Levitt, the co-author of the publications listed below, do hereby give Assegid Hellebo (Student number: HLLASS001) permission to include these publications in his PhD thesis. The status of each publication (under review and prepared for submission) is correct at the time of writing.

List of Papers:
1. Hellebo A, Kenge AP, Obse A, Levitt N, Myers B, Cleary S, Alaba, O. Health-Related Quality of Life and Its Predictors Among Individuals With Diabetes. The Case of the Western Cape, South Africa. Elsevier SSM-Health Systems (Upcoming submission for publication).
2. Hellebo A, Kenge AP, Obse A, Levitt N, Myers B, Cleary S, Alaba, O. Social Determinants of Health and Diabetes Self-Care Management in South Africa. BMC Public Health: 68b4473a-e5e8-4145-b75c-eaa75fabd72c (Under-review for publication).

Yours sincerely,

Signed by candidate

Professor Naomi S Levitt
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Chronic Disease Initiative for Africa
Senior Research Scholar
Department of Medicine
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