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Increasing Access to Essential Surgery in Resource Restricted Settings: An Economic Analysis

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Abstract

Globally, 5 billion people lack access to safe, timely, and affordable surgical, obstetric, and anaesthetic care. Increasing access to surgery saves lives, promotes economic growth, and drives equitable global development. Essential surgery includes caesarean section, laparotomy, and open fracture treatment, otherwise known as the Bellwether procedures. Thesis objectives included conducting a systematic review examining cost-effectiveness of undergoing or increasing access to Bellwether procedures in resource restricted settings and performing an economic evaluation of increasing access to caesarean section for obstructed labour compared to existing care in the South African Development Community region. Our systematic review found that Bellwether procedures were likely to be highly cost-effective. Our economic evaluation demonstrated that increasing access to caesarean section to 80% costs $52.97 per disability-adjusted life year averted from a health systems perspective, relative to existing care (30% access). Future research should focus on improved estimates of cost, effectiveness, and unmet need related to essential surgery.

Keywords

Cost-Utility Analysis, Health Economic Evaluation, Global Surgery, Caesarean Section, Bellwether Procedures, Low-and Middle-Income Countries

Summary for Lay Audience

Globally, 5 billion people lack access to safe, timely, and affordable surgical care. Lack of surgical access is inequitably distributed in low-and middle-income countries and is largely responsible for the number of deaths and time spent in disability from conditions that can be treated. The three procedures that account for most of this burden are caesarean section, laparotomy, and treatment of open fracture, otherwise known as the Bellwether procedures. Research has found that increasing access to essential surgery, defined as the Bellwether procedures, is likely to be cost-effective. However, limitations such as lack of high-quality synthesized evidence and funding impede health policy decision-making. Therefore, it is important to examine best available evidence on health and economic impacts of increasing access to essential surgery in resource restricted settings to address this gap in knowledge and better inform policymakers and stakeholders. The objectives of this thesis were to first, systematically review all existing cost-effectiveness analyses on increasing access or undergoing the Bellwether procedures in low-and middle-income countries; and second, to inform a subsequent de novo economic model that evaluates the costs and health impacts of increasing access to caesarean section to 80% for obstructed labour compared to existing care (30% access) in the South African Development Community region. From the review of existing studies, we found that undergoing a Bellwether procedure was likely to be highly cost effective. However, the identified studies varied in quality, context, and methodology, while excluding neonates and unmet need from their analyses. Consequently, an economic model was constructed to assess the costs and health impacts of increasing access to caesarean section for treatment of obstructed labour to 80% compared to the 30% level of access in existing care. Results from our analyses suggested that increasing access is likely cost-effective at $52.97 and $19.77 per disability-adjusted life year averted compared to existing care for mothers and babies, respectively. A combined estimate for mothers and babies cost $32.00 per disability-adjusted life year averted, assuming additivity. Future economic evaluations would greatly benefit from improved evidence in essential surgery related to costs, effectiveness, and the number of individuals in need of care that cannot access it.

Co-Authorship Statement

This submitted thesis is in integrated article format and consists of two articles being prepared for journal submission.

Chapter 2: Zhao A, Jeong JH, Ali S, and Martin J. Health and Economic Impacts of Improving Access to Essential Surgery in Resource Restricted Settings: A Systematic Review. Currently being prepared for journal submission.

Anne Zhao contributed to conceptualizing the research question, designed and ran all analyses, and wrote the manuscript. Joo-Hyun Jeong was second reviewer for screening, data extraction, and risk of bias). Dr. Janet Martin participated in study design and conceptualization, resolved reviewer conflicts, and provided insight on clinical concepts and health economic concepts. Dr. Shehzad Ali participated in study design and conceptualization, resolved reviewer conflicts, and provided insight on health economic concepts. All members revised the manuscript. Dr. Janet Martin and Dr. Shehzad Ali are senior authors and contributed equally to this work.

Chapter 3: Zhao A, Ali S, and Martin J. Cost-Effectiveness of Increasing Access to Caesarean Section for Obstructed Labour in the South African Development Community (SADC) Region. Currently being prepared for journal submission.

Anne Zhao contributed to conceptualization of the research question, designed and ran all analyses, and wrote the manuscript. Dr. Janet Martin and Dr. Shehzad Ali helped to conceptualize the research question and provided technical advice. All members revised the manuscript. Dr. Janet Martin and Dr. Shehzad Ali are senior authors and contributed equally to this work.

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Table of Contents

List of Tables

List of Figures

List of Appendices

Abbreviations

ACO	Average Cost Per Outcome
AIDS	Acquired Immunodeficiency Syndrome
BCR	Benefit-Cost Ratio
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
CO	Clinical Officer
CS	Caesarean Section
CUA	Cost-Utility Analysis
DA	Decision-Analytic
DALY	Disability-Adjusted Life Year
DSA	Deterministic Sensitivity Analysis
ECOBIAS	Bias in Economic Evaluation
GBD	Global Burden of Disease
GDP	Gross Domestic Product
HIE	Hypoxic-Ischemic Encephalopathy
HIV	Human Immunodeficiency Virus
ICER	Incremental Cost-Effectiveness Ratio
ICU	Intensive Care Unit
ID	Instrumental Delivery
KBD	Korean Burden of Disease
LCoGS	The Lancet Commission on Global Surgery
LMIC	Low-and Middle-Income Countries
LY	Life Year
MANDATE	Maternal and Neonatal Directed Assessment of Technology
MNHR	Maternal and Newborn Health Registry
MSF	Médecins Sans Frontières
NR	Not Reported
NGO	Non-Governmental Organisation
NHS	National Health Service
NICHD	Eunice Kennedy Shriver National Institute of Child Health and Human Development

NICU	Neonatal Intensive Care Unit
NSOAP	National Surgical, Obstetric and Anesthesia Plan
OECD	Organisation for Economic Co-operation and Development
OL	Obstructed Labour
OOP	Out-Of-Pocket
OPD	Out-Patient Department
OT	Operating Theatre
PPP	Purchasing Power Parity
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	The International Prospective Register of Systematic Reviews
PSA	Probabilistic Sensitivity Analysis
QALY	Quality-Adjusted Life Year
QUARITE	Quality of Care, Risk Management and Technology in Obstetrics Trial
SADC	South African Development Community
SDG	Sustainable Development Goals
SSA	Sub-Saharan Africa
SSI	Surgical Site Infection
UHC	Universal Health Coverage
UN	United Nations
UNFPA	United Nations Population Fund
UP	Uterine Prolapse
UR	Uterine Rupture
WHA	World Health Assembly
WHO	World Health Organization
WHO-CHOICE	Choosing Interventions that are Cost Effective
WOMAN	World Maternal Antifibrinolytic Trial
WTP	Willingness-To-Pay

Chapter 1

1 Introduction

Lack of access to essential surgical care in low-and middle-income countries (LMICs) contributes greatly to premature death and disability from surgically treatable conditions.[1,2] Findings from the Lancet Commission on Global Surgery (LCoGS) 2030 advocate for the prioritization of increasing access to essential surgical procedures to improve health outcomes in impoverished populations.[2] Access to caesarean section, laparotomy, and open fracture reduction (also known as the Bellwether procedures) has been proposed as a proxy for broader access to essential surgery.[2] However, several limitations such as scarcity of funding, lack of high-quality synthesized evidence, and various sociodemographic factors prevent the proposed expansion. The aim of this thesis is to examine best available evidence on health and economic impacts of improving access to essential surgery in LMICs and to use the results of the former to inform a de novo economic evaluation of the most common unmet need in the field of global surgery: increased access to caesarean section for obstructed labour in low-middle income settings (applied specifically to the South African Development Community (SADC) region).

1.1 Thesis Organization

The overall thesis is in integrated article format, structured around two manuscripts prepared for journal publication. The first chapter is an introduction to essential surgery and the Bellwether procedures, global health priorities, and an overview on issues surrounding unmet surgical need in impoverished countries. The second chapter is a systematic review appraising economic evaluations of increasing access to the Bellwether procedures in LMICs. The third chapter is an economic evaluation using decision-analytic modelling to assess cost-effectiveness of increasing access to caesarean section for obstructed labour in the SADC region. The fourth chapter discusses the results of both studies in the context of current evidence and global health policy considerations, while incorporating directions for future research and implementation of the model.

1.2 Essential Surgery and the Bellwether Procedures

Five billion people around the world are unable to access safe, timely, affordable surgical care.[2] Lack of access to essential surgery is also disproportionately distributed in low-and middle-income countries, where only 6% of the 313 million surgical procedures performed annually are occurring.[2] An estimated 1.4 million lives are lost to surgically avertable conditions per year, and this loss could be mitigated by increasing access to safe surgical and anaesthetic care for those in need.[3] The Bellwether procedures, defined as caesarean section, laparotomy, and treatment of open fracture, account for a large proportion of this disparity in global access to surgery.[2,4] Targeting these procedures is ideal due to their high-value, acute nature that allows for significant reductions in death and disability.[1,2] Their consistent provision is also considered to indicate a functional surgical system and effective service delivery.[2]

1.3 Lancet Commission on Global Surgery

In 2015, the 68th World Health Assembly declared surgery and anesthesia care to be an essential component of universal health coverage (UHC) as part of resolution 68.15.[5,6] The WHO targets for UHC align with the Lancet Commission of Global Surgery 2015 core indicators that were proposed to assess strength and capacity of surgical systems to provide timely, safe, affordable care to the Bellwether procedures (Table 1).[2]

Table 1 Lancet Commission on Global Surgery Core Indicators for Monitoring Universal Access to Safe, Affordable Surgical and Anaesthesia Care When Needed

Indicator	Definition	Goal
Access to timely essential surgery	Proportion of the population who can access, within 2 h, a facility that can provide Bellwether procedures (i.e., laparotomy, caesarean section, or open-fracture treatment)	A minimum of 80% coverage of essential surgical and anaesthesia services per country by 2030
Specialist surgical workforce density	Number of specialist surgical, anaesthetic, and obstetric physicians who are working per 100,000 population	100% of countries with at least 20 surgical, anaesthesia, and obstetric physicians per 100 000 population by 2030
Surgical volume	Volume of surgical procedures, per 100,000 population per year	80% of countries by 2020 and 100% of countries by 2030 tracking volume; a minimum of 5000 procedures per 100 000 population by 2030
Perioperative mortality	All-cause death rate in patients who have undergone a surgical procedure, divided by total number of procedures (%)	80% of countries by 2020 and 100% of countries by 2030 tracking postoperative mortality; in 2020, evaluate global data and set national targets for 2030

Protection against impoverishing expenditure	Proportion of households protected against impoverishment from direct out-of-pocket payments for surgical and anesthesia care	100% protection against impoverishment from out-of-pocket payments for surgical and anaesthesia care by 2030
Protection against catastrophic expenditure	Proportion of households protected against catastrophic expenditure from direct out-of-pocket payments for surgical and anesthesia care	100% protection against catastrophic expenditure from out-of-pocket payments for surgical and anaesthesia care by 2030

The purpose behind the development of these six core metrics is monitoring universal access to safe surgery in the context of current global health priorities (Table 1). The metrics are grouped by preparedness, delivery, and effect of surgical and anesthesia care.[2] The decision analytic model developed in Chapter 3 of this thesis engages with the indicators pertaining to access to essential surgery, perioperative mortality, and protection against impoverishing or catastrophic expenditure by assessing impacts of increasing access to timely caesarean section for obstructed labour with regards to reducing premature death and disability at increased costs. Overall, the studies included in this thesis project seek to identify priorities for implementation and address gaps in current knowledge on health and economic impacts of increasing access to essential surgery.

1.4 Obstetric Care and Inequities in Maternal and Neonatal Health

1.4.1 Inequitable Maternal Death in LMICs and the South African Development Community (SADC) region

In 2019 alone, 2.08 million mothers and babies across the world died following complications during pregnancy and childbirth.[7] Ninety-four percent of all maternal deaths occur in developing countries such as those in Sub-Saharan Africa, representing the single largest health disparity between high-income countries and LMICs.[7,8] Within Sub-Saharan Africa, a regional economic community comprised of 16 countries called the South African Development Community (SADC) was established in 1992, consisting of Angola, Botswana, Comoros, the Democratic Republic of Congo, Eswatini, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, Seychelles, South Africa, Tanzania, Zambia, and Zimbabwe.[9] These countries are the focus of the economic evaluation in Chapter 3 due to their connectedness through a shared agenda and mission towards eradication of poverty and achieving increased quality of life.[9]

In parallel, a disproportionately high maternal mortality ratio reflects inequities in access to safe obstetric care.[8,10] The maternal mortality ratio in the SADC region countries range from 61 per 100,000 live births in Mauritius to 487 per 100,000 live births in Lesotho, with an average maternal mortality rate of 353 per 100,000 live births across the SADC region.[11] When compared to the maternal mortality rate of 15.68 per 100,000 live births in high-income countries, the gap in access to obstetric care results in a death toll directly related to increased risk of death following complications such as obstructed labour and secondary sequelae like hemorrhage, sepsis, and uterine rupture.[7,11,12] In recent years, improvements in bolstering surgical capacity at hospitals in LMICs have continued to be pursued.[13,14] Strengthening surgical systems by monitoring and targeting the six LCoGS indicators will lead to substantial reductions in avertable deaths and disability due to decreased health over a lifetime.[2] However, the persisting problem that needs to be addressed is lack of access and availability of surgical procedures for obstetric emergencies and life-threatening conditions that require timely treatment.[2]

1.4.2 Neglected Obstructed Labour

Neglected obstructed labour is a severe obstetric condition that frequently leads to maternal death or lifelong disability due to secondary conditions.[12] Obstructed labour is defined by the World Health Organization (WHO) as "labour with no advance of the presenting part of the fetus despite strong uterine contractions, left untreated or neglected."[12] If labour does not advance, caesarean section is needed, otherwise the mother may experience severe sequelae such as sepsis, hemorrhage, uterine rupture, and death.[12] Associated complications for the neonate include high rates of stillbirth, birth asphyxia and trauma, sepsis, and long-term cognitive or motor impairments for the rest of their lifetime.[12,15,16] Inability to provide treatment for obstructed labour is an urgent health problem that exists across LMICs due to inability to access safe, timely caesarean section for an acute health condition that severely harms health outcomes of mothers and babies. Obstructed labour and secondary uterine rupture were responsible for 5,647 deaths in SSA in 2019 alone, with a corresponding number of 317,565 years of life lost due to premature death and an additional 189,470 years lived with disability.[7] These figures are likely to underestimate the true burden of neglected obstructed labour because death due to obstructed labour may be misclassified as death due to sequelae such as maternal sepsis and haemorrhage.[12] In 2019, maternal haemorrhage and sepsis were responsible for 16,922 and 11,593 deaths in SSA, respectively.[7]

1.4.3 Perinatal Mortality in LMICs

Investing in increased access to caesarean section for women in obstructed labour will significantly reduce perinatal mortality and morbidity.[17–19] Perinatal mortality due to neglected obstructed labour ranges from 25% to 52%, with much uncertainty around the true estimates of this death toll.[20] Neglected obstructed labour also leads to an estimated 25% of babies experiencing birth asphyxia and trauma-related outcomes, which is associated with 30% of babies developing hypoxic-ischemic encephalopathy in those who survive birth[20–22] Death from neonatal disorders led to 761,684 deaths in SSA in 2019, with 281,278 being attributed to neonatal encephalopathy due to birth asphyxia and trauma.[7] If neonates survive birth, the likelihood of remaining with a life-long debilitating condition greatly increases their years of life lived in disability and reduces their quality of life.[7] In SSA, neonatal disorders led to 2.81 million years lived with disability in 2019, with 852,797 directly attributed to neonatal encephalopathy due to birth asphyxia and trauma.[7]

1.4.4 Barriers to Surgical Care

A large proportion of maternal deaths and maternal injury-related disability are preventable with the provision of timely access to safe caesarean section for obstructed labour.[2,23] Women in the SADC region experience barriers to care such as risk of catastrophic impoverishment, inability to access facilities, and inadequate or poor-quality services.[2,11,24] These delays in care result in disproportionate death and disability related to obstructed labour for both mothers and babies.[2,25,26]

Reaching the recommended provision levels set by the LCoGS, including 80% coverage of essential surgery, tracking perioperative mortality, and 100% protection against catastrophic impoverishment will complement the United Nations General Assembly’s Sustainable Development Goals (SDGs) 2030.[10,27] SDG3 aims to reduce maternal mortality ratio to under "70 per 100,000 live births with no country having a maternal mortality rate of more than twice the global average."[10] Achieving these goals is integral to all health systems in the SADC region and will lead to tremendously improved health outcomes for those in need.[10]

1.5 Health Economic Evaluation in the Context of Global Surgery

To support the Lancet Commission on Global Surgery goals, economic evaluations of increasing access to the Bellwether procedures are necessary to inform policymakers and stakeholders in health funding decision-making and prioritization.[28] Results of these economic analyses are reported in the WHO-recommended outcome of cost per disability-adjusted life years (DALYs) to measure cost-effectiveness against a defined willingness-to-pay threshold or benchmark intervention.[29,30] The Global Burden of Disease study uses disability-adjusted life years (DALYs) to represent the loss of one year of healthy life.[31,32] This universal metric allows comparison across varying countries, age groups, and years, which is beneficial to policymakers when making funding decisions.[33] Outdated perceptions around surgical and anesthetic care being too expensive have been replaced by several economic evaluations that suggest investing in essential surgery in LMICs is cost-effective, comparing well to public health or infectious disease interventions that were previously thought to be more cost-effective.[27,34,35] Such examples include $54 for cost per DALY averted for providing repair surgery for obstetric fistula in Uganda, $87 per DALY averted for trauma surgery in Cambodia, and $36 per DALY averted for cataracts surgery in Sub-Saharan Africa.[36–38] Previous research has also been conducted on projected losses in economic productivity that were an estimated $12.3 trillion (2010 $USD), with greatest losses being in LMICs.[27]

However, there is a lack of formal economic evaluations of scaling-up access to the Bellwether procedures in LMICs. To better inform national healthcare resource allocation decisions, further work on quantifying long-term health and economic impacts related to scaling-up surgical access as an investment needs to be done.

1.6 Gaps in Knowledge

1.6.1 Maternal and Neonatal Outcomes

There are known issues with uncertainty around the true number of maternal deaths, obstetric fistula cases, and deaths due to neglected obstructed labour in the SADC region, and in Sub-Saharan Africa as a whole.[12,15,39] Deaths due to neglected obstructed labour are often misclassified as deaths due to various sequelae stemming from obstructed labour such as sepsis, hemorrhage, and uterine rupture.[12] Furthermore, estimating the number of women who are unable to reach a facility for treatment is an additional challenge faced by health systems and researchers.[12,25] Of those estimates, there is a high likelihood that the number is far greater than that reported due to unrecorded stillbirths and maternal deaths.[12,40] Accurate data on the length of delays in care for obstructed labour are often scarce, and detailed information on outcomes following neglected obstructed labour is sparse.[12,15,21,40] The quality of maternal health data available is oftentimes limited to retrospective hospital record reviews, cross-sectional surveys, physician recollection, or short-term observational studies specific to a local hospital.

1.6.2 Economic Evaluations of Essential Surgery in LMICs

Generally, economic evaluations conducted on cost-effectiveness of Bellwether procedures in LMICs are limited by lack of formal decision-analytic modelling, reported outcome measures, short time horizons, and choice of perspective. Most of the existing cost-effectiveness analyses are not realistic in terms of reflecting true access to care. The patient populations in these studies are often those who can reach a facility for treatment, which is highly unrepresentative of the current standard of care available to most individuals in the SADC region.

To date, no economic evaluation exists that evaluates the impact of increasing access to caesarean sections for obstructed labour for both mothers and babies using a decision-analytic model for a life-time time horizon, incorporating long-term disabilities. The model constructed in Chapter 3 of the thesis is the first to address this gap in knowledge.

1.6.3 Relevance and Applicability

Insight into costs and health outcomes related to provision of the Bellwether procedures is crucial yet severely lacking for LMICs, particularly in Sub-Saharan Africa and the SADC sub-region.[41] The results of economic evaluations can be used to inform policymakers and decision-makers to improve resource allocation and healthcare delivery for impoverished populations.

The goals of this thesis are to fill knowledge gaps regarding lack of evidence on feasibility of increasing access to the Bellwether procedures in LMICs. Synthesized results for all relevant economic evaluations assessing health and economic impacts of increasing access to the Bellwether procedures are presented and critically appraised in Chapter 2. Subsequently, the decision-analytic model presented in Chapter 3 addresses the long-term, inequitable disease burden due to obstructed labour by increasing provision of caesarean section to meet the goals of the LCoGS targets for increased access in the SADC region.

1.7 Objectives

The objectives of this thesis are as follows:

1. To conduct a systematic review and critically appraise all existing economic evaluations that examine costs, effects, and feasibility of increasing access to the Bellwether procedures in LMICs.

2. To construct a Markov cycle tree using decision-analytic modelling that compares current standard of care to increased access to caesarean section for women in obstructed labour in the SADC region across a lifetime time horizon. This model accounts for the estimated two-thirds of women in obstructed labour who are unable to receive treatment at a healthcare facility and the long-term disability or premature death that they face due to sequelae such as sepsis, haemorrhage, uterine rupture, and obstetric fistula.[25]

3. To construct an accompanying Markov cycle tree that compares neonatal outcomes from standard care to increased access to caesarean section, accounting for birth asphyxia and trauma-related disability across a life-time time horizon.

4. To provide policymakers and healthcare decision-makers an estimate of the cost per DALY averted for mothers and babies if they were to invest in scaling-up access to safe, timely caesarean section to treat obstructed labour in the SADC region.

Chapter 2

2 Health and Economic Impacts of Improving Access to Essential Surgery in Resource Restricted Settings: A Systematic Review

The following is an unpublished manuscript formatted for journal submission. The planned submission date is September 2021.

Authors: Anne Zhao, Joo-Hyun Jeong, Shehzad Ali*, and Janet Martin

*Janet Martin and Shehzad Ali are senior authors and contributed equally to this work.

2.1 Introduction

Five billion people across the world lack safe, timely, and affordable access to surgical, obstetric, and anaesthetic care.[2] Furthermore, the Lancet Commission on Global Surgery determined that very little information is available on the quality of the 313 million surgical procedures performed annually.[2] A recent analysis by Nepogodiev et al. 2019 indicated that the 30-day death toll following surgery was at least 4.2 million, half of which occurred in low and middle-income countries (LMICs).[4,35] The perioperative surgical death toll surpasses the combined death toll from HIV/AIDS, malaria and tuberculosis.[4] The burden of illness, due to lack of access and poor quality of surgical care, is disproportionately distributed in low-income households. Closing this gap in access, particularly in LMICs, could lead to a reduction of 1.5 million deaths per year, or 6.7% of all avertable deaths in LMICs.[42]

Globally, the highest impact of poor access to surgeries is due to low rates of caesarean section, laparotomy, and treatment of open fracture, i.e. the Bellwether procedures.[4] Targeting the Bellwether procedures is especially important for LMICs as they are acute, high-value procedures that can significantly reduce mortality from treatable conditions.[4] Recent reports on the burden of non-communicable diseases and injuries highlight the need for increase in availability of surgical care.[43,44] Failure to address this lack of access to surgical procedures results in considerable economic loss as well as reduced quality of life.[2,35,42]

In 2015, the World Health Assembly declared essential surgical and anaesthesia care to be a component of universal health coverage (UHC).[2,5] The WHO target for UHC is 80% essential health services coverage and 100% financial protection from out-of-pocket health services payments by 2030.[2] Reaching these goals will also complement the Sustainable Development Goals set by the United Nations General Assembly.[10]

To identify priority surgical procedures for implementation in LMICs, cost-effectiveness has been established as an important criterion.[1,35] To date, there remains a gap in knowledge about the cost-effectiveness of Bellwether procedures in LMICs. While a number of economic analyses have been published, they vary in quality, study context, reported outcomes and costs, time horizon and perspective. There is urgent need to synthesize this evidence to inform resource allocation decisions and set priorities for implementation as well as future research. To address this gap, the objective of this study was to conduct a systematic review of economic evaluation studies that examine the costs, effects, and feasibility of increasing access to the Bellwether procedures in LMICs.

2.2 Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used for this systematic review (see Appendix D for completed checklist).[45]

2.2.1 Search Strategy

A comprehensive literature search following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines was conducted.[45] MEDLINE and EMBASE on the OVID platform, PubMed, CINAHL, EconLit, NHS Economic Evaluation Database, Health Technology Assessment Database, the WHO Global Index Medicus, and the Cochrane Library were searched for the controlled vocabulary and keywords: “cost-utility” AND “Bellwether procedures” AND “low middle-income countries" (see Appendix A for search strategy). Additional articles were retrieved using citation tracing of identified studies from the search. The last search was performed on June 20, 2021.

2.2.2 Selection Criteria

Inclusion criteria included economic evaluations of patients undergoing or in need of an essential procedure (defined as the Bellwether procedures: caesarean section, laparotomy, or treatment of open fracture) in low and middle-income countries as defined by the World Bank.[46] Outcomes measured in cost per quality-adjusted life year (QALY), cost per disability-adjusted life year (DALY), incremental cost-effectiveness ratios (ICERs), DALYs averted, unmet surgical need, or years of life lost.

Clinical trials and observational studies were excluded from the review. There were no language restrictions placed on the search.

All inclusion and exclusion criteria were finalized *a priori*.

2.2.3 Study Selection

Two reviewers (AZ and JHJ) independently reviewed abstracts and full text articles for inclusion and exclusion criteria. AZ and JHJ extracted data from finalized articles and independently conducted risk of bias assessments using the ECOBIAS checklist.[47] Discrepancies at any stage were resolved by discussion with JM and SA. The PRISMA diagram (Figure 1) describes the detailed search and screening process, with reasons for exclusion.

2.2.4 Data Extraction and Quality Assessment

Data was extracted using a piloted form agreed upon by all authors. Thirteen measurements were classified as economic evaluations of undergoing or increasing access to one or more Bellwether procedures. Twenty-five measurements of cost-utility and cost-effectiveness were included. Due to potential risk of high heterogeneity from differing countries, baseline disease conditions, and delivery methods, quantitative summary measures were not calculated across articles.

All articles classified as economic evaluations were assessed for quality and bias related to structure, data, and consistency using the ECOBIAS Checklist, a tool developed to assess model-based economic evaluations.[47] Although this tool was developed for model-based economic evaluations, most elements of the tool were effectively applicable to non-model-based studies and broad economic evaluations.

Results from all studies that reported cost-utility were converted to international dollars ($I) using purchasing power parities (PPP) before inflation. Costs were then inflated to PPP-adjusted 2020 United States Dollars ($USD) using GDP Implicit Price Deflators to allow for comparability across studies.[48] If not otherwise stated, market exchange rate was used to convert costs into original local currency before calculating PPP-adjusted 2020 $USD. Outcome measures for different procedures were reported as separate occurrences despite originating from a single study.

2.2.5 Statistical Analysis and Software

Data was entered and compiled into Microsoft Excel 2021 (Version 16.44; Microsoft Corporation, Redmond, WA, USA). Results were grouped by Bellwether procedure and presented in table format.

2.3 Results

2.3.1 Overall results

A total of 6054 articles were identified through database searching, of which 5,952 were excluded for not meeting inclusion criteria. One hundred and two articles were identified for full-text review and 13 articles published between 1998 and 2020 from 49 countries met the pre-specified inclusion criteria to be included for data extraction, quality assessment, and subsequent qualitative analyses (Tables 2 and 3). Of these 13 articles, 6 were identified through citation tracing of systematic reviews captured in the initial search.[37,49–53] Table 4 and Appendix B summarize the ECOBIAS checklist results for quality assessment.

We identified and included 13 cost-effectiveness analyses. Five articles exclusively looked at caesarean section,[19,54–57] three articles examined only laparotomy,[51,53,58] one article examined only open fracture treatment,[52] two articles looked at laparotomy and treatment of open fracture,[37,50] and one article looked at all three Bellwether procedures.[59] Surgery type included both elective and emergency procedures.

Across the Bellwether procedures, the most cost-effective procedures included $7.93 per DALY averted for exploratory laparotomy in Uganda,[58] $10.18 per DALY averted for emergency hernia repair in a Zambian hospital calculated using global life expectancy,[59] $15.55 per DALY averted for emergency hernia repair in Zambia,[59] and $16.90 per DALY averted for emergency caesarean section in a Zambian hospital calculated using global life expectancy.[59] The least cost-effective procedures included $491.81 per DALY averted for emergency caesarean section for obstructed labour across 49 low-middle income countries[55] and $786.13 per DALY averted for fracture dislocation fixation in Zambia.[59]

Ten studies used no surgery as a comparator,[37,49–55,58,59] 2 used vaginal birth,[56,57]and 1 used care as usual.[19] 5 studies evaluated cost per DALY averted,[51,53,55,58,59] 3 studies evaluated ICERs,[54,56,57] 2 evaluated cost per maternal death avoided,[56,57] 1 evaluated total number of deaths averted,[19] 1 evaluated cost per life year saved,[49] and 1 evaluated cost-benefit ratio.[55] Five studies were population-based economic analyses assessing increasing access to surgery[19,49,55–57] and the remaining eight studies were cohort-based economic analyses examining costs and outcomes of those undergoing surgery in a specific setting.

Key study characteristics are presented in Tables 2 and 3.

2.3.2 Risk of Bias

Risk of bias was assessed using the ECOBIAS Tool developed by Adarkwah et al. and presented in Table 4 and Appendix B.[47] The ECOBIAS Tool assesses overall bias in economic evaluation, and specifically bias related to structure and data as well. Overall, there was a considerable amount of bias and uncertainty across a number of domains.

Regarding overall bias in economic evaluation (Table 4), bias related to narrow perspective, inefficient comparator, and reporting and dissemination bias was present across most of the studies included. There were few studies with cost measurement omission bias, intermittent data collection bias, and invalid valuation bias. Ordinal ICER bias was not identifiable in most studies due to lack of formal modelling but was present in both Brazilian studies by Entringer and colleagues.[56,57] It was unclear whether double-counting bias and sponsor bias was present across multiple studies. However, sponsor bias was partly present in two studies.[19,53] Inappropriate discounting bias was present in 5 studies[19,37,50,52,59] and partly present in 4 others.[51,53–55] Limited sensitivity analysis bias was present in 4 studies[37,49,50,59] and partly present in 5 others.[19,52,54,55,58]

In particular, bias related to structure (see Appendix B) was largely unavailable and not reported in 11 out of 13 studies. Bias related to data regarding baseline data and quality-of-life weights was also unavailable in 11 out of 13 studies. Bias related to limited scope was present in 4 studies[37,49,50,59] and partly present in 5 others.[19,37,54,55,58] There was little-to-no bias found related to treatment effects, non-transparent incorporation of data, and internal consistency. There was bias related to data identification partly present in 3 studies.[19,56,57]

2.3.1 Caesarean Section

Across 7 studies that evaluated cost-effectiveness of caesarean section, there were 13 varying outcome measures in total: 5 reported cost per DALY averted, 2 reported cost per maternal mortality avoided, 3 reported ICERs, 1 reported cost per LY saved, 1 provided cost per newborn death avoided per 1000 procedures, 1 provided cost-benefit ratio, and 1 reported deaths averted per $100,000. Of these, 4 studies evaluated emergency caesarean sections, 2 evaluated elective caesarean section, and 1 study included both (Table 5).

The costs per procedure ranged from $98.92 in the Republic of Guinea[49] to $1,723 in Brazil.[56] Two studies did not report costs per procedure.[55,59] Effect measures ranged from 106 DALYs averted for elective caesarean in a Zambian hospital to 7956 DALYs averted globally for emergency caesarean section.[59] Elective caesarean sections accounted for the lower end of effect measures.[56,57] Cost per DALY varied from $16.90 per DALY averted in a Zambian hospital calculated using global life expectancy[59] to $491.81 per DALY averted across 49 countries (Table 5).[55]

Hounton and colleagues reported a range of $230.79 to $247.23 per caesarean section by training clinical officers and doctors respectively.[54] The resulting ICER was $238.86 per newborn death avoided per 1000 caesarean sections when training doctors instead of clinical officers.[54] Verguet and colleagues reported that a $486,383 investment for a 10% increase in provision of caesarean section would avert 590 deaths in one year, resulting in 122 deaths averted per $100,000 spent (Table 5).[19]

2.3.2 Laparotomy

Across 7 studies that evaluated cost-effectiveness of laparotomy, there were 11 measures of average cost per outcome in total: 9 of these were cost per DALY averted and 2 were cost per LY saved. The mean costs per surgery ranged from $123.45 to $1049.46.[50,53] Two studies did not report mean costs per surgery.[37,50] Effect measures ranged from 6.4 DALYs to 18.51 DALYs averted per person,[53,58] and from 98 DALYs to 1424 DALYs in total per individual hospital.[37,59] Life years saved per person ranged from 0.71 to 1.86.[49] Cost per DALY varied from $7.93 per DALY averted[58] to $164.31 per DALY averted,[53] where hernia repair[53,59] was more costly per DALY averted than exploratory and emergency laparotomy.[58,59] Cost per LY saved ranged from $83.46 to $171.70, where hernia repair represented the higher end of costs.[49] Two studies did not report intervention-specific cost-utility (Table 6).[37,50]

2.3.3 Open Fracture

Across 4 studies that evaluated cost-effectiveness of open fracture reduction, there were 4 measures of average cost per outcome in total, all being cost per DALY averted. The mean costs per surgery were not reported. Effect measures ranged from 35 to 2,780 total DALYs averted at a local hospital.[37,59] Cost per DALY varied from $161.13 per DALY averted to $786.13 per DALY averted, where fracture dislocation fixation in Zambia occupied the high end of costs and fracture dislocation reduction in a Zambian hospital calculated using global life expectancy made up the lower end.[59] Three studies did not report intervention-specific cost-utility (Table 7).[37,50,52]

2.4 Discussion

2.4.1 Applicability Compared to WTP Thresholds

Our findings highlight the importance of published cost-effectiveness data on global surgery for understanding the unmet surgical need in low-middle income countries worldwide. Under the World Health Organization's Choosing Interventions that are Cost-Effective (WHO-CHOICE) project, previous suggestions stated that an intervention whose cost per DALY averted is less than three times the national annual GDP per capita of the country is considered cost-effective.[60] A cost per DALY averted that is less than the national annual GDP per capita is considered highly cost-effective.[60] In lieu of these recommendations, more conservative willingness-to-pay (WTP) thresholds estimated by Woods and colleagues that reflect opportunity costs of health care spending are used for comparison.[61] Woods and colleagues' predicted thresholds are markedly lower than the WHO-CHOICE recommendations after accounting for the relationship between marginal productivity, healthcare spending, and income elasticity.[61]

In Tables 5 through 7, the PPP-adjusted WTP thresholds of each country is reported, which allows for direct comparison with the associated cost per DALY averted. Using this comparison threshold, we found that all procedures included in our review except elective caesarean section in Brazil are considered cost-effective, being within the proposed range for WTP.[56,57] Most procedures have economic measures less than the lower end of the estimated WTP and are considered highly cost-effective. Predominantly, the range of cost-effectiveness across multiple studies shows a noticeable variation depending on country, procedure, and whether the surgery was elective or emergency in nature. For example, cost-effectiveness of caesarean sections varied from $16.90 per DALY averted in a Zambian hospital calculated using global life expectancy[59] to $491.81 per DALY averted across 49 countries.[55]

2.4.2 Benchmark Interventions and Current Evidence

Another commonly used approach is by using benchmark interventions from comparable countries as a threshold.[60] Several widely accepted health intervention strategies in low-middle income countries include general surgery and hospital care, including emergency obstetric care in Bangladesh ($17.04 per DALY averted),[62] cleft lip and cleft palate repair in Nepal ($45.45 per DALY),[63] management of obstructed labour in Sub-Saharan Africa ($93.17 per DALY averted),[64] intrapartum care in Mexico ($349.96 per DALY averted),[13] and non-emergency orthopedic surgery in Nicaragua ($407.91 - $613.58 per DALY averted).[14,65]

When comparing the cost utilities reported in our review to those widely accepted in literature, several estimates reported for laparotomy were comparable to general surgery and hospital care in Bangladesh.[62] Cost- effectiveness of open fracture reduction in Zambia compares favourably to that for intrapartum care in Mexico.[13] Treatment for obstructed labour across 49 countries also compares favourably to non-emergency orthopedic surgery in Nicaragua, being less costly.[14,65] A notable exception is elective caesarean section in Brazil, ranging from $1,358.14 to 1,727.92 per maternal mortality avoided).[56,57] Elective caesarean rates have been steadily increasing globally beyond rates considered medically necessary, particularly in Latin America and North America, which is associated with excess risk, increased maternal mortality, unnecessary cost, and reduced cost-effectiveness.[66–68] Efforts to reduce harm and minimize the overuse of caesarean sections have been introduced but further work is required to address these issues to optimize resource allocation for better return on investment in other underfunded aspects of public health.[68–70]

2.4.3 Limitations of Existing Economic Evaluations

Given our inclusive search strategy, we were able to capture economic evaluations across multiple countries and regions. However, since there is no global standard for cost-effectiveness analyses, the outcomes and methodology used in each study varied heavily. Results from the review were qualitatively summarized due to the high heterogeneity across outcomes, patient population, procedure, and costing methods. For example, laparotomy varied from general emergency laparotomy[37,59] to more specific procedures such as elective and emergency inguinal hernia,[49–51,53,59] and emergency appendectomy.[49]

Issues arose with many of the studies and their use of comparator. 7 out of 9 studies using no surgery as a comparator did not explicitly state as such, meaning that it had to be inferred.[37,49,50,52,55,58,59] In addition to being unclear, issues with using comparators of no cost and no effect are evident. The true cost of not receiving surgical treatment could vary from incurring costs from seeking alternate care, or even monetary damages related to not being able to work. Additionally, costs saved from avoiding complications were not captured either.

Only 2 of the 13 studies performed a formal cost-effectiveness analysis using a decision-analytic tree model.[56,57] One other study quantitatively calculated ICERs without using formal health economic modelling techniques.[54] Time horizon was stated in only 2 out of 13 studies[56,57] but was clearly limited in all studies to only immediate, acute outcomes associated with surgery without consideration of long-term costs and effects. In evaluating costs, several articles used WHO-CHOICE guidelines,[54] others used a differing regional guideline, and several did not report use of a standard costing procedure.

Only five of the 13 studies reported economic outcomes as cost per DALY averted.[51,53,55,58,59] The differing use of various health effect metrics had an impact on the results of the review. While the generic outcome of DALYs are the accepted metric used by the WHO and Institute for Health Metrics and Evaluation,[71,72] several included studies reported specific outcomes such as life years or cost per maternal death avoided, which mitigates comparisons across studies.[49,54] It is recommended to only compare higher quality economic evaluations with cost per DALY estimates against each other, as lower quality studies evaluating cost per natural outcome (i.e. cost per death avoided) cannot be compared to cost-utility studies. Results elucidate a basic overview of the immediate deaths and disability prevented in the short term but there remains a large gap regarding long term complications and sequelae. Solely evaluating short term costs without capturing long term cost and effect of lives saved and disability averted may skew the effect measures toward lower estimates of effect.

2.4.4 Generalizability and Future Directions

An issue regarding unmet need in global surgery, and specifically the Bellwether procedures, is that a large component of individuals who require care are unable to reach the operating room or the hospital due to barriers related to geographic distance and/or affordability.[2,68,70] These patients are by default not included in economic evaluations since most economic evaluations draw from those who are able to arrive at hospital for treatment. This inequity should be addressed in future economic evaluations to better reflect the issue of disproportionate access to essential surgery in LMICs.

From the appraisal of existing economic evaluations on increasing access to the Bellwether procedures, it is recommended that future economic evaluations be conducted using standardized metrics such as cost per DALY averted across longer time horizons for a population-based analysis when possible. Analyses assessing cost per natural outcome (i.e. maternal death avoided) should be presented as additional analyses to supplement the reference case but are not adequate replacements for cost-utility estimates. Model-based analyses should also be distinguished from cohort-specific cost and DALY estimates, with careful consideration for choice of comparator.

Despite evidence supporting the cost-effectiveness of increasing access to essential surgery in developing countries, barriers such as financial, political, workforce, and sociodemographic factors continue to limit patient access to life-saving care.[73–75] Recent efforts to address these limitations have been broadly successful. Several health service providers, hospitals, and organizations have created local or international programs to train mid-level health workers such as medical officers or nurses in surgery for improved patient health outcomes.[54,76–78] Task-shifting has not only been successful in saving lives but is also cost-effective for reducing the healthcare worker shortage, directly contributing to both the WHO targets and UN Sustainable Development Goals for 2030.[54,76–78] Other examples of successful interventions include providing altered fee scheduling and vouchers for caesarean section.[79–81] Future economic evaluations should continue to assess the feasibility of implementing these programs and policy interventions in addition to analyses of providing surgical procedures. Continued focus on increasing access to high-value, low-cost interventions such as the Bellwether procedures is a priority that needs to be further supported by policymakers and stakeholders to reach global targets.

2.4.5 Conclusion

The results of our systematic review indicate that many essential surgeries are highly cost-effective in low-middle income countries and represent good value for money compared to alternate use of resources. The importance and feasibility of the LCoGS target for 80% coverage of essential surgical and anaesthesia services per country by 2030 are supported by the findings from this review and the growing evidence base of essential surgery. It is recommended that future economic evaluations follow standardized guidelines, such as those proposed by the WHO, to ensure comparability across cost-effectiveness studies in LMICs.

Despite challenges in improving access to the Bellwether procedures in developing countries, the corresponding health gains from reducing substantial amounts of death and disability emphasize the urgent need to reduce these inequities in access. Considerable efforts are still necessary to reach the WHO 2015 and UN SDG global targets for scaling-up surgical access and reducing perioperative mortality by 2030.[5,6,10] Effective investment by policymakers, health systems, and organizations into improving access to essential surgery will lead to expansive growth and advancement in health systems and human welfare in LMICs.

2.4.6 Acknowledgements and Conflicts of Interest

A.Z is supported by a Canadian Institutes of Health Research Canada Graduate Scholarship award and a Western Graduate Research Scholarship at Western University in London. Ontario. The authors declare no conflicts of interests. S.A holds a Tier II Canada Research Chair in Public Health Economics.

The review protocol is registered on PROSPERO (Registration ID CRD42020196737) and can be freely accessed online. Due to unavailability of information on inequity in access and budget impact in current literature, these additional outcomes were not able to be included in the review. Sub-group analyses were restricted to type of Bellwether procedure for similar reasons.

2.5 Tables and Figures for Chapter 2

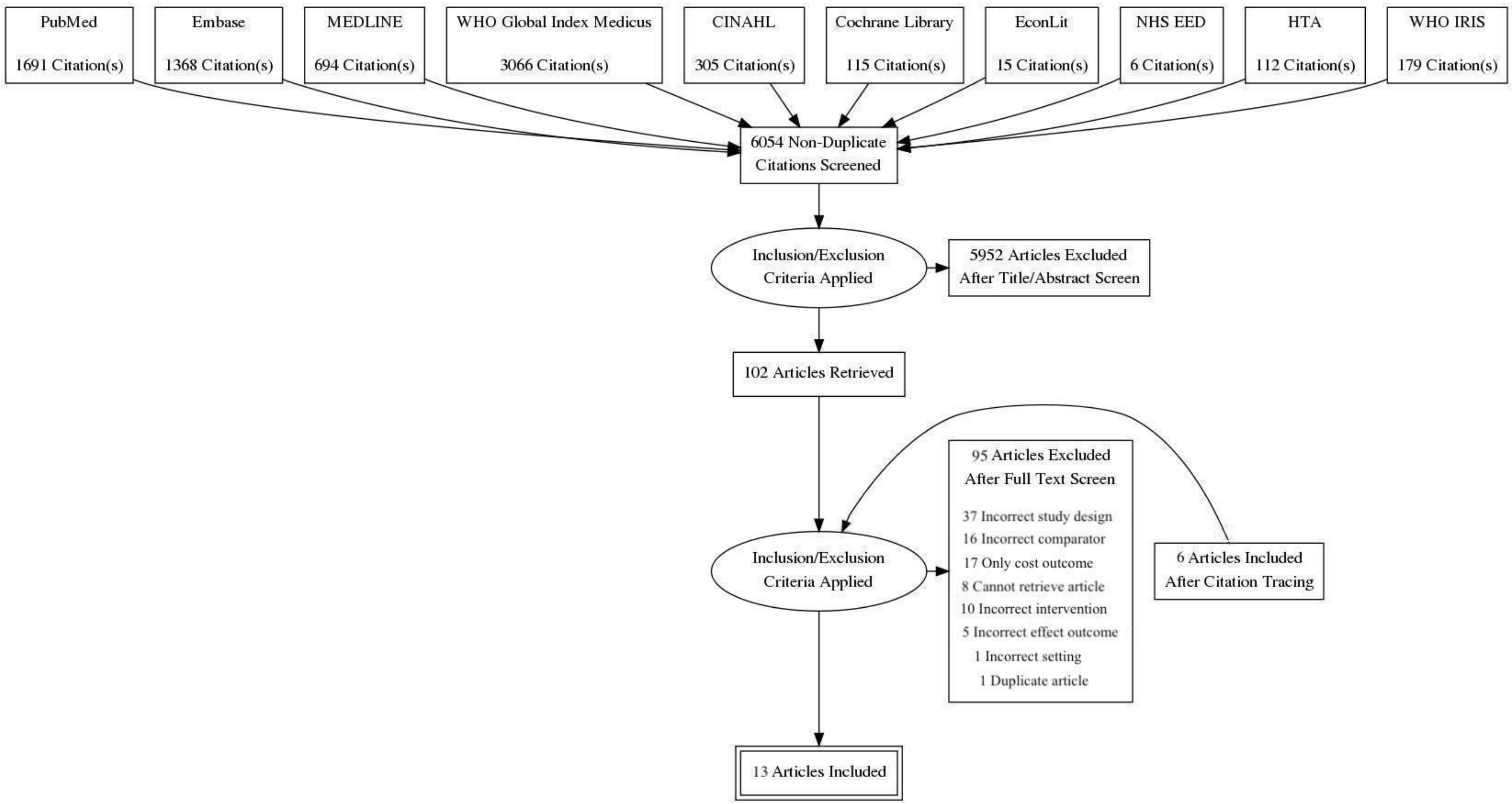

Figure 1. PRISMA Diagram

Table 2 Study Characteristics

Study	Country	Sample Size[a]	Baseline status	Sex	Length of Study	Intervention	Comparator	Outcome
Jha et al. 1998[49]	Republic of Guinea	5600 procedures	NR	NR	NR	Caesarean section for obstructed delivery, surgery for hernia, surgery for appendicitis	No surgery[b]	Cost per LY saved
Gosselin et al. 2006[50]	Sierra Leone	177 cases	Patients needing general care, orthopedic surgical care, pediatric out- patient and inpatient care	NR	July to Sept 2004	Acute abdomen surgery, hernia surgery, fractures	No surgery[b]	Cost per DALY averted
Gosselin et al. 2008[37]	Cambodia	395 cases	Patients in the emergency room, intensive care unit (ICU), and operating theaters	78% Male	Oct to Dec 2006	Laparotomy and open fractures	No surgery[b]	Cost per DALY averted
Hounton et al. 2009[54]	Burkina Faso	2305 caesarean deliveries	Patients with obstructed labour, ruptured uterus, eclampsia, or haemorrhage	All female	2004 to 2005	Caesarean section	Varying caesarean section providers (CO, D, O)	ICER, case fatality rate
Shilcutt et al. 2010[51]	Ghana	113 referred patients	Referred or presenting patients from rural areas with inguinal hernias of various sizes	Male 95%	Nov 2007 (5 days)	Lichtenstein method of inguinal hernia repair	No surgery	Cost per DALY averted
Gosselin et al. 2010[52]	Nigeria, Haiti	788 cases	Patients from the outpatient department (OPD), the operating theaters (OT), and all wards	NR	Aug to Oct 2008	External fixation of significantly open fractures of long bones	No surgery[b]	Cost per DALY averted
Shillcutt et al. 2013[53]	Ecuador	102 patients	Patients with inguinal hernias of various size from rural areas.	Male 82%	July 2010 (2 weeks), Nov to Dec 2010 (2 weeks)	Lichtenstein method of inguinal hernia repair	No surgery	Cost per DALY averted
Alkire et al. 2015[55]	47 countries	811,629 caesarean deliveries	Patients in obstructed labour	All female	NR	Caesarean section	No surgery[b]	Cost per DALY averted, cost-benefit ratio
Roberts et al. 2015[59]	Zambia	405 patients	NR	Laparotomy male 48%, CS all female, hernia repair all male, open fracture male 71%	Sept to Dec 2012	Caesarean section, laparotomy, inguinal hernia repair, fracture reduction	No surgery[b]	Cost per DALY averted
Verguet et al. 2015[19]	Ethiopia	NR	NR	NR	Time period in which 10% increase in access is achievable (i.e. 1 year)	Caesarean section	Usual coverage of intervention	Total number of deaths averted
Entringer et al. 2018a[56]	Brazil	NR	Normal risk pregnant women	All female	NR	Cesarean section	Vaginal delivery	ICER for cost per averted maternal mortality, cost per averted maternal mortality
Entringer et al. 2018b[57]	Brazil	NR	Normal risk pregnant women undergoing spontaneous vaginal delivery or elective cesarean (with no clinical indication)	All female	NR	Cesarean section	Vaginal delivery	ICER for cost per averted maternal mortality, cost per averted neonatal death
Bellamkonda et al. 2020[58]	Uganda	103 patients	Patients presenting with bowel obstruction, gut perforation, intussusception, penetrating trauma, and abdominal mass/tumor, or blunt trauma	Male 46%	Feb to April 2017, June to Dec 2018	Emergency laparotomy	No surgery[b]	Cost per DALY averted

NR = Not reported, LY = life year, DALY = disability-adjusted life year, ICER = incremental cost-effectiveness ratio, CO = clinical officer, D = doctor, O = obstetrician, CS = caesarean section OOP = out of pocket, GBD = Global Burden of Disease

[a] Distinction was made between number of procedures and patients, since it is possible that double-counting could have occurred for studies that count total procedures
[b] Comparator was inferred and not explicitly stated

Table 3 Economic Model

		Parameter Sources							
Study	**Analysis Type**[a]	**Population**	**Costs**	**Intervention Effect**	**Perspective**[b]	**Time Horizon**	**Discounting**	**Costing Year (Currency)**	**Sensitivity Analyses**
Jha et al. 1998[49]	PB	Local data from health centres, first referral hospitals, and national programs	Labour costs from monthly salaries; drug, supplies, and equipment from Central Pharmacy, direct health centre purchases or independent distributors; overhead costs from national non-recurrent salary budget	Published literature and expert opinion	*Health system*	NR	3% on cost and DALYs	1994 (USD)	NR
Gosselin et al. 2006[50]	CB	Local data from NGO hospital	Fixed costs (land purchase, construction, equipment) and local operating costs (salaries, drugs, utilities, fuel, etc.)	Hospital admission logs and patient charts and published literature	*Hospital*	NR	None	2004 (USD)	NR
Gosselin et al. 2008[37]	CB	Local data from emergency hospital	Fixed costs (construction, medical equipment and other equipment), and local operating costs (salaries, medical material, drugs, cargo, utilities, etc.)	Published literature	*Hospital*	NR	Life expectancy	2006 (USD)	NR
Hounton et al. 2009[54]	CB	Hospital records and patient case notes	Costs incurred by the hospital, salaries, pension, training, time spent on surgical tasks	Facility records	*Health system*	NR	3% on training cost	2006 (CFA)	Major cost categories
Shilcutt et al. 2010[51]	CB	Referred or presenting patients	Variable costs (drug unit costs taken from International Drug Price Indicator Guide, Ghana Pharmaceutical Pricing Study, WHO-CHOICE project, out-of-pocket costs by survey) and fixed costs (WHO-CHOICE study, building and refurbishment costs, equipment costs and utilities)	Expert opinion for counterfactual, WHO burden of disease equations for health outcomes, and published literature	Health Provider	NR	3% on DALYs	2008 (USD)	PSA DALY assumptions, patient perspective (including OOP costs)
Gosselin et al. 2010[52]	CB	Local data from MSF surgical trauma centers	Fixed costs (medical and other equipment, cars, etc). Operating costs from MSF internal accountancy, costs for drugs and medical material from pharmacy management software.	Published literature using discounted, age-weighted life expectancy tables and disability weights	*Hospital*	NR	NR	2008 (USD)	DALY calculation (severity of condition, probabilities for success of treatment)
Shillcutt et al. 2013[53]	CB	Private rural local hospital	Local supply companies or literature for component costs of program. Patient out-of-pocket costs (patient survey). Unit costs from pharmacies, WHO-CHOICE project, and catalog prices from medical suppliers.	Published literature; inguinal hernia disability weight and mortality for untreated case based on expert opinion	Health provider	NR	3% on DALYs	2011 (USD)	Monte-Carlo simulation for uncertainty in patient-level data; variation in disability weight; scenario analysis for life tables, costing perspective, and mortality

Alkire et al. 2015[55]	PB	Published literature (cross-sectional and cohort studies)	Published literature and WHO estimates	Published literature	*Health system*	NR	NR	2010 (USD)	PSA using Monte-Carlo simulation (incidence of cases, incidence of maternal mortality, cost proportions of vaginal delivery to caesarean delivery)
Roberts et al. 2015[59]	CB	Single-district local hospital	Hospital cost records, government-funded distribution network for drugs and consumables (WHO African essential price indicator), and online wholesalers	Published literature	*Health system*	NR	NR (but 3% inflation rate for equipment)	2012 (USD)	Range of caesarean section disability weights accounted for
Verguet et al. 2015[19]	PB	Ethiopia Central Statistical Agency, ICF International	Secondary data and published literature	Published literature	*Health system*	NR	NR	2011 (USD)	Evaluated sensitivity to change in coverage increments
Entringer et al. 2018a[56]	**PB**	Hospital Information System of the Unified Health System (SIH-SUS) and DATASUS	Brazilian Hierarchial Classification of Medical Procedures 2016 (CBHPM), National health plan operators' pricing tables, expert opinion, Simpro Hospitalar Magazine, and the Brasindice Pharmaceutical Guide	Published literature	Health subsystem financing (private care)	Between admission for delivery to maternity hospital discharge	None due to short time horizon	2016 (Reais)	DSA and PSA for costs and probabilities, effectiveness parameters were varied
Entringer et al. 2018b[57]	**PB**	Brazilian Unified National Health System	Expert opinion, cost analyses, and public databases (Health Price Bank, Federal Government Purchasing Portal (Comprasnet), Support System for the Development of Health Investment Projects (SomaSus)	SUS Hospital Information System, (SIH-SUS) DATASUS, hospital records, consultation with specialists	Health system	Between hospitaliz ation for delivery until delivery	None due to short time horizon	2014 (Reais)	DSA and PSA (Monte-Carlo simulation)
Bellamkonda et al. 2020[58]	CB	Soroti regional referral hospital	Hospital records	Expert opinion	*Hospital*	NR	3% on DALYs	2014 (USD)	Scenario-analysis (conservative assumption on survival benefit, DALYs averted, salaries).

NR = Not reported, PB = population-based economic analysis, CB = cohort-based economic analysis, DA = decision analytic, OOP = out of pocket costs, MSF = medecins sans frontieres, GBD study = Global Burden of Disease Study, PSA = probabilistic sensitivity analysis, DSA = deterministic sensitivity analysis

a = Analysis type was inferred when not directly reported by authors. Bolded analysis type meant that the model used was a decision-analytic model. If not a decision-analytic model (model-based), the analysis was based on an observational cohort study
b = Perspectives were inferred when not directly reported by authors. Perspectives that were inferred were italicized.

Table 4 Summary of Risk of Bias Assessment using ECOBIAS Tool

Part A: Overall checklist for bias in economic evaluation											
Study	**Narrow perspective bias**	**Inefficient comparator bias**	**Cost measurement omission bias**	**Intermittent data collection bias**	**Invalid valuation bias**	**Ordinal ICER bias**	**Double-counting bias**	**Inappropriate discounting bias**	**Limited sensitivity analysis bias**	**Sponsor bias**	**Reporting and dissemination bias**
Jha et al. 1998[49]	Yes	Yes	No	No	No	N/A	Unclear	No	Yes	Unclear	Yes
Gosselin et al. 2006[50]	Yes	Yes	No	No	Partly	N/A	Unclear	Yes	Yes	Unclear	Yes
Gosselin et al. 2008[37]	Yes	Yes	No	No	Partly	N/A	Unclear	Yes	Yes	Unclear	Yes
Hounton et al. 2009[54]	Yes	Yes	No	No	No	No	Unclear	Partly	Partly	No	Yes
Shilcutt et al. 2010[51]	Yes	Yes	No	No	No	No	Unclear	Partly	No	No	Yes
Gosselin et al. 2010[52]	Yes	Yes	No	No	Partly	N/A	Unclear	Yes	Partly	Unclear	Yes
Shillcutt et al. 2013[53]	No	Yes	No	Unclear	Yes	No	Unclear	Partly	No	Partly	Yes
Alkire et al. 2015[55]	Yes	Yes	No	No	No	N/A	Unclear	Partly	Partly	Unclear	Yes
Roberts et al. 2015[59]	Yes	Yes	No	No	No	N/A	Unclear	Yes	Yes	No	Yes
Verguet et al. 2015[19]	No	Yes	Unclear	No	No	N/A	Unclear	Yes	Partly	Partly	Yes
Entringer et al. 2018a[56]	Yes	No	No	Unclear	No	Yes	Unclear	No	No	No	No
Entringer et al. 2018b[57]	Yes	No	No	Unclear	No	Partly	Unclear	No	No	No	No
Bellamkonda et al. 2020[58]	Yes	Yes	No	No	No	N/A	Unclear	No	Partly	No	Yes

Table 5 Summary of Findings for Caesarean Section

Study	Procedure Type	GDP per capita[a] (in PPP-adjusted 2020 $USD)	Costs (in PPP-adjusted 2020 $USD)		Effect	Measure	Economic Outcome (in original reported currency)[b]	Economic Outcome (in PPP-adjusted 2020 $USD)[b]
			Mean costs	Currency				
Non-model-based studies								
Jha et al. 1998[49]	Emergency	$25 - $720	$98 per surgery	USD	2.309	Life years saved	$18 USD per LY saved	$98.92 per LY saved
Alkire et al. 2015[55]	Emergency	$18 - $600	NR	USD	NR	DALYs averted	$416 USD per DALY averted *4:1*[c]	$491.81 per DALY averted
Roberts et al. 2015[59]	Emergency (Global)	$127 - $1,826	NR	USD	7956 (6376-9098)	DALYs averted	$7.24 USD per DALY averted	$16.90 per DALY averted
Roberts et al. 2015[59]	Emergency (Zambia)	$127 - $1,826	NR	USD	5329 (4264-6106)	DALYs averted	$11.07 USD per DALY averted	$25.84 per DALY averted
Roberts et al. 2015[59]	Elective (Global)	$127 - $1,826	NR	USD	158	DALYs averted	$15.26 USD per DALY averted	$47.85 per DALY averted
Roberts et al. 2015[59]	Elective (Zambia)	$127 - $1,826	NR	USD	106	DALYs averted	$24.03 USD per DALY averted	$62.88 per DALY averted
Verguet et al. 2015[19]	Emergency	$29 - $777	$486,383(for 10% increase)	USD	590	Deaths averted	141 deaths averted per $100,000 USD	122 deaths averted per $100,000
Hounton et al. 2009[54]	Emergency	$42 - $938	$229.79 per caesarean by training clinical officer (CO)	USD	198	Newborn Lives per 1000 c-sections	$36,260 CFA per newborn death avoided per 1000 procedures (from CO to D)*	$238.86 per newborn death avoided per 1000 procedures (from CO to D)*
Hounton et al. 2009[54]	Emergency	$42 - $938	$247.23 per caesarean by doctor (D)	USD	125	Newborn Lives per 1000 c-sections	NR	NR
Model-based Studies								
Entringer et al. 2018a[56]	Elective	$3,584 - $11,303)	$1727.92 (primiparous) per procedure	USD[d]	1 (-0.02%)	Probability of maternal death (compared to vaginal birth)	$3,429.27 Brazilian Reais per maternal mortality avoided (from vaginal birth to caesarean section)* C-section dominated in all outcomes, natural childbirth more cost-effective for normal risk pregnant women	$1,727.92 per maternal mortality avoided (from vaginal birth to caesarean section)*
Entringer et al. 2018b[57]	Elective	$3,584 - $11,303)	$1358.14 (primiparous) per procedure	USD[d]	1 (-0.02%)	Avoided maternal mortality (probability/"effectiveness" compared to vaginal birth)	$2,245.86 Brazilian Reais per maternal mortality avoided $2,659,339 Brazilian Reais per maternal mortality avoided (from vaginal birth to caesarean section)*	$1,358.14 per maternal mortality avoided $1,608,216.17 per maternal mortality avoided (from vaginal birth to caesarean section)*

LY = Life year, DALY = disability-adjusted life year, CO = clinical officer, D = doctor, NR = not reported
a = Willingness-to-pay thresholds estimated by Woods and colleagues 2016 in PPP-adjusted 2020 USD$
b = Reported as either average cost per outcome (ACO), incremental cost-effectiveness ratio (ICER)*, or *benefit cost ratio (BCR)*
c = Benefit-cost ratio calculated by dividing gross economic benefit by total cost
d = Study originally reported local currency, results are converted to PPP-adjusted USD of corresponding costing year

Table 6 Summary of Findings for Laparotomy

Study	Type of Laparotomy	GDP per capita[a] (in 2020 $USD)	Costs (2020 $USD)		Effect	Measure	Economic Outcome (in original reported currency)[b]	Economic Outcome (in 2020 $USD)[b]
			Mean costs	Currency				
Jha et al. 1998[49]	Emergency Appendectomy	$25 - $720	$156.96 per surgery	USD	1.86	Life years saved per person	$36 USD per LY saved	$83.46 per LY saved
Jha et al. 1998[49]	Hernia repair	$25 - $720	$123.45 per surgery	USD	0.71	Life years saved per person	$74 USD per LY saved	$171.70 per LY saved
Gosselin et al. 2006[50]	Acute abdomen surgery	$59 - $1,106	NR	USD	1019	Total DALYs averted	NR	NR
Gosselin et al. 2006[50]	Inguinal hernia	$59 - $1,106	NR	USD	450	Total DALYs averted	NR	NR
Gosselin et al. 2008[37]	Emergency laparotomy	$146 - $1,746	NR	USD	1424	Total DALYs averted	NR	NR
Shilcutt et al. 2010[51]	Tension-free inguinal hernia repair	$250 - $2,281	$312.33 per surgery	USD	9.3	DALYs averted per person	$12.9 USD per DALY averted	$33.52 per DALY averted
Shillcutt et al. 2013[53]	Tension-free inguinal hernia repair	$1,739 - $6,463	$1049.46 per surgery	USD	6.4	DALYs averted per person	$78.2 USD per DALY averted	$164.31 per DALY averted
Roberts et al. 2015[59]	Emergency laparotomy (Global)	$127 - $1,826	NR	USD	2080	Total DALYs averted	$8.62 USD per DALY averted	$20.12 per DALY averted
Roberts et al. 2015[59]	Emergency laparotomy (Zambia)	$127 - $1,826	NR	USD	1418	Total DALYs averted	$12.64 USD per DALY averted	$29.51 per DALY averted
Roberts et al. 2015[59]	Emergency hernia repair (Global)	$127 - $1,826	NR	USD	328	Total DALYs averted	$4.36 USD per DALY averted	$10.18 per DALY averted
Roberts et al. 2015[59]	Emergency hernia repair (Zambia)	$127 - $1,826	NR	USD	215	Total DALYs averted	$6.66 USD per DALY averted	$15.55 per DALY averted
Roberts et al. 2015[59]	Elective hernia repair (Global)	$127 - $1,826	NR	USD	154	Total DALYs averted	$15.26 USD per DALY averted	$35.62 per DALY averted
Roberts et al. 2015[59]	Elective hernia repair (Zambia)	$127 - $1,826	NR	USD	98	Total DALYs averted	$24.03 USD per DALY averted	$56.09 per DALY averted
Bellamkonda et al. 2020[58]	Exploratory laparotomy	$31 - $810	$146.68 per surgery	USD	18.51	DALYs averted per person	$4.08 USD per DALY averted	$7.93 per DALY averted

LY = Life year, DALY = disability-adjusted life year, CO = clinical officer, D = doctor, NR = not reported
a = Willingness-to-pay thresholds estimated by Woods and colleagues 2016 in PPP-adjusted 2020 USD$
b = Reported as average cost per outcome (ACO), either cost per DALY averted or cost per LY saved

Table 7 Summary of Findings for Open Fracture

Study	Type of Laparotomy	GDP per capita[a] (in 2020 $USD)	Costs (2019 USD$)		Effect	Measure	Cost Utility (in original reported currency)	Cost Utility (in 2020 $USD)
			Mean costs	Currency				
Gosselin et al. 2006[50]	Fractures (conservative treatment, reduction, and fixation)	$59 - $1,105	NR	USD	531	Total DALYs averted	NR	NR
Gosselin et al. 2008[37]	Fractures	$146 - $1,746	NR	USD	2,780	Total DALYs averted	NR	NR
Gosselin et al. 2010[52]	External fixation of long bone open fractures (Teme Hospital)	$498-$3,216[b] $46 - $977[c]	NR	USD	1,676	Total DALYs averted	NR	NR
Gosselin et al. 2010[52]	External fixation of long bone open fractures (La Trinité Hospital)	$498-$3,216[b] $46 - $977[c]	NR	USD	976	Total DALYs averted	NR	NR
Roberts et al. 2015[59]	Fracture dislocation reduction (Global)	$127 - $1,826	NR	USD	238	Total DALYs averted	$69.03 USD per DALY averted	$161.13 per DALY averted
Roberts et al. 2015[59]	Fracture dislocation reduction (Zambia)	$127 - $1,826	NR	USD	166	Total DALYs averted	$98.73 USD per DALY averted	$230.46 per DALY averted
Roberts et al. 2015[59]	Fracture dislocation fixation (Global)	$127 - $1,826	NR	USD	52	Total DALYs averted	$225.9 USD per DALY averted	$527.29 per DALY averted
Roberts et al. 2015[59]	Fracture dislocation fixation (Zambia)	$127 - $1,826	NR	USD	35	Total DALYs averted	$336.8 USD per DALY averted	$786.13 per DALY averted

NR = not reported
a = Willingness-to-pay thresholds estimated by Woods and colleagues 2016 in PPP-adjusted 2020 USD$
b = Willingness-to-pay threshold for Nigeria
c = Willingness-to-pay threshold for Haiti

Chapter 3

3 Cost-Effectiveness of Increasing Access to Caesarean Section for Obstructed Labour in the South African Development Community (SADC) Region

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3.1 Introduction

3.1.1 Neglected Obstructed Labour and Associated Sequelae

Globally, there were an estimated 196,000 maternal deaths related to obstetric complications that occurred in 2019.[7] Of these deaths, an estimated 94% occurred in low- and middle-income countries (LMICs), resulting from global inequities in accessing emergency obstetric care, including safe and timely access to caesarean section for obstructed labour (WHO).[2,24,82] One of the most common causes of death due to lack of emergency obstetric care is neglected obstructed labour, defined by the World Health Organization (WHO) as "labour with no advance of the presenting part of the fetus despite strong uterine contractions, left untreated or neglected."[12,83] The global incidence of obstructed labour is approximately 5% of all pregnancies, with markedly higher estimates in LMICs compared to high-income countries.[84] Incidence estimates for obstructed labour range from 12% to 20% in LMICs like Ethiopia but are essentially negligible in developed countries where individuals can readily access timely care.[20,83,85] Obstructed labour is also one of the largest contributors to years lived with disability of all maternal conditions because it affects young women of childbearing age.[7,12,15] The highest disability-adjusted life year (DALY) burdens due to obstructed labour and associated sequelae occur in Sub-Saharan Africa.[7,12,17] Obstructed labour and uterine rupture combined were directly responsible for 507,034 DALYs and 5,646 deaths in Sub-Saharan Africa in 2019 alone.[7]

Obstructed labour is typically managed through caesarean section or instrumental delivery.[12,15] Appropriate use of caesarean section or instrumental delivery reduces the risk of life-threatening sequelae such as sepsis, hemorrhage, surgical site infections, uterine rupture, and death.[12,15,39] Obstetric fistula, a severe but preventable condition, is a chronic condition caused by neglected obstructed labour that may lead to life-long disability and adverse psychosocial outcomes such as being shunned from their homes due to stress incontinence.[86,87] Obstetric fistula occurs after ischemic damage and necrosis of vaginal tissue due to prolonged obstructed labour, resulting in a hole between the bladder and vagina (vesicovaginal) or vagina and rectum (rectovaginal).[88] There are an estimated 33,000 cases of obstetric fistula occurring each year in Sub-Saharan Africa that lead to severe life-long disability for this population of women due to unmet need for repair surgery.[89]

Obstructed labour is also directly associated with high rates of perinatal mortality and morbidity.[90] For babies born to mothers in prolonged obstructed labour, an estimated 26% are affected by perinatal asphyxia following neglected obstructed labour, which may lead to stillbirths, encephalopathy, or motor and cognitive impairments.[21,22] Stillbirth rates for babies born from prolonged obstructed labour range from 25% to 52%, depending on the setting and source of data.[20] Despite an estimated 2.60 million stillbirths occurring yearly worldwide, focus on the targets set for reducing national stillbirth rates to 12 per 1,000 livebirths by 2030 has been limited in global surgery research to date.[91,92]

3.1.2 Treatment and Scaling Up Access to Timely Caesarean Section for Obstructed Labour in the SADC Region

Within Sub-Saharan Africa, a regional economic community of 16 member countries called the South African Development Community (SADC) was formed with goals for achieving economic development, enhanced quality of life, growth, and security.[9] The SADC region includes sixteen Sub-Saharan African countries: Angola, Botswana, Comoros, the Democratic Republic of Congo, Eswatini, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, Seychelles, South Africa, Tanzania, Zambia, and Zimbabwe.[9] There have been significant efforts in improving health outcomes in the SADC region because it represents the highest burden of disease globally.[7,9] In 2019, the maternal mortality ratio in the SADC region ranged from 61 per 100,000 live births in Mauritius to 525 per 100,000 live births in Zimbabwe.[11] Of the 16 member countries, only Mauritius and Seychelles are on track to reaching the Sustainable Development Goals (SDGs) proposed by the United Nations to reduce maternal mortality ratio to under 70 per 100,000 live births.[11] Major direct causes of maternal mortality in the SADC region include obstetric hemorrhage, obstructed labour, pregnancy-induced hypertension, sepsis, and abortion complications.[11]

Prolonged obstructed labour and the associated excess maternal death are preventable if timely access to surgical and anaesthetic care is made available in developing countries.[11] Despite promising evidence, insufficient funding towards maternal and child health is a significant barrier to reducing health inequities, maternal death, and neonatal death in SADC countries.[11]

3.1.3 Statement of Inquiry

The proposed study evaluates the costs and effects associated with scaling-up access to timely caesarean section compared to existing care for women of childbearing age experiencing obstructed labour in the SADC region. Using previously published literature, a decision analytic model was built to evaluate the incremental cost per disability-adjusted life year averted for mothers and babies from a health systems perspective. To our knowledge, this is the first study to use decision analytic modelling using a lifetime time horizon to quantify the health and economic impacts associated with increasing access to caesarean section compared to maintaining existing level of coverage.

3.2 Methods

This economic evaluation is reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guidelines, and in alignment with WHO guidelines for economic evaluation (see Appendix M for the completed checklist).[93]

3.2.1 Type of Economic Evaluation

A cost-utility analysis was conducted to examine the health and economic impacts of increasing the use of caesarean section for treatment of obstructed labour to support decision-makers with broad health system budgets. This cost-utility analysis examined incremental costs per disability-adjusted life years averted for mothers and babies following obstructed labour.

3.2.2 Target Population

The base case population of the analysis was women requiring caesarean section for treatment of obstructed labour and their neonates. The economic evaluation is specific to women in the SADC region between the ages of 15 and 49. Obstructed labour is defined as labour with no advance of the presenting part of the fetus despite strong uterine contractions, left untreated or neglected.[12]

3.2.3 Perspective

This analysis was conducted from a health systems perspective.

3.2.4 Treatment Comparators

In the existing care strategy, 30% of women in obstructed labour received caesarean section, 3.33% received instrumental delivery, and 66.67% had no intervention for obstructed labour. In the increased access strategy, 80% of women in obstructed labour received caesarean section, 6.7% received instrumental delivery, and 13.3% had no intervention for obstructed labour. Estimates of existing care are derived from Demographic Health Surveys data for health facility deliveries in SSA and WHO descriptive analyses estimating the incidence of neglected obstructed labour.[12,25] Within those who can access a health facility, the proportion of those receiving caesarean section and instrumental delivery are based on WHO assumptions of 90% caesarean section and 10% instrumental delivery.[12] The estimates for the increased access strategy are based on the 68th WHA resolutions on universal health coverage and the Lancet Commission of Global Surgery (LCoGS) 2030 goals for global surgery provision (see Appendix G1 for details).[2,6]

3.2.5 Discounting and Time Horizon

Costs and effects were discounted at 3% to reflect WHO recommendations for conducting cost-effectiveness analysis.[94] Sensitivity analyses were conducted varying the discount rate to 0% for health effects and 6% for costs as per recommendations by the WHO guidelines for cost-effectiveness analysis.[94] Costs and health impacts were examined over a lifetime time horizon to incorporate the long-term effects of potential sequelae caused by obstructed labour.

3.2.6 Modelling

3.2.6.1 Maternal Outcomes

3.2.6.1.1 Decision Tree Model

The decision analytic model is comprised of a decision tree to represent in-hospital or in-community outcomes and costs in the short-run, followed by a Markov model that projects long-term survival, health outcomes, and costs of increasing access to caesarean section for obstructed labour (Figures 2-4). Two alternative strategies were modeled: (a) continuing current level of coverage of access to caesarean section (existing care: 30% of all obstructed labor); and (b) increased access to caesarean section (expanded access: 80% of all obstructed labor). For each management strategy in the decision tree (caesarean section, instrumental delivery, and being unable to reach the hospital), branches were constructed to represent the seven short-term sequelae that a woman in obstructed labour may experience: (1) sepsis, (2) hemorrhage, (3) surgical site infections, (4) uterine rupture, (5) uterine prolapse, (6a) maternal hospital discharge without sequelae or (6b) survival without sequelae, and (7) death.[12,21,90] For women unable to reach a hospital for treatment, the corresponding branch for (6a) maternal hospital discharge without sequelae in the caesarean section and instrumental delivery subtrees was (6b) survival without sequelae in the prolonged obstructed labour subtree. Uterine prolapse was assumed to be applicable only to women unable to reach the hospital, since it is attributed to prolonged obstructed labour and difficult vaginal delivery.[95,96] Disability weights were applied based on the sequelae branch. In the event of uterine rupture occurring after caesarean section or instrumental delivery, additional nodes were constructed for women requiring hysterectomy to control severe cases of haemorrhage.[97] If premature maternal death occurred, years of life lost were calculated relative to each woman's remainder of life based on the total healthy life expectancy in the SADC region of 61 years.[11]

3.2.6.1.2 Markov Model

Women surviving obstructed labour from the decision tree entered the Markov model (with an annual cycle) to reflect long-term survival, effects of sepsis (assumed to last up to 2 years), and long-term disability due to obstetric fistula for the remainder of their lifetime.[86,90] The Markov nodes for long-term survival without fistula were comprised of two states: i) survival and ii) death. If women developed sepsis, additional costs for treatment and disability associated with the sequela were applied for two years in the survive state.[98,99] In following cycles, women surviving without obstetric fistula either remained in the survival state or transitioned to death due to external causes.

In the model, women with obstetric fistula either underwent repair surgery or remained untreated, and then transitioned to (i) alive without disability, (ii) alive with vesicovaginal fistula, (iii) alive with rectovaginal fistula, (iv) alive with stress incontinence), or (v) death, depending on surgical success or failure.[100–102] In following cycles, women then remained in the same state for the remainder of their lifetime or transitioned to death due to external causes, which applies a simplifying assumption that women only attempt repair surgery once in their lifetime. We assumed that women could have developed obstetric fistula only if they survived prolonged obstructed labour without treatment.[12] The Markov nodes for obstetric fistula were partially based on a published model by Epiu and colleagues evaluating the cost-effectiveness of repairing obstetric fistula compared to no repair in Uganda.[36] Our analyses also included the probability of developing obstetric fistula in the decision tree model with the two alternative strategies (existing care and increased access to caesarean section), SADC-specific parameters (where possible), and long-term costs related to healthcare expenditure to reflect a health systems perspective.[12,103] To estimate the long-term costs related to healthcare expenditure for women who survive, an average cost for healthcare expenditure per capita representative of the SADC region was incorporated into each Markov node (see Appendix F).[103]

3.2.6.2 Neonatal Outcomes

3.2.6.2.1 Decision Tree Model

For the neonates, a separate decision tree was constructed to represent an outcome of i) stillbirth or ii) survival, based on the management strategies (caesarean section, instrumental delivery, and unable to reach hospital) used in the maternal model (Figures 5 and 6). For neonates born in-hospital from caesarean section or instrumental delivery, an additional branch for iii) admission to the neonatal intensive care unit was included.[104] The number of neonates correlated to the number of mothers in the maternal model to account for cases of obstructed labour where maternal mortality occurred, but the neonate survived. We assumed that all mothers had singleton pregnancies to simplify the model structure. Years of life lost from untimely death were calculated in the event of stillbirth or death in the neonatal intensive care unit based on the healthy life expectancy in the SADC region of 61 years.[11,31] As neonates experience certain health states, the associated costs for treatment and DALYs are accumulated to estimate a cost per DALY averted comparing the two alternative strategies: (a) continuing current level of coverage of emergency obstetric care; and (b) increasing access to caesarean section for obstructed labour to 80%.

3.2.6.2.2 Markov Model

Following survival or neonatal hospital discharge, neonates entered a Markov model (with an annual cycle) to reflect the long-term effects of birth asphyxia and hypoxic-ischemic encephalopathy from obstructed labour depending on if they received hospital treatment (either caesarean section or instrumental delivery) or did not arrive at the hospital in a timely fashion (prolonged obstructed labour).[21,22] The Markov nodes for long-term survival following caesarean section or instrumental delivery were comprised of two states: i) survival without sequelae and ii) death from external causes. In following cycles, neonates either remained in the survive state for the remainder of their lifetime or transitioned to death due to external causes. The Markov nodes for long-term survival after prolonged obstructed labour were comprised of three states: i) survival without sequelae, ii) survival with intrapartum hypoxia with a probability of experiencing hypoxic-ischemic encephalopathy, or iii) death from external causes. In following cycles, neonates either remained the survival without sequelae state or the survival with intrapartum hypoxia-related complications state for the remainder of their lifetime, or transitioned to death due to external causes.

3.2.7 Event Probabilities

A literature review was conducted to parameterize the decision analytic model probabilities using information from published systematic reviews and meta-analyses, cohort studies, or cross-sectional studies. Due to lack of high-quality data from the SADC region, parameters were evaluated and selected in the following order of preference: (1) SADC region, (2) Sub-Saharan Africa, (3) Country-specific in the SADC region, (4) Country-specific in Sub-Saharan Africa, (5) Low-and middle-income countries, (6) High-income countries and (7) Based on expert opinion or assumptions (see Appendix G2 for details and assumptions surrounding each source). Sensitivity analyses accounting for how results differ based on uncertainty in event probabilities are presented in the results (see Section 3.3) and Appendix (see Appendices I and J).

3.2.7.1 Maternal Sequelae Related to Obstructed Labour

The probability of developing sequelae following obstructed labour differed based on whether the woman received caesarean section, had an instrumental delivery, or was unable to receive treatment and experienced prolonged obstructed labour.[105,106] Probabilities specific to each treatment option were sourced for each sequela where possible: (1) sepsis, (2) hemorrhage, (3) surgical site infections, (4) uterine rupture, (5) uterine prolapse, and (6) maternal hospital discharge or survival without sequelae (Table 8). Probabilities were sourced from various registries, observational studies, and systematic reviews and meta-analyses due to lack of SADC-specific estimates for procedure-specific outcomes (see Appendix G2 for detailed information on all parameter sources, study type, and assumptions). For women experiencing prolonged obstructed labour, probabilities of developing obstetric fistula, repair rate, surgical success, and subsequent outcomes (alive without disability, alive with vesicovaginal fistula, alive with rectovaginal fistula, and alive with stress incontinence) were sourced from observational studies from Zambia, Ethiopia, and Sub-Saharan Africa (Table 9).[100–102]

3.2.7.2 Maternal Mortality Related to Obstructed Labour

Mortality due to sequelae experienced by women receiving in-hospital treatment for obstructed labour were assumed to be the same across delivery methods (Table 11).[107–109] Probabilities of death following sepsis, hemorrhage, and uterine rupture were sourced from a population-based survey of West African women experiencing obstructed labour.[107] Probability of death following surgical site infection and hysterectomy were also included from SSA estimates from MSF and LMIC estimates from the WOMAN trial, respectively.[108,109]

Estimates of mortality due to sequelae (hemorrhage, surgical site infection, and uterine rupture) following prolonged obstructed labour were primarily taken from the MANDATE analysis, a mathematical model aiming to estimate reductions of maternal mortality from obstructed labour following treatment in Sub-Saharan Africa conducted by Harrison and colleagues.[106] Probability of death following sepsis after prolonged obstructed labour was estimated based on severity of uterine rupture between hospital and no-hospital due to lack of available evidence.[107] The age-specific annual probability of mortality was sourced from the GBD 2019 study for the Sub-Saharan African region.[7] See Table 11 and Appendix G2 for detailed information on all parameter sources, study type, calculations, and settings.

3.2.7.3 Neonatal Sequelae Related to Obstructed Labour

Probabilities of events related to neonatal outcomes such as stillbirth, mortality in neonatal intensive care units, perinatal asphyxia, and hypoxic-ischemic encephalopathy were sourced from observational studies from LMICs, SSA, Ghana, and South Africa (Table 10).[21,104,105,110] Probabilities of stillbirth following caesarean section or instrumental delivery were derived from an analysis done by Harrison and colleagues using data from a prospective community-based registry called the Maternal and Newborn Health Registry established by the Eunice Kennedy Shriver National Institute of Child Health and Human Development.[105] The registry collected information on births occurring from January 1, 2010 through December 31, 2013 in six LMICs (Guatemala, India, Pakistan, Argentina, and Zambia).[105] Stillbirth probabilities were derived from these six LMICs because SADC-specific stillbirth probabilities based on delivery method were unavailable in literature (see Appendix G2).[105] Evidence of NICU admission rates and neonatal mortality following NICU admission specific to instrumental delivery and caesarean section was also not available in literature. Therefore, it was assumed that NICU admission rate and neonatal mortality following NICU was the same for both delivery methods, due to neonates receiving hospital treatment in both cases (see Appendix G2). These estimates were sourced from observational studies in South Africa and Ghana.[104,110] Probabilities of neonates experiencing intrapartum hypoxia and hypoxic-ischemic encephalopathy were also included for those born following prolonged obstructed labour without treatment.[20–22] The age-specific annual probability of mortality was sourced from the GBD 2019 study for the Sub-Saharan African region.[7] Details, assumptions, and information on sources is available in Appendix G2.

3.2.8 Health Impacts of Increasing Access to Caesarean Section

Disability-adjusted life years (DALYs) were used to measure health impact of increasing access to caesarean section in the management of obstructed labour for mothers and babies (Table 12). DALYs were calculated as the sum of years of life lost to premature death and time lived with disability.[31,33] Years of life lost were calculated as the difference between each woman's age at time of death and the healthy life expectancy in the SADC region of 61 years for each premature death.[11,31] Years lived in disability were calculated using disability weights for a given health state multiplied against the length of time spent in the health state for a life-time horizon.[31,32] Disability weights were sourced from The Institute of Health Metrics and Evaluation Global Burden of Disease Study (GBD) 2019, as it is the most comprehensive and consistent estimate for mortality and morbidity at a regional or global level.[7] The GBD 2019 gives updated estimates for disability weights that reflect severity of disease, where 0 represents perfect health and 1 represents death.[31,33,72] Sources were selected in the same order of priority as probabilities (see Section 3.2.7). Detailed information disability weight sources and calculations are available in Appendix H.

3.2.8.1 Maternal Outcomes Related to Obstructed Labour

Disability weights for caesarean section, instrumental delivery, and short-term and long-term sequelae following obstructed labour were incorporated in the model (Table 12). Disability weights for in-hospital and in-community conditions were applied up to the duration of hospital stay. For long-term sequelae, disability weights specific to each health states were incurred for each year spent in the health state. Disability weights While GBD 2019 disability weights were used for health conditions or states when available, the disability weights for caesarean section and stress incontinence were taken from the GBD 1990 due to lack of updated information.[111] The disability weight for uterine prolapse was adapted from the Korean Burden of Disease Study (KBD) 2015 due to regional information in literature being unavailable.[112] Disability weights for instrumental delivery, acute sepsis, and hysterectomy were estimated as well using GBD 2019 and KBD 2015 data, expert opinion, and published literature (details on all assumptions and calculations in Appendix H).[7,111–114] It was assumed that women who survive obstructed labour and do not develop obstetric fistula or sepsis return to full health, meaning that a disability weight of 0.01 was associated with survival following recovery (see rationale in Appendix H). Sensitivity analyses were conducted to assess how assumptions affected the results of our analysis, presented in Section 3.3 and Appendices I and J.

3.2.8.2 Neonatal Outcomes Related to Obstructed Labour

Disability weights for hypoxic-ischemic encephalopathy were incorporated for a proportion of neonates experiencing birth asphyxia after prolonged obstructed labour.[21,22] These estimates were taken from GBD 2019 data (see Table 12 and Appendix H).[7] Neonates were assumed to return to full health after surviving the neonatal intensive care unit and did not experience disability due to lack of available published estimates (see Appendix H for assumptions). Similarly, neonates surviving prolonged obstructed labour without experiencing birth asphyxia were also assumed to return to full health for the remainder of their lifetime. Sensitivity analyses were conducted to assess the impact of these assumptions on the base case analyses, presented in Section 3.3 and Appendices I and J.

3.2.9 Resources and Costs Estimation

A health systems perspective was taken in determining costs (see Table 13). Costs across different treatment paths and adverse events were sourced primarily from published literature and evaluated for quality in the same order as probabilities and effectiveness (see Section 3.2.7). Costs included variable and fixed costs such as cost of procedure, associated devices and drugs, operative facility time, personnel, and facility maintenance. Further details on calculations and assumptions for each cost can be found in Appendix F. Cost of caesarean section was estimated to be $303.48 USD from nine SADC countries included in a cost-benefit analysis by Alkire and colleagues.[55] Cost of instrumental delivery was $177.36 USD, calculated by taking the ratio between costs of caesarean section and instrumental delivery from Adamu and colleagues and applying it to cost of caesarean section derived from Alkire and colleagues.[55,115] It was assumed that no short-term costs were associated with remaining in prolonged obstructed labour and not receiving timely treatment, which has been widely used in other economic evaluations for receiving essential surgery in LMICs.[36,53,55] However, our analyses include an average yearly health expenditure per capita of $53.03 USD for essential health services utilization, applicable to all women who survive obstructed labour.[103] This annual cost per capita is the minimum investment recommended by the Taskforce on Innovative International Financing for Health Systems and is likely not achieved in the

SADC region.[103] Treatment costs for each sequela related to obstructed labour (hemorrhage, sepsis, surgical site infection, uterine rupture, hysterectomy, and fistula repair) and neonatal intensive care for the neonates can be found in Table 13 with assumptions and rationale in Appendix F.

Purchasing power parity (PPP) from the source country was used to convert values to international dollars ($I) before inflation. Values were then inflated to PPP-adjusted 2020 United States Dollars ($USD) for analysis using GDP Implicit Price Deflators to ensure comparability across costs from varying countries (see Appendix F). If PPP-adjustment was not specified in the published source, market exchange rate was used to first convert costs into original local currency before conversion to PPP-adjusted $USD for 2020 estimates to ensure consistency in methodology (see Appendix F).[48]

3.2.10 Analytic Methods

3.2.10.1 Base Case Analysis

In the decision tree, costs and associated DALYs were estimated based on probabilities of experiencing specific health conditions. Years of life lost due to premature death were calculated based on healthy life expectancy of 61 years for the SADC region, whether that is in-hospital for those able to access caesarean section or instrumental delivery or no treatment for women in prolonged obstructed labour.[11,31] For those who survive hospital discharge or prolonged obstructed labour, costs and DALY burdens were estimated depending on the probability of experiencing health states and length of time spent in them.[31] Since provision of caesarean section for treatment of obstructed labour is intended for the combined benefit of mother and baby, a combined cost per DALY averted when considering the health and economic impacts of mother and baby together was also estimated. In this estimate, we are assuming that the costs and effects are additive (Table 20, see Appendix K for calculation).

A Monte Carlo microsimulation with 10,000 trials was conducted to estimate the incremental cost-effectiveness ratios (cost per DALY averted) comparing increased access to caesarean section to 80% and existing care for a life-time time horizon using a health systems perspective. Cost per DALY averted was calculated for (a) maternal health outcomes and costs; (b) neonatal health outcomes and costs; and (c) a combined estimate for both mothers and babies. The cycle length for the Markov model was one year and the termination condition for the microsimulation was when individual reached or surpassed the age of 100 years old. Costs and effects were discounted at 3% to reflect WHO guidelines for conducting cost-effectiveness analyses.[94] To correct for the traditional Markov model assumption that transitioning between health states occurs only at the end of a cycle, a half-cycle correction was included to assume that events occurred in the middle of each cycle.[116] Model construction and analyses were conducted using TreeAge Healthcare Pro 2021 (Treeage Software. Inc., Williamstown, MA, USA).

The willingness-to-pay (WTP) threshold for the SADC region ranges from $574 to $2,763 per DALY averted in 2020 PPP-adjusted USD, which was calculated as a population-weighted average of SADC country-specific WTP thresholds estimated by Woods and colleagues (see Appendix E).[61] Woods and colleagues provide more conservative estimates for WTP that reflect opportunity cost and PPP-adjusted GDP per capita in comparison to those previously suggested by the WHO-CHOICE project.[60,61] The Report of the WHO Commission on Macro-Economics and Health suggested that interventions costing less than three times the national annual GDP per capita per DALY averted is considered cost-effective and should be supported by the international community if a country cannot undertake the implementation of the intervention on its own.[60]

3.2.10.2 Variability and Uncertainty

Assumptions surrounding model inputs were tested through one-way sensitivity analyses to identify parameters that contributed the most to uncertainty surrounding ICERs using published 95% confidence intervals or an estimated range of $\pm 10\%$ (see Appendix J for assumptions and rationale). A probabilistic sensitivity analysis (PSA) was performed using a Monte Carlo simulation with 10,000 iterations to examine stability of the results. Probabilities were defined using beta or Dirichlet distributions, utilities were defined using beta distributions, and costs were defined using gamma distributions. Details on the range of values used in one-way sensitivity analyses and distributions for the PSA were included in Appendix I and J. A cost-effectiveness acceptability curve was generated to assess the probability of the increased access to caesarean section strategy being cost-effective across a range of willingness-to-pay thresholds. Sensitivity of the results to a 0% discount rate for health effects and 6% for costs were examined as a scenario analysis as per recommendations by the WHO guidelines.[94]

3.3 Results

Increasing access to caesarean section has impacts on health outcomes and costs for both the mother and the neonate. Results are reported using three approaches: (a) using maternal health outcomes and costs; (b) using newborn health outcomes and costs; and (c) aggregating maternal and newborn health outcomes and costs.

3.3.1 Maternal Outcomes

3.3.1.1 Base Case Analysis

The cost of increasing access to caesarean section from 30% to 80% was $1,191 with 2.85 DALYs accumulated over a lifetime. For the existing level of coverage, the cost was $843 with 9.42 DALYs accumulated over a lifetime. Compared to the existing level of coverage, increasing access to caesarean section is expected to avert 6.57 DALYs for an additional $348 per woman experiencing obstructed labour between the ages of 15 and 50 (Table 14). Over a lifetime time horizon, increasing access to caesarean section from 30% to 80% cost the health system $52.97 per DALY averted. Results of the maternal model were assessed for sensitivity to a 0% discount rate for DALYs and 6% for costs, resulting in an estimate of $44.57 cost per DALY averted (Table 15).

3.3.1.2 Deterministic Sensitivity Analysis

Results from our one-way sensitivity analyses are presented in a tornado diagram including parameters that affected the model outputs most substantially (Figure 7). Additional tornado diagrams for all variables and by parameter-type are available in Appendix J. Results indicate that the model varies the most with changes in average cost per capita spent on healthcare expenditure, cost of caesarean section, and probability of surgical site infection following caesarean section. Increasing these parameter values resulted in increased ICERs relative to the base case for the increased access strategy compared to existing care. ICERs decreased when mortality rate from hemorrhage after obstructed labour increased and when the disability weight for experiencing obstructed labour increased. Across all variables tested in the one-way sensitivity analyses, the ICER ranged from $51.69 to $57.35 per DALY averted. ICERs slightly increased when cost of treating surgical site infection increased, when probability of developing sepsis after caesarean section increased, and when the disability weight for undergoing caesarean section increased. Adjusting other model parameters resulted in very slight adjustments to ICER values, with results presented in Appendix J.

3.3.1.3 Probabilistic Sensitivity Analysis

Probabilistic sensitivity analyses suggested that the mean ICER was $50.16 per DALY averted (Table 16). The probability of increasing access to caesarean section being cost-effective approaches 100% at a willingness-to-pay threshold of $172 per DALY averted, which is significantly lower than the SADC-specific lower-end threshold of $574 per DALY averted (Figure 8; see Appendix I for additional information). Results from the ICER scatterplot show that incremental costs and effectiveness are found in the top-right quadrant, indicating that outputs from the model consistently result in additional cost for additional DALYs averted. Cost of increasing access to caesarean section was within the range of $280 to $380 higher than existing care and resulted in a range of 2 and 10 DALYs averted per woman in obstructed labour (Figure 9).

3.3.2 Neonatal Outcomes

3.3.2.1 Base Case Analysis

The cost of the increased access to caesarean section strategy was $1,053 with an accumulated 6.37 DALYs. In the existing care strategy, cost was $830 with 17.64 DALYs accumulated. Compared to existing coverage, increasing access to caesarean section led to a reduction of 11.27 DALYs for an additional $223 per neonate born from a mother experiencing obstructed labour (Table 17). Over a lifetime time horizon, providing increased access to caesarean section cost the health system $19.77 per DALY averted. Results of the neonatal model were assessed for sensitivity to a 0% discount rate for DALYs averted and 6% for costs, resulting in an estimate of $12.93 cost per DALY averted (Table 18).

3.3.2.2 Deterministic Sensitivity Analysis

Results from our one-way sensitivity analyses (Figure 10; see Appendix J for additional information) indicate that the model varies the most with changes to the average cost per capita spent on healthcare expenditure, probability of stillbirth from prolonged obstructed labour, and disability weight of hypoxic-ischemic encephalopathy. Increasing the average cost per capita spent on healthcare expenditure led to a higher ICER for increased access to caesarean section relative to base case results. ICERs decreased when probability of stillbirth after prolonged obstructed labour and disability weight of hypoxic-ischemic encephalopathy increased. ICERs slightly increased when the probability of admission into the neonatal intensive care unit following caesarean section and the cost of treatment in the neonatal intensive care unit increased. Adjusting other model parameters resulted in very slight changes in ICER values (Appendix J). Across all variables tested in the one-way sensitivity analyses, the ICER ranged from $18.04 to $21.51.

3.3.2.3 Probabilistic Sensitivity Analysis

Probabilistic sensitivity analyses suggested that the mean ICER was $24.16 per DALY averted (Table 19). The probability of increasing access to caesarean section being cost-effective approaches 100% at a willingness-to-pay threshold of $32.50 per DALY averted, which is significantly lower than the SADC-specific lower-end threshold of $574 per DALY averted (Figure 12; see Appendix I for additional information). Results from the ICER scatterplot show that incremental costs and effectiveness are also found in the top-right quadrant, meaning that outputs from the model consistently result in additional cost for additional DALYs averted. Cost of increasing access to caesarean section was within the range of $130 to $320 higher than existing care and resulted in a range between 6 to 13 DALYs averted per neonate (Figure 12).

3.3.3 Combined Estimates for Mother and Baby

The combined cost of the increased access to caesarean strategy was $2,244 with an accumulated 9.22 DALYs. In the existing care strategy, combined cost was $1,673 with an accumulated 27.06 DALYs. Compared to existing coverage, increasing access to caesarean section led to a reduction of 17.84 total DALYs for an additional $571 per mother and baby treated (Table 20). Over a lifetime time horizon, providing increased access to caesarean section cost the health system $32.00 per DALY averted, assuming the health and economic impacts for mother and baby are additive**.**

3.4 Discussion

3.4.1 Summary of Findings and Applicability

The results from our model suggest that increasing access to caesarean section to ensure 80% of all women presenting with obstructed labor receive treatment reduces DALYs due to years of life lost and years lived in disability at a cost of $52.97 per DALY averted over a lifetime time horizon for childbearing women. Accompanying the maternal estimate is an ICER of $19.77 per DALY averted for neonates born from mothers in obstructed labour. Sensitivity analyses showed that above a threshold of $172 and $32.50, increasing access to caesarean section is likely to be more cost-effective than existing care for mothers and babies, respectively. Combining the health and economic impacts for mother and baby cost $32.00 per DALY averted, assuming they can be additive. Importantly, our model estimates cost per DALY averted for mothers and babies both separately and combined while accounting for long-term health and economic impacts, which strengthens and adds to the current evidence base. These estimates support that scaling up access to caesarean section to reduce DALY burdens in mothers and newborns is likely cost-effective and should be considered a high-value intervention worthy of investment for health systems in the SADC region.

When comparing the cost per DALY averted for increased access to caesarean section to benchmark interventions reported in the Disease Control Priorities 3 Volume 1, our estimates are comparable or lower than cleft lip and cleft palate repair in Nepal ($45.45 per DALY), intrapartum care in Mexico ($349.96 per DALY averted), and non-emergency orthopedic surgery in Nicaragua ($407.91 - $613.58 per DALY averted).[3,13,14,65,116] Furthermore, the estimates for both maternal and neonatal outcomes are markedly lower than the willingness-to-pay threshold calculated for the SADC region.

Previous recommendations by the WHO-CHOICE project suggested three times the national annual GDP per capita of the country to be cost-effective and one times GDP to be very cost-effective.[60] However, these willingness-to-pay thresholds have been found to bias towards higher estimates than what patients are reporting.[117,118] The WHO-CHOICE thresholds are based on previous research that require more rigorous estimation to avoid misallocation of limited resources in LMICs after further exploration of cost-effectiveness, budget feasibility, and broader consideration of opportunity costs.[117] In comparing model estimates to more conservative willingness-to-pay thresholds derived by Woods and colleagues that reflect opportunity costs of health care spending, the weighted threshold range calculated for the SADC region is between $574 and $2,763 PPP-adjusted USD 2020 per DALY averted (see Appendix E).[61] Even by these more precise standards, increasing access to caesarean section remains highly cost-effective in the SADC region.

3.4.2 Comparison to Existing Economic Evaluations and Modelling Studies

Our model improves upon previously conducted cost-effectiveness analyses of caesarean section for obstructed labour that are restricted to cohort-based estimates of those receiving treatment for a short time horizon (generally up until hospital discharge) by including long-term health and economic impacts and unmet need for caesarean section.[49,56,59]

The findings from our model also support previous mathematical and epidemiological modelling studies. Verguet and colleagues performed an extended cost-effectiveness analysis to assess health gains and financial risk protection afforded if caesarean section were made universally available.[19] Their findings demonstrated that government investment in scaling up access to caesarean section led to 122 deaths averted per

$100,000 spent and 85 cases of poverty averted per $100,000 spent.[19] To examine health impacts, Higashi and colleagues quantified the burden of maternal and neonatal conditions in LMICs that could be averted by full access to first-level obstetric surgical procedures through epidemiological modelling and GBD 2010 data.[17] They found that 21.1 million DALYs of a total estimated 56.6 million DALYs related to obstructed labour, maternal haemorrhage, obstetric fistula, abortion, and neonatal encephalopathy are avertable by full coverage of obstetric surgery in LMICs.[17] In parallel, Molina and colleagues estimated a potential reduction of up to 163,513 maternal and 803,129 neonatal deaths averted annually if countries with low rates of caesarean section increased their rates and those with high rates decreased their rates of caesarean section to meet ideal thresholds.[18] Furthermore, Alkire and colleagues performed a cost-benefit analysis of caesarean delivery for obstructed labour in 47 LMICs, estimating the number of caesarean deliveries required to prevent 80% of obstructed labour cases, as well as cost per DALY averted per country.[55] The estimated cost per DALY averted was $492, which is markedly higher than our model estimates due to their exclusion of neonates and lack of comparison to the null (e.g. existing care).[55] Alkire and colleagues' estimates remain the most comprehensive and relevant in published literature that address research objectives related to our model. While these modelling studies seek to address the issues of unmet need, inequitable DALY burdens, and catastrophic expenditure in global surgery, ours is the first to use formal decision analytic modelling in an economic evaluation assessing the health and economic impacts of scaling-up access to caesarean section while addressing key limitations in Alkire and colleagues' estimates. Overall, our findings align with epidemiological modelling and support that increasing access to caesarean section for obstructed labour results in substantial health gains while addressing unmet need in caesarean section in resource-restricted settings.

3.4.3 Strengths

To our knowledge, this is the first decision-analytic model that estimates DALYs averted for scaling-up caesarean section compared to existing care for a lifetime time horizon for both mothers and babies. Notably, the model incorporates multiple interventions that reflect the burden of obstructed labour and estimated proportion of those who receive treatment into each overall strategy (existing care versus increased access). It also includes obstetric complications related to instrumental delivery, caesarean section, and prolonged obstructed labour to best represent existing standard of care and clinical pathways following obstructed labour. The model incorporates years of life lost due to premature death from obstructed labour or resulting sequelae while also incorporating years lived in disability for those who develop obstetric fistula or severe sepsis for the remainder of their lives. The decision-analytic model constructed for treatment of obstructed labour also makes novel contributions to existing literature by incorporating perinatal outcomes for neonates, including long-term disability related to birth asphyxia and hypoxic-ischemic encephalopathy. Reductions in neonatal mortality are incorporated into years of life lost in neonates who are stillborn or die in the NICU. To date, estimates have largely excluded neonates, despite neonatal mortality due to obstructed labour accounting for 29% to 44% of stillbirths.[21,119]

An important aspect of unmet need in global surgery is the number of individuals in need of care who are unable to reach the hospital due to barriers related to affordability or distance.[2] These patients are generally excluded from economic evaluations as most patient populations are drawn from hospitals which, by definition, includes only those, and therefore represent data from populations who have actually reached care, but fails to account for those who did not reach care.[53,56,58,59] Our model attempts to address this disparity in access by modelling health gains associated with reducing the proportion of women who remain in prolonged obstructed labour without access to caesarean section.

3.4.4 Limitations

3.4.4.1 Limitations in Estimating Probabilities

Primarily, our analysis was dependent on data from publicly available sources. The parameter estimates in our model reflect best available evidence but remain limited by the quality of data available from the SADC region, or next closest alternative source. In particular, there are constraints with estimating the incidence of prolonged or neglected obstructed labour, which are done through proxy measures using proportion of pregnant women able to reach a health facility and number of live facility births.[12,25] Due to scarcity of data specific to the SADC region, several estimates were taken from Sub-Saharan African or country-specific data which may reduce applicability of our results to the SADC region. Our model also applies the simplifying assumption that women experience one short-term sequela at a time, which is assumed to be the primary cause of morbidity or mortality. In reality, short-term sequelae following obstructed labour are likely not mutually exclusive and a woman may experience more than one sequela at the same time.[15,120] We also assumed that women only developed obstetric fistula when remaining in neglected obstructed labour following delays in care, but a small proportion of women treated late with caesarean section or instrumental delivery may also develop obstetric fistula.[121,122] This exclusion was largely due to our treatment strategies being defined by proportions of women able to receive safe, timely, affordable treatment as per WHA resolutions and LCoGs 2030 targets for global surgery.[2,6]

3.4.4.2 Limitations in Estimating Disability Weights

Another limitation of the model is lack of information on expanded contributors to long-term disability due to prolonged obstructed labour. While this was largely accounted for by the inclusion of obstetric fistula in our analysis, current literature does not provide estimates for other potential contributors to disability associated with neglected obstructed labour which may also be mitigated by access to caesarean section. This could result in underestimation of the disability experienced by these women across a life-time horizon, and potentially underestimation of the number of DALYs avertable through increased access to caesarean section. Consequently, our estimates may be an underestimation of benefit, and estimates incorporating more accurate estimates of long-term disability are likely to remain cost-effective at the threshold range of $574 to $2,763 per DALY averted in the SADC region.

3.4.4.3 Limitations in Estimating Costs

Due to lack of costing information for the SADC region, certain model parameters were limited by the calculation method of applying costing ratios from other countries (see Appendix F for details on calculations). This approach was used in the estimation of costs of instrumental delivery, hysterectomy, long-term sepsis, and uterine rupture, and could have resulted in underestimated or overestimated cost per DALY estimates. In particular, costs are known to vary based on the setting and there is a lack of SADC-specific cost estimates for the parameters included in our model.[123] Future efforts should focus on country-specific estimates and costing information applicable to specific settings. Our analyses also assumed that provision of surgery was the primary cause for reductions in DALY burdens. The costs of caesarean section used in our model were primarily focused on cost per procedure and facility maintenance at present levels. Health system costs of scale-up related to healthcare professional training to expand access to obstetricians, surgeons, anaesthesiologists, and related infrastructure and supplies have not been incorporated, but current estimates of cost per capita for surgery system scale-up from the SADC countries indicate that the ICER will remain highly cost-effective even after incorporation into the model.[124]

3.4.4.4 Limitations in Analyses

While the results of the sensitivity analyses produced estimates that are relatively precise, sourcing probabilities from a mixture of published evidence and de novo sources did not always allow for the full range of potential heterogeneity to be incorporated. The methodology used for conducting sensitivity analyses follows WHO cost-effectiveness guidelines, but the true population-level uncertainty is likely to be much larger than the 95% confidence limits reported in literature, and the assumption of 10% variation in costs.

Regarding perspective, a societal perspective would be more comprehensive since observational studies find that neglected obstructed labour and related sequelae are associated with reduced workforce capability and economic losses to society.[21,125] However, a health systems perspective was taken due to lack of data as well as methodological uncertainty surrounding the valuation and incorporation of productivity and societal costs. A societal perspective would likely result in higher incremental benefit and lower incremental cost related to improved social productivity across the maternal and neonatal lifespan, suggesting even higher value to society of increasing access to caesarean section in the SADC region.

3.4.5 Conclusion & Implications

The cost of increasing access to caesarean section (80% of all obstructed labour) is relatively low, while the health gains are relatively high. Therefore, increasing access to caesarean section to treat 80% of women in obstructed labour is likely cost-effective. When considering the associated health gains for neonates born to these women, the cost-utility estimates appear to be even more cost-effective. Validated health system costing data will need to be estimated and used for future cost-effectiveness research in the area before we can definitively conclude cost-effectiveness.

Overall, our model supports previous research that suggests investing in caesarean section is both cost-effective and of high value for health systems in the SADC region.[19,55,64] Further work is encouraged to develop improved, country-specific estimates for SADC countries that address the uncertainty in our model parameters due to lack of evidence. Our results support the United Nations Sustainable Development Goals 2030 of reducing maternal mortality rates and the Lancet Commission on Global Surgery 2030 targets for increased access to safe, timely surgical care.[2,6,10] Investment in continued strategies to strengthen existing health systems and increase access to caesarean section for treatment of obstructed labour in developing countries is necessary to achieve health gains for impoverished populations that inequitably cannot access essential care.

3.5 Tables and Figures for Chapter 3

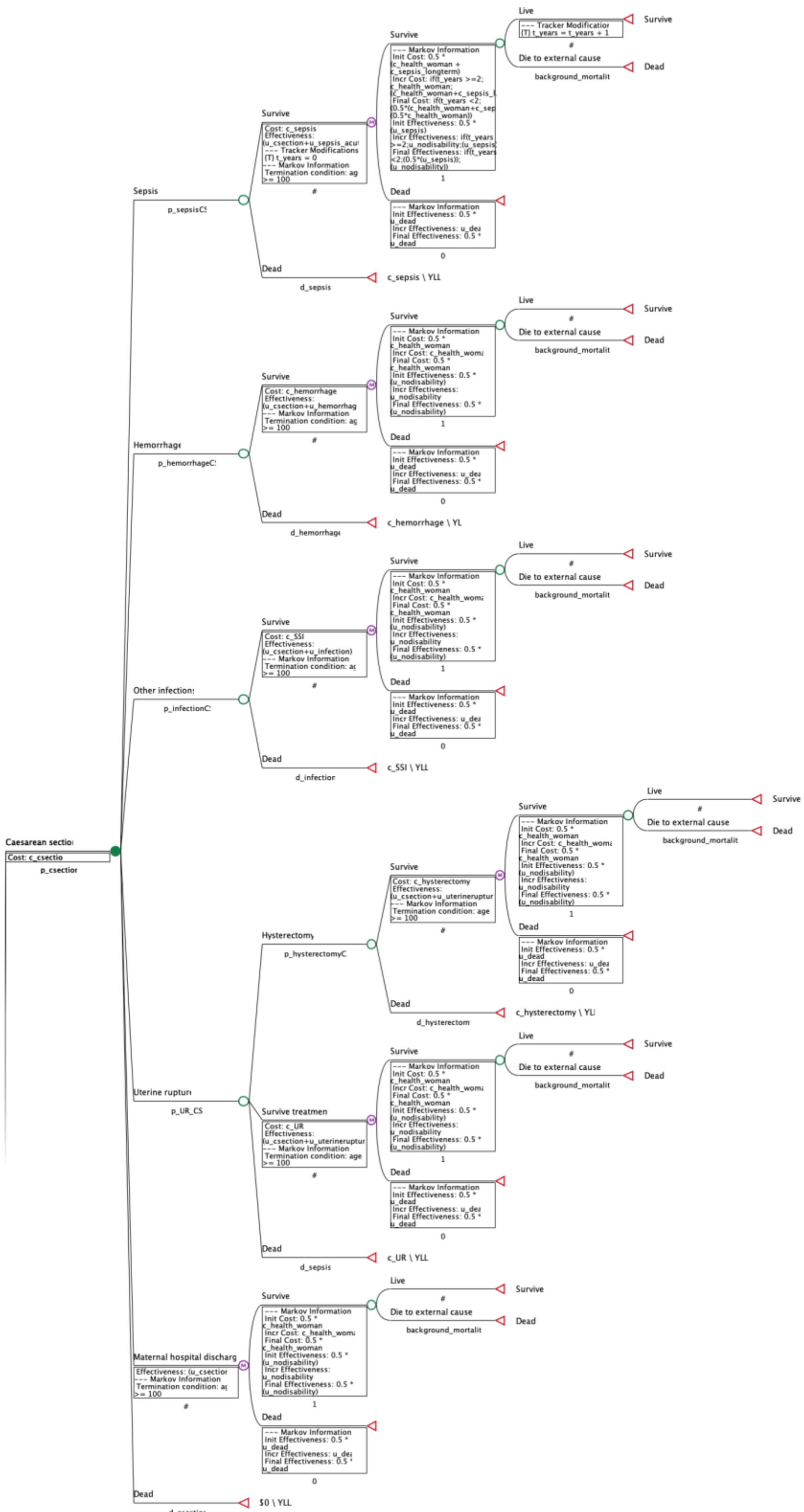

Figure 2 Maternal Decision Analytic Model (Caesarean Section Subtree)

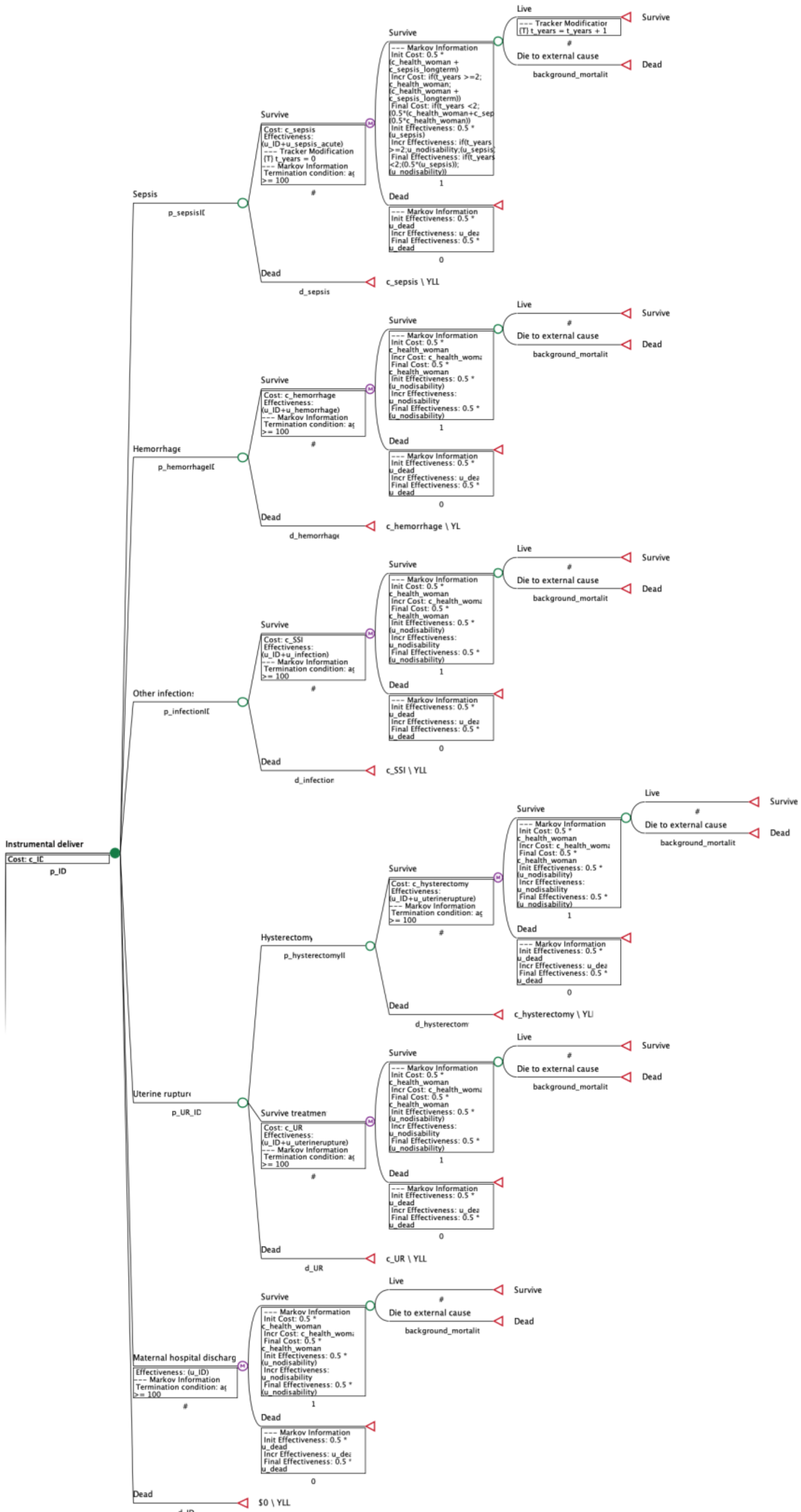

Figure 3 Maternal Decision Analytic Model (Instrumental Delivery Subtree)

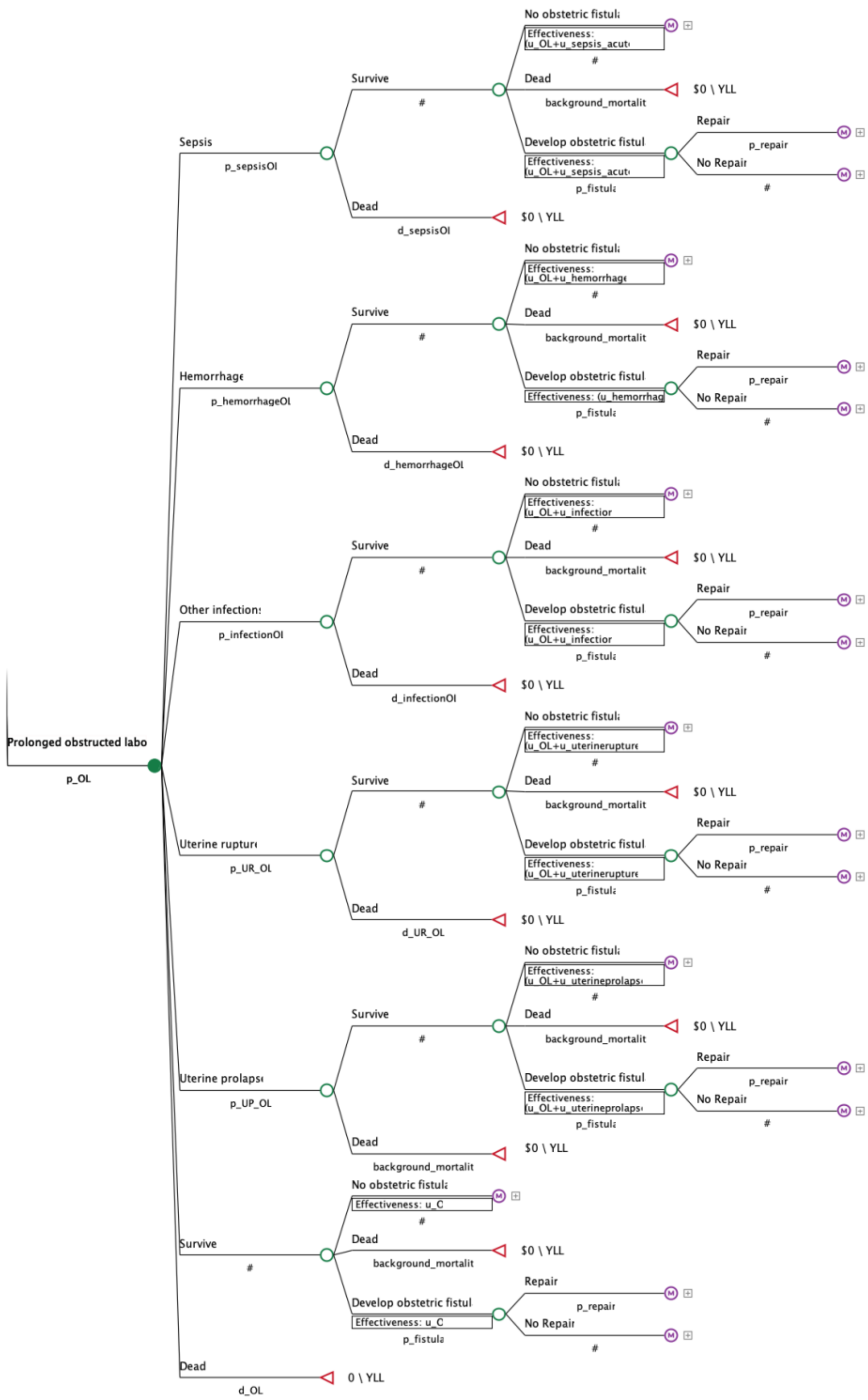

Figure 4a Maternal Decision Analytic Model (Prolonged Obstructed Labour Subtree: Collapsed Markov Model). Collapsed Markov model to show individual pathways following each sequela.

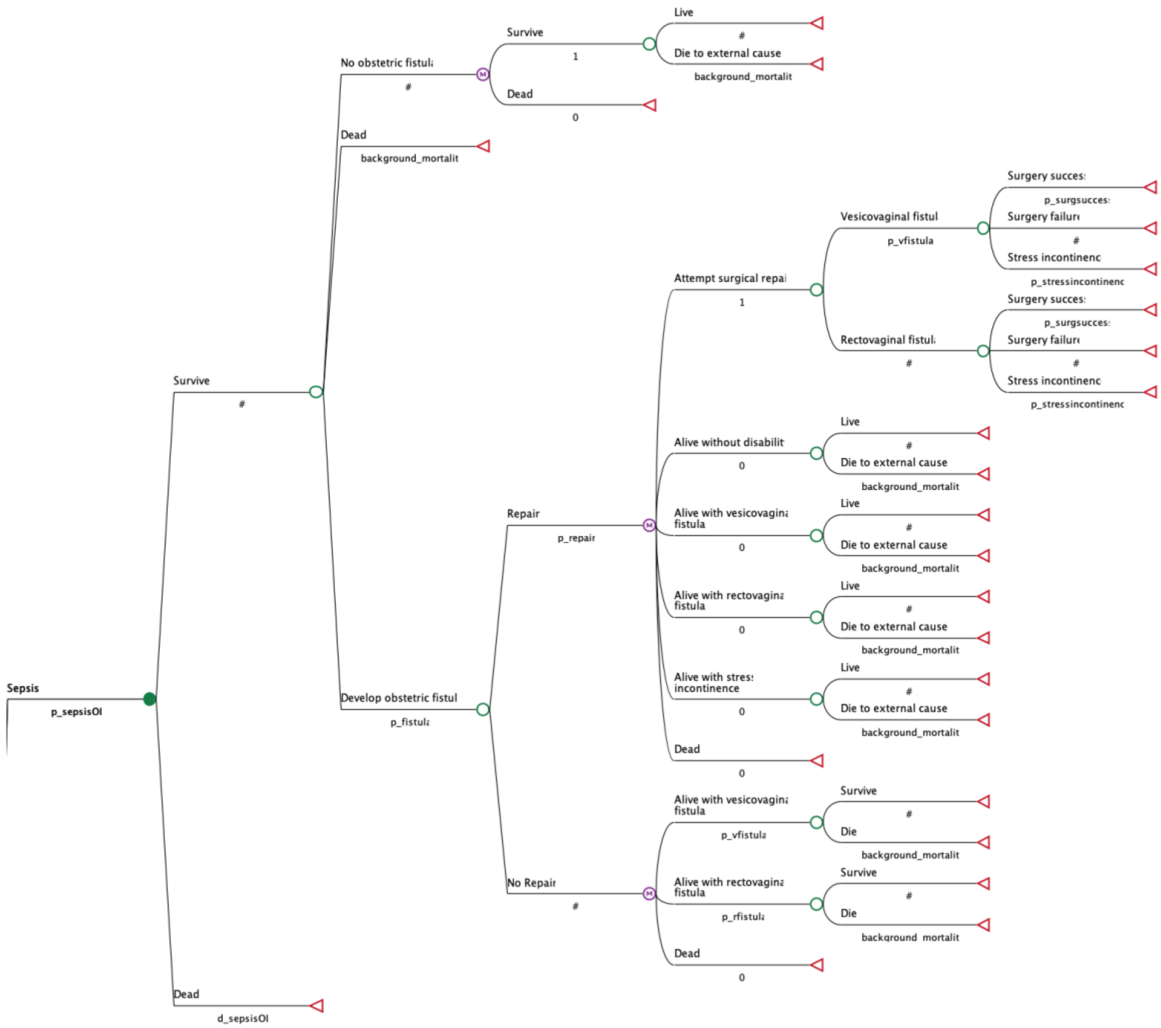

Figure 4b Maternal Decision Analytic Model (Prolonged Obstructed Labour Subtree: Expanded Markov Model). Prolonged obstructed labour subtree: expanded sample branch to show all possible events occurring after sepsis and health states in the Markov model. The same model structure applies to other sequelae shown in Figure 4a.

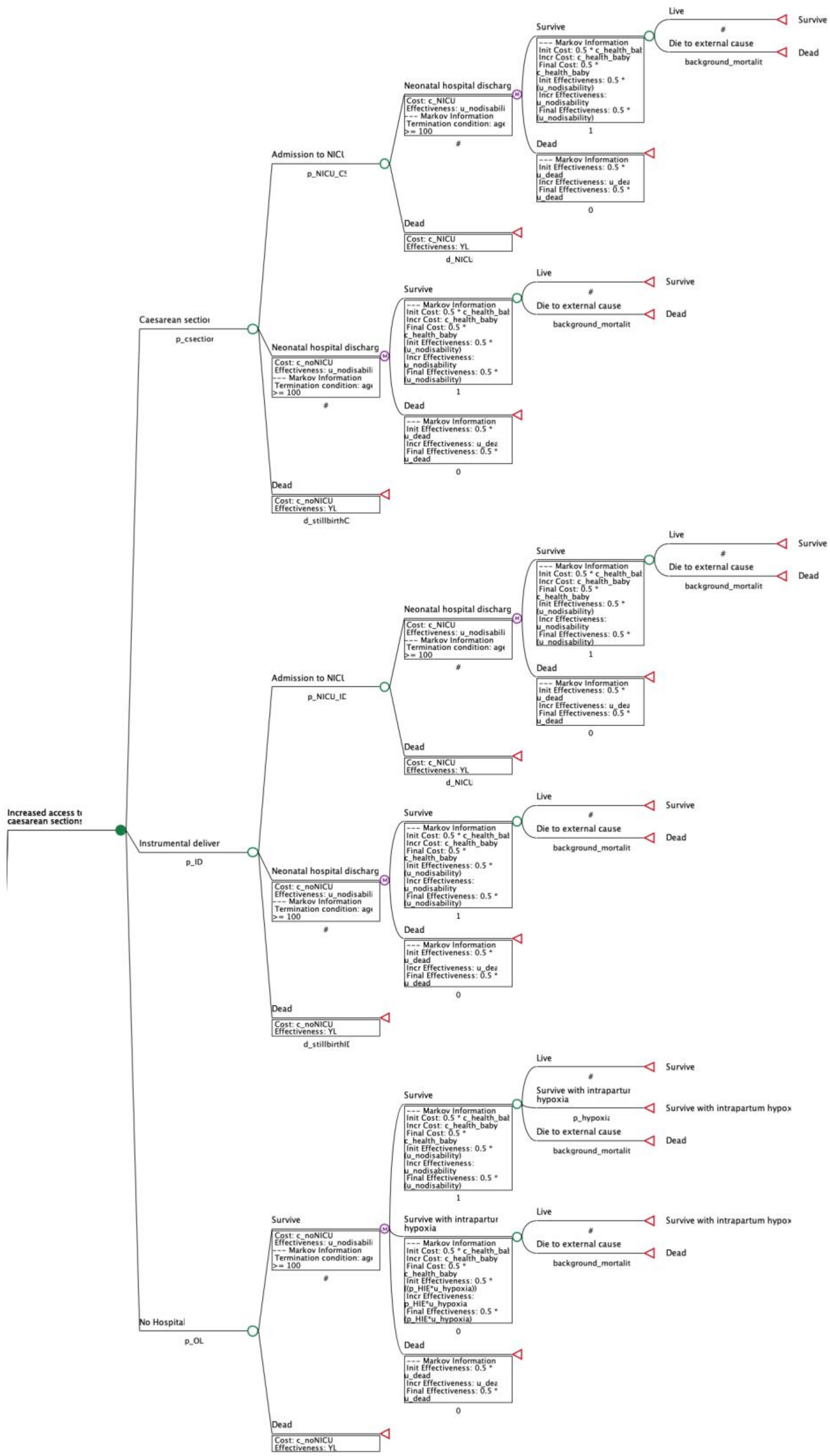

Figure 5 Neonatal Decision Analytic Model (Increased Access Subtree)

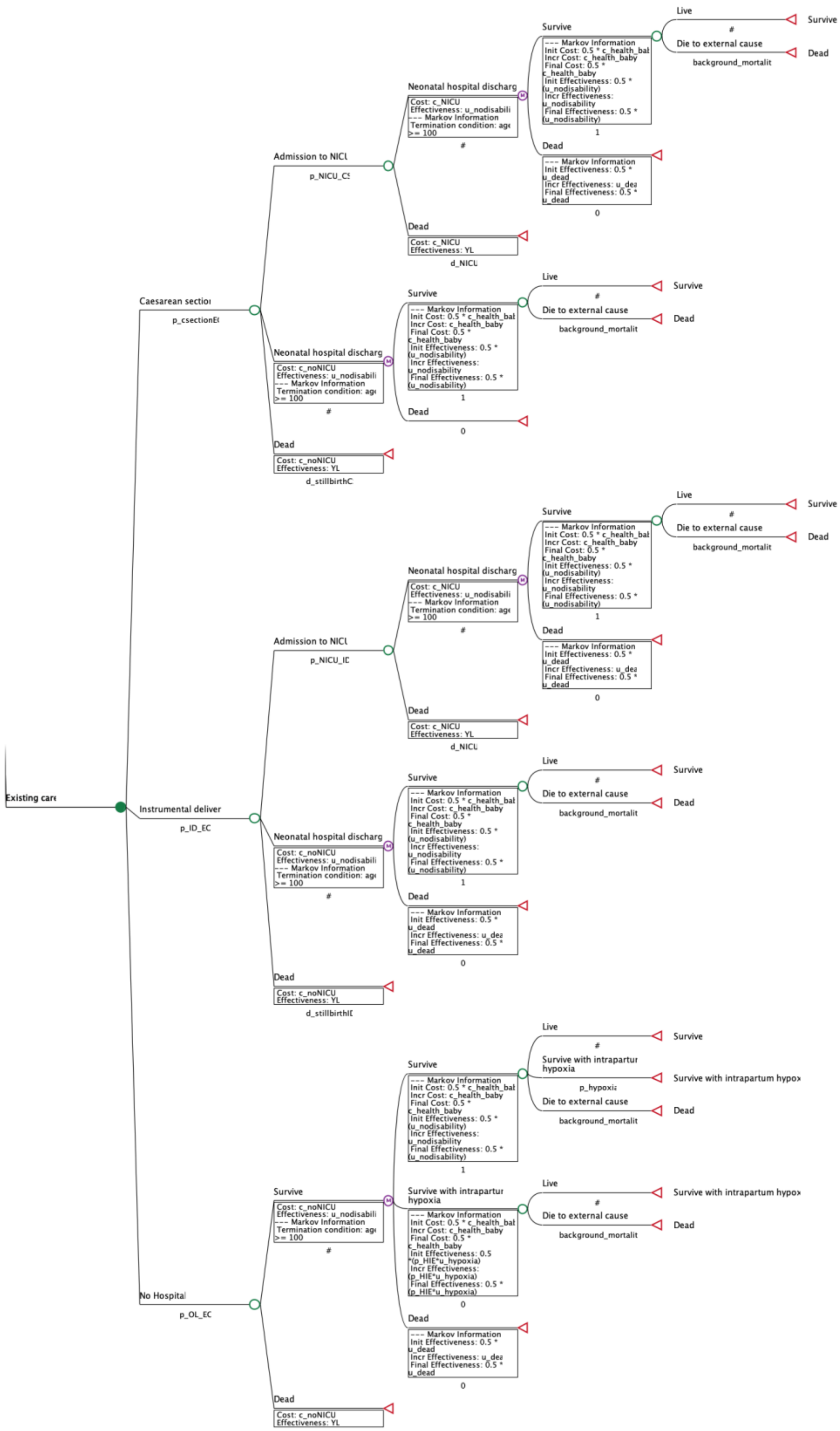

Figure 6 Neonatal Decision Analytic Model (Existing Care Subtree)

Table 8 Probabilities of Short-Term Maternal Outcomes Following Obstructed Labour

	Parameter	**Mean**	**Distribution**	**Source**
Increased Access to Caesarean Section Strategy	Caesarean Section	0.800	—	Meara et al. 2015[2]
	Instrumental Delivery	0.067	—	Dolea et al. 2000[12]
	Prolonged Obstructed Labour	0.133	—	Dolea et al. 2000[12]
Existing Care Strategy	Caesarean Section	0.300	—	Doctor et al. 2018,[25] Dolea et al. 2000[12]
	Instrumental Delivery	0.033	—	Dolea et al. 2000[12]
	Prolonged Obstructed Labour	0.667	—	Doctor et al. 2018,[25] Dolea et al. 2000[12]
Caesarean Section	Sepsis	0.0173	Beta	Dare et al. 1998[126]
	Hemorrhage	0.0104	Beta	Harrison et al. 2015[105]
	Surgical site infection	0.0729	Beta	Chu et al. 2015[108]
	Uterine rupture	0.000150	Beta	Liu et al. 2007[127]
	Hysterectomy	0.00631	Beta	Briand et al. 2012[128]
	Maternal Death	0.00227	Beta	Harrison et al. 2015[105]
Instrumental Delivery	Sepsis	0.0173	Beta	Dare et al. 1998[126]
	Hemorrhage	0.0777	Beta	Harrison et al. 2015[105]
	Surgical site infection	0.0254	Beta	Son et al. 2017[129]
	Uterine rupture	0.0245	Beta	Astatikie et al. 2017[130]
	Hysterectomy	0.00	Beta	Briand et al. 2012[128]
	Maternal Death	0.00209	Beta	Harrison et al. 2015[105]
Prolonged Obstructed Labour	Sepsis	0.194	Dirichlet	Roa et al. 2020[21]
	Hemorrhage	0.130	Dirichlet	Harrison et al. 2016[106]
	Surgical site infection	0.114	Dirichlet	Roa et al. 2020[21]
	Uterine rupture	0.300	Dirichlet	Ayenew et al. 2021[20]
	Uterine prolapse	0.158	Dirichlet	Roa et al. 2020[21]
	Obstetric fistula	0.0215	Beta	Dolea et al. 2000[12]
	Maternal Death	0.0910	Dirichlet	Gaym et al. 2002[131]

Outcomes within each management strategy (caesarean section, instrumental delivery, and prolonged obstructed labour) were not mutually exclusive but are assumed to be the primary cause of morbidity or mortality experienced by individual women.

Table 9 Probabilities of Long-Term Maternal Outcomes Following Obstructed Labour

Parameter	Mean	Distribution	Source
Rectovaginal fistula	0.212	Beta	Kelly et al. 1998[100]
Vesicovaginal fistula	0.788	Beta	Kelly et al. 1998[100]
Repair[a]	0.250	Beta	Gebremedhin et al. 2019[101]
Surgical success	0.726	Dirichlet	Holme et al. 2007[102]
Surgical failure	0.0992	Dirichlet	Holme et al. 2007[102]
Stress incontinence	0.175	Dirichlet	Holme et al. 2007[102]

a = Repair surgery occurred once in the woman's lifetime, with 3 possible outcomes (success, failure, remain with stress incontinence). There was no probability of death associated with repair surgery[102]

Table 10 Probabilities of Neonatal Events Following Obstructed Labour

	Parameter	Mean	Distribution	Source
Caesarean Section	Stillbirths	0.0163	Beta	Harrison et al. 2015[105]
	NICU Admission	0.151	Beta	Amegan-Aho et al. 2018[104]
	Neonatal mortality in NICU	0.202	Beta	Hoque et al. 2011[110]
Instrumental Delivery	Stillbirths	0.0694	Beta	Harrison et al. 2015[105]
	NICU Admission	0.151	Beta	Amegan-Aho et al. 2018[104]
	Neonatal mortality in NICU	0.202	Beta	Hoque et al. 2011[110]
Prolonged Obstructed Labour	Stillbirths	0.386	Beta	Ayenew et al. 2021[20]
	Intrapartum hypoxia	0.256	Beta	Roa et al. 2020[21]
	Hypoxic-ischemic encephalopathy (HIE)[a]	0.303	Beta	Graham et al. 2008[22]

Abbreviations: NICU, Neonatal Intensive Care Unit.
a = Hypoxic-ischemic encephalopathy occurs conditionally upon experiencing intrapartum hypoxia

Table 11 Maternal Mortality Following Sequelae due to Obstructed Labour

	Parameter	Mean	Distribution	Source
Hospital (Caesarean Section and Instrumental Delivery)	Sepsis	0.333	Beta	Prual et al. 2000[107]
	Hemorrhage	0.0322	Beta	Prual et al. 2000[107]
	Surgical site infection	0.0551	Beta	Chu et al. 2015[108]
	Uterine rupture	0.304	Beta	Prual et al. 2000[107]
	Hysterectomy	0.200	Beta	Huque et al. 2018[109]
No Hospital (Prolonged Obstructed Labour)	Sepsis	0.493	Beta	Prual et al. 2000[107]
	Hemorrhage	*0.250*	Beta	Harrison et al. 2016[106]
	Surgical site infection	*0.0500*	Beta	Harrison et al. 2016[106]
	Uterine rupture	*0.450*	Beta	Harrison et al. 2016[106]
In-hospital mortality due to obstructed labour sequelae following caesarean section and instrumental delivery were assumed to be the same[107]				

Table 12 Disability Weights for Maternal and Neonatal Outcomes

	Parameter	Disability Weight	Distribution	Source
Short-Term In-Hospital and In-Community Maternal Outcomes	Caesarean Section	0.349	Beta	GBD 1990[111]
	Instrumental Delivery*	0.375	Beta	Estimate
	Obstructed Labour	0.324	Beta	GBD 2019[7]
	Sepsis (acute)*	0.499	Beta	KBD 2015,[112] Estimate
	Hemorrhage	0.324	Beta	GBD 2019[7]
	Surgical site infection	0.051	Beta	GBD 2019[7]
	Uterine prolapse	0.404	Beta	KBD 2015[112]
	Uterine rupture	0.490	Beta	Gilbert et al. 2013,[114] Chung et al. 2001[113]
	Hysterectomy*	0.324	Beta	GBD 2019[7]
Long-Term Maternal Outcomes	Stress incontinence	0.0250	Beta	GBD 1990[111]
	Rectovaginal fistula	0.501	Beta	GBD 2019[7]
	Vesicovaginal fistula	0.342	Beta	GBD 2019[7]
	Sepsis (long-term)	0.133	Beta	GBD 2019[7]
	Full Health	0.0100	Beta	Estimate
Long-Term Neonatal Outcomes	Hypoxic-Ischemic Encephalopathy	0.351	Beta	GBD 2019[7]
	Full Health	0.0100	Beta	Estimate
Abbreviations: GBD, Global Burden of Disease Study; KBD, Korean Burden of Disease Study.				

Table 13 Costs Related to Interventions and Sequelae for Obstructed Labour

Parameter	**Mean (PPP-adjusted $USD 2020)**	**Distribution**	**Source**
Caesarean Section	$303.48	Gamma	Alkire et al. 2015[55]
Instrumental Delivery	$177.36	Gamma	Adamu et al. 2013[115] *
Hemorrhage	$123.02	Gamma	Levin et al. 2003[132]
Hysterectomy	$584.48	Gamma	Lorenzoni et al. 2015[133] *
Fistula repair	$406.30	Gamma	Epiu et al. 2018[36]
Sepsis (acute)	$464.32	Gamma	Fenny et al. 2020[134]
Sepsis (long-term)	$239.11	Gamma	Farrah et al. 2020[99] *
Surgical site infection	$509.53	Gamma	Silverstein et al. 2016,[135] Monahan et al. 2020[136]
Uterine rupture	$510.14	Gamma	Alsuwaidan et al. 2020[137] *
Current healthcare expenditure per capita (SADC)	$53.03	Gamma	Taskforce on Innovative International Financing for Health Systems[103]
Neonatal Intensive Care	$363.77	Gamma	Enweronu-Laryea et al. 2018[138]
Current healthcare expenditure per capita (SADC)	$53.03	Gamma	Taskforce on Innovative International Financing for Health Systems[103]

Abbreviations: USD, United States Dollar; PPP, Purchasing Power Parity; SADC, South-African Development Community.

* = Estimated costs using relative proportions of costs of other health states. Methodology available in Appendix F

Table 14 Base Case Results for Maternal Model

Strategy	Cost ($USD 2020)	Incremental Cost ($USD 2020)	Effectiveness (DALYs)	Incremental Effectiveness (DALYs)	Incremental Cost-Effectiveness Ratio (ICER)
Existing Care	843.04	—	9.42	—	—
Increased Access to Caesarean Sections	1191.00	347.96	2.85	6.57	52.97

Table 15 Sensitivity Analysis Results for Maternal Model (Discounted 0% effect, 6% costs)

Strategy	Cost ($USD 2020)	Incremental Cost ($USD 2020)	Effectiveness (DALYs)	Incremental Effectiveness (DALYs)	Incremental Cost-Effectiveness Ratio (ICER)
Existing Care	622.03	—	9.73	—	—
Increased Access to Caesarean Sections	912.93	290.91	3.20	6.53	44.57

Table 16 Probabilistic Sensitivity Analysis Results for Maternal Model (Mean Expected Value)

Strategy	Cost ($USD 2020)	Incremental Cost ($USD 2020)	Effectiveness (DALYs)	Incremental Effectiveness (DALYs)	Incremental Cost-Effectiveness Ratio (ICER)
Existing Care	910.93	—	9.33	—	—
Increased Access to Caesarean Sections	1245.91	334.98	2.66	6.67	50.16

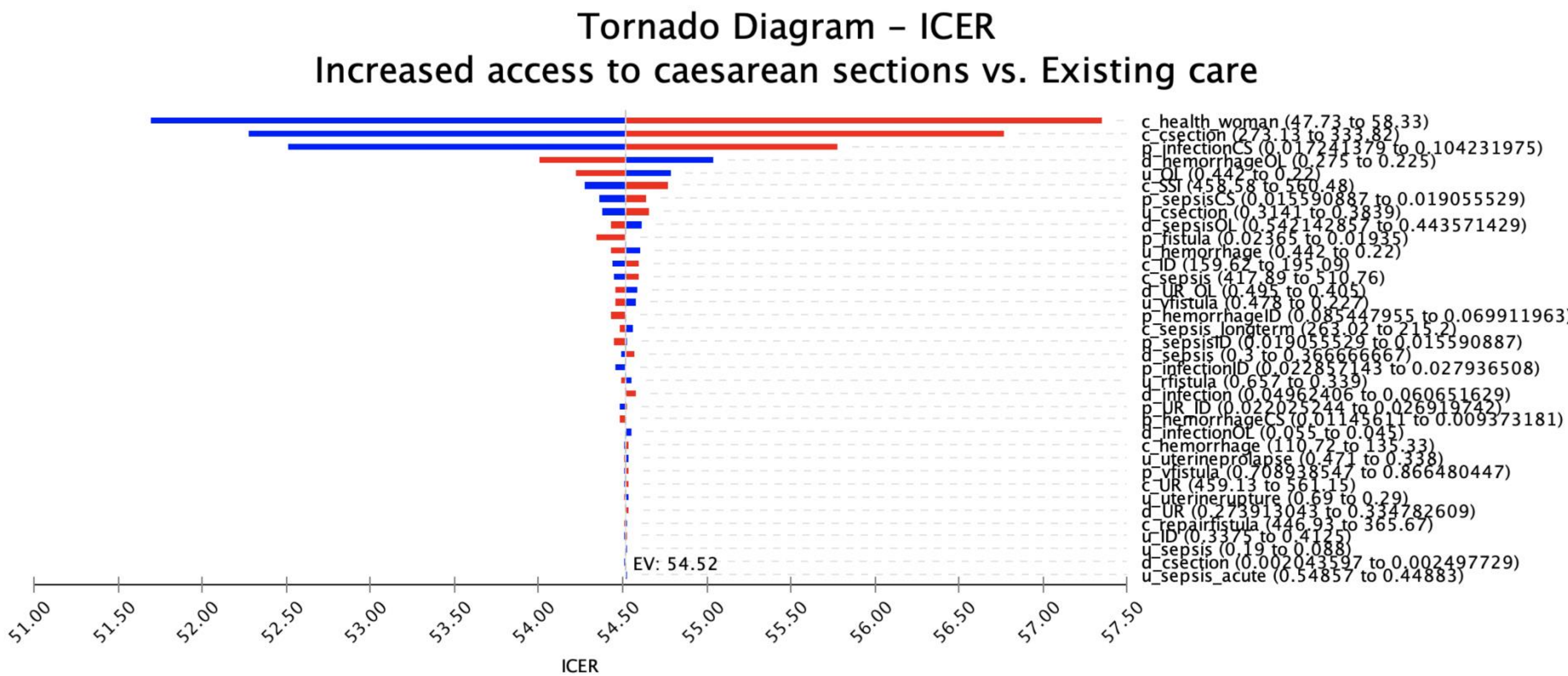

Figure 7 Tornado Diagram. Expected value of $54.52 refers to cost per disability-adjusted life year averted.

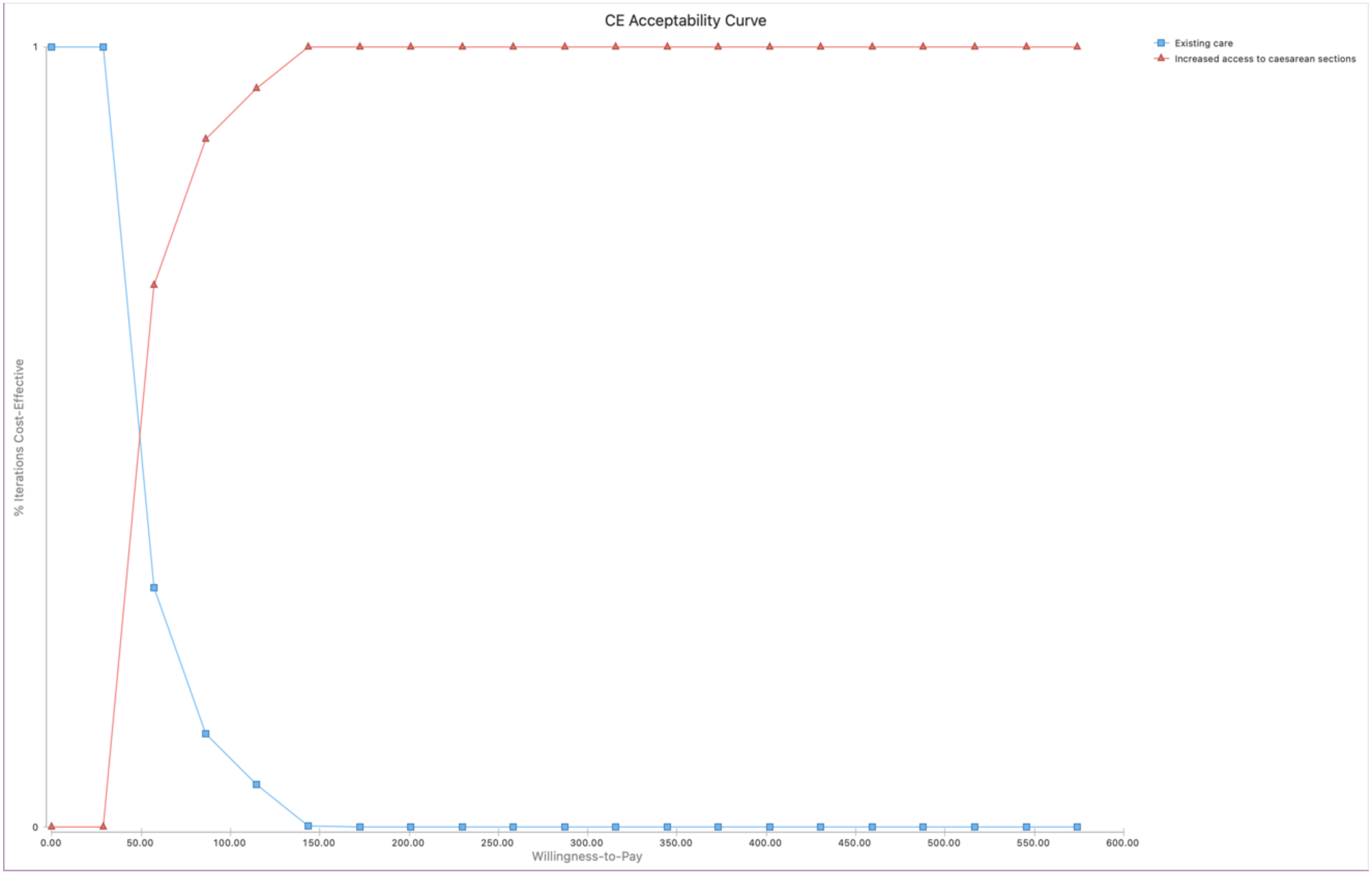

Figure 8 Probabilistic Sensitivity Analysis (10,000 iterations) using Monte Carlo Simulation for Maternal Model (WTP = $574)

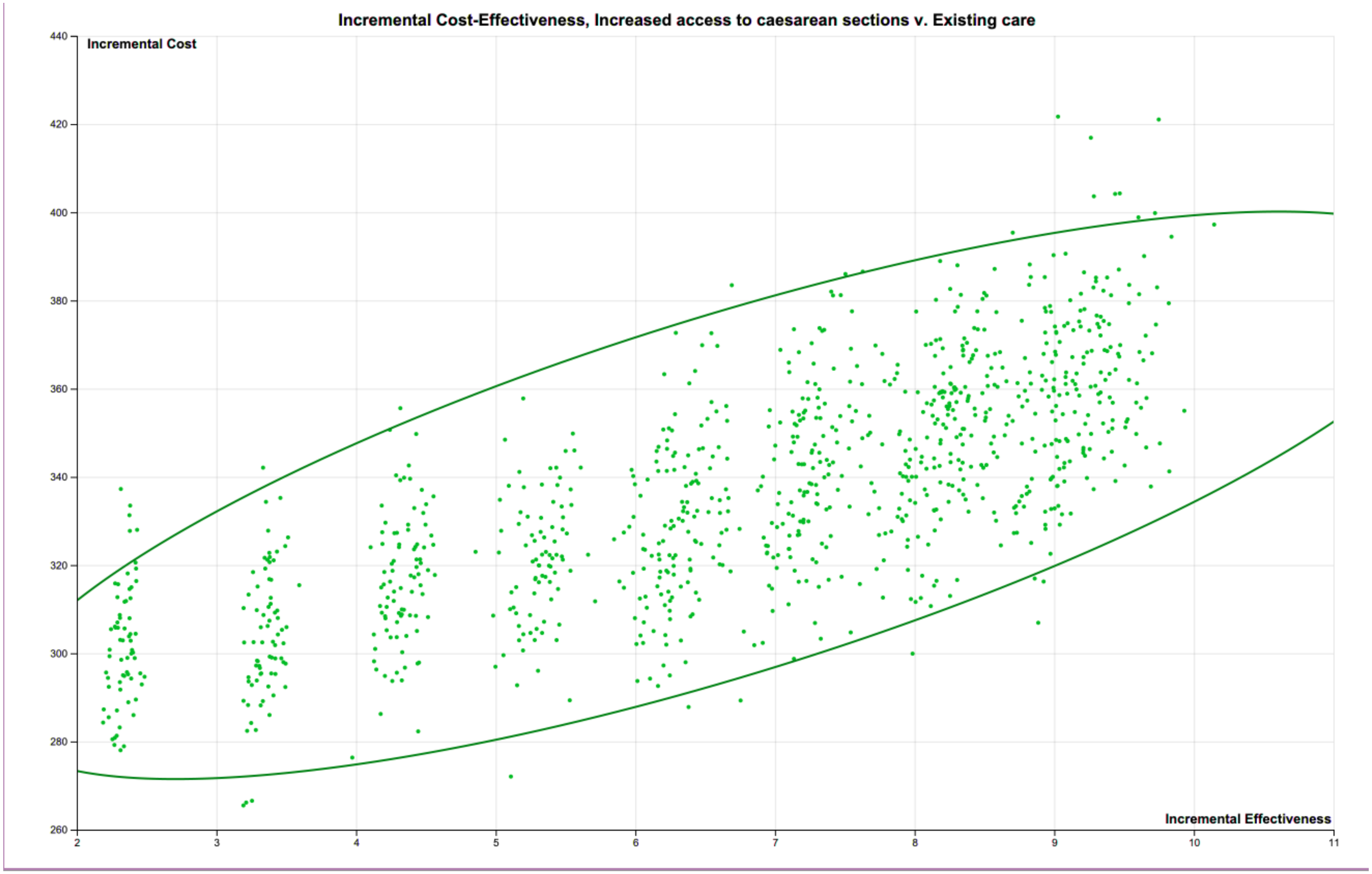

Figure 9 ICE Scatterplot for Maternal Model. Incremental costs presented in PPP-adjusted $USD 2020 and incremental effectiveness presented in disability-adjusted life years averted.

Table 17 Base Case Results for Neonatal Model

Strategy	Cost ($USD 2020)	Incremental Cost ($USD 2020)	Effectiveness (DALYs)	Incremental Effectiveness (DALYs)	Incremental Cost-Effectiveness Ratio (ICER)
Existing Care	829.69	—	17.64	—	—
Increased Access to Caesarean Sections	1052.56	222.87	6.37	11.27	19.77

Table 18 Sensitivity Analysis Results for Neonatal Model (Discounted at 0% effect, 6% costs)

Strategy	Cost ($USD 2020)	Incremental Cost ($USD 2020)	Effectiveness (DALYs)	Incremental Effectiveness (DALYs)	Incremental Cost-Effectiveness Ratio (ICER)
Existing Care	534.64	—	18.70	—	—
Increased Access to Caesarean Sections	686.01	151.37	6.98	11.72	12.93

Table 19 Probabilistic Sensitivity Analysis for Neonatal Model (Mean Expected Value)

Strategy	Cost ($USD 2020)	Incremental Cost ($USD 2020)	Effectiveness (DALYs)	Incremental Effectiveness (DALYs)	Incremental Cost-Effectiveness Ratio (ICER)
Existing Care	828.51	—	25.62	—	—
Increased Access to Caesarean Sections	1057.59	229.09	16.13	9.49	24.16

Table 20 Combined Cost-Utility Estimates for Mother and Baby

Strategy	Cost ($USD 2020)	Incremental Cost ($USD 2020)	Effectiveness (DALYs)	Incremental Effectiveness (DALYs)	Incremental Cost-Effectiveness Ratio (ICER)
Existing Care	1672.73	—	27.06	—	—
Increased Access to Caesarean Sections	2243.56	570.83	9.22	17.84	32.00

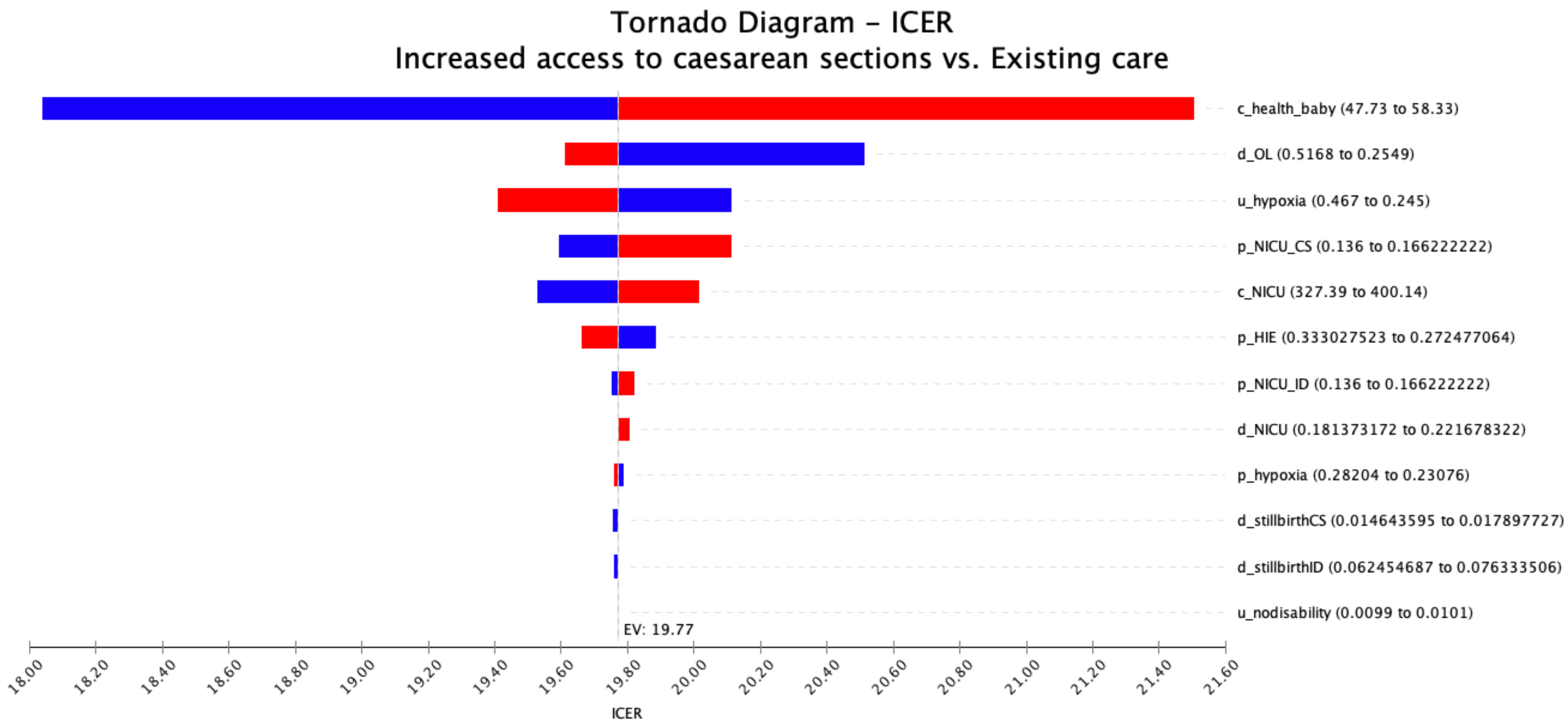

Figure 10 Tornado Diagram. Expected value of $19.77 refers to cost per disability-adjusted life year averted.

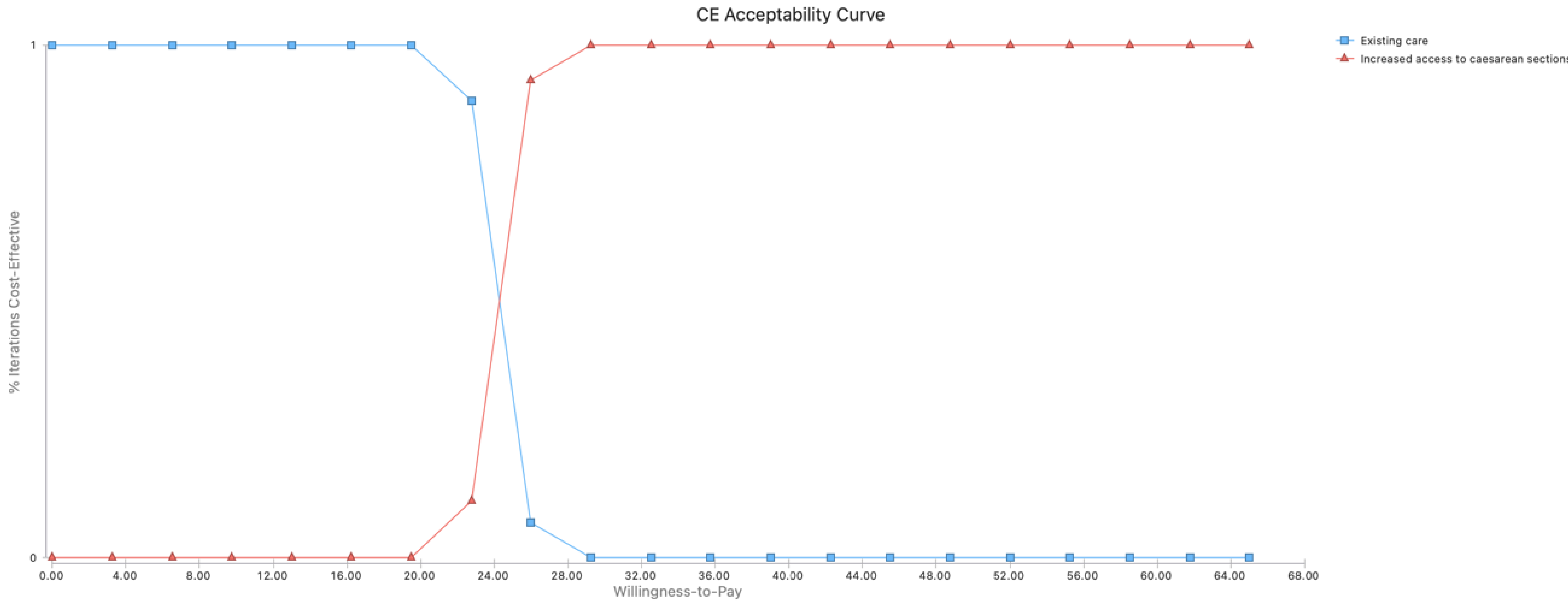

Figure 11 Probabilistic Sensitivity Analysis (10,000 iterations) using Monte Carlo Simulation for Neonatal Model (WTP = $574)

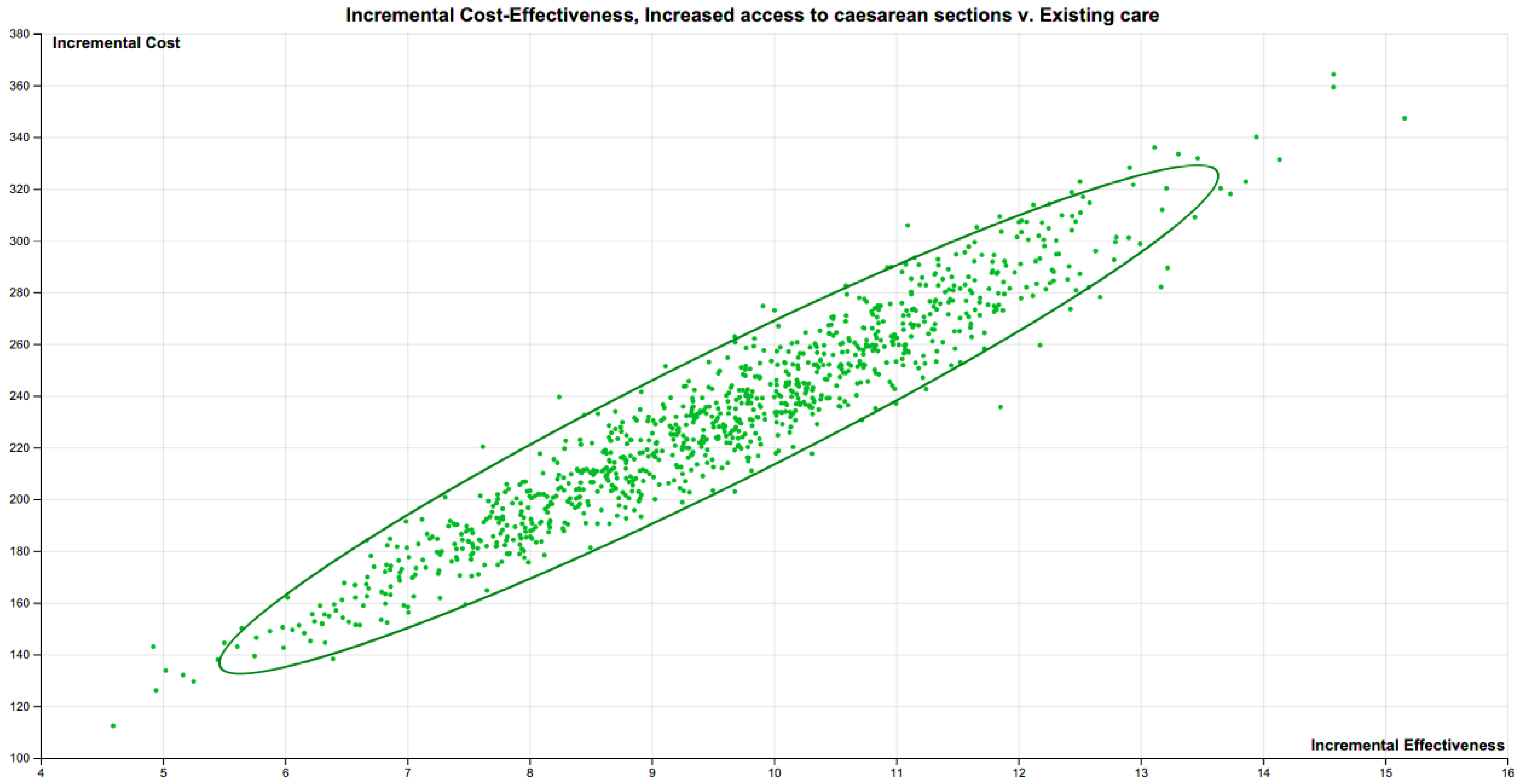

Figure 12 ICE Scatterplot for Neonatal Model. Incremental costs presented in PPP-adjusted $USD 2020 and incremental effectiveness presented in disability-adjusted life years averted.

Chapter 4

4 Conclusion

4.1 Summary of Findings

The results from the systematic review on essential surgery in LMICs and the subsequent economic evaluation of increasing access to caesarean section in the SADC region demonstrated that increasing access to the Bellwether procedures in developing countries is likely cost-effective in the context of benchmark interventions and willingness-to-pay thresholds derived from opportunity cost and PPP-adjusted GDP per capita.[60,61]

The systematic review on increasing access to the Bellwether procedures in LMICs included 13 economic evaluations that estimated the cost-effectiveness of caesarean section, laparotomy, and treatment of open fracture. Surgery type included both elective and emergency procedures across 49 countries between 1998 and 2020. Several studies reported generic outcomes such as cost per DALY, cost per LY saved, and cost-benefit ratio while others reported specific outcomes such as cost per maternal mortality avoided and cost per newborn death avoided per 1000 procedures. Due to inadequate comparator groups, most economic measures were classified as average cost per outcome for a specific cohort. It was thus only possible to compare five studies that included cost per DALY averted estimates, as recommended by the WHO and IHME.[29,30,32] The most cost-effective procedures were exploratory laparotomy in Uganda ($7.93 per DALY averted),[58] emergency hernia repair in Zambia ($15.55 per DALY averted),[59] and caesarean section in Zambia ($16.90 per DALY averted).[59] The least cost-effective procedures were emergency caesarean section for obstructed labour across 49 low-middle income countries ($491.81 per DALY averted)[55] and fracture dislocation fixation in Zambia ($786.13 per DALY averted).[59] These estimates remain cost-effective under benchmark WTP thresholds and PPP-adjusted WTP thresholds for each country.[60,61]

Overall bias as assessed with the ECOBIAS Checklist across the included studies was high, with main biases being inefficient comparator, reporting and dissemination bias, limited sensitivity analyses, and cost measurement omission bias.[47] Notably, most studies did not use formal decision-analytic modelling to estimate economic measures and were cohort-specific analyses instead of population-based.

Following the results of the systematic review, a Markov tree cycle was constructed to assess the cost-effectiveness of increasing access to caesarean section for obstructed labour in the SADC region compared to existing care. The cost of the increased access strategy was $1,191 with 2.85 DALYs compared to $843 with 9.42 DALYs for the existing care strategy. Increasing access to caesarean section from 30% to 80% and reducing the proportion of women remaining in neglected obstructed labour from 66.67% to 13.3% is expected to reduce a disability burden of 6.57 DALYs for an additional $348 per woman in obstructed labour, resulting in an ICER of $52.97 per DALY averted in 2020 PPP-adjusted $USD. Model outputs were most sensitive to the average cost per capita spent on healthcare expenditure, cost of caesarean section, and probability of surgical site infection following caesarean section. Probabilistic sensitivity analyses demonstrated stable results with increased access being cost-effective 100% of the time at a willingness-to-pay threshold of $172 per DALY averted.

Accompanying results for the neonates were $1,053 with an accumulated 6.37 DALYs for the increased access strategy compared to $830 with 17.64 DALYs for the existing care strategy. The increased access strategy led to a reduction of 11.27 DALYs for an additional $223 per neonate born relative to the existing care strategy, resulting in an ICER of $19.77 per DALY averted. Probabilistic sensitivity analyses were cost-effective 100% of the time at a willingness-to-pay threshold of $32.50 per DALY averted. A combined estimate of cost-utility for mothers and babies cost $32.00 per DALY averted comparing increased access to existing care.

Compared to SADC-specific willingness-to-pay thresholds ranging from $574 to $2,763 per DALY averted in 2020 PPP-adjusted $USD, all results were found to be likely cost-effective. However, given that our results are sensitive to health system costs, these costs must be validated and incorporated into these cost-utility estimates before we can definitively conclude cost-effectiveness.[124] Our findings are consistent with other published economic evaluations and epidemiological modelling studies that find provision of safe, timely caesarean section for obstructed labour to result in substantial health gains and likely be cost-effective in LMICs.[17–19,55,64]

4.2 Strengths and Limitations

4.2.1 Systematic Review

The systematic review has several strengths. It is the first systematic review to synthesize and appraise evidence on all cost-effectiveness estimates for increasing access to the Bellwether procedures in LMICs, which is much needed in the context of supporting global targets for surgical access by 2030. Importantly, gaps and limitations in the quality in existing evidence were identified, providing opportunity to establish a standard for future cost-effectiveness analyses conducted in LMIC settings. The findings show that increasing access to Bellwether procedures to reduce disability and premature death is highly cost-effective but remains limited by aspects of the economic evaluations pertaining to lack of formal decision-analytic modelling, short time horizons, restricting cohorts of only those who can access care, and lack of generalizability due to the limited study settings. Limitations of this review mostly stem from the methodology and data from the included studies which restricted the possibility of further quantitative analyses due to high heterogeneity and incomparability across studies.

4.2.2 Economic Evaluation

Similarly, the model constructed to address the knowledge gap surrounding increasing access to caesarean section for obstructed labour has several strengths. Primarily, it is the first decision-analytic model to incorporate a Markov cycle decision tree to represent the impact of increasing safe, timely caesarean section compared to existing care for women in obstructed labour. Furthermore, the model accounts for long-term disability due to secondary conditions following obstructed labour, such as sepsis and obstetric fistula, across a life-time time horizon. The model employs methods recommended by the WHO to evaluate sets of interventions to better address resource constraints by modelling the treatment options that most accurately represent standard care.[94] Most importantly, the model addresses a largely ignored issue of unmet need in global surgery health economics, being that a staggering proportion of women in obstructed labour are unable to reach the operating room or the hospital.[2] These patients have been generally excluded from economic evaluations on global surgery to date, leaving a gaping inequity in access that the model is able to address. Finally, the model also includes an accompanying analysis for neonates that have also been typically excluded from economic evaluations conducted in LMICs. This is particularly impactful due to the number of stillbirths and asphyxia-related disabilities attributed to obstructed labour that would be prevented with access to safe, timely caesarean section.[17]

The model also has limitations, primarily the limited quality of data available for the SADC region. In many cases, SADC-specific estimates were not available and estimates from the super-region, Sub-Saharan Africa, were used to populate the model. The proportion of those receiving caesarean section, undergoing instrumental delivery, or unable to receive treatment were also extrapolated from pooled Demographic Health Surveys data and WHO estimates of health facility access and deliveries in Sub-Saharan Africa.[12,25] Another limitation to the model is lack of information surrounding long-term disability for mothers and babies after obstructed labour, besides disability due to obstetric fistula, which remains understudied and difficult to estimate.

4.3 Health Policy Implications

Prioritizing high-value, low-cost interventions such as the Bellwether procedures is a practical use of healthcare resources with considerable health benefits for reasonably low cost.[2,3] The goal of the systematic review and the Markov cycle model are to demonstrate to policymakers that increasing access to safe surgery to meet the LCoGS 2030 targets for safe surgery is likely achievable at a cost-effective capacity. Evidently, achieving the Sustainable Development Goals in reducing maternal mortality also heavily relies on the availability and extent of access to safe surgical management of obstructed labour.[1,9,49 53]

While implementing measures to increase access to essential surgery continues to be a global priority, there are several challenges to successful realization of these goals. High cost, infrastructure demands, political factors, shortage of trained workers, patient perceptions of surgery, and various demographic factors are examples of barriers that exist between patients and life-saving access to essential surgery.[42-45] However, meaningful efforts have been made to lessen the severity of these limitations, such as surgical workforce training, task-shifting, alternative fee programs, and maternal care packages for essential obstetric care.[54,64,81,139]

To close the gap in access by 2030, it is crucial that the unmet need in global surgery is as accurately and comprehensively defined as possible. National Surgical, Obstetric and Anesthesia Plans (NSOAPs) are a framework for strengthening surgical systems through three core concepts, one of which is to define current gaps in surgical access and delivery through the LCoGS indicators.[140] Groundwork for developing NSOAPs is in various stages globally and several countries in Sub-Saharan Africa have successfully implemented NSOAPS to improve their national health strategic plans.[140] As the amount of country-specific data on the LCoGS core indicators expands, future economic evaluations will be able to use higher quality data to accurately represent surgical access in existing care and yield cost-utility estimates that are closer to reality.

4.4 Future Directions

Based on the findings of these studies, future directions for global surgery economic evaluation should be expanded in two ways: i) to develop and implement more rigorous standards for cost-effectiveness analyses conducted in LMICs and ii) to adapt the novel decision-analytic model to country-specific data to provide specific estimates for individual health systems in the SADC region. The model was created with the goal to demonstrate to policymakers and stakeholders that death and disability due to prolonged obstructed labour in LMICs is preventable in a cost-effective manner and worth investing in. However, the model currently can only broadly estimate cost per DALY averted due to the paucity of data from the SADC region. Our cost estimates for caesarean section also solely focus on costs related to procedure and facility maintenance while excluding health system costs of scale-up related to healthcare professional training to expand access to obstetricians, surgeons, and anaesthesiologists. Validated estimates of these health system costs should be developed and used for future cost-effectiveness research in this area. Future work includes developing a clinician survey on REDCap for costs, event probabilities, and effectiveness to drive accompanying economic evaluations forward and improve the current evidence base for better global health outcomes. Open access to the model will be established to allow policy advisors, researchers, and clinicians to input country-specific or regional data for their own assessments.

While the results of the study find increasing access to essential surgery to be cost-effective, it is important to note that cost-effectiveness thresholds should not be the only criteria for making public health decisions at a national level.[141] Evidence-to-decision or multi-criteria decision analysis frameworks, context, and further deliberation are necessary to supplement the decision-making process.[141] For this reason, significant efforts are still required to reach the WHO targets for strengthening emergency and essential surgical care and anaesthesia as a component of universal health coverage by 2030, as well as the UN SDG goals for reducing maternal mortality to under 70 per 100,000 live births.[6,10] Despite the numerous challenges to global expansion of access to safe and timely essential surgery, their cost-effectiveness in saving lives and potential to reduce long-term disabilities underscores the urgent need to implement equitable, increased access to safe surgical care.[2,34] Successful achievement of these goals will advance global development, maintain resilient health systems, and enhance human welfare in LMICs through global commitment and partnership to guide policy and action.[10]

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Appendices

Appendix A: Search Strategy for Electronic Databases and Grey Literature

Embase (Ovid)
1 developing country/ (96047)
2 ((developing or low or middle) adj3 (countr* or nation*)).mp. (180576)
3 ((third adj2 world) and (countr* or nation*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word] (2930)
4 ((underdeveloped or under-developed) adj2 (countr* or nation*)).mp. (1911)
5 (least-developed adj2 (countr* or nation*)).mp. (304)
6 middle income country/ (8679)
7 low income country/ (6029)
8 LMIC.mp. (2752)
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 (182891)
10 bellwether.mp. (125)
11 (c?section* or c?esar?an* or c-section*).mp. (124122)
12 ((abdominal* or surgical) adj2 (deliver* or birth*)).mp. (2571)
13 exp obstetric operation/ (173801)
14 exp obstetric anesthesia/ (15172)
15 (obstetric adj2 (anesthesia or operation* or surgery)).mp. (14070)
16 laparotomy/ (85823)
17 (laparotom* or minilaparotom*).mp. (111940)
18 exp open fracture/ (6508)
19 open fracture treatment.mp. (31)
20 (fracture* adj3 (open or compound)).mp. (13971)
21 fractures/su [Surgery] (8982)

22	open fracture/ (6508)
23	open fracture reduction/ or "open reduction (procedure)"/ (3591)
24	exp laparoscopy/ (161382)
25	laparoscop*.mp. (241531)
26	minilaparoscop*.mp. (388)
27	minilaparoscop*.mp. (8)
28	celloscop*.mp. (32)
29	peritoneoscop*.mp. (1383)
30	laparoendoscop*.mp. (3240)
31	(abdom* adj3 (surgery or surgical or surgeries or surgically or operation* or operating or operativ* or operated)).ti,ab. (44405)
32	10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 (581365)
33	socioeconomics/ (146503)
34	cost benefit analysis/ (84628)
35	cost effectiveness analysis/ (151274)
36	cost of illness/ (19182)
37	cost control/ (68383)
38	economic aspect/ (118180)
39	financial management/ (117224)
40	health care cost/ (190180)
41	health care financing/ (13318)
42	hospital cost/ (21578)
43	(fiscal or financial or finance or funding).tw. (201427)
44	Cost minimization analysis/ (3507)
45	(cost adj estimate$).mp. (3454)
46	(cost adj variable$).mp. (267)
47	(unit adj cost$).mp. (4561)

48	cost*effect*.mp. (5158)
49	cost-effect*.mp. (252753)
50	exp "cost"/ (353958)
51	cost.mp. (893345)
52	cost*analysis.mp. (20)
53	cost-analysis.mp. (13631)
54	exp quality adjusted life year/ (26575)
55	quality adjusted life year.mp. (27923)
56	QALY.mp. (16675)
57	exp "quality of life"/ (490822)
58	life year*.mp. (38423)
59	exp disability-adjusted life year/ (2027)
60	disability-adjusted life year.mp. (2617)
61	DALY.mp. (2383)
62	budget impact.mp. (4120)
63	inequity.mp. (4188)
64	exp health care disparity/ (15339)
65	inequalit*.mp. (39269)
66	equit*.mp. (30320)
67	equal*.mp. (453297)
68	health inequality aversion.mp. (6)
69	health inequality.mp. (1421)
70	exp health disparity/ (19690)
71	exp health care need/ (29929)
72	surgical need.mp. (199)
73	exp "cost utility analysis"/ (9690)

74	cost utility analysis.mp. (10645)
75	exp "cost benefit analysis"/ (84628)
76	exp health economics/ (864297)
77	budget/ (29609)
78	budget*.ti,ab,kw. (39980)
79	(economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 (412465)
80	(cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kw. (229933)
81	(value adj2 (money or monetary)).ti,ab,kw. (3333)
82	statistical model/ (160542)
83	economic model*.ab,kw. (4916)
84	probability/ (108625)
85	markov.ti,ab,kw. (29715)
86	monte carlo method/ (40260)
87	monte carlo.ti,ab,kw. (50440)
88	decision theory/ (1768)
89	decision tree/ (12957)
90	(decision* adj2 (tree* or analy* or model*)).ti,ab,kw. (34477)
91	33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 (2891764)
92	9 and 32 and 91 (1353)

Appendix B Risk of Bias Using the ECOBIAS Tool

Part B: Model-specific aspects of bias in economic evaluation										
	I. Bias related to structure				**II. Bias related to data**						**III. Bias related to consistency**
Study	Structural assumption bias	No treatment comparator bias	Wrong model bias	Limited time horizon bias	Bias related to data identification	Bias related to baseline data	Bias related to treatment effects	Bias related to quality-of-life weights (utilities)	Non-transparent data incorporation bias	Limited scope bias	Bias related to internal consistency
Jha et al. 1998	N/A	N/A	N/A	N/A	No	N/A	No	N/A	No	Yes	No
Gosselin et al. 2006	N/A	N/A	N/A	N/A	No	N/A	No	N/A	No	Yes	No
Gosselin et al. 2008	N/A	N/A	N/A	N/A	No	N/A	No	N/A	No	Yes	No
Hounton et al. 2009	N/A	N/A	N/A	N/A	No	N/A	No	N/A	No	Partly	No
Shilcutt et al. 2010	N/A	N/A	N/A	N/A	No	N/A	No	N/A	No	No	No
Gosselin et al. 2010	N/A	N/A	N/A	N/A	No	N/A	No	N/A	No	Partly	No
Shillcutt et al. 2013	N/A	N/A	N/A	N/A	No	N/A	No	N/A	No	No	No
Alkire et al. 2015	N/A	N/A	N/A	N/A	No	N/A	No	N/A	No	Partly	No
Roberts et al. 2015	N/A	N/A	N/A	N/A	No	N/A	No	N/A	No	Yes	No
Verguet et al. 2015	N/A	N/A	N/A	N/A	Partly	N/A	No	N/A	Partly	Partly	No
Entringer et al. 2018	No	No	Partly	Partly	Partly	No	No	Yes	No	No	No
Entringer et al. 2018	No	No	Partly	Partly	Partly	No	No	Yes	No	No	No
Bellamkonda et al. 2020	N/A	N/A	N/A	N/A	No	N/A	No	N/A	No	Partly	No

Appendix C Currency Conversions

Table C.1 Costs Conversion and Inflation for Caesarean Section

Study	Cost	Currency	Costing Year	PPP Exchange Rate	Cost ($I)	GDP Implicit Price Deflator (Original)	GDP Implicit Price Deflator (Adjusted)	Ratio	Adjusted Cost (2020)
Jha et al. 1998	41,481	Guinean Francs	1994	676.887	$61.28	70.392	113.626	1.61418911	$98.92
Jha et al. 1998	18,000	Guinean Francs	1994	676.887	$26.59	70.392	113.626	1.61418911	$42.93
Alkire 2015	38,124.00	USD	2010	1	$416.00	96.111	113.626	1.1822372	$491.81
Roberts et al. 2015	58,291.70	Zambian kwacha	2012	2563.23	$14.87	100	113.626	1.13626	$16.90
Roberts et al. 2015	107,948.00	Zambian kwacha	2012	2563.23	$22.74	100	113.626	1.13626	$25.84
Roberts et al. 2015	161,184	Zambian kwacha	2012	2563.23	$42.11	100	113.626	1.13626	$47.85
Roberts et al. 2015	38,124.00	Zambian kwacha	2012	2563.23	$62.88	100	113.626	1.13626	$62.88
Verguet et al. 2015	420,000	USD	2011	--	$420,000	98.118	113.626	1.15805459	$486,382.93
Verguet et al. 2015	140 deaths per 100,000	USD	2011	--	--	98.118	113.626	--	122 deaths per 100,000
Hounton et al. 2009	34884	Burkina Faso (CFA)	2006	191.518	$182.14	90.066	113.626	1.26158595	229.7912688
Hounton et al. 2009	37531	Burkina Faso (CFA)	2006	191.518	$195.97	90.066	113.626	1.26158595	$247.23
Hounton et al. 2009	36260	Burkina Faso (CFA)	2006	191.518	$189.33	90.066	113.626	1.26158595	238.8553895
Entringer et al. 2018a	3,429.27	Brazilian Reais	2016	2.133	$1,607.72	105.722	113.626	1.07476211	1727.918175
Entringer et al. 2018b	2245.86	Brazilian Reais	2014	1.813	$1,238.75	103.638	113.626	1.09637392	1358.136969
Entringer et al. 2018b	2659399.2	Brazilian Reais	2014	1.813	$1,466,850.08	103.638	113.626	1.09637392	1608216.171

Table C.2 Costs Conversion and Inflation for Laparotomy

Study	Cost	Currency	Costing Year	PPP Exchange Rate	Cost ($I)	GDP Implicit Price Deflator (Original)	GDP Implicit Price Deflator (Adjusted)	Ratio	Adjusted Cost (2020)
Jha et al. 1998	65,819	Guinean Francs	1994	676.887	$97.24	70.392	113.626	1.61418911	156.9601916
Jha et al. 1998	35,000	Guinean Francs	1994	676.887	$51.71	70.392	113.626	1.61418911	83.46536266
Jha et al. 1998	51,768	Guinean Francs	1994	676.887	$76.48	70.392	113.626	1.61418911	123.4524255
Jha et al. 1998	72,000	Guinean Francs	1994	676.887	$106.37	70.392	113.626	1.61418911	171.7001746
Shillcutt et al. 2010	$122.328	Ghanian New Cedi	2008	0.472	$259.17	94.285	113.626	1.20513337	312.3338033
Shillcutt et al. 2010	$13.1277	Ghanian New Cedi	2008	0.472	$27.81	94.285	113.626	1.20513337	33.51828256
Shillcutt et al. 2013	499.33	USD	2011	0.551	$906.23	98.118	113.626	1.15805459	$1,049.46
Shillcutt et al. 2013	78.18	USD	2011	0.551	$141.89	98.118	113.626	1.15805459	164.313444
Roberts et al. 2015	45,390.70	Zambian kwacha	2012	2563.23	$17.71	100	113.626	1.13626	20.12134564
Roberts et al. 2015	66,559.00	Zambian kwacha	2012	2563.23	$25.97	100	113.626	1.13626	29.50508902
Roberts et al. 2015	22,958.60	Zambian kwacha	2012	2563.23	$8.96	100	113.626	1.13626	10.1773695
Roberts et al. 2015	35,069.80	Zambian kwacha	2012	2563.23	$13.68	100	113.626	1.13626	15.54617063
Roberts et al. 2015	80,355.20	Zambian kwacha	2012	2563.23	$31.35	100	113.626	1.13626	35.6208376
Roberts et al. 2015	126,536	Zambian kwacha	2012	2563.23	$49.37	100	113.626	1.13626	56.09242844
Bellamkonda et al. 2020	10,005.50	Ugandan shilling	2018	1,300.42	$7.69	110.296	113.626	1.03019148	7.926359755
Bellamkonda et al. 2020	185,150	Ugandan shilling	2018	1,300.42	$142.38	110.296	113.626	1.03019148	146.6758791

Table C.3 Costs Conversions and Inflation for Open Fracture

Study		Cost	Currency	Costing Year	PPP Exchange Rate	Cost ($I)	GDP Implicit Price Deflator (Original)	GDP Implicit Price Deflator (Adjusted)	Ratio	Adjusted Cost (2020)
Roberts et al. 2015	Fracture dislocation reduction (Global)	363,494	Zambian kwacha	2012	2563.23	$141.81	100	113.626	1.13626	161.134074
Roberts et al. 2015	Fracture dislocation reduction (Zambia)	519,887	Zambian kwacha	2012	2563.23	$202.82	100	113.626	1.13626	230.4618792
Roberts et al. 2015	Fracture dislocation fixation (Global)	1,189,480	Zambian kwacha	2012	2563.23	$464.06	100	113.626	1.13626	527.2872683
Roberts et al. 2015	Fracture dislocation fixation (Zambia)	1,773,400	Zambian kwacha	2012	2563.23	$691.86	100	113.626	1.13626	786.1344803

Appendix D PRISMA Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	pg. 10
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	N/A
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	pg. 10 - 11
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	pg. 10 - 11
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	pg. 12
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	pg. 11 - 12
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	pg. 11 Appendix A
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	pg. 12
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	pg. 12 - 13
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	pg. 12
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	pg. 12 - 13
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	pg. 12 - 13
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	pg. 12
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	N/A
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	pg. 12 - 13
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	pg. 13
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	pg. 13
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	pg. 13
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	pg. 12 - 13 & Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	pg. 14 - 16 & Tables 2-3
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	pg. 15, Table 4, Appendix B
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Tables 5 - 7
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	pg. 14 - 16
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Table 4, Appendix B
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	pg. 17 - 18
	23b	Discuss any limitations of the evidence included in the review.	pg. 19 - 20
	23c	Discuss any limitations of the review processes used.	pg. 19
	23d	Discuss implications of the results for practice, policy, and future research.	pg. 20 - 21
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	pg. 22
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	pg. 22
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	pg. 22
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	pg. 22
Competing interests	26	Declare any competing interests of review authors.	pg. 22
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	pg. 22

Appendix E Willingness-To-Pay Thresholds for SADC Countries

Country	Population	Weight	Low threshold	High Threshold	Weighted low	Weighted high
Angola	31,825,295	0.08991821	901.1466955	4327.067466	81.02950035	389.0821733
Botswana	2,303,697	0.00650879	3897.152376	11634.50734	25.36576543	75.72662177
Comoros	850,886	0.00240407	39.08319002	894.4467201	0.093958616	2.150310039
Democratic Republic of Congo	86,790,567	0.24521541	8.933300575	428.7984276	2.190582939	105.147981
Eswatini	1,148,130	0.00324389	707.9640706	3836.852597	2.296558492	12.44633277
Lesotho	2,125,268	0.00600467	106.0829443	1484.044558	0.636992761	8.911193462
Madagascar	26,969,307	0.07619825	31.26655201	800.647064	2.382456647	61.0079077
Malawi	18,628,747	0.05263309	10.04996315	447.7816913	0.528960622	23.56813436
Mauritius	1,265,711	0.0035761	4692.216127	12408.3545	16.77983905	44.37352963
Mozambique	30,366,036	0.08579527	17.86660115	599.6478011	1.532869819	51.44694331
Namibia	2,494,530	0.00704797	1487.394546	5559.862945	10.48311003	39.18573938
Seychelles	97,625	0.00027583	9279.465972	15715.90904	2.559524311	4.334867046
South Africa	58,558,267	0.16544873	2480.107572	9948.346853	410.3306539	1645.941376
Tanzania	58,005,463	0.16388686	50.24981573	1018.396266	8.235284359	166.901763
Zambia	17,861,030	0.05046401	160.7994103	1825.743305	8.114582504	92.13432218
Zimbabwe	14,645,468	0.04137886	45.78316545	975.9630878	1.894455024	40.38423636
Total	353,936,027				574.4550948	2762.743431

Appendix F Costs

Methodology for Calculating PPP-adjusted $USD and Inflation of Costs

To adjust the costs used in the model for varying currencies and inflation, the following general procedure was used:

i) Adjust costs in original currency to account for purchasing power parity (PPP). Purchasing power parity incorporates the prices of specific goods to compare the absolute purchasing power of a country's currency. PPPs incorporate price information for a representative basket of products and services across countries to allow for comparison.

$$Cost\ adjusted\ with\ PPP = \frac{Cost\ in\ original\ currency}{PPP\ exchange\ rate}$$

Costs adjusted with PPP are in the units of international dollars ($I) but will be referred to as PPP-adjusted $USD to maintain comparability. One international dollar has the same purchasing power for goods and services in a cited country as one United States Dollar ($USD) in the United States at a given point in time.[48] PPP exchange rates were taken from the International Monetary Fund: World Economic Outlook database.[142]

ii) Adjust PPP-adjusted USD for inflation and convert all costs to a single base year, 2020. Costs were inflated using Gross Domestic Product (GDP) implicit price deflators which reflect price changes of all goods contributing to GDP and average annual rate of inflation during the specific period.[48]

$$Adjusted\ cost\ (2020\ price) = Cost\ (original\ costing\ year) \times \frac{GDP\ implicit\ price\ deflator\ for\ 2020}{GDP\ implicit\ price\ deflator\ for\ original\ year}$$

US inflation rates more accurately reflect price changes of tradeable resources in comparison to local inflation rates. GDP implicit price deflators were taken from the International Monetary Fund: World Economic Outlook database.[142]

A sample calculation follows below:

The cost for treatment of acute sepsis was $934.50 in 2019 Ghanaian Cedi.

$$Cost\ adjusted\ with\ PPP = \frac{\$934.50}{2.037} = \$458.76$$

The PPP-adjusted cost in USD for treatment of acute sepsis was then inflated to 2020 prices from the original costing year of 2019.

$$Adjusted\ cost\ (2020\ price) = \$458.76 \times \frac{113.626}{112.265} = \$464.32$$

The adjusted cost to account for PPP and inflation was $464.32 USD for treating acute sepsis. Additional assumptions and details for costs used in the analyses can be found in Table 26 and 27.

Due to scarcity of information, assumptions in cost were necessary for cost of instrumental delivery, hysterectomy, treatment for long-term sepsis, and uterine rupture (details in Table 26). Costs for instrumental delivery, hysterectomy, and uterine rupture were estimated by calculating the ratio between cost of procedure and cost of caesarean section in the source country. The ratio was then applied to the cost of caesarean section estimated for the SADC region using Alkire and colleagues' calculations. A sample calculation follows below:

$$Cost\ of\ instrumental\ delivery\ (SADC) = \frac{Cost\ of\ instrumental\ delivery\ in\ Nigeria}{Cost\ of\ caesarean\ section\ in\ Nigeria} \times Cost\ of\ caesarean\ section\ (SADC)$$

$$Cost\ of\ instrumental\ delivery\ (SADC) = \frac{\$28{,}800}{\$49{,}300} \times \$303.48 = \$177.36$$

Cost of treating long-term sepsis was estimated by calculating a ratio of sepsis treatment costs in year 2 to treatment in year 1 and applying it similarly to the cost of caesarean section estimated for the SADC region.

Table F.1 Details and Assumptions for Costs

Parameter	**Costing Details and Assumptions**	**Preference Order**	**Source**
Caesarean Section	Standardized profile including costs for caesarean section, associated devices and medicines, operative facility time, medical human resources time, post-operative hospital stay for stabilization, facility maintenance, and equipment. Estimated average cost for 9 SADC countries: Comoros, the Democratic Republic of Congo, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Tanzania, and Zambia.	SADC Region (1)	Alkire et al. 2015
Instrumental Delivery	Estimated with the proportion of costs of caesarean section compared to instrumental delivery from Adamu et al. 2013, applied to the cost of caesarean section in the SADC region.	SADC Region (1), assumptions (7)	Adamu et al. 2013*
Hemorrhage	Cost of treating postpartum haemorrhage in a public hospital in Malawi (from two facilities). Costs included drugs and supplies (unit costs) and variable costs including personnel, maintenance, and utilities.	Country-specific in the SADC region (3)	Levin et al. 2003

Hysterectomy	Estimated average cost using proportion of costs of caesarean section compared to hysterectomy in South Africa, applied to the cost of caesarean section in the SADC region. Original cost sourced is for private hospital costs of hysterectomy in South Africa from OECD Health Working Paper No. 85. Costs included cost of procedure, drugs, equipment, staff, facility maintenance, and hospital stay.	Country-specific in the SADC region (3), assumptions (7)	Lorenzoni et al. 2015*
Fistula repair	Cost of providing repair surgery for obstetric fistula in Uganda (the Centre for Fistula Care in Mulago National Referral Hospital and the Kitovu Regional Referral Hospital). Costs included costs of procedure, supplies, drugs, infrastructure, equipment, personnel, and patient accommodation.	Country-specific in Sub-Saharan Africa (4)	Epiu et al. 2018
Sepsis (acute)	Costs of treating puerperal sepsis in Ghana (Eastern Regional Hospital and Greater Accra Regional Hospital) Costs included costs of treatment, diagnostic tests, medical procedures, supplies, drugs, clinical support, and staff-related costs.	Country-specific in Sub-Saharan Africa (4)	Fenny et al. 2020
Sepsis (long-term)	Estimated average cost using proportion of costs for sepsis treatment in year 1 compared to year 2 in Ontario, Canada, applied to the long-term cost of sepsis. Costs included costs of treatment, diagnostic tests, laboratory services, professional fees, medication, and inpatient hospitalizations.	High-income countries (6), (assumptions (7)	Farrah et al. 2020*
Surgical site infection	Costs of treating surgical site infection following abdominal surgery in Rwanda (Rwanda Military Hospital). Costs included costs for treatment, supplies, drugs, tests, hospitalization, and additional ancillary fees for transportation.	Country-specific in Sub-Saharan Africa (4), assumptions (7)	Silverstein et al. 2016, Monahan et al. 2020

Uterine rupture	Estimated average cost using proportion of costs of caesarean section compared to uterine rupture in Saudi Arabia, applied to the cost of caesarean section in the SADC region. Original cost sourced is for uterine rupture treatment at King Saud Medical City in Saudi Arabia. Costs included cost of surgical intervention, consultations, drugs, laboratory work, equipment, and hospitalization.	High-income countries (6), (assumptions (7)	Alsuwaidan et al. 2020*
Current healthcare expenditure per capita (SADC) for mothers	The minimum recommended per capita spending on health for LMICs to provide essential health services. Investment would go towards strengthening health systems and universal coverage of interventions that reduce maternal mortality, diagnosis, prevention and treatment of infectious diseases, primary care, and health promotion.	Sub-Saharan Africa (2)	Taskforce on Innovative International Financing for Health Systems
Neonatal Intensive Care	Costs for in-patient neonatal services (neonatal intensive care unit) for perinatal asphyxia in a regional hospital and largest district hospital in the Greater Accra Region of Ghana. Costs included costs for diagnostics, treatment and therapeutics, medicines, clinical supplies, laboratory services, and hospitalization.	Country-specific in Sub-Saharan Africa (4)	Enweronu-Laryea et al. 2018
Current healthcare expenditure per capita (SADC) for neonates	The minimum recommended per capita spending on health for LMICs to provide essential health services. Investment would go towards strengthening health systems and universal coverage of interventions that reduce maternal mortality, diagnosis, prevention and treatment of infectious diseases, primary care, and health promotion.	Sub-Saharan Africa (2)	Taskforce on Innovative International Financing for Health Systems

Appendix C.2 Cost Conversions and Inflation

Parameter	Cost	Currency	Costing Year	PPP Exchange Rate	Cost ($I)	GDP Implicit Price Inflator (Original)	GDP Implicit Price Inflator (Adjusted)	Adjusted Cost (2020)	Source
Caesarean Section	$256.70	USD	2010	1	$256.70	96.111	113.626	$303.48	Alkire et al. 2015
Instrumental Delivery[a]	$28,800	Nigerian Naira	2011	--	--	--	--	$177.36	Adamu et al. 2013
Hemorrhage	$1,107	Malawian Kwacha	1998	35.2	$81.51	75.283	113.626	$123.02	Levin et al. 2003
Hysterectomy[b]	$34,432	South African Rand	2013	5.296	$6,501.51	101.755	113.626	$584.48	Lorenzoni et al. 2015
Fistula repair	$378	USD	2016	1	$378.04	105.722	113.626	$406.30	Epiu et al. 2018
Sepsis (acute)	$934.50	Ghanaian Cedi	2019	2.037	$458.76	112.265	113.626	$464.32	Fenny et al. 2020
Sepsis (long-term)[c]	--	--	--	--	--	--	--	$239.11	Farrah et al. 2020
Surgical site infection	$483	USD	2017	1	$483	107.71	113.626	$509.53	Silverstein et al. 2016, Monahan et al. 2020
Uterine rupture[d]	$10,086.00	Saudi Riyal	2020	--	--	--	--	$510.14	Alsuwaidan et al. 2020
Current healthcare expenditure per capita (SADC)	$44	USD	2008	1	$44	94.285	113.626	$53.03	Taskforce on Innovative International Financing for Health Systems
Neonatal Intensive Care	$522.59	Ghanaian Cedi	2016	1.544	$338.46	105.722	113.626	$363.77	Enweronu-Laryea et al. 2018
Current healthcare expenditure per capita (SADC)	$44	USD	2008	1	$44	94.285	113.626	$53.03	Taskforce on Innovative International Financing for Health Systems

a = Estimated, cost of caesarean section was $28,800 Nigerian Naira in Nigeria (Adamu and colleagues)
b = Estimated, cost of caesarean section was estimated to be $3,200 USD in South Africa
c = Estimated, cost of sepsis in year 1 and 2 were $65,682 and $33,824 CAD respectively (Farrah and colleagues)
d = Estimated, cost of caesarean section was estimated to be $6,000 Saudi Riyal

Appendix G Probabilities

G.1 Treatment Proportions for Existing Care and Increased Access to Caesarean Section

In the existing coverage arm, the proportion of women in neglected obstructed labour is derived from Demographic Health Surveys data for health facility deliveries in SSA and WHO estimates.[12,25] The estimated incidence of obstructed labour is 6.0 per 100 live births. The proportion of deliveries in health facilities (33 per 100 live births) was used as a proxy measure for the incidence of neglected obstructed labour, which was estimated to be 4.0 per 100 live births (or two-thirds of women in obstructed labour).[12] The proportion of women receiving caesarean section or instrumental delivery is based on a WHO estimate of 90% undergoing caesarean section and 10% undergoing instrumental delivery if receiving treatment for obstructed labour.[12] The 'existing care' strategy is therefore defined as 66.67% of women remaining in prolonged obstructed labour, 30% accessing caesarean section, and 3.33% receiving instrumental delivery.

The target coverage level was based on the 68th WHA resolutions and Lancet Commission on Global Surgery 2030 goals to provide a minimum of 80% coverage of essential surgical and anesthesia services per country by 2030.[2,6] The 'increased access to caesarean section' strategy is defined as 80% of women receiving caesarean section, a proportional two-thirds of the remainder unable to access care and experiencing neglected obstructed labour based on previous facility access estimates (13.3%), and 6.7% undergoing instrumental delivery.[2,6,25]

G2 Details and Assumptions for Probabilities

Appendix G2.1 Details and Assumptions for Short-Term Probabilities

	Parameter	Details and Assumptions	Preference Order	Source[a]
Caesarean Section and Instrumental Delivery	Sepsis	Retrospective observational study examining patients with puerperal sepsis admitted to Ife State Hospital (ISH) in Nigeria between January 1986 to December 1995. Country-specific estimates from Nigeria were assumed to be applicable to the SADC region and representative of caesarean section and instrumental delivery.	Country-specific in Sub-Saharan Africa (4)	Dare et al. 1998
	Hemorrhage	Prospective population-based observational study examining maternal, fetal, and neonatal outcomes following prolonged labour, obstructed labour, and failure to progress in LMICs. Data was collected from Argentina, Guatemala, India, Kenya, Pakistan, and Zambia between January 1, 2010 to December 31, 2013. Data was taken from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) using the Maternal and Newborn Health Registry (MNHR). Estimates specific to Africa stratified by delivery mode were unavailable so we elected to use LMIC-specific estimates that differed by instrumental and caesarean section.	Low-and middle-income countries (5)	Harrison et al. 2015
	Hysterectomy	Cross-sectional survey nested in a randomized cluster trial (QUARITE) examining maternal and perinatal outcomes by delivery mode in Senegal and Mali between January 10, 2007 and January 10, 2008. Estimates stratified by delivery mode were available and assumed to be representative of the SADC region.	Country-specific in Sub-Saharan Africa (4)	Briand et al. 2012
	Maternal Death	See above assumptions for "hemorrhage"	Low-and middle-income countries (5)	Harrison et al. 2015
Caesarean Section	Surgical site infection	Retrospective observational study examining post-operative surgical site infection after caesarean section in three LMIC countries. Analyses used data from four emergency obstetric programs supported by Médecins Sans Frontières (Burundi, Democratic Republic of Congo, and Sierra Leone) between August 1, 2010 to January 31, 2011.	Country-specific in the SADC region (3) and Sub-Saharan Africa (4)	Chu et al. 2015
	Uterine rupture	Retrospective population-basd cohort study of all women in Canada (excluding Quebec and Manitoba) giving birth between April 1991 through March 2005, stratified by delivery mode.	High-income country (6)	Liu et al. 2007

Instrumental Delivery	Surgical site infection	Retrospective secondary analysis of data from the Caesarean Registry from the NICHD on maternal and neonatal outcomes stratified by delivery mode between 2008 and 2011. Endometritis after operative vaginal delivery was assumed to be representative of postpartum infection (or surgical site infection). Data following caesarean section were comparable to estimates sourced from SSA (see Chu and colleagues above).	High-income country (6)	Son et al. 2017
	Uterine rupture	Cross-sectional study examining maternal and fetal outcomes of uterine rupture conducted in Northwest Ethiopia in December 2015. Data was assumed to be representative of instrumental delivery although a proportion were assisted by caesarean sections (17.4%).	Country-specific in Sub-Saharan Africa (4)	Astatikie et al. 2017
Prolonged Obstructed Labour	Sepsis	Cross-sectional clinician survey and epidemiological modelling study of burden of disease related to prolonged obstructed labour comorbidities in Asia and Africa in November and December 2018. 83.1% of clinician respondents worked primarily in sub-Saharan Africa	Sub-Saharan Africa (2), includes some Asian countries (5)	Roa et al. 2020
	Hemorrhage	Mathematical model (MANDATE) evaluating interventions to reduce maternal mortality from prolonged labour, obstructed labour, and prolonged obstructed labour in Sub-Saharan Africa. Estimate for hemorrhage incorporated published literature and expert opinion.	Sub-Saharan Africa (2)	Harrison et al. 2016
	Surgical site infection	See above assumptions for "sepsis"	Sub-Saharan Africa (2), includes some Asian countries (5)	Roa et al. 2020
	Uterine rupture	Systematic review and meta-analysis examining incidence, causes, and maternofetal outcomes of obstructed labour in Ethiopia. Pooled estimate from 16 primary studies with 28,591 mothers giving birth. Estimates from Ethiopia were assumed to be applicable to the SADC region due to lack of data.	Country-specific in Sub-Saharan Africa (4)	Ayenew et al. 2021
	Uterine prolapse	See above assumptions for "sepsis"	Sub-Saharan Africa (2), includes some Asian countries (5)	Roa et al. 2020
	Obstetric fistula	WHO descriptive study on burden of disease related to obstructed labour and sequelae, stratified by WHO region. The incidence rate of obstetric fistula is expressed as the proportion of the neglected obstructed labour cases for SSA	Sub-Saharan Africa (2)	Dolea et al. 2000
	Maternal Death	Retrospective observational study of all deliveries occurring at a district hospital to assess incidence and outcomes of obstructed labour in Ethiopia from September 1990 to May 1999. Estimates from Ethiopia were assumed to be applicable to the SADC region due to lack of data.	Country-specific in Sub-Saharan Africa (4)	Gaym et al. 2002

Appendix G2.2 Details and Assumptions for Long-Term Probabilities

Parameter	**Details and Assumptions**	**Preference Order**	**Source**
Rectovaginal fistula	Retrospective review of patients (716) treated for vesicovaginal and rectovaginal fistulae in Africa (578) at Addis Ababa Fistula Hospital and Britain (138 patients). It was assumed that patients did not experience direct mortality due to obstetric fistula and that estimates from Ethiopia were representative of the SADC region due to lack of data.	Country-specific in Sub-Saharan Africa (4)	Kelly et al. 1998
Vesicovaginal fistula	See above assumptions for "rectovaginal fistula"	Country-specific in Sub-Saharan Africa (4)	Kelly et al. 1998
Repair	Retrospective secondary analysis using 16 national Demographic and Health Surveys in SSA between 2010 and 2017 to describe health-seeking behaviour of women with obstetric fistula in SSA. Estimates from Zambia were assumed to be applicable to the SADC region due to lack of data.	Sub-Saharan Africa (2)	Gebremedhin et al. 2019
Surgical success	Retrospective review of patients receiving treatment for obstetric fistula at the Monze Mission Hospital in Zambia between August 2003 and December 2005.	Country-specific in the SADC region (3)	Holme et al. 2007
Surgical failure	See above assumptions for "surgical success"	Country-specific in the SADC region (3)	Holme et al. 2007
Stress Incontinence	See above assumptions for "surgical success"	Country-specific in the SADC region (3)	Holme et al. 2007

Appendix G2.3 Probabilities of Neonatal Events Following Obstructed Labour

	Parameter	Details and Assumptions	Preference Order	Source
Caesarean Section and Instrumental Delivery	Stillbirths	Prospective population-based observational study examining maternal, fetal, and neonatal outcomes following prolonged labour, obstructed labour, and failure to progress in LMICs. Data was collected from Argentina, Guatemala, India, Kenya, Pakistan, and Zambia between January 1, 2010 to December 31, 2013. Data was taken from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) using the Maternal and Newborn Health Registry (MNHR). Estimates specific to Africa stratified by delivery mode were unavailable so we elected to use LMIC-specific estimates that differed by instrumental and caesarean section.	Low-and middle-income countries (5)	Harrison et al. 2015
	Neonatal mortality in NICU	Retrospective descriptive review of neonatal admissions and outcomes at Empangeni Hospital in South Africa between January and December 2005. Estimates for mortality were stratified by mode of delivery and assumed to be applicable to the SADC region due to lack of data.	Country-specific in the SADC region (3)	Hoque et al. 2011
	NICU Admission	A descriptive review of neonatal intensive care unit admissions stratified by cause for admission over a six-month period at the Volta Regional Hospital in Ethiopia from September 2016 to March 2017. Estimates from Ghana were assumed to be applicable to the SADC region due to lack of data.	Country-specific in Sub-Saharan Africa (4)	Amegan-Aho et al. 2018
Prolonged Obstructed Labour	Stillbirths	Systematic review and meta-analysis examining incidence, causes, and maternofetal outcomes of obstructed labour in Ethiopia. Pooled estimate from 16 primary studies with 28,591 mothers giving birth. Estimates from Ethiopia were assumed to be applicable to the SADC region due to lack of data.	Country-specific in Sub-Saharan Africa (4)	Ayenew et al. 2021
	Intrapartum hypoxia	Cross-sectional clinician survey and epidemiological modelling study of burden of disease related to prolonged obstructed labour comorbidities in Asia and Africa in November and December 2018. 83.1% of clinician respondents worked primarily in sub-Saharan Africa	Sub-Saharan Africa (2), includes some Asian countries (5)	Roa et al, 2020
	Hypoxic-ischemic encephalopathy (HIE)	Systematic review and meta-analysis examining infants with intrapartum hypoxia-ischemia and related outcomes in the USA. Pooled estimates were assumed to be applicable to the SADC region due to lack of data.	High-income country (6)	Graham et al. 2008

Appendix G2.4 Probabilities of Maternal Mortality Following Obstructed Labour

	Parameter	Details and Assumptions	Preference Order	Source
Hospital (Caesarean Section and Instrumental Delivery)	Sepsis	Multicentre, prospective population-based study to measure incidence of maternal morbidity in West Africa (December 1994 to June 1996) mainly in Burkina Faso, Côte d'Ivoire, Mali, Mauritania, Niger, and Senegal. Case fatality rates stratified by delivery mode were unavailable, so it was assumed that case fatality after a woman develops the condition (e.g. sepsis) is the same across caesarean section and instrumental delivery since they are able to reach a hospital. It was assumed that these estimates were applicable to the SADC region due to lack of data.	Sub-Saharan Africa (2), country-specific in Sub-Saharan Africa (4)	Prual et al. 2000
	Hemorrhage	See above assumptions for "sepsis"	Sub-Saharan Africa (2), country-specific in Sub-Saharan Africa (4)	Prual et al. 2000
	Surgical site infection	Retrospective observational study examining post-operative surgical site infection after caesarean section in three LMIC countries. Analyses used data from four emergency obstetric programs supported by Médecins Sans Frontières (Burundi, Democratic Republic of Congo, and Sierra Leone) between August 1, 2010 to January 31, 2011.	Country-specific in the SADC region (3) and Sub-Saharan Africa (4)	Chu et al. 2015
	Uterine rupture	See above assumptions for "sepsis"	Sub-Saharan Africa (2), country-specific in Sub-Saharan Africa (4)	Prual et al. 2000
	Hysterectomy	Retrospective secondary analysis using data from the WOMAN trial carried out in 21 countries. Death rate among hysterectomy cases was calculated specific to Africa and assumed to be representative of the SADC region overall.	Sub-Saharan Africa (2)	Huque et al. 2018
No Hospital (Prolonged Obstructed Labour)	*Sepsis*	Mathematical model (MANDATE) evaluating interventions to reduce maternal mortality from prolonged labour, obstructed labour, and prolonged obstructed labour in Sub-Saharan Africa. The mortality from uterine rupture estimated for caesarean and instrumental delivery (in-hospital) was calculated against that of prolonged obstructed labour (no hospital) as a proportion and applied to the in-hospital estimate of mortality from sepsis. This was assumed to be applicable to the SADC region due to lack of data.	Sub-Saharan Africa (2), assumptions (7)	Prual et al. 2000, Harrison et al. 2016
	Hemorrhage	See above for information on the MANDATE model. Estimate was for postpartum hemorrhage and incorporated published literature and expert opinion.	Sub-Saharan Africa (2)	Harrison et al. 2016
	Surgical site infection	See above for information on the MANDATE model. Estimate incorporated published literature and expert opinion.	Sub-Saharan Africa (2)	Harrison et al. 2016
	Uterine rupture	See above for information on the MANDATE model. Estimate incorporated published literature and expert opinion.	Sub-Saharan Africa (2)	Harrison et al. 2016

Appendix H Disability Weight Modifications

Methodology for Calculating Disability Weight for Acute Sepsis

To estimate utility when information was unavailable, the following methodology was used:

i) Calculate proportions between the disability weights of various health states

$$Proportion = \frac{DW\ of\ hemorrhage\ (SSA)}{DW\ of\ hemorrhage\ (Korea)}$$

$$Proportion = \frac{0.324}{0.514} = 0.6304$$

ii) Repeat for obstructed labour and genital prolapse and average the proportions.

iii) Apply the proportion to the disability weight of maternal sepsis from the KBD 2015[112]

$$Disability\ weight\ sepsis = DW\ of\ sepsis\ (Korea) \times\ average\ proportion\ (between\ GBD\ 2019\ and\ KBD\ 2015)$$

$$Disability\ weight\ sepsis = 0.749\ \times\ 0.666 = 0.499$$

Table H.1 Details and Assumptions for Disability Weights

	Health Condition or State	Details and Assumptions	Preference Order	Reference
Short-Term In-Hospital and In-Community Maternal Outcomes	Caesarean Section	Disability weight for undergoing caesarean section.	Sub-Saharan Africa (2)	GBD 1990
	Instrumental Delivery	Disability weight estimated for instrumental delivery through expert opinion, using disability weights for caesarean section, uterine prolapse, hysterectomy, and uterine rupture as benchmarks for severity of condition.	Assumptions (7)	Estimate
	Obstructed Labour	Disability weight for experiencing obstructed labour (acute event).	Sub-Saharan Africa (2)	GBD 2019
	Sepsis (acute)	Disability weight for experiencing acute sepsis, estimated using proportion of GBD 2019 to KBD 2015 disability weights and applied to the KBD 2015 disability weight of experiencing sepsis (see above for sample calculation).	High-income country (6), assumption (7)	KBD 2015, Estimate
	Hemorrhage	Disability weight for experiencing maternal hemorrhage (> 1L blood lost).	Sub-Saharan Africa (2)	GBD 2019
	Surgical site infection	Disability weight for experiencing infectious disease (acute episode, moderate).	Sub-Saharan Africa (2)	GBD 2019
	Uterine prolapse	Disability weight for experiencing uterine prolapse, assumed to be applicable based on comparison of other health state disability weights as benchmark comparisons to the GBD 2019 values.	High-income country (6)	KBD 2015
	Uterine rupture	Disability weight for uterine rupture taken from an economic evaluation of trial of labour after caesarean section in the United States. The original study used disutility, which was assumed to be efficient to estimate disability weight in our analyses. Original disutility was calculated using the Quality of Well-Being classification system.	High-income country (6)	Gilbert et al. 2013, Chung et al. 2001
	Hysterectomy	Disability weight for undergoing hysterectomy following uterine rupture. Value was estimated by associating the relevant health state lay description "severe pain in belly, unable to carry out daily activities" from the GBD 2019 study.	Sub-Saharan Africa (2), assumptions (7)	GBD 2019

Long-Term Maternal Outcomes	Stress incontinence	Disability weight of experiencing stress incontinence (long-term)	Sub-Saharan Africa (2)	GBD 1990
	Rectovaginal fistula	Disability weight for living with rectovaginal fistula. If women experienced both rectovaginal fistula and vesicovaginal fistula, the more severe disability weight associated with rectovaginal fistula was applied.	Sub-Saharan Africa (2)	GBD 2019
	Vesicovaginal fistula	Disability weight for living with vesicovaginal fistula.	Sub-Saharan Africa (2)	GBD 2019
	Sepsis (long-term)	Disability weight for experiencing puerperal sepsis. It was assumed that this lower estimate was applicable to long-term sepsis through expert opinion. See above for acute sepsis estimates.	Sub-Saharan Africa (2)	GBD 2019
Long-Term Neonatal Outcomes	Hypoxic-ischemic encephalopathy (neonatal)	Applied proportionally to the those who experience birth asphyxiation	Sub-Saharan Africa (2)	GBD 2019
	Full Health	Disability weight of returning to full health was assumed to be 0.01 due to lack of estimates of baseline disability weights for women living in the SADC region. It is likely that the baseline disability is higher but lack of accurate information exists in current literature.	Assumptions (7)	Estimate
Abbreviations: GBD, Global Burden of Disease Study; KBD, Korean Burden of Disease Study.				

Appendix I Probabilistic Sensitivity Analysis for the Maternal Model

I.1 Methodology for Probabilistic Sensitivity Analyses

For the probabilistic sensitivity analysis (PSA), distributions were used in calculations depending on the type of parameter. Beta distributions were used for parameter values bound between 0 and 1, such as utilities and probabilities.[143] Dirichlet distributions were used in the case of health states leading to multiple outcomes such as short-term outcomes following neglected obstructed labour (i.e. sepsis, hemorrhage, surgical site infection, uterine rupture, uterine prolapse, survival, or death) or outcomes following repair surgery for obstetric fistula (i.e. surgery success, failure, or remaining in stress incontinence). Uncertainty surrounding costs was accounted for using gamma distributions, bound between 0 and infinity and ideal for skewed data.[143] Results were calculated across 10,000 iterations to examine stability of the base case results.

Distributions for probabilities were calculated by inputting sample size integer parameters from sourced literature on TreeAge Healthcare Pro 2021 where possible (e.g. total number of women receiving caesarean section and those that developed hemorrhage from that cohort). If sample size and number of events was unavailable, a lower and upper limit of $\pm 10\%$ was applied to calculate alpha and beta values. See Appendix G2 for information regarding literature sources and assumptions.

Distributions for utility used upper and lower limits (95% confidence intervals) from their original source (i.e. Global Burden of Disease 2019 study, Korean Burden of Disease 2015 study, Chung and colleagues, or Gilbert and colleagues).[7,112-14] If published 95% confidence intervals were not available, a lower and upper limit of $\pm 10\%$ was applied to calculate alpha and beta values.

Distributions for costs applied the assumption of a lower and upper limit of $\pm 10\%$ to calculate alpha, beta, and lambda values.

All alpha and beta values used in the PSA are presented in tables below.

I.2 Tables for Values Used in Probabilistic Sensitivity Analysis

I.2.1 Probabilities for Maternal Events Following Obstructed Labour

	Parameter	Mean	Distribution	Number of Events	Total Sample Size	Alpha	Beta	Source[a]
Caesarean Section	Sepsis	0.0173	Beta	146	8428	--	--	Dare et al. 1998
	Hemorrhage	0.0104	Beta	161	15459	--	--	Harrison et al. 2015
	Surgical site infection	0.0729	Beta	93	1276	--	--	Chu et al. 2015
	Uterine rupture	0.000150	Beta	7	46766	--	--	Liu et al. 2007
	Hysterectomy	0.00631	Beta	71	11255	--	--	Briand et al. 2012
	Maternal Death	0.00227	Beta	35	15414	--	--	Harrison et al. 2015
Instrumental Delivery	Sepsis	0.0173	Beta	146	8428	--	--	Dare et al. 1998
	Hemorrhage	0.0777	Beta	150	1931	--	--	Harrison et al. 2015
	Surgical site infection	0.0254	Beta	24	945	--	--	Son et al. 2017
	Uterine rupture	0.0245	Beta	254	10379	--	--	Astatikie et al. 2017
	Hysterectomy	0.00	Beta	0	0	--	--	Briand et al. 2012
	Maternal Death	0.00209	Beta	4	1916	--	--	Harrison et al. 2015
Prolonged Obstructed Labour	Sepsis	0.194	Dirichlet	--	--	*73*	*304*	Roa et al. 2020
	Hemorrhage	*0.130*	Dirichlet	--	--	*334*	*2236*	Harrison et al. 2016
	Surgical site infection	0.114	Dirichlet	--	--	*59*	*454*	Roa et al. 2020
	Uterine rupture	0.300	Dirichlet	--	--	*30*	*69*	Ayenew et al. 2021
	Uterine prolapse	0.158	Dirichlet	--	--	*68*	*366*	Roa et al. 2020
	Obstetric fistula	*0.0215*	Beta	--	--	*376*	*17107*	Dolea et al. 2000
	Maternal Death	0.0910	Dirichlet	86	945	--	--	Gaym et al. 2002
	Rectovaginal fistula	0.212	Beta	152	716	--	--	Kelly et al. 1998
	Vesicovaginal fistula	0.788	Beta	564	716	--	--	Kelly et al. 1998
	Repair	0.250	Beta	329	1317	--	--	Gebremedhin et al. 2019
	Surgical success	0.726	Dirichlet	183	252	--	--	Holme et al. 2007
	Surgical failure	0.0992	Dirichlet	25	252	--	--	Holme et al. 2007
	Stress incontinence	0.175	Dirichlet	44	252	--	--	Holme et al. 2007
Italicized parameters used the assumption of +/- 10% of the mean as upper and lower confidence limits								

I.2.2 Probabilities of Neonatal Events Following Obstructed Labour

	Parameter	Mean	Distribution	Number of Events	Total Sample Size	Alpha	Beta	Source
Caesarean Section	Stillbirths	0.0163	Beta	252	15488	--	--	Harrison et al. 2015
	Neonatal mortality in NICU	0.202	Beta	317	1573	--	--	Hoque et al. 2011
	NICU Admission	0.151	Beta	136	900	--	--	Amegan-Aho et al. 2018
Instrumental Delivery	Stillbirths	0.0694	Beta	134	1931	--	--	Harrison et al. 2015
	Neonatal mortality in NICU	0.202	Beta	317	1573	--	--	Hoque et al. 2011
	NICU Admission	0.151	Beta	136	900	--	--	Amegan-Aho et al. 2018
Prolonged Obstructed Labour	Stillbirths	0.386	Beta	--	--	20	32	Ayenew et al. 2021
	Intrapartum hypoxia	0.256	Beta	--	--	77	222	Roa et al. 2020
	Hypoxic-ischemic encephalopathy (HIE)	0.303	Beta	33	109	--	--	Graham et al. 2008
Italicized parameters used the assumption of +/- 10% of the mean as upper and lower confidence limits								

I.2.3 Mortality Following Sequelae due to Obstructed Labour and Distributions for PSA

	Parameter	Mean	Distribution	Number of Events	Total Sample Size	Alpha	Beta	Source
Hospital (Caesarean Section and Instrumental Delivery)	Sepsis	0.333	Beta	6	18	--	--	Prual et al. 2000
	Hemorrhage	0.0322	Beta	11	342	--	--	Prual et al. 2000
	Surgical site infection	0.0551	Beta	22	399	--	--	Chu et al. 2015
	Uterine rupture	0.304	Beta	7	23	--	--	Prual et al. 2000
	Hysterectomy	0.200	Beta	204	1020	--	--	Huque et al. 2018
No Hospital (Prolonged Obstructed Labour)	*Sepsis*	0.493	Beta	--	--	194	200	Prual et al. 2000
	Hemorrhage	*0.250*	Beta	--	--	288	864	Harrison et al. 2016
	Surgical site infection	*0.0500*	Beta	--	--	365	6933	Harrison et al. 2016
	Uterine rupture	*0.450*	Beta	--	--	211	258	Harrison et al. 2016
Italicized parameters used the assumption of +/- 10% of the mean as upper and lower confidence limits								

I.2.4 Disability Weights for Maternal Model and Distributions for PSA

	Parameter	Disability Weight	Distribution	Alpha	Beta	Source
Short-Term In-Hospital and In-Community Maternal Outcomes	*Caesarean Section*	0.349	Beta	250	466	GBD 1990
	*Instrumental Delivery**	0.375	Beta	240	400	Estimate
	Obstructed Labour	0.324	Beta	22	45	GBD 2019
	*Sepsis (acute)**	0.499	Beta	192	193	KBD 2015, Estimate
	Hemorrhage	0.324	Beta	22	45	GBD 2019
	Surgical site infection	0.051	Beta	21	399	GBD 2019
	Uterine prolapse	0.404	Beta	84	124	KBD 2015
	Uterine rupture	0.490	Beta	11	12	Gilbert et al. 2013, Chung et al. 2001
	Hysterectomy*	0.324	Beta	22	45	GBD 2019
Long-Term Maternal Outcomes	*Stress incontinence*	0.0250	Beta	375	14607	GBD 1990
	Rectovaginal fistula	0.501	Beta	19	18	GBD 2019
	Vesicovaginal fistula	0.342	Beta	18	35	GBD 2019
	Sepsis (long-term)	0.133	Beta	23	147	GBD 2019
	Full Health	0.0100	Beta	38032	3765151	Estimate
Long-Term Neonatal Outcomes	Hypoxic-Ischemic Encephalopathy	0.351	Beta	25	56	GBD 2019
	Full Health	0.0100	Beta	38032	3765151	Estimate

* = Estimated disability weights (see Appendix F for calculation methods and assumptions)
Italicized parameters use the assumption of +/- 10% of the mean as upper and lower confidence limits

I.2.5 Costs Related to Interventions and Sequelae for Obstructed Labour

Parameter	Mean	Distribution	Alpha	Beta	Source
Caesarean Section	$303.48	Gamma	384	0.79	Alkire et al. 2015
Instrumental Delivery	$177.36	Gamma	384	0.46	Adamu et al. 2013
Hemorrhage	$123.02	Gamma	384	0.32	Levin et al. 2003
Hysterectomy	$584.48	Gamma	384	1.52	Lorenzoni et al. 2015
Fistula repair	$406.30	Gamma	384	1.06	Epiu et al. 2018
Sepsis (acute)	$464.32	Gamma	384	1.21	Fenny et al. 2020
Sepsis (long-term)	$239.11	Gamma	384	0.62	Farrah et al. 2020
Surgical site infection	$509.53	Gamma	384	1.33	Silverstein et al. 2016, Monahan et al. 2020
Uterine rupture	$510.14	Gamma	384	1.33	Alsuwaidan et al. 2020
Current healthcare expenditure per capita (SADC)	$53.03	Gamma	384	0.14	Taskforce on Innovative International Financing for Health Systems
Neonatal Intensive Care	$363.77	Gamma	384	0.95	Enweronu-Laryea et al. 2018
Current healthcare expenditure per capita (SADC)	$53.03	Gamma	384	0.14	Taskforce on Innovative International Financing for Health Systems
All cost parameters used the assumption of +/- 10% of the mean as upper and lower confidence limits					

I.3 Acceptability values at willingness-to-pay from the PSA

I.3.1 Maternal Model Acceptability at WTP

Willingness-to-pay ($)	Acceptability
0	0
28.7	0
57.4	0.6938
86.1	0.8809
114.8	0.946
143.5	0.999
172.2	1

Acceptability is defined as the probability of the ‘increased access to caesarean section’ strategy being cost-effective

I.3.2 Neonatal Model Acceptability at WTP

Willingness-to-pay ($)	Acceptability
16.25	0
19.5	0.0001
22.75	0.1095
26	0.9316
29.25	0.9997
32.5	1

Acceptability is defined as the probability of the ‘increased access to caesarean section’ strategy being cost-effective

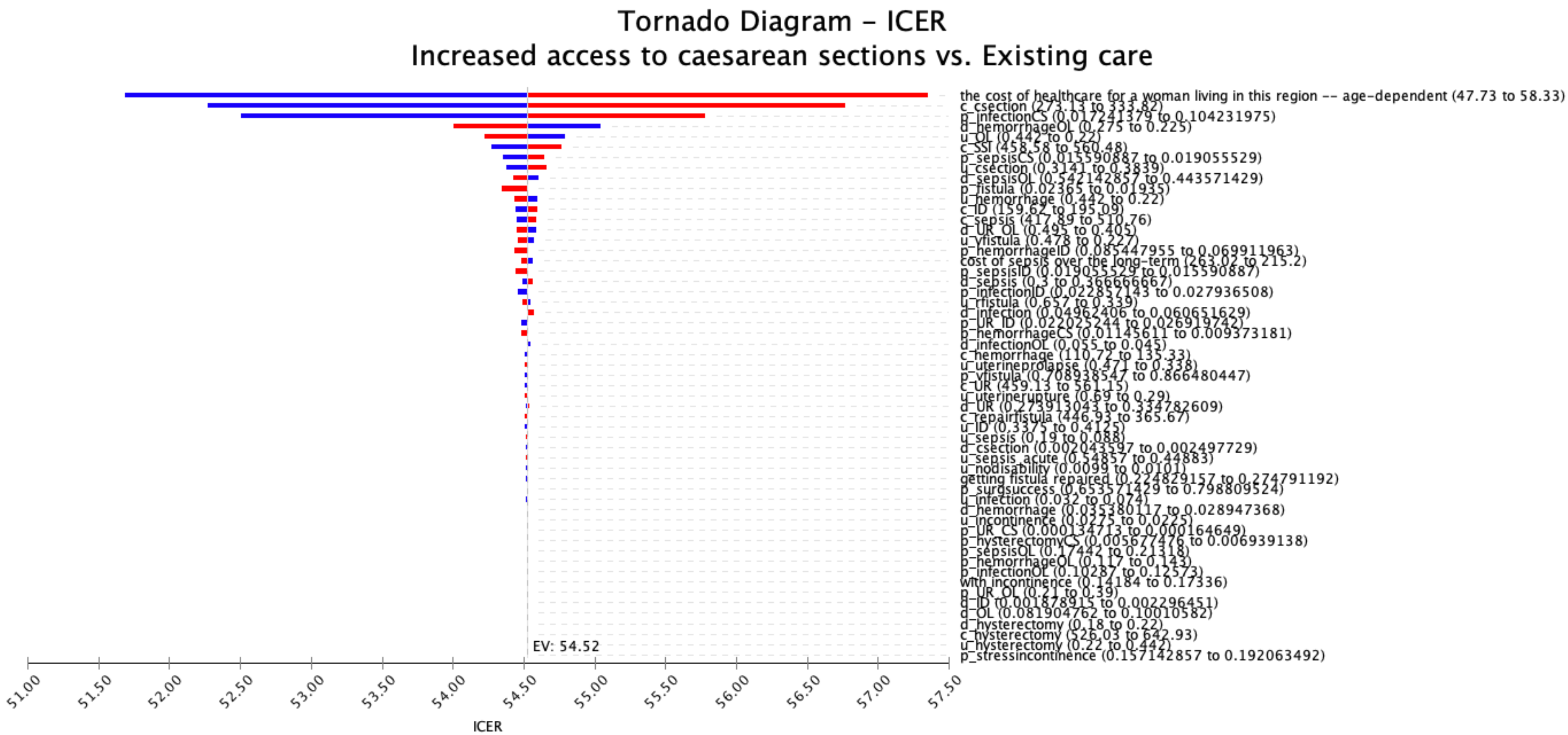
Appendix J One-Way Sensitivity Analyses

J.1 Methodology for One-Way Sensitivity Analyses

One-way sensitivity analyses were calculated across model parameters to assess how changes in a parameter affect the cost-utility estimates. Results were presented in tornado diagrams that show the impact (increase or decrease) as well as the range in ICER values.[143] The range in parameters were taken from published 95% confidence intervals from the source literature. When published values were not available, a lower and upper limit of $\pm 10\%$ was applied. Supplementary tornado diagrams and outputs for the maternal model (all parameters, costs, disability weights, and mortality) and outputs for the neonatal model (all parameters) are presented below.

J.2 Tornado Diagrams and Outputs for Maternal Outcomes

J.2.1 Tornado Diagram (All Variables)

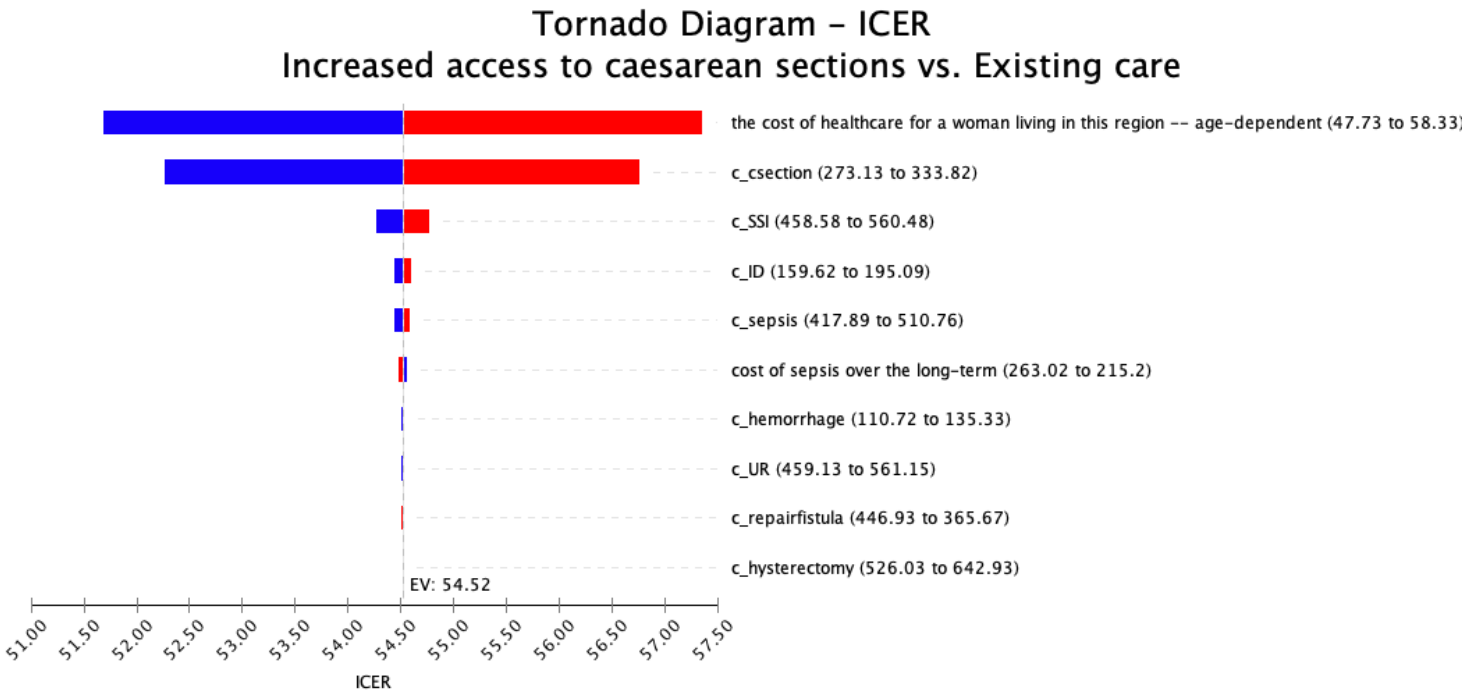


J.2.2 Tornado Diagram Outputs (All Variables)

Variable Name	Variable Low	Variable Base	Variable High	Impact	Low	High	Spread	Spread2	Risk %	Cumulative Risk %
c_health_woman	47.73	53.03	58.33	Increase	51.68925	57.35303	5.66378	32.07843	0.494	0.494
c_csection	273.13	303.48	333.82	Increase	52.27548	56.76605	4.49058	20.16528	0.31	0.804
p_infectionCS	0.01724	0.07288	0.10423	Increase	52.50818	55.78007	3.27189	10.70525	0.165	0.969
d_hemorrhageOL	0.225	0.25	0.275	Decrease	54.00231	55.04327	1.04096	1.0836	0.017	0.986
u_OL	0.22	0.324	0.442	Decrease	54.22099	54.78844	0.56745	0.322	0.005	0.991
c_SSI	458.58	509.53	560.48	Increase	54.27443	54.76784	0.49341	0.24346	0.004	0.994
p_sepsisCS	0.01559	0.01732	0.01906	Increase	54.35708	54.64274	0.28566	0.0816	0.001	0.996
u_csection	0.3141	0.349	0.3839	Increase	54.38241	54.66058	0.27817	0.07738	0.001	0.997
d_sepsisOL	0.44357	0.49286	0.54214	Decrease	54.4314	54.60977	0.17838	0.03182	0	0.997
p_fistula	0.01935	0.0215	0.02365	Decrease	54.34717	54.52114	0.17397	0.03026	0	0.998
u_hemorrhage	0.22	0.324	0.442	Decrease	54.43158	54.60031	0.16874	0.02847	0	0.998
c_ID	159.62	177.36	195.09	Increase	54.4424	54.59983	0.15744	0.02479	0	0.998
c_sepsis	417.89	464.32	510.76	Increase	54.44897	54.59332	0.14434	0.02084	0	0.999
d_UR_OL	0.405	0.45	0.495	Decrease	54.45263	54.5878	0.13517	0.01827	0	0.999
u_vfistula	0.227	0.342	0.478	Decrease	54.4559	54.57643	0.12053	0.01453	0	0.999
p_hemorrhageID	0.06991	0.07768	0.08545	Decrease	54.43239	54.52114	0.08875	0.00788	0	0.999
c_sepsis_longterm	215.2	239.11	263.02	Decrease	54.48015	54.56212	0.08197	0.00672	0	1
p_sepsisID	0.01559	0.01732	0.01906	Decrease	54.44568	54.52427	0.07859	0.00618	0	1
d_sepsis	0.3	0.33333	0.36667	Increase	54.49282	54.56899	0.07617	0.0058	0	1
p_infectionID	0.02286	0.0254	0.02794	Increase	54.45911	54.52114	0.06202	0.00385	0	1
u_rfistula	0.339	0.501	0.657	Decrease	54.49105	54.55242	0.06137	0.00377	0	1
d_infection	0.04962	0.05	0.06065	Increase	54.52114	54.57456	0.05342	0.00285	0	1
p_UR_ID	0.02203	0.02447	0.02692	Increase	54.48712	54.52831	0.04118	0.0017	0	1
p_hemorrhageCS	0.00937	0.01041	0.01146	Decrease	54.48095	54.52114	0.04019	0.00162	0	1
d_infectionOL	0.045	0.05514	0.055	Decrease	54.52114	54.55231	0.03117	0.00097	0	1
c_hemorrhage	110.72	123.02	135.33	Increase	54.50698	54.5353	0.02832	0.0008	0	1

u_uterineprolapse	0.338	0.404	0.471	Decrease	54.50782	54.53426	0.02644	0.0007	0	1
p_vfistula	0.70894	0.7877	0.86648	Increase	54.50981	54.53364	0.02383	0.00057	0	1
c_UR	459.13	510.14	561.15	Increase	54.5097	54.53257	0.02287	0.00052	0	1
u_uterinerupture	0.29	0.49	0.69	Decrease	54.51152	54.53075	0.01923	0.00037	0	1
d_UR	0.27391	0.30435	0.33478	Increase	54.51915	54.53792	0.01877	0.00035	0	1
c_repairfistula	365.67	406.3	446.93	Decrease	54.51203	54.53024	0.01822	0.00033	0	1
u_ID	0.3375	0.375	0.4125	Increase	54.51231	54.52997	0.01766	0.00031	0	1
u_sepsis	0.088	0.133	0.19	Decrease	54.51581	54.52534	0.00953	0.00009	0	1
d_csection	0.00204	0.00227	0.0025	Increase	54.51274	54.52114	0.0084	0.00007	0	1
u_sepsis_acute	0.44883	0.4987	0.54857	Decrease	54.51793	54.52435	0.00642	0.00004	0	1
u_nodisability	0.0099	0.01	0.0101	Increase	54.51815	54.52413	0.00598	0.00004	0	1
p_repair	0.22483	0.24981	0.27479	Increase	54.51632	54.52114	0.00482	0.00002	0	1
p_surgsuccess	0.65357	0.72619	0.79881	Increase	54.52114	54.52531	0.00417	0.00002	0	1
u_infection	0.032	0.051	0.074	Increase	54.51993	54.5226	0.00267	0.00001	0	1
d_hemorrhage	0.02895	0.03216	0.03538	Decrease	54.52114	54.52204	0.0009	0	0	1
u_incontinence	0.0225	0.025	0.0275	Decrease	54.52111	54.52117	0.00006	0	0	1
p_UR_CS	0.00013	0.00015	0.00016	Increase	54.52114	54.52114	0	0	0	1
p_hysterectomyCS	0.00568	0.00631	0.00694	Increase	54.52114	54.52114	0	0	0	1
p_sepsisOL	0.17442	0.1938	0.21318	Increase	54.52114	54.52114	0	0	0	1
p_hemorrhageOL	0.117	0.13	0.143	Increase	54.52114	54.52114	0	0	0	1
p_infectionOL	0.10287	0.1143	0.12573	Increase	54.52114	54.52114	0	0	0	1
p_UP_OL	0.14184	0.1576	0.17336	Increase	54.52114	54.52114	0	0	0	1
p_UR_OL	0.21	0.3	0.39	Increase	54.52114	54.52114	0	0	0	1
d_ID	0.00188	0.00209	0.0023	Increase	54.52114	54.52114	0	0	0	1
d_OL	0.0819	0.09101	0.10011	Increase	54.52114	54.52114	0	0	0	1
d_hysterectomy	0.18	0.2	0.22	Increase	54.52114	54.52114	0	0	0	1
c_hysterectomy	526.03	584.47795	642.93	Increase	54.52114	54.52114	0	0	0	1
u_hysterectomy	0.22	0.324	0.442	Increase	54.52114	54.52114	0	0	0	1
p_stressincontinence	0.15714	0.1746	0.19206	Increase	54.52114	54.52114	0	0	0	1

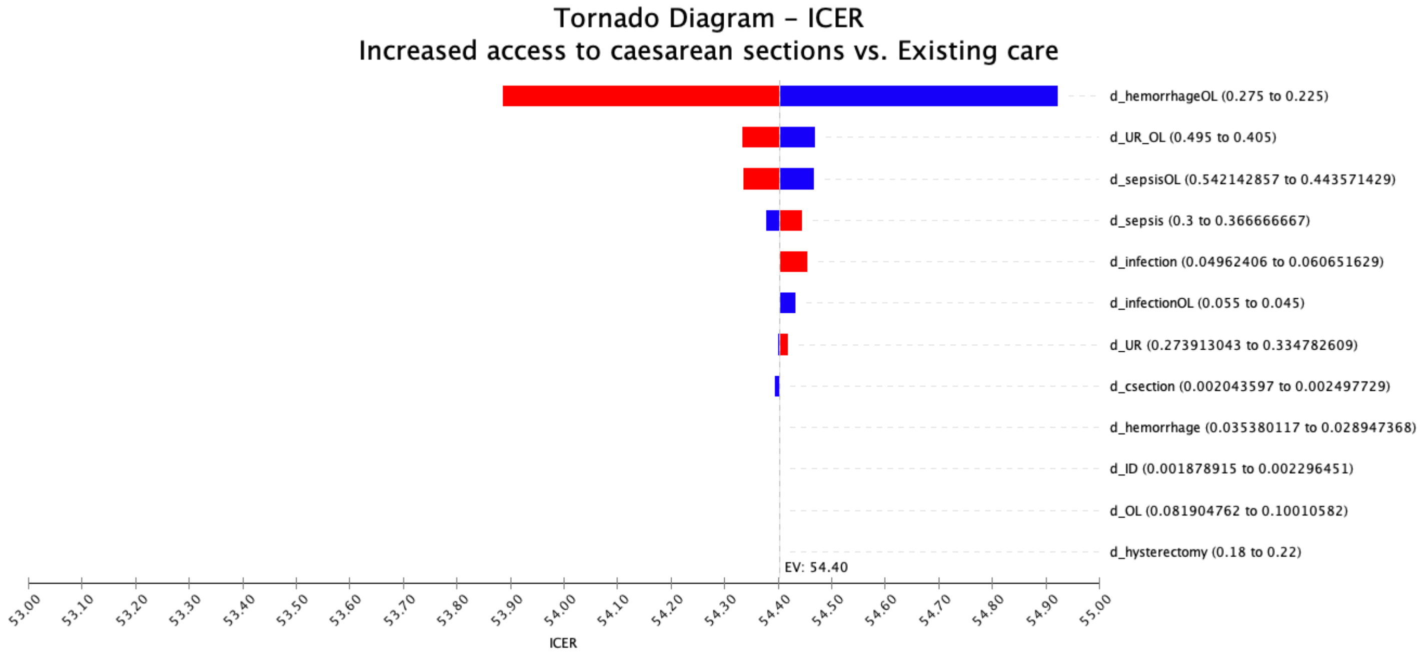
J.2.3 Tornado Diagram for Costs Related to Maternal Outcomes



J.2.4 Tornado Diagram Outputs for Costs Related to Maternal Outcomes

Variable Name	Variable Low	Variable Base	Variable High	Impact	Low	High	Spread	Spread2	Risk %	Cumulative Risk %
c_health_woman	47.73	53.03	58.33	Increase	51.68925	57.35303	5.66378	32.07843	0.611	0.611
c_csection	273.13	303.48	333.82	Increase	52.27548	56.76605	4.49058	20.16528	0.384	0.994
c_SSI	458.58	509.53	560.48	Increase	54.27443	54.76784	0.49341	0.24346	0.005	0.999
c_ID	159.62	177.36	195.09	Increase	54.4424	54.59983	0.15744	0.02479	0	0.999
c_sepsis	417.89	464.32	510.76	Increase	54.44897	54.59332	0.14434	0.02084	0	1
c_sepsis_longterm	215.2	239.11	263.02	Decrease	54.48015	54.56212	0.08197	0.00672	0	1
c_hemorrhage	110.72	123.02	135.33	Increase	54.50698	54.5353	0.02832	0.0008	0	1
c_UR	459.13	510.14	561.15	Increase	54.5097	54.53257	0.02287	0.00052	0	1
c_repairfistula	365.67	406.3	446.93	Decrease	54.51203	54.53024	0.01822	0.00033	0	1
c_hysterectomy	526.03	584.47795	642.93	Increase	54.52114	54.52114	0	0	0	1

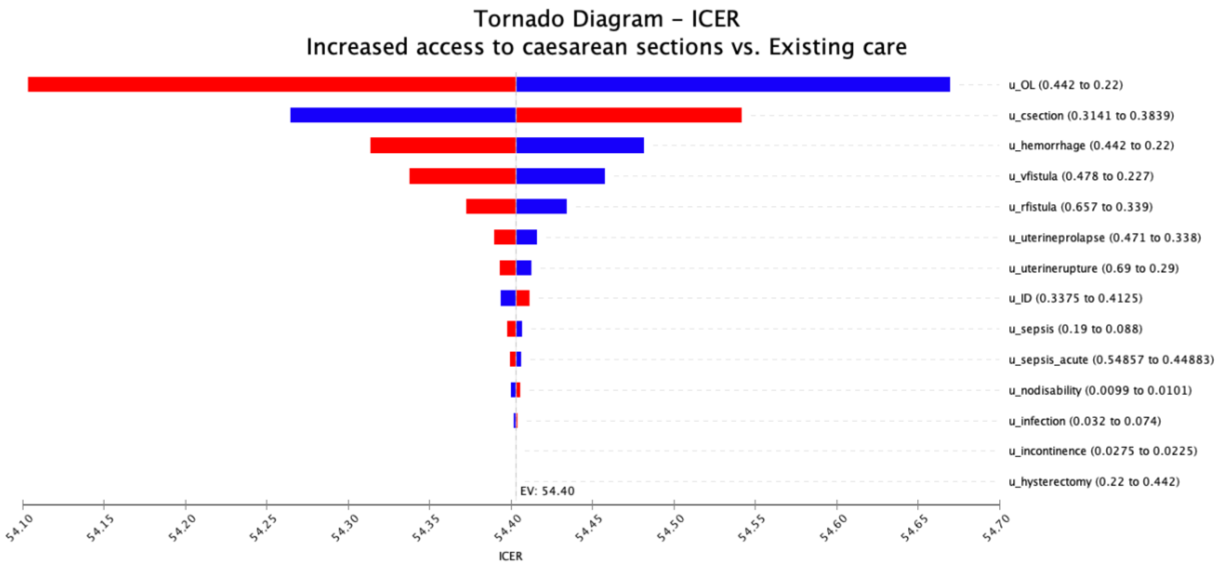
J.2.5 Tornado Diagram for Maternal Mortality due to Obstructed Labour Sequelae



J.2.6 Tornado Diagram Outputs for Maternal Mortality due to Obstructed Labour Sequelae

Variable Name	Variable Low	Variable Base	Variable High	Impact	Low	High	Spread	Spread2	Risk %	Cumulative Risk %
d_hemorrhageOL	0.225	0.25	0.275	Decrease	53.88624	54.92288	1.03665	1.07464	0.961	0.961
d_UR_OL	0.405	0.45	0.495	Decrease	54.33458	54.46922	0.13464	0.01813	0.016	0.977
d_sepsisOL	0.44357	0.49286	0.54214	Decrease	54.33652	54.46825	0.13173	0.01735	0.016	0.992
d_sepsis	0.3	0.33333	0.36667	Increase	54.3793	54.44598	0.06668	0.00445	0.004	0.996
d_infection	0.04962	0.05	0.06065	Increase	54.40286	54.45599	0.05314	0.00282	0.003	0.999
d_infectionOL	0.045	0.05514	0.055	Decrease	54.40286	54.43386	0.031	0.00096	0.001	1
d_UR	0.27391	0.30435	0.33478	Increase	54.40088	54.41957	0.01869	0.00035	0	1
d_csection	0.00204	0.00227	0.0025	Increase	54.39451	54.40286	0.00835	0.00007	0	1
d_hemorrhage	0.02895	0.03216	0.03538	Decrease	54.40286	54.4038	0.00094	0	0	1
d_ID	0.00188	0.00209	0.0023	Increase	54.40286	54.40286	0	0	0	1
d_OL	0.0819	0.09101	0.10011	Increase	54.40286	54.40286	0	0	0	1
d_hysterectomy	0.18	0.2	0.22	Increase	54.40286	54.40286	0	0	0	1

J.2.6 Tornado Diagram for Disability Weights Related to Obstructed Labour



J.2.7 Tornado Diagram Outputs for Disability Weights Related to Obstructed Labour

Variable Name	Variable Low	Variable Base	Variable High	Impact	Low	High	Spread	Spread2	Risk %	Cumulative Risk %
u_OL	0.22	0.324	0.442	Decrease	54.10336	54.66958	0.56622	0.3206	0.719	0.719
u_csection	0.3141	0.349	0.3839	Increase	54.26443	54.542	0.27757	0.07704	0.173	0.892
u_hemorrhage	0.22	0.324	0.442	Decrease	54.31349	54.48186	0.16837	0.02835	0.064	0.956
u_vfistula	0.227	0.342	0.478	Decrease	54.33776	54.45803	0.12027	0.01446	0.032	0.988
u_rfistula	0.339	0.501	0.657	Decrease	54.37284	54.43407	0.06123	0.00375	0.008	0.997
u_uterineprolapse	0.338	0.404	0.471	Decrease	54.38957	54.41595	0.02638	0.0007	0.002	0.998
u_uterinerupture	0.29	0.49	0.69	Decrease	54.39327	54.41245	0.01919	0.00037	0.001	0.999
u_ID	0.3375	0.375	0.4125	Increase	54.39405	54.41167	0.01762	0.00031	0.001	1
u_sepsis	0.088	0.133	0.19	Decrease	54.39754	54.40706	0.00951	0.00009	0	1
u_sepsis_acute	0.44883	0.4987	0.54857	Decrease	54.39966	54.40606	0.00641	0.00004	0	1
u_nodisability	0.0099	0.01	0.0101	Increase	54.39987	54.40584	0.00597	0.00004	0	1
u_infection	0.032	0.051	0.074	Increase	54.40165	54.40432	0.00266	0.00001	0	1
u_incontinence	0.0225	0.025	0.0275	Decrease	54.40283	54.40289	0.00006	0	0	1
u_hysterectomy	0.22	0.324	0.442	Increase	54.40286	54.40286	0	0	0	1

J.3 Tornado Diagram Outputs for Neonatal Outcomes

Variable Name	Variable Low	Variable Base	Variable High	Impact	Low	High	Spread	Spread2	Risk %	Cumulative Risk %
c_health_baby	47.73	53.03	58.33	Increase	18.0409	21.50559	3.46469	12.00407	0.865	0.865
d_OL	0.2549	0.3859	0.5168	Decrease	19.61213	20.51514	0.903	0.81541	0.059	0.923
u_hypoxia	0.245	0.351	0.467	Decrease	19.41185	20.11546	0.70361	0.49507	0.036	0.959
p_NICU_CS	0.136	0.15111	0.16622	Increase	19.59296	20.11548	0.52252	0.27303	0.02	0.979
c_NICU	327.39	363.77	400.14	Increase	19.52922	20.0172	0.48797	0.23812	0.017	0.996
p_HIE	0.27248	0.3028	0.33303	Decrease	19.66267	19.88542	0.22276	0.04962	0.004	1
p_NICU_ID	0.136	0.15111	0.16622	Increase	19.75519	19.82033	0.06514	0.00424	0	1
d_NICU	0.18137	0.20153	0.22168	Increase	19.77324	19.80667	0.03342	0.00112	0	1
p_hypoxia	0.23076	0.2564	0.28204	Decrease	19.76094	19.78955	0.02861	0.00082	0	1
d_stillbirthCS	0.01464	0.01627	0.0179	Increase	19.75532	19.77544	0.02012	0.0004	0	1
d_stillbirthID	0.06245	0.06939	0.07633	Increase	19.76143	19.77511	0.01368	0.00019	0	1
u_nodisability	0.0099	0.01	0.0101	Increase	19.77152	19.77497	0.00345	0.00001	0	1

Appendix K Calculation and Assumptions for Combined Cost-Utility Estimate for Mother and Baby

To provide an estimate of the combined benefits of increasing access to caesarean section for mothers and babies, a combined cost-utility estimate was calculated under the assumption that the costs and effects were additive. The follow methodology was used:

i) Costs and effectiveness estimates were combined for mother and baby for the existing care strategy

$$Combined\ Cost\ for\ Existing\ Care\ Strategy\ = Costs\ for\ mother + Costs\ for\ baby$$

$$Combined\ Cost\ for\ Existing\ Care\ Strategy\ = \$843.04 + \$829.69$$

$$Combined\ Effectiveness\ for\ Existing\ Care\ Strategy\ = DALYs\ for\ mother + DALYs\ for\ baby$$

$$Combined\ Effectiveness\ for\ Existing\ Care\ Strategy\ = 9.42\ DALYs + 17.64\ DALYs$$

ii) Procedure was repeated for the increased access strategy

$$Combined\ Cost\ for\ Increased\ Access\ Strategy\ = Costs\ for\ mother + Costs\ for\ baby$$

$$Combined\ Cost\ for\ Increased\ Access\ Strategy\ = \$1191.00 + \$1052.56$$

$$Combined\ Effectiveness\ for\ Increased\ Access\ Strategy\ = DALYs\ for\ mother + DALYs\ for\ baby$$

$$Combined\ Effectiveness\ for\ Increased\ Access\ Strategy\ = 2.85\ DALYs + 6.37\ DALYs$$

iii) Incremental costs and effectiveness were calculated

$$Incremental\ Cost = Combined\ cost\ of\ Increased\ Access\ - Combined\ cost\ of\ Existing\ Care$$

$$Incremental\ Cost = \$2243.56\ - \$1679.51$$

$$Incremental\ Effectiveness = \ Combined\ DALYs\ of\ Existing\ Care - \ Combined\ DALYs\ for\ Increased\ Access$$

$$Incremental\ Effectiveness = \ 27.06\ DALYs - 9.22\ DALYs$$

iv) Incremental cost-effectiveness ratio was calculated for cost per DALY averted

$$Incremental\ Cost - effectiveness\ Ratio = \frac{Incremental\ Cost}{Incremental\ Effect}$$

$$Incremental\ Cost - effectiveness\ Ratio = \frac{\$570.83}{17.84\ DALYs} = \$32.00\ per\ DALY\ averted$$

Appendix L Age and Mortality Tables for Mothers and Babies

L.1 Age Table Calculation for Start Age in Model

To account for the age distribution among women aged 15 to 49 in the SADC region, the population proportions for each age group were calculated using the total population and applied to women entering the decision tree to determine their starting age. The following table used data from the GBD 2019 study for population estimates in Sub-Saharan Africa. The GBD 2019 study used census and population registry location-years.[7]

L.1.1 Age Table for Women Age 15 – 49 in SSA

Age Group	Measure	Metric	Value	Lower Limit	Upper Limit
15 to 19	Population	Number	118045517.7	113300465.4	122545528
20 to 24	Population	Number	99335866.48	95388169.81	103145714.9
25 to 29	Population	Number	83646132.09	80388969.94	86864450.69
30 to 34	Population	Number	70920863.67	68221072.58	73587350.53
35 to 39	Population	Number	59437282.44	57192430.73	61661005.61
40 to 44	Population	Number	48429447.2	46610500.17	50219735.77
45 to 49	Population	Number	38565376.13	37089622	40015277.47

L.2 Background Mortality for Mothers and Babies

Background mortality was estimated using GBD 2019 Life Tables that give probability of death for each age group in SSA, presented in the table below. The GBD 2019 study used vital registration systems, household surveys, sample registration systems, census, disease surveillance, and demographic surveillance systems to estimate probability of death.[7]

L.2.1 Age-Specific Background Mortality for Women in SSA

Age Group	Measure	Value	Lower Limit	Upper Limit
10 to 14	Probability of death	0.00322702	0.00283939	0.00369285
15 to 19	Probability of death	0.00522938	0.00449112	0.00613231
20 to 24	Probability of death	0.007505	0.00642428	0.00880502
25 to 29	Probability of death	0.01080307	0.00909925	0.01301689
30 to 34	Probability of death	0.01511975	0.01307455	0.01764319
35 to 39	Probability of death	0.0200597	0.01743614	0.02304425
40 to 44	Probability of death	0.02606931	0.0231992	0.0294146
45 to 49	Probability of death	0.03347585	0.029844	0.03801584
50 to 54	Probability of death	0.04476215	0.03967667	0.05072255
55 to 59	Probability of death	0.06019755	0.05328658	0.06861861
60 to 64	Probability of death	0.08781039	0.07886011	0.09841783
65 to 69	Probability of death	0.12624893	0.11596635	0.13862625
70 to 74	Probability of death	0.19336296	0.18119522	0.20781046
75 to 79	Probability of death	0.28124691	0.26845174	0.29713757
80 to 84	Probability of death	0.41340369	0.40045789	0.4296512
85 to 89	Probability of death	0.53083965	0.51393211	0.5546191
90 to 94	Probability of death	0.67053432	0.65194081	0.69011415
95 to 99	Probability of death	0.7958159	0.7789731	0.80978189
100 plus	Probability of death	0.88536033	0.87287437	0.89425456

L.2.2 Age-Specific Background Mortality for Neonates in SSA

Age Group	Measure	Value	Lower Limit	Upper Limit
<1 year	Probability of death	0.04852258	0.04279735	0.05557117
1 to 4	Probability of death	0.02679061	0.0233071	0.03127402
5 to 9	Probability of death	0.00502385	0.00430445	0.00590262
10 to 14	Probability of death	0.00374959	0.00331268	0.00427001
15 to 19	Probability of death	0.00635538	0.00555295	0.00725204
20 to 24	Probability of death	0.00895272	0.00784897	0.01017167
25 to 29	Probability of death	0.01198776	0.01046481	0.01379842
30 to 34	Probability of death	0.01658756	0.01457848	0.01906661
35 to 39	Probability of death	0.02253893	0.01980338	0.02576687
40 to 44	Probability of death	0.03060471	0.02733187	0.03426385
45 to 49	Probability of death	0.04019339	0.03618192	0.04517133
50 to 54	Probability of death	0.0548082	0.04932792	0.06116604
55 to 59	Probability of death	0.07395989	0.06675291	0.08286859
60 to 64	Probability of death	0.10698647	0.09761727	0.1177657
65 to 69	Probability of death	0.15021095	0.13953834	0.16245587
70 to 74	Probability of death	0.21952617	0.20799598	0.23310687
75 to 79	Probability of death	0.30739389	0.29647574	0.32135717
80 to 84	Probability of death	0.4344075	0.42251731	0.44925169
85 to 89	Probability of death	0.55606159	0.54284982	0.57369999
90 to 94	Probability of death	0.69127857	0.67658325	0.70657172
95 to 99	Probability of death	0.8079571	0.79487548	0.81969626
100 plus	Probability of death	0.89263383	0.8830638	0.90030513

Appendix M Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Checklist

Section/Item	Item No.	Recommendation	Reported on Page No.
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared	31
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions	N/A
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions	31-33
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analyzed, including why they were chosen	34
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made	34-35
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated	34
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen	34-35
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate	35
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate	35
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	34
Measure of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	N/A

	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data	38-39, Appendix G1 and G2
Measurement and valuation of preference- based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes	N/A
Estimating resources and costs	13a	*Single study-based economic evaluation*: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs	N/A
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs	42-43 Appendix F
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	42-43
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	43, Figures 2-6
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	35-38, Appendix F-K
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	43 - 45 Appendix E, G, I-K
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	60-63, Appendix F-J

Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	45-48, 64, and 68
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	N/A
	20b	*Model-based economic evaluation*: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	45-47
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	N/A
Discussion			
Study findings, limitations, generalizability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	48-54
Other			
Sources of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	N/A
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	N/A

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