

ASSESSING THE COST-EFFECTIVENESS OF FACILITY-BASED EMERGENCY CARE IN LOW RESOURCE SETTINGS

by

Kalin Werner

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Supervisor(s):

Professor Lee A. Wallis Division of Emergency Medicine, University of Cape Town

Tracy Kuo Lin, PhD Department of Social and Behavioral Sciences, University of California San Francisco

Dr. Teri A. Reynolds Emergency, Trauma and Acute Care, World Health Organization

Dr. Nicholas Risko Department of Emergency Medicine, Johns Hopkins University

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Signature:

Signed by candidate

Date: March 17, 2021

Student Name: Kalin Werner

Student Number: WRNKAL001

ABSTRACT

Background

Emergency conditions comprise nearly half of the total global burden of disease, and disproportionately affect low-resource settings (LRS). This burden of life-threatening yet treatable conditions can be ameliorated by effective, timely emergency care (EC) interventions, so significantly that the Disease Control Priorities project estimates over half of deaths in the lowest-income countries could be addressed through the implementation of effective EC. Interest in developing better facility-based EC is expanding rapidly, yet there is a large gap in the cost-effectiveness literature to support informed resource allocation. Distinguishing the "value for money" of EC is crucial, especially in contexts of extreme resource limitations. Developing robust and setting-specific data on the cost of implementing EC cultivates the ability to understand the impacts of, and plan improvements in, EC in LRS. The aim of this thesis was to investigate the cost-effectiveness of interventions forming a systematic approach to EC in health facilities in LRS.

Aims and Objectives

The primary aim of this research was to investigate the cost-effectiveness of implementing the WHO emergency care toolkit to reduce mortality related to emergency conditions in health facilities in an LRS. To achieve this aim, the following objectives were established: synthesise evidence relating to the cost-effectiveness of EC in LRS, enumerate context specific costs of delivering facility-based EC, and retrospectively study the impact of implementing a low-cost set of EC interventions in low-resource EC naïve health facilities on cost and outcome (mortality), to derive a measure of cost effectiveness.

Methods

The dissertation is comprised of 3 studies. First, Chapter 3 undertakes a systematic review of literature on EC interventions in LRS, using PRISMA guidelines and the Consolidated Health Economics Evaluation Reporting Standards (CHEERS) checklist. Secondly, to enumerate context specific costs of delivering facility-based EC, data were collected over a 4-week period in Uganda using direct activity-based costing and presented in Chapter 6. Measures of central tendency were derived by condition and by intervention. Variations in cost between conditions were explored using a Kruskal-Wallis H test and a post-hoc Nemenyi test were performed to make pairwise comparisons between conditions. Third, in Chapter 7 a cost-effectiveness analysis model was developed using Microsoft Excel to calculate both the costs and effects of scalable investments strengthening facility-based EC on morbidity and mortality. Costs and consequences associated with piloting the WHO Emergency Care Toolkit package of interventions in Uganda were analysed using the decision tree model. Pre- and post-intervention groups were compared from a societal perspective. Cost and health outcomes were discounted using a micro-simulation and parameter uncertainty assessed using Monte-Carlo simulation probabilistic sensitivity analyses.

Results

35 studies were included in the final review; most were methodologically weak and focused on single-intervention analyses rather than intervention packages or system changes. This body of literature represented only 24 of 137 low- and middle-income countries (LMICs) globally, and was heterogeneous in methods, settings, and presentation of results of the identified studies. Accordingly, formulating a general conclusion about the wider implication of the findings on the cost-effectiveness of EC is problematic. The overall median (IQR) cost of care across all conditions was \$15.53 (14.44 to 19.22). A Kruskal-Wallis test yielded statistically significant difference in cost values between sentinel conditions

($H=94.89$, $p=1.20E-19$). At a P value of $< .05$, the post-hoc Nemenyi test revealed paediatric diarrhoea has a statistically significant lower median cost compared to all other conditions, but did not yield any significant differences in median cost between the remaining four sentinel conditions. In running the decision tree model with a 1753 patient cohort, sampled 10000 times, the intervention averted 509 DALYs over standard care. The model found implementing the WHO Toolkit saved \$664,231 (\$658,552 to \$669,910), and yielded an additional 27 lives saved, or an additional 1,826 life years.

Conclusions and relevance

This dissertation makes important conceptual, analytical and empirical contributions in exploring the application of local economic evidence-informed priority setting to ensure that decisions made around EC are guided by the populations they serve. In conducting one of the first cost-effectiveness analyses of investments that create a systematic approach to facility-based EC, we found that this is a very low-cost, high-yield intervention. In many cases it may not only be cost-effective, but actually cost saving. This finding is especially relevant in LRS contexts where associated additional costs may be considered affordable given the high burden of emergency conditions.

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ACRONYMS AND ABBREVIATIONS

BEC	Basic Emergency Care
BMGF	The Bill and Melinda Gates Foundation
CEA	Cost-effectiveness analyses
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
DALYs	Disability-adjusted life years
DCP	Disease Control Priorities project
DCP3	3 rd edition Disease Control Priorities report
EC	Emergency Care
ECOP	Emergency Care Outcomes Project
ECS	Emergency Care System
EmOC	Emergency Obstetric Care
EU	Emergency Unit
DAH	Development Assistance for Health
GDP	Gross Domestic Product
The Global Fund	The Global Fund to Fight Aids, Tuberculosis and Malaria
GNI	Gross National Income
HCA	Human capital approach
HICs	High-income countries
HRBA	Human rights based approach
HTA	Health technology assessments
ICU	Intensive care unit
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
JMS	Joint Medical Stores
LICs	Low-income countries
LMICs	Low- and middle-income countries
LRS	Low resource settings
LYS	Life years saved
MoH	Ministry of Health
NMS	National Medical Stores

OOP	Out-of-pocket payments
PPH	Post-partum haemorrhage
QALYs	Quality-adjusted life years
REDCap	Research Electronic Data Capture
RRH	Regional Referral Hospital
RTI	Road traffic incident
WHO	World Health Organization
WHO-CHOICE	World Health Organization CHoosing Interventions that are Cost Effective
YLL	Years of Life Lost

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Chapter 1

GENERAL INTRODUCTION

“Emergencies occur everywhere, and each day they consume resources regardless of whether there are systems capable of achieving good outcomes. With better planning, the ongoing costs of emergency care can result in better outcomes and better cost-effectiveness” -Kobusingye 2005

Emergency conditions contribute substantially to the global burden of disease and represent a key cause of disability and premature death worldwide. This single factor contributes to nearly half of the total global burden of disease.¹ Traumatic injury alone accounts for 11% of all global deaths per year and is forecast to account for 20% of all ill-health in the world by 2020.^{2,3} These conditions disproportionately affect the lowest income countries where over 90% of all injury-related deaths occur.⁴ Emergency conditions are nearly 60% worse in low-resource settings (LRS), which experience a burden of 25,186 disability-adjusted life years (DALYs) per 100,000 population, compared to the 15,691 DALYs per 100,000 in middle-income countries.⁵ Although injury and trauma add most significantly to this burden, non-communicable diseases, obstetric conditions, and infectious diseases all significantly contribute to the incidence of emergency conditions. Rapid urbanisation, economic growth, and the resulting increase in the number of motorised vehicles in LRS indicate a likelihood that the weight of trauma will only increase in the coming decade. Furthermore, the growth of non-communicable diseases such as hypertension, cardiac disorders and diabetes, and increased motor vehicle use are expected to contribute to rising incidents of emergencies such as cardiac arrest, stroke and road-traffic incidents.

Death and disability resulting from these conditions exact a weighty societal and economic toll. The primary victims of injury-related mortality cases are young economic contributors between the ages of 15 and 44 years old.⁶ Much of this comes from life-threatening, yet treatable, sequelae that can be ameliorated by effective, timely emergency care (EC). Even with such a considerable undertaking, EC garners little attention and consideration from health stakeholders worldwide, contributing to its moniker as the “neglected disease of modern society”.⁷

The diseases treated through EC are diverse and often unavoidable. Organised EC provides crucial access to immediate and urgent medical interventions for life-threatening conditions. The timing and appropriateness of these interventions are vital in reducing the incidence of morbidity and mortality. This is so significant that the Disease Control Priorities (DCP) project estimates over half of the deaths in low- and middle- income countries (LMICs) could be addressed through the implementation of effective EC.⁸ For emergency conditions, delays in care or delivery of inappropriate care can mean the difference between life and death. However, defining effective emergency care from a health system perspective is persistently imprecise.

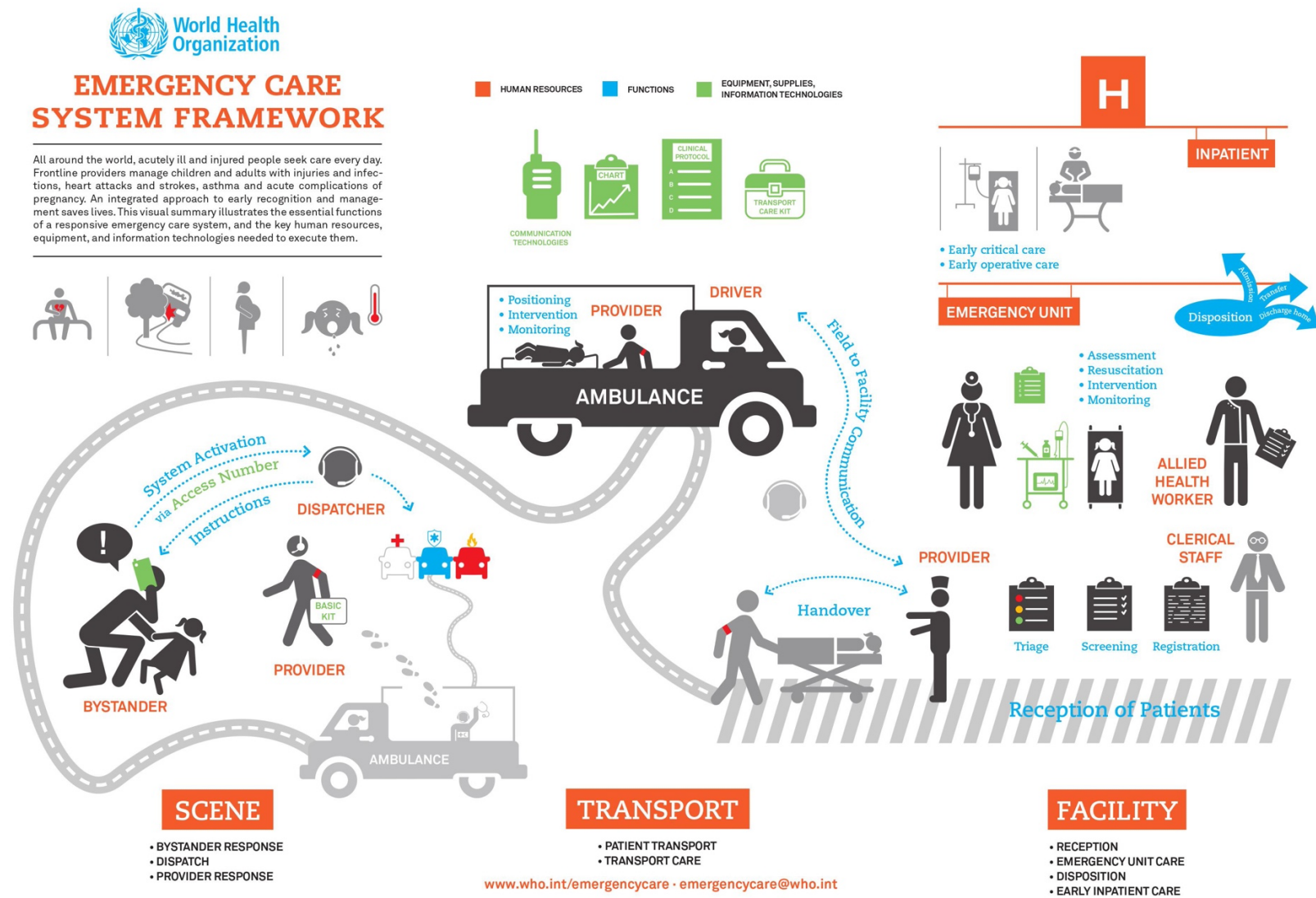
Many of the prominent global causes of death and disability in developing countries, such as diarrheal disease, lower respiratory infections, ischemic heart disease, and road traffic injuries, are responsive to improvements in the delivery of EC.⁹ Meeting these challenges requires

organised EC which matches patients rapidly with necessary clinical services. Despite the prevalence of emergency conditions and consequential negative health and economic impact, most LRS lack relevant EC policies and capacities. In high-income countries (HICs) the implementation of state-wide trauma systems has resulted in reductions in risk-adjusted mortality, and up to a 15% reduction in overall mortality.^{10,11} Evidence suggests that organised systems of care can lead to significant improvements in mortality outcomes.^{12,13} An estimated 54% of annual deaths in LRS could be addressed with pre-hospital and facility-based EC.¹⁴

Emergency Care Systems Framework

EC can be differentiated from other medical specialties due to the complexity of care and provision across many areas of the health system and cross-cutting and interlinking functions. The World Health Organization (WHO) Emergency Care System (ECS) framework (**Figure 1.1**) takes the complex and interconnected mechanism of delivering EC and designates how the various elements are interrelated.¹⁵ The framework identifies essential functional components of EC at the *scene*, during *transport*, and in *facilities*. In each of these three domains, critical functions are specified. By providing a shared language which encompasses the interlinked functions, it becomes possible to discuss and evaluate ECS. This guide was used to inform decisions about resources specified throughout this research.

Figure 1.1 World Health Organization Emergency Care Systems Framework



Source: The World Health Organization¹⁵

Aside from managing urgent conditions, ECS deliver competencies that are essential for public health emergencies, conflict settings, and disasters, and can improve both access and financial protection for patients. EC plays a central role in the delivery of a range of essential care services that contribute to the achievement of universal health coverage (UHC). Calls to align EC with existing global health priorities would ensure access to these critical life-saving interventions which could save more than 400,000 lives globally each year.¹⁶

Facilities

There are many locally appropriate and resource relevant interventions for strengthening ECS which show promise, especially those which work with the existing infrastructure of LRS to enhance the delivery of EC. For example, layperson first aid responder programmes and boda-boda ambulances have shown promising outcomes and are likely an effect of their alignment with existing networks of transportation in LRS.^{17,18} Solutions which create synergies with existing resources are desperately needed.

While considerable research has been conducted into the benefits of both scene and transport care, little has been done concerning urgent care provided within facilities.¹⁸⁻²² However, care delivered in facilities is an essential part of a broader continuum of care for emergency conditions. For example, improving pre-hospital care – such as ambulance transport – may improve the capacity to stabilise critical patients in the field, but ultimately their survival and recovery will be compromised should they not receive quality care upon arrival at a facility. Positive outcomes from EC are highly dependent on the alignment of these various areas to reduce adverse outcomes.

Facilities are the point in the ECS where patients are expected to receive definitive care, which heavily relies on appropriate triage, adequate supplies and staff, and physical infrastructure. Under the WHO ECS Framework, responsibilities of facility care include reception (registration, screening, triage, and handover), emergency unit (EU) care (assessment, monitoring, diagnostic studies, and treatment), and disposition (admission, discharge, or transfer). This dissertation uses this definition to delineate the services considered for costing in subsequent analyses.

Advancing access to hospital-based EC is also an important driver of overall service availability and capacity to deliver timely care. Access is of particular importance in emergencies, where proximity to equipped facilities can greatly affect the timeliness of care.²³ Recent geospatial analyses reveal that more than 30% of populations in Sub-Saharan African countries live more than two hours away from a hospital that can deliver EC.²⁴ This coverage gap can influence the time it takes for patients to receive urgent life-saving care, which can depend on a matter of minutes rather than hours. Moreover, these findings likely underestimate the impact which other measures of access may have, such as trained providers, affordability, medical supply availability, and infrastructure.^{25,26}

Where facilities are available, most lack a dedicated space for an EU which may mean that EC is dispersed across several areas of the facility. Various assessments of EC capacity at public hospitals in Zambia, eSwatini, and Uganda have identified serious infrastructure gaps that hinder the provision of these essential services.²⁶⁻²⁹ Expansion of dedicated facility space is therefore an essential part of any coverage strategy to increase the availability of EC services and has been noted as a key building block for the achievement of UHC.

In analysing which of the components of the ECS framework are likely to yield cost-effective solutions, it is important to identify where such infrastructure is already in place. Facilities already exist in many LRS communities even where transport services are absent. Although few LRS have national ambulances services, nearly all have existing clinics and hospitals that serve their populations. Facility-based interventions may be able to tap into the existing (but fragile) health systems, thereby reducing the need to recruit new staff or develop additional infrastructure. This alignment could make a measurable difference in reducing the impact of improvements to EC on limited budgets whilst still reaping the benefits. The realisation of simple interventions to improve facility-based care has the potential to tackle key bottlenecks for EC whilst significantly contributing to the strengthening of the overall health care system.

Emergency care in low-income countries and low-resource settings

ECS are not evenly distributed around the world. Despite being a critical component of any effective health care system, the organisation and function of EC varies considerably from across countries. Though LRS experience the highest burden of emergency conditions, they are least equipped to handle this load. This creates a significant discrepancy between the needs and services provided in these locations. Like most health programmes in LRS, providers are overburdened and under-resourced. Unlike other disease areas, few providers who deliver EC have been trained in principles of emergency management.

In LRS, which by definition face significant financial challenges, the reality of EC is one of extreme resource constraints coupled with high patient volumes and mortality. Weak EC systems exist with delays in initiating appropriate care, resulting in many preventable deaths. The absence of well-coordinated ECS leads to in lower quality of care and poorer health outcomes.

Studies show that as few as 19% of hospitals in sub-Saharan Africa have the capacity to deliver 24-hour EC.²⁶ Treatment ability of facilities varies widely, and health systems are plagued by a scarcity of clinicians trained in EC. In a study of 192 facilities across 59 low-income countries (LICs), only 18% had physicians on staff with specialised emergency training, and only 4% surveyed had staff with these skills available fulltime.³⁰ In locations where EC has not yet been established within a medical speciality, and which suffer from weak ECS, populations remain at risk of avoidable mortality and morbidity. Where present, ECS in LRS struggle to meet demand. The volume of patients presenting at these facilities is nearly ten times those of HICs.⁹ It is a circumstance where the greatest burden of injury occurs in systems least prepared to meet the

challenge. This is a reality further confirmed by the fact that individuals with life-threatening but treatable injuries are six times more likely to die in a LIC than in a HIC.⁴

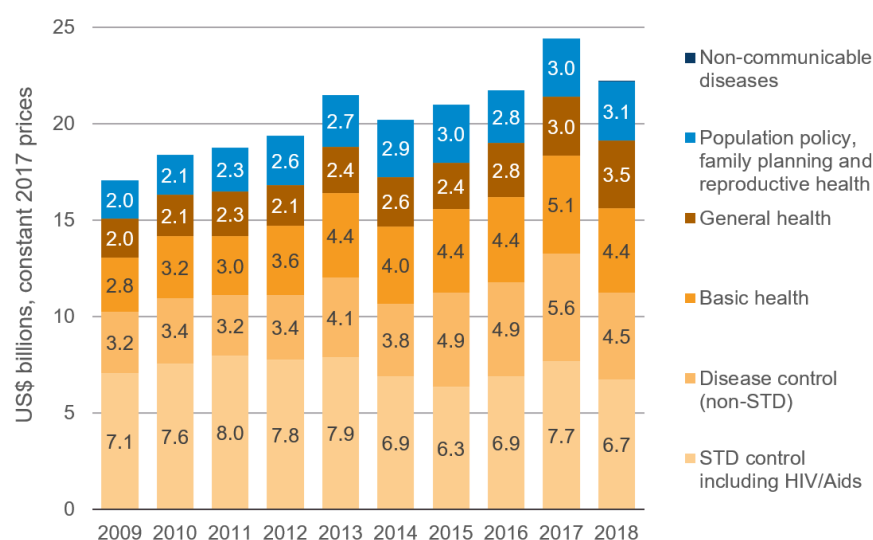
Contextualising the need for emergency care in situations of resource scarcity

EC is often associated with being complex and resource intensive. The truth, however, is that many life threatening conditions are highly treatable with very simple EC interventions.³¹ The third edition of the DCP Project report, DCP3, which sets global priorities for disease control, identified the weak fundamentals of organised EC as a priority area. These included the lack of basic pre-hospital care and transport, a dedicated area and standards for hospital-based EC, and a core of non-rotating providers trained in the care of emergencies and assigned to the EU, which are reflected in the global discrepancy in outcomes across the range of emergency conditions.³² Simple interventions in EC may provide a promising solution for even the most resource-limited settings.⁹ This is especially true for interventions that require limited new investments in infrastructure.³³

Investigations into how improved triage, patient flow, and supervision can lead to reductions in mortality are underway.³⁴ Opportunities to systematise care using these simple interventions move beyond the perception that EC is a high-technology field and aim to prove that averting death and disability may be helped by new resource inputs that are achievable, such as in-service training of existing hospital staff.³⁵ Further low-cost interventions such as team and facility organisation, communication, and protocols have also shown promise in improving access to life-saving care.³⁴

Although resolving issues of health financing fall outside of the scope of this study, it is important to comment on the urgent need for more accurate cost data to serve as evidence for broader financing process. A series of WHO Emergency Care System Assessments (ECSAs) identified both insufficient funding and lack of dedicated funding streams as a shared challenge across multiple LRS.³⁶ Unfortunately, global funding for EC is sparse, especially when contrasted to that for vertical disease programmes, such as HIV/AIDs, TB, or malaria. This is reflective of the wider health financing environment in LRS health systems where development aid and donor assistance may be responsible for almost a quarter of health spending.³⁷ Over half of all overseas development funding for health is dedicated to specific health subsectors. Some of the most prominent and powerful global health initiatives such as Bill and Melinda Gates Foundation (BMGF), The Global Fund to Fight Aids, Tuberculosis and Malaria (The Global Fund), the Global Alliance for Vaccines and Immunizations, and the President's Emergency Plan for AIDS Relief have disease specific mandates which guide distribution of their reserves. For example the BMGF and The Global Fund provided nearly half of the \$26 billion spent on health in 2018.³⁸ **Figure 1.2** summarises the distribution of health aid by subsector and illustrates that non-communicable disease receives the smallest fraction at only \$15 million USD in 2018.

Figure 1.2 Health aid by subsector, 2009-2018



*levels to the NCD subsector are not visible due to scale

*Source: Development Initiatives, based on the Organisation for Economic Cooperation and Development (OECD) Creditor Reporting System (CRS)*³⁸

With very few major global donors or development agencies committed to the mandate of EC, proving the viability and impact of emergency services is imperative. Research and economic analyses can provide foundational evidence to drive the agenda of future health financing plans. Likewise, governments are confronted with determining how and where to prioritise interventions in health.³⁹ Financial constraints and concerns of cost are frequently mentioned as the motivation behind the lack of investment in EC. In order to help mobilise resources, robust economic evaluation research and findings are needed. Results can reveal the true impact of EC and to guide decision-makers towards a better understanding of the value of EC; one which fits the urgent needs of both their citizens and their budgets. If acute care remains outside the mandate of health care strengthening efforts, countries will continue to experience limited ability to implement even low-cost strategies.

Cost information is important in circumstances under which resource limitations necessitate tough resource allocation decisions.³⁴ Sound planning and organisation of health care systems in LRS are regularly inhibited by the lack of context-relevant cost analyses. Most of the existing literature is derived from HICs, which is problematic when seeking locally appropriate solutions for EC in LRS. How EC is implemented and what it costs are reflective of the distinctive systems under which it operates. Therefore, very few of the currently published findings can speak to the conditions experienced by LRS.

There are several studies that suggest EC systems are likely to be cost-effective compared to current care under the state of high disease burden affecting LRS, but there is an urgent need for more robust findings.^{40,41} To make matters more challenging, research findings are often not reported in a manner which speaks to the metrics used by health stakeholders, such as DALYs and years

of life lost (YLL).⁴² Perceptions of EC as resource demanding are only furthered by a lack of robust cost data and persistently impede the ability to understand the impacts of and plan improvements for EC in LRS.

EC is an essential part of an effective health care system. Delivery of this vital component requires several integrated services, which together function to provide prompt, safe, and effective access to health care in times of urgent need. Distinguishing the "value for money" of EC is critical, especially for LRS. Developing robust data on the cost of implementing emergency care within low-income contexts will greatly aid in sound planning and priority setting of countries carrying some of the highest burdens of morbidity and mortality related to EC treatable disease.

Interest in developing better facility-based EC is expanding rapidly, and there is a significant gap in the cost-effectiveness literature in this area. However, the introduction of any intervention must be accompanied by rigorous evaluations to maintain appropriateness to the fiscal setting. Therefore, there is an urgent need to strengthen the evidence taken into account for both policy and practice. LRS include countries with some of the highest EC needs so health programmes must prove not only their ability to save lives, but the relative effectiveness given competing issues within a limited budget.

Early iterations of the proposed work (see **Appendix A**) sought to prospectively collect data related to the roll-out of a WHO package of interventions to systematise EC. Due to unexpected delays in the implementation process, the study objectives were slightly modified to adequately address research questions regarding the cost-effectiveness of EC given time and data constraints. In particular, the cost-effectiveness analysis (CEA) presented in Chapter 7 used retrospective rather than prospective data. Prospective data collection is ongoing and will constitute the basis for future research in this area.

1.1 AIM AND OBJECTIVES

1.1.1 Aim

The primary aim of this research was to investigate the cost-effectiveness of interventions that create a systematic approach to emergency care in health facilities in low-resource settings.

1.1.2 Objectives

To achieve this aim, the following objectives were established:

1. Synthesise evidence relating to the cost-effectiveness of emergency care in low-resource settings.
2. Enumerate context specific costs of delivering facility-based emergency care.

3. Retrospectively evaluate the impact of implementing a low-cost set of emergency care interventions in low resource emergency care naïve health facilities on cost and outcome (mortality), to derive a measure of cost-effectiveness.

1.2 METHODOLOGY AND ETHICS OVERVIEW

1.2.1 Methodology

To achieve the aim of this dissertation a variety of quantitative methods were employed which are provided in further detail within each chapter. First, a systematic review of the literature was performed to assess the existing body of work on EC interventions in LRS. Here a PRISMA systematic review was conducted of published articles in 5 databases including PubMed, Scopus, EMBASE, Cochrane, and Web of Science, applying Cochrane LMIC filter to search results. The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist is a validated tool and was used to grade the quality of available evidence. In Chapter 6, a bottom-up micro-costing approach is used to provide robust data on the cost of providing EC in a LRS facilities. Chapter 7 takes the lessons from previous chapters and empirical inputs derived in the micro-costing to conduct a retrospective CEA of the pilot implementation of the WHO EC toolkit in Uganda.

1.2.2 Ethics

Ethical approval for all of the work in this thesis was granted by the University of Cape Town (HREC REF: 549/2019). The full proposal is included in **Appendix A**. Additionally, for all research conducted in Uganda (including Chapters 4 and 5) ethical approval was granted by the Institutional Review Board of Makerere University School of Medicine (REC REF: 2019-035). Approval and authorisation of data collection at regional referral sites, as well as cost data from government suppliers, was granted by the Ministry of Health of the Republic of Uganda. Copies of all three approvals can be found in **Appendices B-D**. To protect confidentiality all data collected were anonymised to ensure that no participant's details were recorded.

1.3 OVERVIEW OF SETTING

This section offers background to the context of LRS. It provides details of the geographic, demographic, and socio-economic features, and gives an overview of the structure of health care systems, their capacities, and funding sources in these settings. Equivalent details are then given for Uganda, the country that serves as the principal area of this research.

1.3.1 Low resource settings

The research in the following chapters focuses specifically on issues in EC and health economics in “low-resource settings”. Understanding the parameters of what this identifier entails is imperative to understanding the scope of the following chapters. The World Bank introduced the classification of countries by income in 1978 and updates these thresholds annually. Today, low- and middle-income country (LMICs) are classified as nations with a gross national income (GNI) per capita below \$3,995. As of 2020, there are 29 countries whose GNI per capita fall below

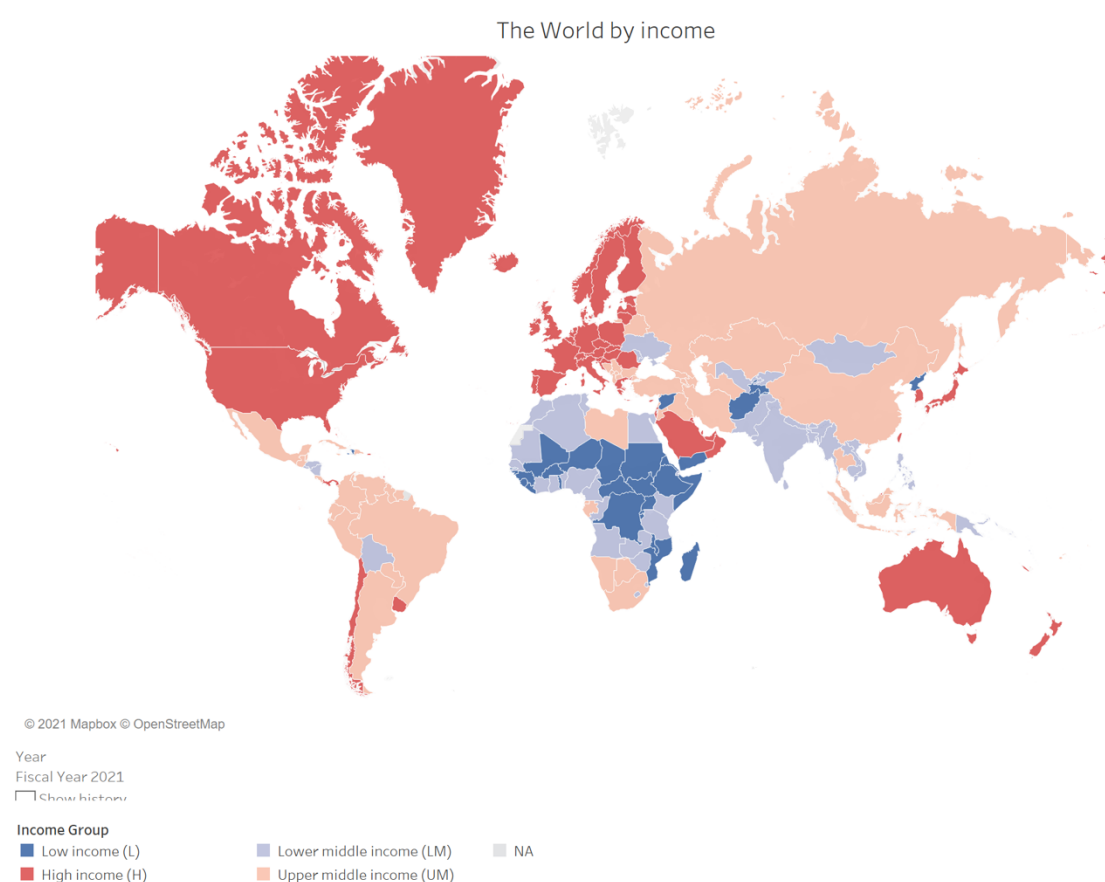
\$1,026 and are therefore considered low-income economies. This list is provided in **Table 1.1** and in a summary map in **Figure 1.3**.

Income is only one of many ways to categorise countries, but it is this characterisation that reveals the strain experienced by these countries in providing public services to their populations, including the health sector. It acts as an important identifier of nation-states that are likely to experience hardships and difficulties in providing social services. Although all but six of these countries are located on the African continent, this list is still comprised of nations with diverse economic and epidemiological characteristics with heterogeneous health systems structures. Note that both LRS and LMIC are utilised throughout this dissertation. The term LMIC is engaged only when referenced specifically in published works which are copied verbatim in this thesis, such as Chapters 3, 6, and 7. Otherwise all empiric data were captured in a low, rather than middle, income setting and the term LRS is therefore used in all other areas of this thesis to accurately label the analysis setting.

Table 1.1 Low-Income Economies (\$1,035 or less GNI per capita) by geographical region

<i>Region</i>	<i>Countries</i>
<i>Sub Saharan African Region</i>	Burkina Faso, Central African Republic, Chad, Democratic Republic of Congo, Eritrea, Ethiopia, Gambia, Guinea, Guinea Bissau, Liberia, Madagascar, Malawi, Mali, Mozambique, Niger, Rwanda, Sierra Leone, Somalia, South Sudan, Sudan, Togo, Uganda
<i>Middle East North Africa</i>	Syria, Yemen
<i>Latin America and Caribbean</i>	Haiti
<i>Europe and Central Asia</i>	Tajikistan
<i>East Asia Pacific</i>	Democratic People's Republic of Korea
<i>South Asia</i>	Afghanistan

Figure 1.3 World by income



Source: *The World Bank* ⁴³

Geographic, demographic, and socio-economic information

LRS populations are overwhelmingly young and faced with a high burden of both communicable and non-communicable diseases. **Table 1.2** presents a series of selected indicators that provide insight into the population, their health, and financial station.

Table 1.2 Demographic, Health and Socio-economic of indicators for LRS

Indicator variable	Value and units
<i>Demographics</i>	
Population	668,454,965
Growth rate (annual)	2.6%
Population between ages 0-14 (% of total)	279,473,861 (41.8%)
Population between ages 15-64 (% of total)	367,076,891 (54.9%)
Population above 65 (% of total)	21,904,213 (3.3%)
% of total global population	8.6%
<i>Health</i>	
Life expectancy at birth	63.5 years
Under five mortality rate	67.6 per 100,000 people
Mortality caused by road traffic injury	27.8 per 100,000 people
<i>Socio-economic</i>	
GDP per capita	2,489 (international \$)
GDP growth rate	1.2%

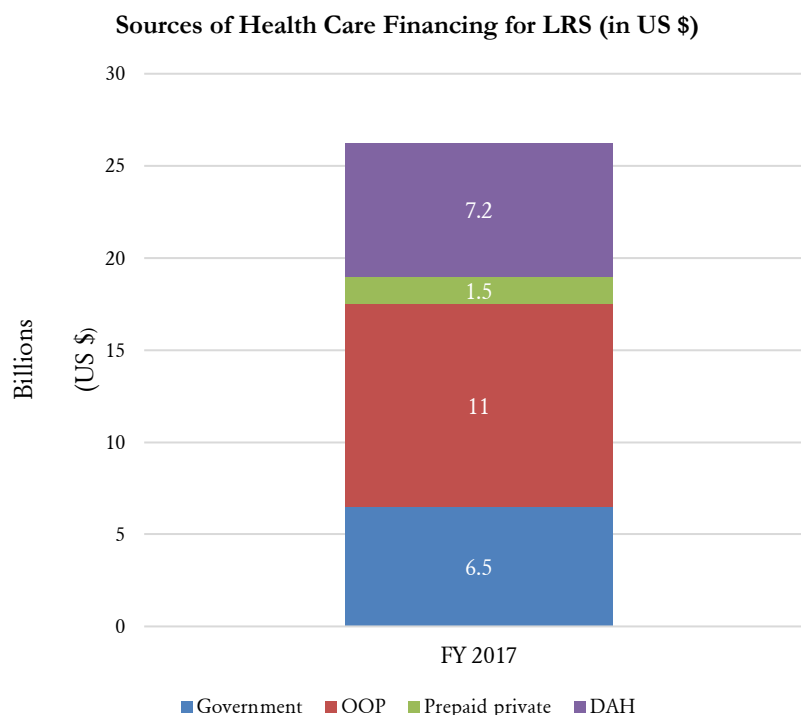
Source: *The World Bank World Development Indicators* ⁴⁴

Health systems in LRS and key health indicators

LRS face unique challenges in health: persistent shortfalls in financing for health system development and many competing health priorities. As a result of wider scarcity, LRS often lack investments in infrastructure, supply chain, and trained health professionals. In this work, the term LRS is used to classify the context of resource constraint.

Figure 1.4 illustrates the distribution of sources of health care financing in LRS during the 2017 fiscal year. Of a total of US\$ 26.2 billion, nearly half of all health care provided in LRS is financed from out-of-pocket payments (OPP) by patients, while over a quarter is financed from global donors via development assistance for health (DAH). There is a noteworthy imbalance between the proportion of costs covered by the government and the heavy presence of DAH and financial burden borne by patients. Very little financial protection exists for those seeking care.

Figure 1.4 LRS sources of health care financing



Source: Institute of Health Metrics and Evaluation ⁴⁵

Issues of scarcity exist across the health infrastructure spectrum, ranging from a lack of human resources for health, to a shortage of facilities, medical supplies, and equipment to meet population needs. **Table 1.3** presents a summary of key health system indicators in LRS where these challenges are endemic. The poor performance of many indicators makes it abundantly clear that more must be done with fewer resources in LRS, and signals the substantial strain experienced by these nations in providing public services to their populations.

Table 1.3 Health system indicators for LRS

Indicator variable	Value and units
<i>Financing</i>	
Current health expenditure (% of GDP)	5.7%
Domestic general government health expenditure (% of current health expenditure)	20.1%
External health expenditure (% of current health expenditure)	22.3%
Out-of-pocket expenditure (% of current health expenditure)	51.5%
<i>Infrastructure</i>	
Hospital beds (per 1,000 people)	0.8
Nurses and midwives(per 1,000 people)	0.9
Physicians (per 1,000 people)	0.3
UHC Service Coverage Index	42.1
<i>Financial protection</i>	
Proportion of population spending more than 25% of household consumption or income on OOP health care expenditure (%)	1.5%
Proportion of population pushed below \$1.90 poverty line by OOP healthcare spending	0.9%
% pushed below \$1.90 poverty line by out-of-pocket health care expenditure	1.2%

Source: *The World Bank World Development Indicators* ⁴⁴

1.3.2 Uganda

During the period of this study, immense strides forward and opportunities were occurring in Uganda. The time-sensitive ability to assess the ongoing implementation of a WHO package to systematise EC presented a unique occasion to conduct empirical assessments of the theory presented in this thesis and contribute robust evidence to the cost-effectiveness of facility-based interventions. For this reason, Uganda acts as the primary location for the empiric data which forms the basis of later chapters. In this section, key health and demographic indicators are summarised and a brief overview of the Ugandan health system is provided.

Geographic, Demographic and Socio-Economic information

The East African nation of the Republic of Uganda shares borders with five other countries. The Democratic Republic of the Congo sits to the west, Kenya to the east, Rwanda and Tanzania to the south, and South Sudan to the north. Conflict afflicts some of these meeting points and has driven refugees from these areas to seek refuge within Uganda's borders. As a result, populations near these borders surge, adding to the capacity needs of the health care system of these regions.

The population is young, with nearly half of the total population under the age of 15 and over 40% living of the below the poverty line. Trauma conditions are prevalent, and the country remains among the top-ranking countries for Road Traffic Injuries.⁴⁶ **Table 1.4** presents a summary of selected indicators that provide insight into the population, their health, and financial standing.

Table 1.4 Demographic, Health and Socio-economic indicators for Uganda

Indicator variable	Value and units
<i>Demographics</i>	
Population	44,269,594
Growth rate (annual)	3.6%
Population between ages 0-14	46.5%
Population between ages 15-64	51.5%
Population above 65	2.0%
<i>Health</i>	
Life expectancy at birth	63 years
Under five mortality rate	45.8 (per 1,000 live births)
Mortality caused by RTI	29.0 (per 100,000 people)
<i>Socio-economic</i>	
GDP per capita	2,272 (International \$)
GDP per capita growth rate	2.8%
% below poverty line	41.5

Source: *The World Bank World Development Indicators* ⁴⁴

Health system in Uganda

The Ugandan health system is comprised of both private and public health facilities. A majority of care is accessed at public facilities where it is provided free of charge to citizens. Services are delivered across four tiers of facilities including Health Care Centre IV, District Hospital, Regional Referral Hospital, National Referral Hospital which are all managed by the Ministry of Health in coordination with District Health Officers. **Table 1.5** presents a summary of key health system indicators.

Table 1.5 Health system indicators for Uganda

Indicator variable	Value and units
<i>Financing</i>	
Current health expenditure (% of GDP)	6.5%
Domestic general government health expenditure (% of current health expenditure)	15.8%
External health expenditure (% of current health expenditure)	43.1%
Out-of-pocket expenditure (% of current health expenditure)	38.4%
<i>Infrastructure</i>	
Hospital beds (per 1,000 people)	0.5
Nurses and midwives(per 1,000 people)	1.2
Physicians (per 1,000 people)	0.2
UHC Service Coverage Index	45
<i>Financial protection</i>	
Proportion of population spending more than 25% of household consumption or income on OOP health care expenditure (%)	3.8%
Proportion of population pushed below \$1.90 poverty line by OOP healthcare spending	41.5%
% pushed below \$1.90 poverty line by out-of-pocket health care expenditure	3.2%

Source: *The World Bank World Development Indicators* ⁴⁴

The country is divided into geo-administrative regions (Northern, Eastern, Central, and Western), each catering to a population of approximately nine million.⁴⁷ Regional Referral Hospitals

(RRH) which are the referral centres for multiple districts, provide specialised clinical services and act as centres for teaching and training. Placed strategically around the country, these sites provide higher-level referral coverage to the district health care delivery system. **Figure 1.5** shows the distribution of RRHs across the country.

Figure 1.5 Map of Regional Referral Hospitals in Uganda



Emergency care in Uganda

Some hospitals, commonly higher-level centres of care such as RRHs or National Referral Hospitals, maintain EUs. These facilities are a rare occurrence at the district level. At higher level sites, EC services are still limited by gaps in clinical documentation, equipment, regulation, and clinical protocols, including response capacity to mass casualty incidents.⁴⁸ During 2017-2018, injuries from trauma and road traffic incidents alone accounted for 7% of all mortality in public Ugandan health facilities.⁴⁹ Lack of training, variation of triage protocols from one hospital to another, shortage of staff on duty, absence of national guidelines on triage and poor administrative support are all major barriers to improvement and development of formal triage in all these hospitals.^{48,50} EC as service has evolved in recent years alongside the creation of the

department of Emergency Medical Services within the Ministry of Health (MoH) and current efforts towards a national emergency medical services policy.

Sources of health financing

Sources of health financing include public, household out-of-pocket expenditures, voluntary health insurance, and development partners. Even though user-fees and cost-sharing were abolished at government hospitals, OPP contribute 40% of total health spending. In comparing, DAH received (\$830 million) relative to government health expenditure (\$280 million) in 2017, it becomes clear that donors outspend government contributions to health.⁴⁵ Despite an increase for financing health services of 93% over the recent 5 years (2011-2016), from 660 billion UGX to 1,271 billion UGX, limited funds are dedicated to the management of ECS.⁵¹

1.4 STRUCTURE OF THE DISSERTATION

To achieve the stated objectives, this dissertation is composed of three empirical studies and a guiding conceptual framework presented throughout eight chapters. Of these chapters, three (3, 6, and 7) are published or submitted works and reproduced here verbatim. Thus certain abbreviations that are outlined in earlier chapters may be repeatedly defined in these selected chapters to maintain an exact reproduction of the published text. The dissertation adheres to the following structure:

This first chapter provides an introduction to the dissertation including an overview of the motivation for the research, objectives, and aims. It also provides background to EC, the study setting, LRS, and details about the country (Uganda) where the primary research was conducted.

Chapter 2 lays out the theoretical frameworks and approaches taken in this work. In reviewing discourse around the application of economic principles to health in LRS, it establishes an efficiency criterion which is used throughout the chapters that follow to evaluate the achievement of health objectives.

In Chapter 3, a robust systematic review is presented to summarise the current knowledge of the cost-effectiveness of EC in LMICs.

From here, Chapter 4 progresses to explore the concepts and approaches for CEA of EC interventions, and uses the findings and lessons to guide the development of a conceptual framework for assessing the cost-effectiveness of facility-based EC interventions.

Chapter 5 identifies and discusses the methodological challenges of employing cost-effectiveness in EC.

In Chapter 6 a micro-costing study of facility-based EC interventions is presented to determine the true cost of EC in the setting of interest and to address the lack of robust context-specific data about the cost of EC in LRS. Empirical data from this study is then applied to a decision

analytic model to conduct a retrospective CEA of the outcomes reported in a 2016-2017 pilot study of the WHO toolkit in Uganda. Methods and results of this analysis are presented in Chapter 7.

Chapter 8 finishes with a discussion on the contributions to the literature. Consideration is given to the limitations of these findings and attention is paid to the implications for decision-makers regarding the development of EC in LRS.

In Chapter 9 recommendations for future research are made and conclusions drawn.

Chapter 2

THEORETICAL FRAMEWORK AND APPROACHES TO ASSESSING COST-EFFECTIVENESS

“The complicated analyses which economists endeavour to carry through are not mere gymnastic. They are instruments for the bettering of human life.” - Pigou 1928

Answering the primary research aim of this work concerning the cost-effectiveness of facility based EC first requires establishing a basis from which value is measured and the criteria for judging efficiency goals. This chapter aims to demonstrate the importance of inherent value judgements in this process, and illustrate how they shape the approach taken throughout this dissertation. Theoretical literature is reviewed, and the ideologies, frameworks, and tools adopted in this research are outlined. Foundational frameworks and theories are detailed to establish an understanding of both health economics and EC before moving on to the analytical and empirical efforts in the following chapters.

The discussion uses the following structure. First, key economic terms are defined and arguments and concepts on measuring efficiency are summarised. Next, the implied ethical frameworks underpinning decision analysis are discussed and various consequentialist theories are introduced in more depth. Section 2.4 reviews the various normative frameworks for assessing and measuring value. Following this, Section 2.5 explores the use of economic evaluation as a decision support tool, paying particular attention to the use of CEAs. This is followed by a detailed discussion on why CEAs are used. Specific challenges faced in conducting analyses in LRS are identified to account for why CEAs are less commonly used in this context. Finally, suggestions are made into how CEAs could be applied to policymaking in low resource environments.

2.1 INTRODUCTION

This dissertation builds on the intersection of decision theory and health economics, endeavouring to develop an economic argument for the value of EC. The ensuing chapters are shaped by the dichotomy of two fields of study which until now have not been naturally linked. This includes economic evaluation and EC. To understand the cross-disciplinary approach taken in this dissertation the inherent basis for decisions and how choices are made are first studied to determine how success is measured in later chapters. Certain critical theoretical assumptions are taken in the remainder of this dissertation and outlined here.

Principally this study is concerned with matters of how choices are evaluated to guide decision-making. It is important that the foundation of the theoretical approach be outlined, and key concepts defined ahead of composing the remaining chapters. This establishes the criteria upon which evaluations and assessments can be made, and how the health care system is examined for

inefficiencies in resource allocation. The use of economic efficiency criteria, rather than explicitly ethical or political considerations, is justified.

2.2 CONCEPTS IN ECONOMICS AND EFFICIENCY

This section briefly explores the framework of health economic theory to ground subsequent discussions. Key ideas are reviewed to highlight the importance of their roles in assessing concepts of value under health economic theory. Consideration is given to the paradigms and assumptions that define the concept of efficiency based upon this framework. A brief outline is given of the underlying assumptions of opportunity cost, pareto efficiency, utility and utilitarianism, and welfarist and extra-welfarist approaches.

Our world has a finite amount of goods and resources. The reality of this resource scarcity necessitates that choices be made among several alternatives. The field of economics studies human behaviour in the face of this scarcity, and endeavours to make sense of this world where resources are limited, and choices must be made. Economic theory aims to explain and interpret the actions of consumers and sellers interacting in the exchange of goods and services, what is defined as a market. It hinges on the principles of utility maximisation and economic rationality. Both assume that choices are made by rational actors who make their decisions based on a calculation of which choice will give them the most benefit. As a result, trade-offs are always being made between competing services and products in the market. The theory assumes that, when certain conditions exist, rational actors will seek to maximise their consumption of value and choices will be made based on where they derive more satisfaction or value. The phenomena of why and how this rationality influences the distribution of goods and services grounds the approach taken in this dissertation. The empirical and conceptual contributions of this work borrow from the vast literature on health economic theory. In adopting this approach, the remaining chapters are concerned with the principle of efficiency or the amount of useful output produced per cost of resource consumed.

Opportunity costs

In understanding the relationship between scarcity and choice, it is important to recognise that for advances to be made in one area losses must be taken in other areas.⁵² That is to say that to consume one thing means inherently giving up the ability to consume another, thereby resulting in a loss of unrealised gain of the forgone alternative. Thus, the cost of having one option must also include the loss of another that had to be given up. This occurrence is known as an opportunity cost, which establishes that all choices mean that there is a forgone alternative. An example for health decision makers would be if one patient consumes excess resources, or receives inefficient treatment, this may deny treatment to other patients who could have benefited from treatment if the resources had been better used. In exploring EC in LRS from an economic perspective, we consider the opportunity cost of other forgone health services.

Pareto efficiency

According to Vilfredo Pareto's 1906 *Manual of Political Economy*, under certain assumptions the market produces efficient outcomes where no further changes can be made to improve utility for one person without detracting from another.⁵³ This phenomena, coined Pareto efficiency, sets a point at which social welfare is maximised by the allocation of resources. In this state of competitive equilibrium, there is no improved alternative allocation of resources which can occur without reducing utility for someone else. This level of optimality is achieved through a series of choices that create improvements for at least one person without harming others, also known as Pareto improvements. Pareto's theory implies that through these improvements, there is a systematic and measurable way to accomplish optimal societal gains. Ultimately, there exists a point where no further improvements can be made. It establishes a yardstick by which it is feasible to measure "correctness" in the distribution of resources across society and achieve maximum satisfaction.

Implications for resource allocation

The analytical methods performed in this dissertation use a goal-based approach linked to the basic principle of economics, founded in the concept of economic efficiency. Economic efficiency assumes that decision makers seek to maximise the health outcomes gained by resources invested in health to ensure society maximises benefits from its limited supply of resources.⁵⁴ Consequently, efficiency targets seek the point of equilibrium in which maximum productivity of available resources is attained with the least amount of waste. Both this objective, and the proximity to achieving it become quantifiable.

Health is unlike most goods in that it is not directly traded on a market. Wellness cannot be directly purchased, only the health care and services which aim to achieve wellness may be acquired. As a result, attention must be paid to its meaning, measurement, and value in economic theory. Efficiency is a particularly salient task when it comes to the delivery of health. Economists argue that due to persistent market failures, such as uncertainty of disease incidence or efficacy of treatment and information asymmetries, the market will fail to attain efficient outputs on its own. The numerous market failures in health make it possible for inappropriate or poor quality care to continue at high prices unless policy action is taken.⁵⁵ In comparison to other sectors it is widely agreed that in determining health care policy decisionmakers should pursue the objective of efficiency to mediate these challenges. This follows public interest theory, where regulations by decision makers seek to protect and benefit of the public at large.

Health care decisions are concerned with productive efficiency, or optimal production of health, and allocative efficiency, or the optimal distribution of health. These multiple dimensions address avoiding waste and reducing costs through technically efficient methods of production. Importantly, depending on the values set by society, utilitarianism does not always achieve socially desirable distributions of resources, but rather efficient ones. For example, it may be more cost-effective to place human resources for health in metropolitan areas over rural areas. In a metropole setting each clinician has the capacity to treat more patients with the same level of investment costs. Although this might be the most efficient use of a limited basket of resources,

doing the most for the most people, it does not address potentially unequal distribution of health care resources. In fact the efficient choice in this case could worsen geographic inequality.

There are a number of weaknesses associated with using considerations of efficiency to drive decision making in health. First, efficiency may not address inequality as an efficient approach could still mean an unequal one. However, given the limited means available in LRS, convincing arguments have been made that efficiency and the alleviation of inequality are in fact coherent with one another.⁵⁶ For example, Marseille and Kahn argue “the incremental benefit of investing additional global health dollars for the poor and others with limited access to health care is generally greater than the incremental benefits generated by the same dollars spent on the more affluent and those with better access to health care”.⁵⁷

The remaining chapters of this dissertation continue to use the criteria of economic efficiency as maximising health gains for resources allocated. The counter argument is that inefficiencies exist where resources could be re-allocated to produce better health outcomes. These principles play a role in priority setting in health care decision making.

2.3 IMPLIED ETHICAL FRAMEWORKS

The practice of decision-making is guided by using both social and ethical values to resolve the trade-offs between choices. These parameters help determine how we ought to act, what is considered right and wrong or better and worse, and how these choices are evaluated. However, defining desirability is not value-free and there are numerous ways to approach reaching this conclusion. Both explicit and inherent standards for behaviour are reflected in our value judgements.⁵⁸ Economic analyses, which seeks to weigh these trade-offs, are innately influenced by a variety of important ethical theories. This section traces principles of the implied ethical frameworks that underpin the remaining chapters of this dissertation.

2.3.1 Normative theories and consequentialism

Normative theories are based on what *should* or *ought* to be, rather than observing what is. Under this philosophy, choice is both subjective and prescriptive in nature. Much of the field of economics is characteristically normative, conducting analyses framed by opinions based on what is desirable. Normative theories cannot be proven but are rather used to prescribe what should be done. The value judgements fundamental to normative theories are determined by ethical frameworks. Such frameworks provide a set of principles related to right and wrong conduct to establish what is desirable and the values which drive decisions and influence choice. In setting a basis for what is right, and thus also what is wrong, the grounds for objectives are established and provide the possibility of defining measures of benefit based on what is to be improved or valued on the way towards achieving this the intended goal. The research in this dissertation practices a prescriptive approach encoded by normative theories and analyses to guide decision makers towards optimality.

Consequentialist ethical theory adopts the understanding that choices are made on the basis of their consequences and thus actions are justified only by their outcomes.⁵⁹ Better choices can be determined by the quantity of good consequences produced, and accordingly, the right action is the one which creates the best outcome. For example, if there is only enough of a particular medicine for one very sick patient or three patients whom are less ill, the better choice would be to use the drug to produce the most good consequences for the three patients rather than one. This approach is particularly useful in population level choices where the consequences of decisions may be better for some than others. Consequentialist theories are adopted for the deliberations of this dissertation to justify better choices by their outcomes in both health and economics.

2.3.2 Utility and Utilitarianism

Value is fundamentally subjective, based on personal judgement of desires. For this reason, it can be particularly difficult to measure that which can systematically capture satisfaction derived from the consumption of a good or service. 19th century philosopher Jeremy Bentham sought to establish a single index to capture this “goodness”. He detected that this value was determined by the individual’s instinct to seek that which is pleasurable and avoid that which is painful. He defined this unit as “utility”, a term which has since become the prevailing measure in economics to quantify the perceived value associated with, or satisfaction derived from, a good or service. This expression speaks to what Bentham identified as choices which are made based on individual desire to increase pleasure and decrease pain, resulting in overall improved welfare. Today, the utility principle in economics states that individuals maximise their welfare by rationally seeking to gain the highest level of satisfaction from their decisions. In doing so consistently, these actors can be expected to consistently choose their preferred options, also known as maximising their utility.

The axiom of utility inspired the ethical theory of utilitarianism, first outlined in Bentham’s *An Introduction to the Principles of Morals and Legislation*.⁶⁰ Utilitarianism adopts a normative approach, describing how people should act and provides insight into how policy or laws should be established. The value of the consequences of choice in utilitarian theory are set by the amount of pleasure derived from the good or service in question. In Bentham’s classical utilitarianism approach, social and economic policies should be measured by the consequences they hold for human happiness or utility. Advancing upon Bentham’s work, John Stuart Mill’s 1863 work *Utilitarianism* emphasises that the goal of society should be to seek the “greatest good for the greatest number”, which can be measured by the sum of all individuals’ utilities.⁶¹ This theory persists as one of the most frequent motivations used by policymakers to drive decisions which have population level impact. Maximising outcomes for all involves improving the situation for the most individuals possible.

Although utilitarian theory serves an important basis for the understanding of choice and decision making, there are some notable weaknesses in its usefulness to guide decisions. Principally, it fails to capture considerations of equity, individual choice, and preference, which

may repeatedly result in situations in which efficacy and equity are opposed. Mutually beneficial outcomes are not always reached. For example, it is possible that harming a minority might benefit a majority. Principles of utility and utilitarianism are applied to this research in the pursuit of maximising welfare for society.

2.3.3 Welfarist approaches and social welfare

Individual utility is sometimes called welfare or well-being. In his 20th century work *The Economics of Welfare*, Alfred Pigou (1920) introduces a theory which assesses policies and choices based on the effects on the welfare of a broader community.⁶² Similar to utilitarianism, welfarist approaches identify the possibility for resources to be allocated in a way to maximise the total sum of individual utilities. However, welfarist approaches exclusively focus on the consequences of choices, maximising social welfare, and ignores other factors. Welfarism suggests a very simple central tenant, that social welfare of a society is measured as the sum of all individual welfares in that society and individual welfare is measured only from utility. This suggests that choices can be justified based on preferences of individual members of society. In doing so it is a pragmatic solution to the challenge of assigning scarce health resources and provides an approach capable of identifying that some individuals may value health more highly in comparison to other goods. It accepts that different individuals value the same health states differently and that it is their derived satisfaction which should be measured rather than the health output. This theory was later adapted by the economist Amartya Sen and applied to economic policy, establishing what he termed welfare economics. He argues that social choice is not determined by individual welfare but rather by individual's choice of interest. A benefit of this approach is that it better captures measures of inequality. Although this work draws from Sen's theories, much of his work is concerned with addressing inequality and poverty. For the primary purpose of this dissertation, which is concerned with health policy rather than economic policy, definitions of welfarism rather than welfare economics will suffice.

Critics of welfarist approaches argue that they lead further from efficiency and closer to inequality as a result of preferences being conditioned by other elements of the social environment. In markets of health in particular, using an individual's willingness to pay may not accurately represent the best interest of individuals, since market imperfections in health can cause irrational consumption. Practically, it is cumbersome to find each individuals willingness to pay for improved health.

2.3.4 Extra-welfarist perspective

Coining the term in his 1989 work *The Normative Economics of Health Care Finance and Provision*, Anthony Culyer describes extra-welfarism as moving beyond the traditional considerations of welfare economics to focus on maximising health rather than social preferences.⁶³ He argues that there are characteristics of health the same as a good which make it more appropriate to consider issues beyond the focus of welfarism on the consumption of goods and services. While welfare approaches try to maximise the sum of individual utilities within budget constraints, extra-welfare approaches aim to maximise health outputs. This difference is in how the relationship between

health and utility is observed. The former is defined by the contribution of health to overall welfare, whereas the latter seeks to extend health against all other goods, as if health itself is the utility.

Extra-welfarism moves beyond the individual preferences and towards pursuing societal objectives based purely on outcomes. In doing so, an assumption is made that the value of health states are homogenous across individuals, diminishing the potential differences in value of incremental health. By overriding individual preference, the objective is shifted to maximise societal health outputs given the available resources. Therefore, health becomes the principal output and assessing the consumption thereof focuses solely on the effect of this consumption on health outcomes.⁶⁴ These outcomes move outside of traditional measurements of utility as willingness to pay towards measured natural units of output such as the quality-adjusted life-years (QALYs) and DALYs. It also makes it possible to select a singular most efficient mix of choices to achieve this goal.

2.4 APPROACHES TO VALUE AND BENEFIT ASSESSMENT

Rational planning requires a measurement of output to be able to establish a relationship between inputs and outputs.⁶⁵ Setting the explicit value for loss or gains of health can be approached in numerous ways. Prescriptive in nature, the following approaches set the scope of how outcomes are assessed and what benefits should be valued in analyses.

2.4.1 Human capital approach

One approach to establishing priorities considers economic growth as a function of health, produced as a factor of contribution to the overall gross domestic product (GDP). In 1962 Gary Becker developed this theory in which he identified that what is related to the qualities and abilities that make individuals productive as human capital. In his foundational work, *Investment in Human Capital: A Theoretical Analysis* Becker notes that imbedding resources in people can lead to future real income.⁶⁶ In doing so he established the first grounds of the idea that investments in education and job training to improve the abilities of the individuals receiving them, thereby increasing their prospective income.⁶⁶

In drawing direct links with certain actions and investments to a financial outcome the human capital approach (HCA) uses forgone future earnings as a measure of value. Although the theory has been used in the realm of education and training since the 1960s, it was only applied in depth to the dimension of health during the early 2000s. Various authors have investigated the effect of health on economic growth, or disease in depressing income.^{67,68} Bloom et al. indicated health has a positive and statistically significant effect on economic growth.⁶⁷ Furthermore, Weil was able to measure income gains that result from improvements in the health of populations.⁶⁹ From this perspective authors traced the microeconomic impact of health on individuals which is then applied across entire populations. Countries were modelled to show their outputs as a function of their inputs to consider the efficiency with which these inputs are used. Based on Becker's theories which indicated that certain investments could lead to a higher skilled, higher

functioning, and therefore more productive workforce, improved health has been presented as having impacts on the economic viability and growth of nations in the future.

This theory places importance on a range of inputs that contribute to an individual's productivity. For example, better health means fewer days of missed work due to sickness or disability, either for oneself or in the care of family members. Physical and mental wellness can contribute towards more energetic and productive workers. Fundamentally then, healthier populations will have more hours which they can work and produce. As a result, lost productive years in contributing skills and services to the labour force are considered welfare losses. Measuring the value of life by the contribution the individual can make to society in terms of monetary value captures the impact of a programme upon the larger economy.

There is an established precedent of using HCA for EC in the fields of trauma and injury.⁷⁰ A fundamental reason is the ability of this approach to better capture the economic benefit of saving lives and reducing morbidity which may not be weighted as significantly using an alternative approach, and does not value productive working years as considerably. This is also consistent with many of the existing health technology assessment agencies in HICs.⁷¹

The application of HCA is not without controversy. Arguments have been made that this approach takes too narrow a view by disregarding the multi-dimensional nature of welfare and as a result does not provide a sufficient basis for value. Furthermore, health has an intrinsic value outside of its capacity to contribute to productivity.⁷² In measuring the value an individual provides society exclusively by annual income, other areas of life which may provide utility are not accounted for. The HCA is often criticised for overlooking questions of equity and non-financial measures and representing human life in dollar terms. There are many other considerations in decision-making which are overlooked in adopting an approach so directly linked to economic outputs. Furthermore, by assessing a patient's contribution to society based on income level this approach can imply that a life in a LRS, where GDP per capita is much lower, is of less value than a life in a HIC.

2.4.2 Human rights-based approach

Another such argument for priority setting stems from moral and ethical obligations. A growing body of literature supports the shift towards an inherently human rights-based approach (HRBA), framing health within a government's broader commitment to fulfil human rights. This marks a shift away from determining the provision of health based on the financial usefulness to a nation state and towards an understanding of a human right to health, regardless of economic productivity. The theory fundamentally recognises that the human experience and worth comprise more than simple economic productivity, and there is value to life even if it is not lived in ways which contribute to a growth in GDP. Burkholder et al (2019) propose a human rights approach to EC, which draws from modern thinking regarding the right to health and UHC.⁷³ The authors argue that motivations to improve provision of EC should be framed under the premise of the right to high quality care. This discourse is especially relevant in considering the

commitment of many leaders to the Sustainable Development Goal (SDG) target 3.8 that “aims to extend UHC to one billion more people by 2023”. While a very noble approach, arguments have been made that HRBA does not capture the true willingness to pay of the individual, and may cause an undervaluing of health as a good. This produces distortions in the market which disrupt the capacity to achieve pareto optimal outcomes. Under an economic assumption, this could limit optimal distribution of resources and result in welfare losses.

The decision to apply one approach over the other in this dissertation was closely considered to align with the prevailing frameworks for decision-makers in LRS. While monetary considerations are not the only measures, they are important ones. Financially comfortable nations are better positioned to provide conditions which create and maintain the well-being of their citizens. Using this approach is justified by the fact that financial stability is an important means to many of the other values which have been listed here. Lastly, due to the nature of acute care and trauma care which affect the young and healthy and the significant number of productive years ahead of them, it is important to enumerate the opportunity cost and loss that results from delayed investments in EC.

Although many have presented arguments for EC as a human right, this dissertation takes an HCA to understand what the cost of EC is and whether it is “worth it”. An HCA is relevant to the particular challenges faced by LRS, where decision-makers are inclined to measuring resources, both in how they are spent and how they are generated. It understands the essential scarcity of funds which defines many LRS capabilities to provide public services. Where services, expertise, medical devices, and treatments all have price tags, it is difficult to separate decision making from a financial approach. While there are many further arguments for the advancement of EC, this work focuses on the practicality of what is effective in regard to budgetary constraints experienced by LRS.

2.5 COST-EFFECTIVENESS ANALYSIS AS AN EVALUATION TOOL FOR HEALTH

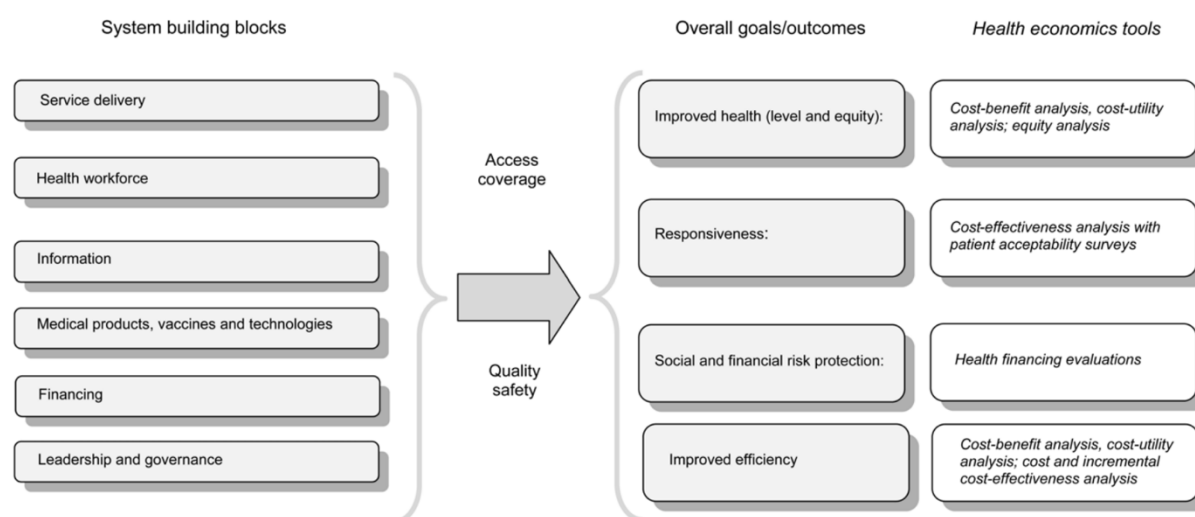
Michael Grossman’s 1972 work *On the Concept of Health Capital and the Demand for Health* provided the first model for demand for the commodity of health as a good.⁷⁴ By establishing this link, he ushered in a period of using analytical methods to extend beyond understanding good investments in health towards achieving optimal investments. In normative economics, the most efficient distribution of resources is identified as the point pareto efficiency is achieved. Thus, under welfarist orientation and Paretian optimality, certain decision tools and techniques use analyses which measure how close we as a society are to reaching this level of optimality.

Economic evaluations examine the relative efficiency of alternative courses of action in improving health.⁵² These analyses provide an indication of where money should be invested and which health services to provide depending on an assessment of incremental costs and benefits.⁷⁵ Under such assumptions, it becomes possible to measure gains across very different health priorities in a comparable manner, which can establish an ideal choice. Foundationally the belief

is that one can use these methods as a decision tool, guiding choices and trade-offs which must be made with limited resources.

Numerous tools are available which offer a prescriptive examination of the distribution of limited resources. Utilising these tools can help decision-makers measure how resources are used to achieve health goals within a system. **Figure 2.1** pairs the function of each of these alongside building blocks in the WHO health systems framework. Each of the techniques to evaluate health maximisation is suited for different overall goals and outcomes of the system. The tools function to translate principles of normative theory and welfarism to guide decision making. These evaluations serve to identify, measure, compare and value alternatives by their costs and consequences.

Figure 2.1 WHO health system framework with health economics tools



Source: Mann et al (2011)⁷⁶

In providing an explicit set of criteria to help determine decisions, economic evaluations allow for the analysis of the costs and consequences of alternative course of actions.⁵² Of the available options, CEAs are the central policy tool for many health systems.^{77,78} CEAs stem from both Paretian welfare economics and extra-welfarist principles which assume that the objective is to maximise health. By using these analytical tools it becomes possible to measure and compare the relative benefits of two programmes using decision analytics to drive rational planning. Assuming normative economic principles, this analysis allows for comparison of different interventions aiming to achieve the same overall goal of improved population health. It is a powerful tool which can help inform decisions seeking to achieve the most efficient distribution of limited resources. Decision-makers can thus comprehensively deal with both cost and consequences of competing course of action.⁵²

In applying natural unit outcome measures the CEA is one of the most widely used analyses for health care policymaking, where there is both an interest in how to spend limited resources as

well as the benefit they will have on the lives of patients. CEAs allow for the full incorporation of both of these needs and for this reason they are one of the most popular analytical methodologies. Accordingly using common natural units affords the advantage of comparing different programs from one another to indicate which is the best allocation of resources.

2.6 COST-EFFECTIVENESS ANALYSES IN LOW RESOURCES SETTINGS (LRS)

Numerous countries have systematised the use of these decision tools in priority setting, known as health technology assessments (HTA). This type of evidence-based analysis provides critical information for a well-functioning health system to direct investments in health, to prioritise health care needs, and to maximise the benefits of tight budgets. Yet, of the countries categorised as the lowest-income by the World Bank, none have recognised HTA governing bodies or guidelines. Of the 44 worldwide pharmacoeconomic guidelines listed on International Society for Pharmacoeconomics and Outcomes Research's (ISPOR) webpage, there are none attributed to LICs, and only 11 from any non-HIC settings.⁷⁹ In a survey conducted by the WHO in 2015, only 13 LICs worldwide reported having a formal process to index information for decision making and only four of these countries indicated having legislative requirements.⁸⁰

For over a decade the literature has acknowledged the disparity of economic analyses conducted globally and called for efforts to develop modelling as a practice for LRS.⁸¹ A 2012 landscape analysis of HTAs in 12 LICs reveals the existence of few formal HTA bodies, indicating potential oversights in the evidence used for decisions which could improve population health.⁸² There is substantial room for improvement. The lowest income setting account for 12% of the global population, and carry 19% of the global burden of disease, yet a 2016 bibliographic review of economic evaluations found that only 4% of the evaluations in the review were conducted in this environment.⁸³ While it is easy to understand how LRS may benefit the most significantly from such evaluations, they often have the fewest resources to do so.

Furthermore, published CEAs are not distributed proportionately across disease areas. Across all country income levels, relative to their disease burden, HIV/AIDS interventions are over-researched while injury and wound interventions are substantially under-researched.⁸³ In regard to EC, most published CEAs only analyse single interventions of one condition and very few are able to capture the economics of scale which EC can provide. The existing literature offers few solutions to these challenges.

Moreover, methodological variation in how the evaluations are conducted in LRS compared to HICs has been well documented.^{84,85} There are a range of barriers which make it difficult to generate economic evidence in LRS and analysts are often hindered by a lack of high quality local data to support analyses.⁸⁶ The results of economic modelling are highly dependent on the quality and appropriateness of the variables used, and much data are not considered transferrable across settings. In contexts where there are difficulties in routine data collection and an absence of electronic records, even hospital records may be sparse. Simply using data that speaks to the clinical effectiveness of an intervention does not bring LRS any closer to understanding the

important consequences they can expect to see from a health programme in their own context and setting.

Along with poor data availability, there is a scarcity of expertise. While commendable efforts are being made to assemble robust local data and share open-source models, such as the WHO *CHOosing Interventions that are Cost-Effective* (WHO CHOICE) project, the deficiency of analytical power persists.⁸⁷ Key stakeholders in LRS cite a lack of information technology, lack of expertise in CEAs, limited data, and limited CEA training as barriers to the uptake of economic evaluations. Although expertise is limited, there is substantial interest in these methods with some indications that over 95% of key actors believe CEAs are important for clinical decision making and policy formulation.⁸⁸ Providing a rigorous yet accessible tool with the functionality to use contextually relevant data, where available, may significantly improve the applicability of the findings to guide decisions of spending in these LRS. Culyer and Chalkidou appraised the literature and identified nine main issues of using both CEA and cost-benefit analyses in LRS. Many of their findings, such as the lack of relevant data, non-comparable outcome measures, and lack of preference elicitation capacity, are echoed later in Chapter 5 of this dissertation and a summary of their findings are provided in **Table 2.1**.⁷⁸

Table 2.1 Nine issues for CEA in LMICs

1	Relevant data are not local; are incomplete; unreliable; or imprecise; are challenged by experts; or are completely absent.
2	High quality analytical capacity is lacking in clinical disciplines, health economics, epidemiology, ethics, biostatistics, systematic reviewing and meta-analyses.
3	Measures of outcome comparable to QALYs or DALYs are absent along with their monetary valuations, rendering the calculation of valuations of QALYs and DALYs irrelevant
4	Eliciting and using experimentally derived outcome valuations is a major research exercise fraught with potential biases over and above those entailed with DALY and QALY measurement and not to be cheaply replicated in every country.
5	It is not uncommon to find a prejudiced and unsympathetic, but dominant, senior cohort of professionals whose cooperation is not guaranteed
6	Political understanding of the value of pricing outcomes is likely to be absent
7	Gaining acceptance of a threshold is already a tough task extending it to valuing many outcomes, including those in nonhealthy sectors could at times be at odds with movement toward UHC.
8	Public understanding and acceptance of a solution modelled on a theoretical market outcome based on individuals' ability to pay is unlikely.
9	Major foreign funders of health care and health care policies have their own disease, or technology, or population level priorities and budgets not based on CEA.

Source: Adapted from Culyer and Chalkidou (2019) ⁷⁸

2.6 PRIORITY SETTING IN LOW RESOURCE SETTINGS

The use of economic evaluations for global health priority setting in LRS is rooted in the 1970's, a period in which economists began to advocate for rational spending practices to guide the work of multilateral and bilateral aid agencies. In his 1972 work *Health Priorities in Developing Countries*:

The Economist's Contribution Brian Abel-Smith argues that “the greatest contribution which the economist can make to health planning is not in the development of models, but in cost-effectiveness studies”.⁶⁵ He makes the point that the deficiency of representative evidence to inform the allocation of health services in LRS cannot be fixed in the use of theory alone. Many of the challenges he cites, such as lack of comprehensive cost studies undertaken in LRS, still hold true nearly fifty years later.

Limited health care resources render conscious resource allocation choice a necessity. Identifying efficiencies becomes paramount to the capacity of LRS to provide services that meet the needs of their populations. The realities of resource scarcity leave a need for systematic ways to assess the cost and benefits of assessments. Tools such as CEAs that can assess a variety of health challenges give scope for synchronise policy across a health system. The results of CEAs, in supplying a cost per health unit gained, provide this evidence-base to guide decisions and fulfil the argument that more rational planning can be achieved. Typically when assessments are conducted in LRS they are used primarily for budgeting and planning purposes as opposed to technology advancement, which speaks to the very different needs placed on low and high resource settings.⁸⁰

Efforts continue to be made to characterise cost-effective investment in LRS. The use of reference case and toolkits are further promoted to structure analytical efforts in this context. One such initiative is the DCP report. First published in 1993 by the World Bank, the report identifies and ranks the most cost-effective interventions for LRS across a wide range of disease areas. Updates have been published in recent years based on the latest available data and shifting burden of disease. Other gains continue to be made towards the growth of economically efficient rational decision making through initiatives such as the International Decision Support Initiative's Health Technology Assessment (HTA) Toolkit, The Guide to Economic Analysis and Research (GEAR) online resource, the Gates Reference Case, and in efforts to establish country-level cost-effectiveness thresholds.^{89,90} Initial findings suggest this guidance improves reporting adherence amongst per DALY registered studies.⁹¹

Lately interest has been shown in shifting away from an ad-hoc priority setting approach towards a standardised approach.^{92,93} Recently multidisciplinary collaborations have sought to identify priorities in research to improve EC in LICs with cost-effectiveness making the short list of priorities time and again.⁹⁴ More than ever there is a need for more CEAs to inform rational decision making. Efforts towards defining the cost-effectiveness of EC parallel the theoretical shift of extra-welfarist approaches towards maximising health outputs. This analysis is adequate for addressing larger health system goals, such as UHC, making it the right tool for the right time.

The benefits of this prioritisation work is of particular importance to LRS where scarcity is an undeniable reality. Conventional opinion echoes both the importance of such evaluations, as well as the dominance of CEAs over other forms of economic evaluation in the context at the given moment.⁷⁸ The transparency of using common objectives across all health care systems through the production of ICERs, facilitates the transfer of evidence. Due in part to the capacity

of such studies to yield practical results which identify the cheapest way to achieve a set of goals, economic analyses became recommended by numerous development agencies. As a result, using economic evaluation to set health care priorities is arguably one of the most effective ways for decision makers to meet their mandates.

Finally, there are notable developments to extend economic analyses beyond the straightforward costs and health outcome consequences of CEA. Although detailed discussion of these approaches such as multi-criteria decision analyses and generalised cost-effectiveness analyses falls beyond the scope of this work, it is important to note the direction of priority setting guidance. These proposed methods aim to better capture important consequences for decision makers, which are not captured in simply maximising health using political or equity factors.^{95,96}

2.7 CHAPTER SUMMARY

This chapter summarises foundational economic theories and value frameworks that set the tone for the work of later chapters. It illustrates the variety of fields from which this work borrows, including decision theory, social policy, and health economics, and the impact of this multi-disciplinary approach on the costs and effects considered throughout this dissertation. It assesses the value of EC based on principles of welfare economics and makes clear assumptions regarding the measurability of efficiency and the value of philosophy on well-being. In using normative decision theory, it is possible to analyse outcomes of choice given constraints and assumptions and explains the choice of using economic efficiency as a criterion for resource allocation decisions.

To assess cost-effectiveness of EC, a theoretical foundation is established. A theoretical foundation is established for following chapters that approach the economic argument for the value of EC in LRS drawing from utilitarian and welfarist principles. These theories lay the basis for the prescriptive rather than descriptive nature of this work, which seeks to describe how resources ought to be used rather than how they are used.

In the next chapter a systematic literature review is presented that summarises and evaluates the current knowledge and evidence on the cost-effectiveness of EC in LRS.

Chapter 3

A SYSTEMATIC REVIEW OF COST-EFFECTIVENESS ANALYSES OF EMERGENCY CARE INTERVENTIONS IN LOW-AND MIDDLE-INCOME COUNTRIES

In order to achieve the first objective of this work, a systematic review of the peer-reviewed literature was conducted to identify and assess all available data on the cost-effectiveness of EC interventions in LMICs. Section 3.1 provides a background and rationale for the study. Section 2 specifies the methods used in the review. In Section 3.3, results are summarised, and Section 3.4 considers both the quality and coverage of the literature. Section 3.5 summarises the study and introduces the subsequent chapter. This review has been published (Werner et al, 2020).⁹⁷ A copy of the published paper, verbatim with citations and table numbers changed to keep consistent format style with this dissertation, follows over the next eight pages.

3.1 INTRODUCTION

Emergency care is a health systems and service delivery innovation that facilitates early recognition and life-saving interventions for time sensitive acute injuries and illnesses, where a delay of hours may result in avoidable death or disability, or make treatments less effective.^{98,99} Frontline providers deliver these interventions across the emergency care system, from scene care to transport to facilities. Conditions addressed by emergency care include trauma, infections, noncommunicable disease and complications of pregnancy. These conditions accounted for nine of the 10 leading causes of death in LICs in 2017.¹⁰⁰ For people aged 5–29 years, the most common cause of death is road traffic crashes, causing over 28 million deaths a year, of which most occurring in low- and middle-income countries.¹ Researchers have estimated that over half of deaths in low- and middle-income countries, and up to 2.5 billion disability-adjusted life-years (DALYs) annually, could be addressed through the implementation of effective emergency care.⁹⁹ These figures are expected to grow due of factors such as increased use of motor vehicles, increased urbanization and lifestyle changes leading to increases in coronary heart disease. Traumatic injury alone is anticipated to represent a fifth of all ill-health worldwide by 2020.^{2,101} Early recognition of acute conditions by the health-care system, and improved access to care, could address much of the ill-health burden and save millions of lives. These facts have been acknowledged by the World Health Assembly Resolution *Emergency care systems for universal health coverage: ensuring timely care for the acutely ill and injured*.¹⁰²

Emergencies occur regardless of whether a health system is prepared to address them. An organised emergency care system can theoretically leverage economies of scope and scale by employing simple low-cost interventions that will save millions of lives. However, little is known about the cost-effectiveness of emergency care interventions in low- and middle- income countries, where such interventions may have the greatest impact.

Cost-effectiveness data is essential to inform the resource allocation decisions of policymakers and regulators. Such data encourages the prioritisation of systems and interventions most likely to provide a health and economic benefit. A survey of policymakers in Brazil, Cuba, Nepal, Norway, and Uganda demonstrated a majority preference for efficiency arguments, such as cost-effectiveness, in formalising the health priority setting process.¹⁰³

Here, we present a systematic review on the cost-effectiveness of emergency care interventions in low- and middle- income countries. Our aim was to characterise the existing knowledge regarding the costs and benefits of delivering emergency care in these settings, to examine the quality of cost-effectiveness analyses and to provide guidance for future research efforts.

3.2 METHODS

3.2.1 Search strategy

We systematically reviewed the literature on emergency care interventions in low- and middle-income countries. We searched for peer-reviewed articles on published before May 2019, in PubMed®, Scopus, Embase®, Cochrane Library and Web of Science. To capture the heterogeneity of emergency care interventions, we included components of both pre-hospital and facility-based emergency care system. An example of the search terms used is shown in **Box 1** and the full search strategy is available in the data repository (**Appendix E**).¹⁰⁴ We applied no language restrictions. To limit search results to our context of interest we applied the Cochrane LMIC filter.¹⁰⁵ The study was designed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses guidelines¹⁰⁶ and was prospectively registered with PROSPERO (CRD42018080145).

Box 1. Example Search Terms

Example of Search Terms for PubMed:

```
("Cost-Benefit Analysis"[mh] OR "cost benefit" OR "cost-benefit" OR "cost effective" OR "cost-effective" OR "cost effectiveness" OR "cost-effectiveness" OR "cost utility" OR "cost-utility")
AND
("Emergency Service, Hospital"[mh] OR "Emergency Medicine"[mh] OR "Emergency medicine"[TW] OR "Emergency services"[TW] OR "Emergency department"[TW] OR "Emergency service"[TW] OR "Emergency departments"[TW] OR "Emergency room"[TW] OR "Emergency rooms"[TW] OR "Emergency ward"[TW] OR "Emergency Unit"[TW] OR "Trauma Centers"[mh] OR "Trauma Center"[TW] OR "Trauma Centers"[TW] OR "emergency health service"[TW] OR "emergency health services"[TW] OR "emergency medical services"[TW] OR "emergency medical service"[TW] OR "accident and emergency"[TW] OR "accident & emergency"[TW] OR "a&e"[TW] OR "A & E"[TW] OR "prehospital"[TW] OR "ambulance"[TW])
AND
Cochrane LMIC Filter
```

3.2.2 Selection of studies

We uploaded all identified studies into the software Covidence (Covidence, Melbourne, Australia) for review. Studies were considered for inclusion if they: (i) described a system-wide or individual emergency care intervention; (ii) were implemented in an low- and middle- income country (according to 2018 World Bank classification) or analysed costing data from an low- and middle- income country; and (iii) undertook a full economic evaluation (either a cost-effectiveness analysis, cost-utility analysis or cost-benefit analysis). We defined emergency care

interventions as interventions that provide or facilitate the early care of acutely injured and ill patients, whether outside or inside a health-care facility. This definition included early critical care or surgical interventions that commonly take place in an emergency department.

Two reviewers independently assessed titles and abstracts for inclusion of the articles for the full text review. The reviewers only selected studies for full text review if both agreed that the studies met the inclusion criteria. Studies then underwent full text reviews for eligibility by two independent reviewers. Disagreements were resolved by consensus within the study team. To identify additional primary studies, we hand searched the reference lists of included studies.

3.2.3 Quality assessment

Two reviewers appraised the included studies using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.¹⁰⁷ To better understand the quality of data, we did a comprehensive scoring of studies, by giving one point for each fulfilled item on the checklist, however, we did not exclude any studies based on quality.

3.2.4 Data abstraction

The following information was extracted from included studies: country; year of publication; intervention; comparator; time horizon; discount rate, study perspective, health outcome, sensitivity analyses and findings. We converted cost results or the cost part of the incremental cost-effectiveness ratios to 2019 United States dollars (US\$) for comparability. Due to the lack of consensus surrounding the use of cost-effectiveness thresholds,^{57,108} we did not apply a global benchmark to each study's results, but left the results to be interpreted within the specific study context.

3.3 RESULTS

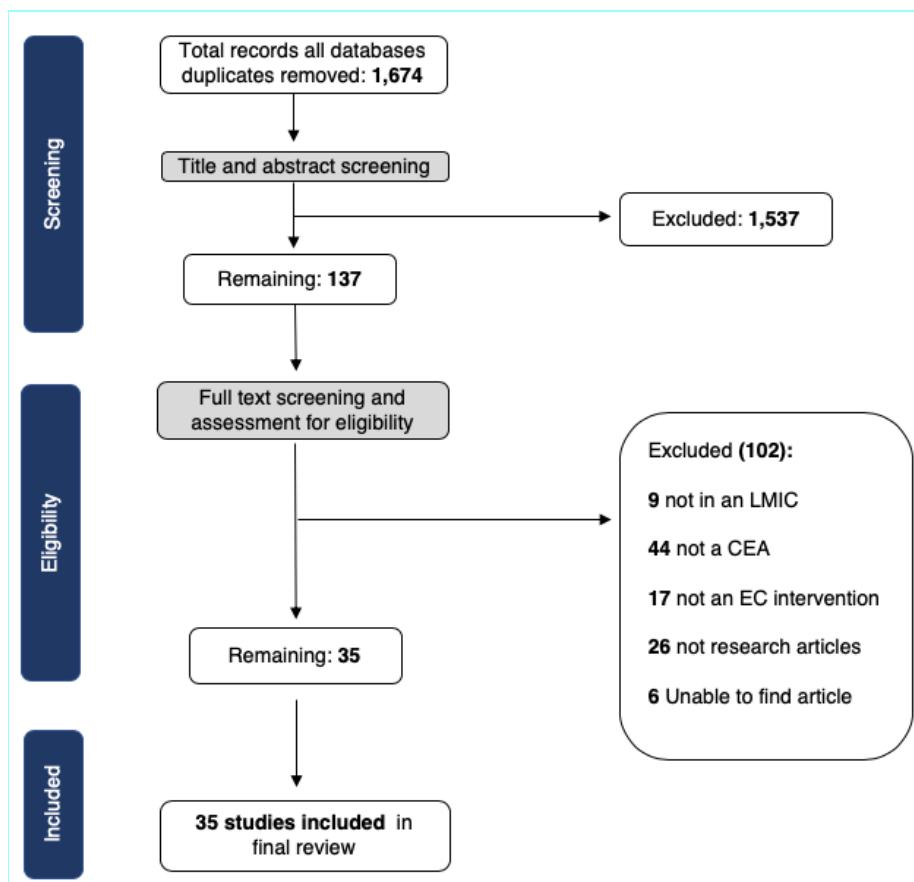
3.3.1 Overview of included studies

By searching the five databases, we identified 1674 unique articles. After screening titles and abstracts for eligibility, 137 articles remained for full text screening. Of these studies, 35 studies met all the inclusion criteria and were eligible for data abstraction. Additionally, we included four eligible studies identified through hand searching of reference lists (**Appendix F**).^{17,19–}

21,41,70,109–141

The reasons for exclusion during the full text screening were: not done in a low- and middle-income country (nine studies); did not contain cost-effectiveness analyses (44 studies); did not address emergency care interventions (17 studies); were not a research article (26 studies); or were not available in full text either online or by request (six studies; **Fig. 3.1**).¹⁰⁴

Figure 3.1 PRISMA Flow Chart



3.3.2 Quality assessment

Appendix G and Table 3.1 shows the overall grading of quality for each article section, the detailed CHEERS scoring of each included article is available in the data repository.¹⁰⁴

Table 3.1 Quality score of included studies on cost-effectiveness analyses for emergency care

	Section/item	Adequately reported Total number of studies, (%)		
Title and abstract	Title	31 (79)	>80%	Green
	Abstract	37 (95)	50-80%	Yellow
Introduction	Background and objectives	38 (97)	0-50%	Red
Methods	Target population and subgroups	37 (95)		
	Setting and Location	36 (92)		
	Study perspective	17 (44)		
	Comparators	28 (72)		
	Time horizon	12 (31)		
	Discount rate	17 (44)		
	Choice of health outcomes	29 (74)		
	Effectiveness	31 (79)		
	Preference valuation**	14 (36)		
	Costs	33 (85)		
	Currency, price date, conversion	30 (77)		
	Choice of model	16 (41)		
	Assumptions	16 (41)		
	Analytical methods	14 (36)		
	Study parameters	17 (44)		
	Incremental costs and outcomes	27 (69)		
Results	Uncertainty	17 (44)		
	Heterogeneity	5 (13)		
	Study findings/ limitations/ generalisability	37 (95)		
Discussion	Source of funding	23 (59)		
Other	Conflict of interest	21 (54)		

Only three studies considered a broader societal perspective,^{126,128,137} while 14 studies considered a health-care perspective.^{19,20,110,124,125,127,129-136} The remaining 22 studies did not clearly indicate the perspective used in the study.^{17,21,41,70,109,111,112,114-122,138-143} Ten studies did not clearly describe the comparator being used.^{19-21,70,109,110,138-141} Standardised metrics for health outcomes that allow for cross-intervention comparison were used in 26 studies. Most studies (13) used the life years saved or gained as health outcome,^{17,19,20,70,109,110,112,119,129-132,138,142} nine studies reported DALYs^{114,117,120,123-125,139-141} and three studies reported quality adjusted life years (QALYs).¹²⁶⁻¹²⁸ The other 13 studies reported findings in unique metrics that prohibit comparison to other disease programmes.^{21,41,111,115,116,118,121,122,133-137}

Only 12 studies clearly stated the structural assumptions underpinning their decision-analytic model^{21,70,114,117,123-129,133} and only 15 studies adequately described the analytical methods used to support their evaluations.^{41,70,114,117,120,124-128,132,133,135,137,144}

Although all studies analysed both costs and health outcomes, 12 studies failed to report an incremental cost-effectiveness ratio.^{21,70,111,112,115,116,118,121,122,132,135,136}

Of the 17 studies reporting uncertainty analyses, 10 were deterministic^{19,117,123,125-128,131,134,135} and seven used probabilistic sensitivity analyses.^{17,20,114,124,129,133,136} The remaining 22 studies did not adequately report the use of sensitivity analyses to assess uncertainty of either parameters or the

model.^{21,41,70,109–112,115,116,118–122,130,132,137–142} Only five studies reported on analysis of heterogeneity, making this item the most poorly reported checklist item.^{122,128,138,140,145}

3.3.3 Description of included studies

Included studies fell within five broad categories: prehospital services; training; treatment interventions; diagnostic tools; and facilities and/or packages of care. These categories are not mutually exclusive but rather reflect the primary nature of the intervention studied. **Appendix F** shows a summary of all included articles, interventions assessed and main findings.¹⁰⁴

Prehospital services

Five studies investigated the impact of either introducing a professional ambulance service or improving ambulance response times. Two studies looked specifically at the establishment of ambulance services for obstetric care,^{19,20} one at establishing a general emergency medical services system,¹³⁸ one for cardiac arrest care,¹¹² and one modelled the impacts of a decrease in response time.²¹ The cost-effectiveness of establishing an ambulance system ranged from US\$ 18 in Uganda to US\$ 568 642 in Malaysia per life year saved.^{20,112} In Thailand, reducing the response time would decrease the yearly national health-care expenditure by US\$ 425 million to US\$ 850 million for each minute saved.²¹ The wide range of results in this category is attributable to significant heterogeneity in the costs, exact interventions provided and impact data used for the analysis.

Provider training

Six studies assessed the impact of training interventions,^{17,41,117,121–123} three of which studied prehospital training.^{17,121,122} These prospective studies assessed training in a variety of cadres, from lay first-responders to orthopaedic specialists. Strengthening the human resource capacity to provide trauma care ranged from US\$ 30 per life year saved for lay first-responders to US\$ 188 per life year saved for orthopaedic trauma residency.

Treatment interventions

Nineteen studies compared different treatments or patient care pathways. Four studies assessed the treatment of acute bleeding, including two for tranexamic acid injection in trauma patients^{109,129} and two studies for recombinant activated factor VII injection in patients with hemophilia.^{127,136} Cost-effectiveness for tranexamic acid was between US\$ 17 and US\$ 76 per life year saved. For recombinant activated factor VII injection, the total direct cost was US\$ 7490 per bleeding episode and US\$ 60 557 per QALY gained. Other studies assessed operative versus non-operative management of appendicitis,¹¹⁶ treatment interventions for severe conditions at first level referral hospitals,¹¹⁰ treatment of abdominal penetrating trauma,¹¹¹ severe asthma,¹¹⁵ acute myocardial infarction,¹²⁶ paediatric respiratory distress,^{120,124,132} acute paediatric diarrhoea,^{135,137} severe sepsis and septic shock,^{119,130,131} protocolised treatment for acute stroke¹¹⁸ and substance abuse interventions.¹³⁴

Emergency diagnostic tools

Two studies assessed emergency care diagnostic tools.^{128,133} For example, a modelling study showed that using an electrocardiogram for patients with chest pain in India costs US\$ 16 per QALY gained.¹²⁸

Facilities and packages of care

Four studies assessed the cost-effectiveness of the provision of facility-based emergency care. Three studies focused on the provision of surgical care¹³⁹⁻¹⁴¹ while one evaluated a stand-alone diarrhoea treatment centre.¹⁴² The cost-effectiveness of facilities providing surgical care varied from US\$ 18 to 265 per DALY averted,¹³⁹⁻¹⁴¹ and US\$ 4032 per death averted for a diarrhoeal treatment centre.¹⁴²

Although most studies analysed actual interventions, three studies used modelling to predict the impact of increased coverage and improved quality of service.^{70,114,125} Authors of one paper estimated that the economic benefit would be within the range of US\$ 758 billion-786 billion per year globally if the mortality rates in low- and middle-income countries were reduced to the rates in high-income countries.⁷⁰ Other findings show that implementing guidelines and improving the standard of care yielded incremental cost-effectiveness ratios between US\$ 47 and US\$ 474 per DALY.¹²⁵

3.4 DISCUSSION

We sought to systematically collect and critically appraise the existing literature on the cost-effectiveness of emergency care interventions in low- and middle- income countries. Cost-effectiveness analyses are important for assessing the value for money of emergency care interventions and to allow for prioritisation and optimal resource allocation.

Formulating a general conclusion about the wider implication of the findings on the cost-effectiveness of emergency care is problematic, because of the heterogeneity of methods, settings, and presentation of results of the identified studies. For example, few studies used health outcomes that are widely comparable against other disease programmes, such as QALYs or DALYs. This lack, coupled with inconsistent reporting of incremental cost-effectiveness ratios, makes the comparison between the findings of these assessments and other programmes difficult for decision-makers with constrained budgets. Furthermore, some studies fell short of using a contextually-oriented study design and, where possible, empirically derived local inputs. For example, one study used parameters from a high-income setting to estimate cost-effectiveness in a middle-income country, generating results that are difficult to interpret.¹¹²

Overall, we noted that most the studies were methodologically weak by the quality criteria we applied, failing to provide detailed descriptions of the assumptions taken. Assumptions used to calculate costs and outcomes can greatly influence the final cost estimate and reporting these

details can help decision-makers understand to what level these findings apply to their setting and what level of uncertainty was taken in the review. Furthermore, not reporting the comparator used will hinder readers to understand the context of the results. Only two-thirds of the studies provided an incremental cost-effectiveness ratio, which aid decision-makers by allowing for comparability across interventions and the application of a cost-effectiveness threshold.

Even in the setting of standardised methods and results reporting, there continues to be a lack of expert consensus surrounding the interpretation of cost-effectiveness data outside the original study context that produced it. While the application of gross domestic product-based global thresholds remains a common approach, consideration of willingness-to-pay for health benefits, identification of benchmark interventions, assessment of budgetary-impact, and incorporation of league tables allow for improved contextualisation of results and utility for decision-makers.^{57,108,146} When comparing the results of our included studies with readily available collated data from other public health interventions, we recommend readers go to the primary literature and ensure context and methodologic comparability.

Another notable finding from our review is that the research focused on single-intervention analyses rather than intervention packages or system changes. An organised emergency care system has the capacity to treat a variety of conditions with a common set of resources, thus gaining efficiencies in per-unit costs by applying economies of scope. Additional positive effects across the health system, such as reducing downstream health-care costs, contributing to public health surveillance and preparedness for disasters, can be also achieved by the organisation and alignment of emergency care services. More research is needed on the cost-effectiveness of system changes, process improvement and intervention packages. Furthermore, an exclusive health-care perspective was used in most the studies, which may undervalue the broad social impacts and economic burden of lost workforce productivity that can be mitigated with emergency care. This narrow scope of analysis may obscure the broader productivity and economic gains that emergency care interventions provide.

Over 80 studies excluded in the review were costing-only assessments (i.e. no measure of efficacy or benefit was assessed). These studies were often descriptive costing studies of a disease entity used to justify spending on preventive measures. For example, the authors of a cost analysis of interpersonal violence in South Africa concluded that the costs of in-hospital care of violence victims warrants investment in primary prevention of these injuries.¹⁴⁷ Costing-only studies were also employed for budget-impact analysis between two choices, including (i) contrasting expenditures between two health-care settings for a single disease entity¹⁴⁸ and (ii) contrasting expenditures between two patient populations.¹⁴⁹ One study reported an incremental cost-effectiveness ratio calculated by using the reduction in treatment time as a primary outcome rather than a health outcome and therefore was not extracted for final review.¹⁵⁰

When evaluating the research gap, we noticed a sizable discrepancy between the breadth of emergency care interventions in low- and middle- income countries and the amount of published

research from these settings. Of the articles we assessed, only 24 out of 137 low- and middle-income countries globally are represented in our findings, indicating a significant gap in research.

Finally, a limitation of our study surrounds the difficulty of labelling emergency care interventions for searchability. Although, we attempted to capture all literature related to emergency care, there may be relevant articles which were not caught in our search criteria. Unless authors clearly tagged the intervention with terms related to “emergency care,” their study may not have been captured by our search. For this reason, we hand-searched references of included articles, yielding several additional studies.

Our systematic review demonstrates a relative sparsity of evidence regarding the cost-effectiveness of emergency care interventions in low-and middle-income countries. Given the breadth of available interventions, numerous potentially low- and high-cost interventions and their impacts remain unevaluated. Our review highlights areas for improvement in the quality of methods and study-design that would facilitate the use of future studies in the decision-making process with regards to the allocation of resources. Overall, the included studies allow us to begin to characterise the literature and establish a research agenda in this area. A primary focus of the future research is the development of cost-effectiveness analyses that evaluate emergency care as a system of integrated care delivery, considering economies of scope and the broader impact of organising and aligning health-care provision.

3.5 CHAPTER SUMMARY

This chapter examined all available records on the cost-effectiveness of EC interventions in LMICs. In doing so it provides an overview of the current efforts to economically evaluate EC in LRS and identifies a paucity of quality evidence. Furthermore, the review finds evidence that many specific EC interventions are indeed cost-effective, from which we can forecast the potential value of these interventions. The work substantiates the need for further high-quality research into the potential savings generated through economies of scale in implementing EC. The next chapter introduces and discusses a conceptual framework to guide the assessment of EC from an economic perspective and outlines approaches for the practice of CEAs on EC specific interventions.

Chapter 4

CONCEPTS AND APPROACHES FOR COST-EFFECTIVENESS ANALYSIS OF EMERGENCY CARE INTERVENTIONS

Health interventions and economic policy goals interact with one another. For example, ill-health affects economic and social welfare, while improvements in economic and social welfare can impact health. Applying economic analytical methods to health offers the opportunity to identify unrealised societal gains. This chapter presents a conceptual framework that serves as a guide to how EC investments could result in changes in costs and health outcomes for societies with limited resources.

The rationale behind the proposed framework is provided and details of the process and pathway through which improved health and reduced costs are gained. Literature surrounding the relationship between investing in a systematic approach to EC and transformations in health outcomes and costs is outlined in Section 4.3. An in-depth rationale of investment strategies and evidence base demonstrates the relationship between investments in systematic approaches to EC and improved service outputs, the effect of improved knowledge and performance on service outcomes, and the resulting health outcomes. This fosters an awareness of how resources are allocated at each stage of the framework by giving attention to each of these areas of transformation.

The latter half of the chapter makes recommendations for a systematic approach to conducting economic evaluations on EC interventions. Section 4.4 draws links between general guidance for economic evaluation and EC by presenting the frameworks, computations, and outputs for both CEAs and BIAs. Section 4.5 briefly discusses the limitations of the recommended instruments. The final section summarises the chapter before moving on to discuss methodological challenges of applying CE to EC in the subsequent chapter, and later empirical testing to validate the instrument.

4.1 BACKGROUND

To assess the cost-effectiveness of EC, decision-makers and researchers must have a framework to understanding how investments in EC produce health, economic, and societal benefits and to interpret the resulting changes in costs and outcomes. Formal priority setting and resource allocation frameworks are used in most levels of governance and administration. Existing methodologies are not very accessible; hence the need to develop easy-to-use procedures that will guide investigators in this process. These frameworks are essential tools for decision-making, but only in so much as they can reflect the setting's true values. Practices in priority setting and resource allocation should endeavour to use tools which reflect the circumstances of LRS and are capable of using data that reflects the values of their populations.

Given the complexity of these evaluations and the limited technical capacity of the setting, clearly establishing the means by which positive impact is accomplished is essential. By identifying characteristics of classical economic evaluations which are appropriate to EC, the framework can support the systematic generation of evidence to better represent the true value of scalable interventions in facility-based EC in LICs. In the latter part of this chapter, solutions and guidance for conducting a simple CEA and BIA for EC are provided.

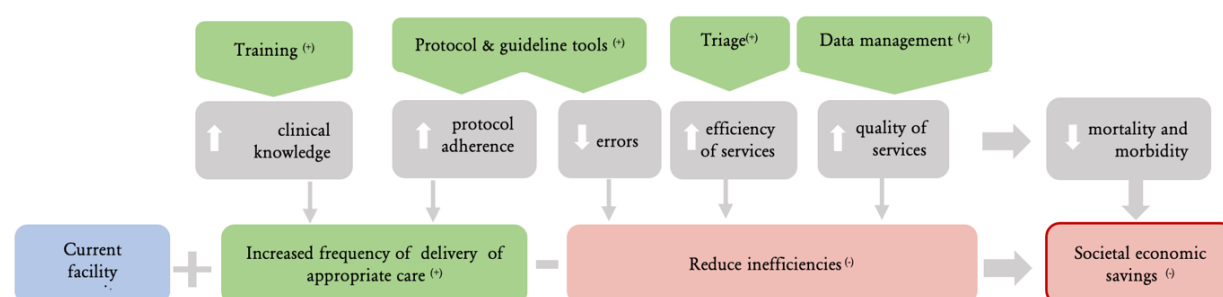
Developing a wider body of evidence of the cost-effectiveness of EC could be accomplished rapidly with a streamlined instrument that is both flexible enough to incorporate significant variations across settings, and simple enough to use where technical capacity may be limited. Furthermore, using a standardised framework with consistent causes, effects and indicators, will facilitate building a coherent body of evidence across varying settings.

4.2 PROPOSING A CONCEPTUAL FRAMEWORK

The framework approach lays out three sequential steps to evaluate the relationship in order to model the correlation between simple interventions and the resulting healthcare spending and outcomes. The first step makes investments to expand the facility-based EC organisational capacity and advance provider skills. These strategies include implementing protocol and guideline tools such as checklists, training providers, and establishing triage systems and trauma registries for data management. Secondly, these investments result in improvements to performance, thereby increasing the frequency of appropriate EC services and reducing inefficiencies. Finally, as a consequence of these improvements, morbidity and mortality are reduced, and societal gains therefore realised.

Figure 4.1 illustrates the conceptual framework created to estimate the effects of various strategies to establish a systematic approach to facility-based EC. It classifies between transformations that result in spending (+) and those which save costs (-).

Figure 4.1 Conceptual framework, investing in a systematic approach to EC and the societal costs and health outcomes



(+) indicates area of spending or increase costs from baseline

(-) indicates areas of savings or decreased costs from baseline

4.3 INVESTING IN A SYSTEMATIC APPROACH TO FACILITY-BASED EMERGENCY CARE

Unlike scene or transport care, a portion of the activities outlined under facility-based EC are already being executed within health systems to some degree. Hospitals are already staffed and delivering care to patients. Nonetheless, many facilities are not adequately equipped and staffed to deal with patients requiring EC. But even where new material resources are limited, simple improvements in organisation and knowledge can positively affect service delivery, performance and productivity. Reductions in the morbidity of a range of conditions have been observed in introducing a systematic approach to EC, centred around acuity-based triage, early recognition and resuscitation, and initial management.^{151,152} These investments have shown sustained health-economic effects in HICs and represent affordable approaches if applied at scale in LRS.¹⁵³

Simple interventions in EC may provide a promising solution for even the most resource limited settings.⁹ This is especially true for interventions that require limited new investments in infrastructure.³⁰ Investigations into how improved triage, patient flow, and supervision can lead to reductions in mortality are underway.³⁴ These simple interventions move beyond the myth that EC is high-technology field, and aim to prove that averting death and disability may be helped as a result of nominal new resource inputs, such as in service training of existing hospital staff.¹⁵² Further low-cost interventions such as team and facility organisation, communication, and protocols have also shown promise in improving access to life saving care.³⁴

Preliminary results indicate that simple developments in organisation and knowledge may contribute to significant advances in health. Strategies such as in-service training, checklists for patient management, and prioritising patient care based on severity have been found to increase clinical knowledge, protocol adherence and quality of services and therefore reduce errors and inappropriate care.^{125,154–156} This impact leads to improved overall efficiency and quality of services resulting in transformations to performance that will achieve better health outcomes.¹⁵⁷ There is some evidence of the benefit of in-service training on enhancements in knowledge, performance, and confidence of health care providers and the reductions in the frequency of inappropriate or potentially harmful practices.^{155,156} These advances extend across both objective assessment measures and subjective confidence levels in a provider's ability to carry out initial assessments and manage ill patients. Basic emergency care (BEC) courses are associated with significant improvements in both knowledge and confidence scores.^{158,159}

4.3.1 The effect of improved knowledge and performance on service outcomes

Improvements in knowledge and performance increase the frequency of appropriate EC services and reduces inefficiencies. This process of transition is based around core clinical elements of EC. These are pertinent as any decision-maker will have to wrestle with these fundamental components in strengthening EC. Training provides educational resources to clinical staff, expanding their skills and job-related knowledge. The establishment of registries improves identification of gaps in care, and the resulting quality improvement initiatives can improve the service delivery efficiency. The adoption of checklists improves patient management and reduces

errors. Implementing triage systems establishes an approach to determine the priority of patient care which improves patient flow and efficiently allocates resources. Based on the existing body of literature, the framework estimates the impact of advancements in knowledge and performance to improve services using the following indicators.

Increasing the delivery of appropriate care

Improving clinical knowledge and protocol adherence results in increased delivery of appropriate care as training and checklists or protocol implementation produce better-trained providers who are thereafter able to perform appropriate care more regularly. Likewise, the use of checklists has been found to increase protocol adherence, thus increasing overall activity significantly.¹⁵⁴ Although no published evidence exists regarding the influence of this increase on budgets, a proxy estimate is derived by using the percentage increase in the number of checklist items completed as indicative of the percentage increase in the total volume of services delivered. In doing so, estimates can be made that checklists could increase costs. The conceptual framework characterises change by gains in knowledge and confidence, leading to delivery of additional services, increasing costs resulting from more care delivery and an increase in total supply-use.

Reducing inefficiencies

Enhanced organisation and systematic approaches to care delivery lead to reductions in existing facility inefficiencies, such as medical errors or inappropriate practices.¹⁵⁷ Simple interventions in EC, such as acuity-based triage systems or checklists and protocols, have shown this capacity.^{160,161} Reorganising hospital intake areas to include dedicated EC areas with formal triage systems is associated with considerable patient mortality reductions.¹⁵⁵ The use of checklists is associated with decreases in medical errors and an increase in appropriate interventions, significantly decreasing the length of stay for patients.^{160,162} Standardised resuscitation protocols are associated with a 25% reduction in all-cause mortality and hospital length of stay for injured patients.¹⁶⁰

Acuity-based triage can transform the process and delivery of care by advancing the ability to prioritise clinical management. This formal process contributes to improved patient flow due to prioritising patients by need, and notable decreases in waiting times for urgent cases.¹⁶³ This increases the efficiency of services by improving the allocation of care to patients based on their severity and need. Reduction in errors and increased quality are excellent markers of the impact on improving efficiency. Reducing errors achieves more efficient use of finite resources. Consequently, by removing inefficient practices from the system, we would expect to see both reductions in costs and an improvement in health outcomes.

4.3.2 Translating care delivery to health impact

EC is an effective way to save lives and reduce disability, with available data suggesting that increasing the frequency of appropriate services and reducing existing inefficiencies will result in lower morbidity and mortality.¹⁶⁴ Due to the nature of acute conditions it is vital to understand

the opportunity cost of delays in investing in EC. For example, trauma conditions disproportionately affect the young and healthy for whom early mortality or disability can have substantial consequences. The following pieces of evidence were used to estimate the impact of improvements in EC delivery to save lives and avoid disability.

Lives saved due to improved emergency care

Modelling studies have estimated that improving EC and reducing fatality rates in LICs to those in HIC settings results in approximately 34-38% of all injury deaths being prevented.⁷⁰ This amounts to between 1.73 to 1.965 million lives saved globally each year.¹⁶⁵ The framework derives estimates of the reduction in morbidity and mortality resulting from increased service coverage and improved delivery of EC. Although there is limited evidence of the impact of in-service training on reductions in mortality, in cases where health outcome data are available, in-hospital training in trauma management has been associated with up to 4.8% reduced mortality for injured patients.¹⁶⁶ In one LRS, these gains were observed without increasing the use of resources.¹⁶⁷ Improving the timely delivery of basic interventions such as monitoring, fluids, and antibiotics, has been shown to reduce mortality for adults with serious infections by 13%.¹⁶⁸ Triage systems are associated with a reduction in mortality of around 10%.^{155,161,163} The use of trauma care checklists alone led to a 50% reduction in mortality for severely injured patients, and findings from a 2017 pilot study suggest that mortality may be reduced by 40% as a result of implementing many of these strategies concurrently.¹⁵⁴

Long-term disability avoided due to improved EC care

Prompt and appropriate acute care, such as splinting of fractures or the appropriate treatment of respiratory failure, can result in reductions of long-term disability. Under such circumstances, the earlier definitive treatment is delivered, the better the prognosis for patients. Often, timely care results in avoiding disability which may incur long-term cost savings in care, and avoid significant productivity losses. The framework suggests that if EC were strengthened, a reduction in disability could be achieved.

4.4 DEVELOPING INSTRUMENTS TO ASSESS INVESTMENTS

While clinical effectiveness had been previously assessed, the cost-effectiveness of such EC interventions to systematise care in LRS has never been measured. In LRS where budgets may be inadequate, it is critical to go beyond clinical effectiveness and begin to quantify the economic impact of introducing a new program. To this end, better instruments for measuring and understanding efficiency in EC are urgently needed. The proposed conceptual framework can be used to draw connections between classic economic approaches to value health and EC. Standardising calculations of cost-effectiveness may allow for comparisons of costs and outcomes between locations and interventions. In this section an overview of recommended economic analytical tools is provided. The analytical frameworks, computations and outputs are reviewed for both CEAs and BIAs as they apply to the context of EC.

A CEA model is suggested to support the empirical testing of the proposed conceptual framework. The approach assesses the addition of low-cost and highly scalable investments to organise EC to the existing platform of care delivery. This tool supports health system planning and the development of a more robust body of evidence concerning the strengthening EC services in LRS.

Details on economic decisions tools use an illustrative example of a suite of tools developed by the WHO Emergency, Trauma and Acute Care programme to support strengthening facility-based EC to best illustrate the core EC competencies introduced in the conceptual framework. The interventions in this package of care include the implementation of BEC training for staff, operation of triage systems, and the adoption of medical and trauma checklists and trauma registries.

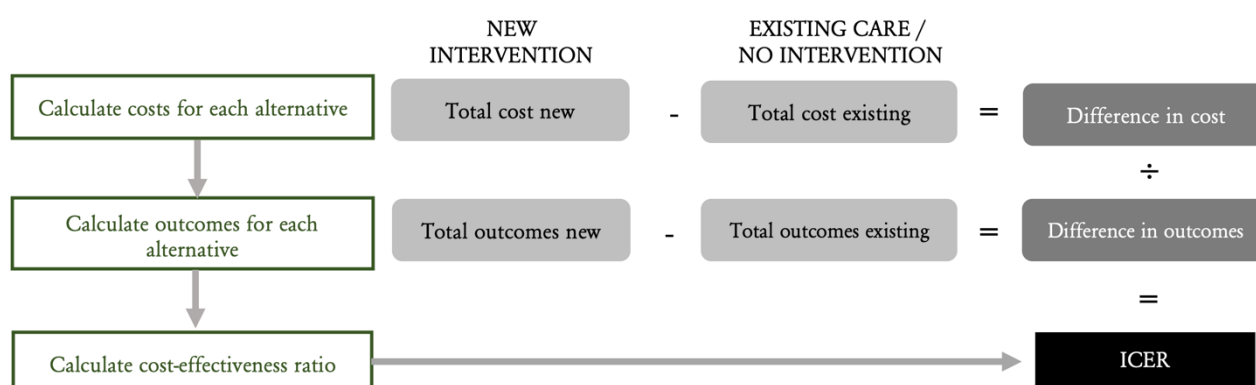
4.4.1 Cost-effectiveness analyses

CEA is a method of economic evaluation that uses modelling to examine both the costs and consequences of health programmes.⁵² Costs of a new intervention and programme are compared against existing care cost. Health outcomes achieved through each approach are then compared.

Analytical framework

The approach used in CEA accounts for the difference between the costs and outcomes of two alternative courses to develop a ratio which demonstrates the incremental cost per outcome unit. **Figure 4.2** illustrates the analytical framework structure of calculating this ratio.

Figure 4.2 Analytic framework for cost-effectiveness analyses



Computations

The final output is a context-relevant measure of efficiency, reported as an incremental cost-effectiveness ratio (ICER) of cost per DALY averted, allowing for comparison against other priority health programmes. Both incremental costs and incremental effectiveness are identified and reported separately. **Figure 4.3** illustrates the equation used in which the difference in the

intervention costs are divided by the difference in its effectiveness. The difference between costs is divided by the difference in outcomes for a ratio of cost per incremental benefit.

Figure 4.3 Incremental Cost-Effectiveness Ratio (ICER) equation

$$\text{ICER} = \frac{\text{Costs}_{\text{Toolkit}} - \text{Costs}_{\text{Current standard of care}}}{\text{DALYs}_{\text{Toolkit}} - \text{DALYs}_{\text{Current standard of care}}}$$

Any assessment should finish with a BIA to understand the true affordability of the programme within the user's wider national health system goals.¹⁶⁹ Further details are outlined in the next section of this chapter.

4.4.2 Budget impact analysis

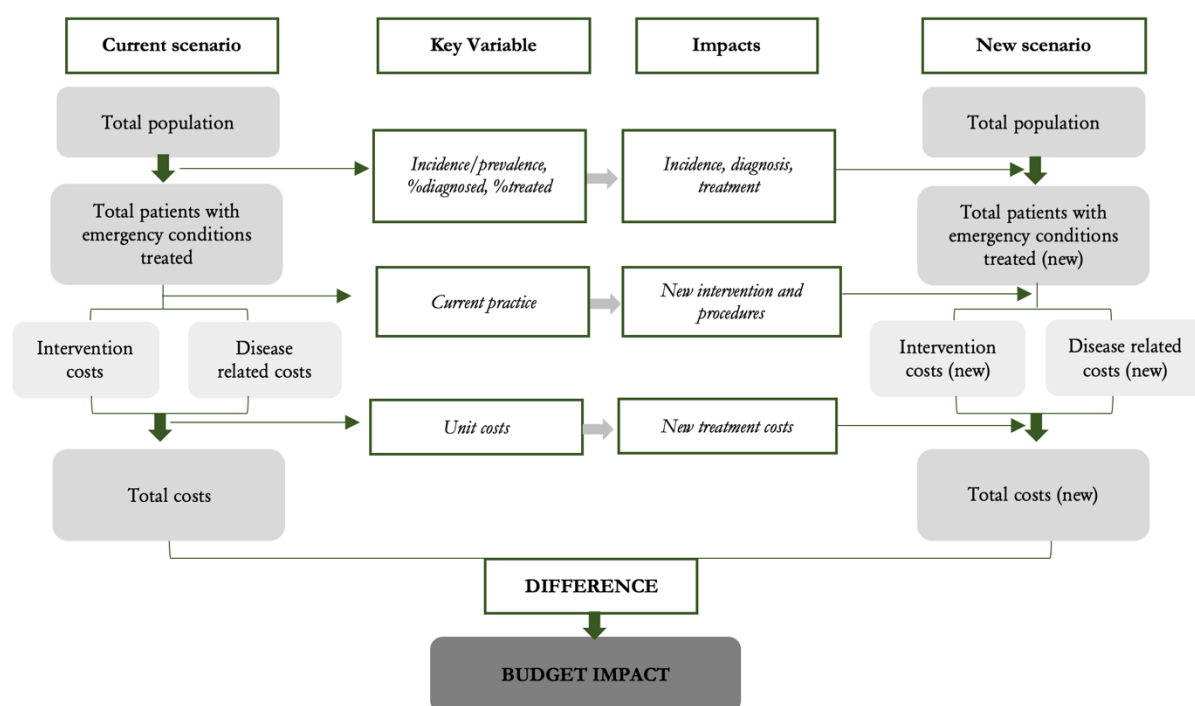
Although the ICER provides insight into the value of the toolkit, it does not offer any indication of the size or scale of the programme under consideration.⁵² Furthermore, we can assume that not all cost-effective interventions are affordable within the context constraints of LRS. That is to say that the specific resources required to fund the intervention may not be available. This is especially true in cases where the chosen comparators are “no intervention” or “standard of care” as in this model. For example, many studies have identified the cost-effectiveness of Hepatitis C vaccination in populations in sub-Saharan Africa. Yet when the population size is explicitly considered, scaling vaccinations to national treatment coverage in a country such as Egypt, where 10% of all adults are Hepatitis C infected, it would necessitate spending 32% of total health expenditure for the country.¹⁷⁰ In such a case, the funds required to introduce national treatment coverage far exceed what is available in the national budget. BIA should be used to measure the true feasibility of a health intervention by framing the effect an intervention will have on the national budget.

Concerns regarding affordability are particularly pressing in resource-limited settings where available health systems funding may not be sufficient. The feasibility of any given health programme is thus determined by knowing the short-term operational costs carried by the payer, making it critical to incorporate analyses that address concerns of affordability.¹⁷¹

Analytical framework

The approach used in the BIA accounts for the difference between the current cost of treating patients seeking unscheduled care at facilities without a systematic approach to EC and the projected cost to the system in which the WHO toolkit has been implemented at facilities as part of a national rollout. **Figure 4.4** Illustrates the analytical framework structure of this simple cost calculation simulation model.

Figure 4.4 Analytic framework for the budget scenario



Source: Adapted from the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Taskforce for Good Research Practices and Manskopf¹⁷²

Computations

Calculating the budget impact involves calculating the difference between the current total costs and the new total costs of the health programme. Importantly this involves accounting for budgetary requirements across a specified time-horizon. **Table 4.1** summarises the considered cost for the comparison in conducting a BIA of EC system strengthening initiatives. Year 1 intervention costs are a function of the total number of sites for roll-out multiplied by the per site cost of the intervention. This is then added to the cost of treatment, calculated by the population per-site multiplied by the number of sites, and the average cost of medical intervention per patient. Based on previous literature on the impacts of checklist implementation and provider training on care process measures, trauma checklists result in an average 13% increase in frequency of a selected list of process measures, and 21% greater overall improvement in care quality measures.^{154,157} Thus a 15% increase in EC intervention costs could be used to estimate the increased activity associated with improvements in care.^{154,157} The analysis assumes that treatment costs vary based on the number of patients seen and training costs fluctuate as a result of the number of sites.

Table 4.1 Example of costs considered, by year, in a budget impact comparison

	Patients with current treatment (no intervention)	Patients treated under new toolkit (with intervention)
Year 1	Treatment costs	Intervention costs + treatment costs
Year 2	Treatment costs	Treatment costs + 15% increase in treatment costs
Year 3	Treatment costs	Treatment costs + 15% increase in treatment costs

Figure 4.4 illustrates the equation used to determine the budget impact of a program change. For each year of the established time horizon both the continued costs of care and any increase in budget as a result of changes to behaviour are calculated to give an accurate representation of the resources required.

Figure 4.4 Budget impact calculation

$$\text{Budget impact} = \underbrace{(C_I + C_T)}_{\text{Costs}_{Yr1}} + \underbrace{(C_T * 1.15)}_{\text{Costs}_{Yr2}} + \underbrace{(C_T * 1.15)}_{\text{Costs}_{Yr3}}$$

*Cost of Intervention (CI) = # of sites * intervention*

*Cost of Treatment (CT) = # of sites * volume of patients per site * average cost of care per patient*

4.5 DISCUSSION

In charting the conceptual framework and conceptualising the analytical approach some of the critical challenges in applying economic evaluations to EC are addressed. This conceptual framework and CEA tool used to assess the cost-effectiveness of integrated improvements in organisation and knowledge illustrate that in organising and systematising EC there are potential benefits for a range of health services and outcomes well beyond acute care. Strengthening the capacity to employ health economic methods at scale will contribute significantly to addressing the current evidence gap. This framework traces the primary drivers of change that result from efforts to strengthen EC such as improved clinical knowledge, increased delivery of appropriate care, and reduction in errors. In doing so the chapter demonstrates the feasibility of using decision analytic tools to estimate the cost-effectiveness of scalable investments in facility-based EC. Decision-makers are given the tools to advocate for improvements in organising and systematising EC and a unit of measure, in the form of the ICER, which can be compared across other health priorities and programmes.

4.5.1 Limitations

Availability of EC services in LRS is affected by factors such as physical infrastructure, equipment, and supplies. These do not feature in our model, although their impact on the success of facility-based care delivery is assured. Rather this analysis focuses on the EC elements intentionally designed to function within existing health infrastructure settings and provides a realistically scalable solution. Costs associated with improving accessibility of care via expanded

physical infrastructure are not considered. Implementing the intervention in this setting may require further investment resources such as hiring more staff or acquiring more equipment, which could impact the financial feasibility of the interventions.

The work of this dissertation is limited to items and activities which incur costs and fall within the scope of facility-care. There are other sources of increased or offset costs that ought to be further considered in undertaking a broader ECS framework. For example, improved clinical outcomes may add costs not previously borne by the existing system such as expensive life support care, or chronic disease management. On the other hand, more rational treatment and testing as a result of better trained and organised staff may reduce costs. Regardless, better EC will result in reduced referrals, decreased length of stay, and better outcomes for many patients, allowing a quicker return to the productive economy of the country and having more far-reaching societal and economic impact than can be covered in this model. A more complex model, capable of considering the full fiscal impact of increased health utilisation stemming from the expansion of health coverage, should be considered in the future. Until then, the basic structure presented here provides meaningful clarity on the potential of cost-effective interventions in EC.

4.6 CHAPTER SUMMARY

This chapter provides details on the causal pathway which shows the impact of creating a systematic approach to EC on health care costs and patient outcomes. The chapter finishes by proposing the application of CEA and BIA methodology under this framework which could be used to assess EC from an economic perspective. The conceptual framework underpinning the correlation between the investments and societal gains was justified, indicating the prospect of a net positive economic benefit to LIC societies. Facility-based EC poses unique challenges to conducting economic evaluations. In the next chapter, the methodological and analytical challenges in applying CEA techniques to interventions in EC are discussed and a compendium of recommended approaches is provided.

Chapter 5

METHODOLOGICAL CHALLENGES OF STUDYING COST-EFFECTIVENESS IN EMERGENCY CARE

“Those few economists who have penetrated beyond theories and generalities and tried to come to grips with the realities of applying quantitative analysis to health, have come to appreciate the peculiar difficulties – most of which have long been appreciated by health administrators” – Abel-Smith (1972)

Previous chapters identified a scarcity of published CEAs concerning EC in LRS. In seeking to tackle this gap, this chapter reports on the prevailing challenges which contribute to this lack of published work. Common debates are reviewed and concepts to consider when employing economic evaluation in EC are outlined. A discussion is held on methods for doing so using the CHEERS Checklist and the ISPOR Principles of Good Practice for Budget Impact Analysis guidelines and reporting format.¹⁷² While BIAs are directly linked to CEAs, structural considerations and parameters vary between the two. In following best practice guidelines, each is systematically reported separately here.¹⁶⁹ Section 5.1 provides background on the current knowledge of challenges so far. Section 5.2 examines the conceptual challenges related to the technical approach of CEA in EC, including the selection of an eligible population, study perspective, comparators, time horizon and discounting, and choice of outcome measures; it continues with a discussion of wider considerations related to the analytical challenges. Section 5.3 summarises challenges in the technical approach of BIA in EC. Section 5.4 touches on the limitations of economic models for EC and, finally, a brief conclusion is provided in Section 5.5.

5.1 BACKGROUND

Economic evaluations, and in particular CEAs, are important policy tools used by decision-makers to inform evidence-based priority setting. Results from such evaluations contribute to maximising the benefits of health interventions and provide insight into their value. This is relevant to any decision-makers who must make choices from a range of options while operating within a given budget.⁵² Classifying both the cost and gains clarifies what benefits can be expected relative to budgetary constraints. A bibliometric analysis conducted on economic evaluations published between 2012-2014 showed that only 4% of the literature addressed LRS.⁸³ The available body of evidence is limited in its relevance to decision makers in these settings. A continued lack of CEAs being produced or tailored to LRS settings, despite the critical need, can be attributed to a variety of technical challenges. These include a lack of quality local clinical data, poor reporting and insufficient data. These negative factors are compounded by limited local research capacity and a lack of funding to strengthen this work.⁸⁶ Where expertise is limited, a simple low-tech tool allowing local decision-makers to input data representative of their setting could be used to support the alignment of spending with local needs.

It is clear that while policymakers are receptive to using CEAs to guide practice, there is a need to strengthen local capacity to conduct context-specific analyses in LRS using evidence that adequately reflects the distinct health system contexts and needs.^{88,173,174} Disease programmes such as HIV, tuberculosis, surgery, vaccines, and maternal and newborn health, have garnered enormous support from global health initiatives. This is in large part due to the extensive body of literature developed by technical experts to provide the financial evidence which can corroborate the worthiness of the investment.¹⁷⁵⁻¹⁷⁹ In a recent appraisal of the Tufts Medical Center Global Health Cost-Effectiveness Analysis Registry, studying published analyses in LICs conducted between 2008-2017, HIV/AIDS and tuberculosis constituted the highest number of studies.¹⁸⁰ Over three-quarters of CEAs from the African region focus on communicable disease, a higher proportion than any of the other regions.⁹² Across all country income levels, relative to their disease burden, HIV/AIDS interventions are over-researched while injury and wound interventions are substantially under-researched.⁸³ Many assessments of cost-effectiveness in EC analyse single interventions of one condition. Very few are able to capture the economics of scale which EC can provide. The existing literature offers few solutions to these challenges.

To assess the feasibility of committing resources towards efforts in EC, a larger body of contextually appropriate cost-effectiveness data is needed. Although evidence continues to mount regarding the effectiveness of ECS investments, the economic value and health financing implications of implementing and enhancing an ECS remain poorly understood. Cost-effectiveness evidence surrounding EC in LRS is mostly limited to single interventions or single functions within the ECS.⁹⁷ In recent literature experts suggest several priorities in global EC research – including the need to develop methodology for economic evaluations that increase meaningful data on the economic value and benefits of EC.^{181,182} Experts with a growing interest in establishing methods to appropriately measure the value of EC are just beginning to map out the presenting challenges such as a lack of quality data and lack of economic analyses.¹⁸²

Still, not enough is known about the costs of delivering EC in LRS and many barriers continue to impede progress in the understanding of its fiscal impacts. This includes a lack of routine data collection systems and patient registries, meaning the costs of EC remain largely unassessed.¹⁸³ There are several studies which suggest that EC systems are likely to be cost-effective under the state of high disease burden affecting LRS, but there is an urgent need for more robust findings.^{40,41} To make things more difficult, where research has been conducted, findings are often not reported in metrics which match those used by health stakeholders, such as DALYs and YLL.⁴² Perceptions of the high cost of EC are furthered by a lack of robust cost data, which impedes the ability to understand the impacts of and to plan improvements for EC in LRS.

Considerations when assessing investments towards facility-based emergency care in low-resource settings

Although the clinical effectiveness of interventions to systematise EC in LRS has been assessed, the cost-effectiveness has never been measured. It is rational to believe that the implementation of an EC package could realise further facility efficiencies rather than drain resources. However,

conducting economic evaluations for EC is not straightforward and the methodological choices taken to adjust for these trials have important implications for the outcomes of such evaluations.

Unlike many other diseases, the severity of emergency conditions can range widely, thus resulting in a broad range of possibilities of health outcomes and use of health service. The provision of EC is complex and there are numerous areas where prevailing economic evaluation theory fails to adequately account for the characteristics endemic to the delivery of acute and urgent care under severe resource constraints. Given variations in disease burden, patient demographics, and infrastructure of the healthcare system, there are some important properties of EC that require consideration when designing an economic evaluation. Reflecting upon these choices is pertinent for analysts to consider when conducting economic analyses for EC in LRS.

5.2 COST-EFFECTIVENESS ANALYSES

A compendium of the challenges faced when applying economic evaluation methodologies to the provision of EC is provided below. The CHEERS checklist is used to organise a discussion of several aspects related to the theoretical and conceptual challenges and considers the implications for preferentially selecting certain methods over others in assessing EC. In this section, considerations are first organised by methodological challenges and followed by analytical challenges. An overview of key issues and their recommended approach are provided in **Table 5.1**.

Table 5.1 Overview of considerations for use of cost-effectiveness analyses in emergency care

Item	Issues	Recommendation
Methods		
<i>Target population and subgroups</i>	Lack of data on the epidemiology of emergency presentations, demand for care is unpredictable	Consider adopting the broadest population approach to capture uncertainty
<i>Setting and location</i>	EC is provided across various settings throughout a continuum of care.	Establish clear boundaries on areas of the hospital where costs and outcomes will be considered and consider using a time (48 hour) limit.
<i>Study perspective</i>	Significant burden of both premature death and disability, with substantial cost implications outside of the hospital such as long-term care costs or lost working productivity.	Utilise a societal perspective to capture all relevant costs and outcomes.
<i>Comparators</i>	The absence of existing formalised EC systems result in a “do nothing” or null comparator, which can lead to	Use a null comparator (and de facto standard of care when possible), but be aware of potential biases in comparing results.
<i>Time horizon</i>	Both short term and life-long financial and health effects, especially in situations of lifelong disability	Adopt a lifetime horizon for all costs and outcomes.
<i>Discount rate</i>	Need to account for a decline in the economic value of improved health later on in life, and preference for paying later rather than now.	Apply discount rates to both costs and outcomes.
<i>Choice of health outcomes</i>	Must seek to account for a range of both short-term and long-term consequences that may develop from each cause of illness.	Select a composite outcome measure that can combine the effects of both morbidity and mortality.
<i>Measurement of effectiveness</i>	Scarcity of data and few RCTs as a result of ethical considerations.	Use single study observational data where possible.
<i>Measurement and valuation of preference-based outcomes</i>	Urgent life-saving nature of the care limit the value of measuring preference between health states	Utilise DALYs rather than QALYs to circumvent the lack of local, context specific health state preference value.
<i>Estimating resources and costs</i>	Lack of formal EC systems leads to a scarcity of EC-specific data on resource use.	When possible collect primary data in setting or use of regional data from comparable context, if available. Otherwise, make all assumptions and sources of data explicit.
<i>Currency, price date, and conversion</i>	Unit costs frequently derived from different price years or expressed in different currencies	Adjust data to achieve a common currency and price year of all inputs.
<i>Choice of model</i>	Fewer health states transitions experienced, many EC treatments have somewhat binary outcomes	Utilise a decision tree model rather than Markov model.
Analysis		
<i>Characterising uncertainty</i>	High parameter uncertainty as a result of limited routine data collection	Use probabilistic sensitivity analysis to allow for all parameters to be varied concurrently.
<i>Methods for extrapolation</i>	Need to account for the life-time horizon and long-term disability costs	Employ a microsimulation methodology to capture the variation in value of costs over time.
<i>Unmeasured confounding</i>	High frequency of observational studies rather than RCTs elevate potential bias of treatment effect	Use Bayesian analytical approaches to accommodate for bias.

5.2.1 Methodological challenges

Target population and subgroups

Throughout LRS there is a lack of data on the epidemiology of emergency presentations, and no agreed metric for measuring the population-level burden of disease.¹⁸⁴ Consequently, accurately describing the characteristics of the base case population used in the analysis may pose certain challenges. This is further complicated by the reality that emergency conditions are not a single condition in itself, but rather a host of heterogeneous ailments for which patients must seek urgent unscheduled care. Efforts have been made to provide a collective measure of these conditions. Chang et al. (2016) classified 31 out of 249 conditions listed in the Global Burden of Disease as emergency medical diseases or those which “if not diagnosed and treated within hours to days of onset, often led to serious physical or mental disability or death”.⁵

Defining the choice of target population taken in analyses has implications regarding the characteristic variables considered in an economic evaluation and scope of the total population. Emergencies can happen to anyone and anywhere, thereby making the nature of the demand for EC unpredictable. Consequently, the entire population stands to benefit from improvements in the delivery of EC. In adopting this broad and comprehensive approach to defining the target population, there is risk of overestimating the true size of the population served and subsequently underestimating the costs relative to patient population due to the cost outlays being spread across a larger number than the actual population. In using a more limited population, for example only conditions like stroke care where immediate care prevents mortality, there is a risk of undervaluing the benefits and overestimating costs.

Setting and location

How EC is implemented and what it costs are highly reflective of the distinctive systems, funding, and political drivers under which it operates. EC is provided across various settings throughout a continuum of care, including scene care and treatment in ambulances during transportation. This dissertation focuses on EC provided within the facility setting, meaning at a hospital. The most relevant characteristic in this setting is the lack of an established EC system, which means care is regularly provided by individuals without dedicated training, on a first-come, first-serve basis. Other common attributes include the lack of legal frameworks, presence of rudimentary ambulance networks, and inadequately equipped and staffed units to deal with patients who require EC. Scarce staff may result in patients experiencing delays in receiving care. Within a facility, EC is typically provided across several areas of the hospital making it challenging to isolate data regarding outcomes and costs attributable to only EC. In contexts where dedicated ECS do not exist, many costs for EC are shared within existing budgets.

Study perspective

The choice of study perspective is important in determining the costs and outcomes considered in an economic evaluation. Emergency conditions can lead to a significant burden of both premature death and disability, which have substantial cost implications outside of the hospital

such as long-term care costs or lost working productivity. Using a less comprehensive approach risks bias of omitted cost and consequences variables.¹⁸⁵ This is particularly relevant for EC conditions where function following illness may be limited. Reducing this burden has implications for a healthier, more robust workforce with better capacity to contribute to economic growth. To reflect this effect, it is necessary to capture the opportunity cost of lost wages for injured, ill, or disabled patients and the non-health consequence of subsequent productivity loss for societies. Therefore, in assessing EC the more expansive societal approach, which considers both direct and indirect costs, should be used to accurately capture broad costs and impacts for society at large. This approach requires inputs including short- and long-term disability care costs, which may be challenging to obtain in LRS where data are scarce and formal disability care services may be limited.

Comparators

Determining the optimal intervention depends on the set of interventions being compared. To reflect the lack of existing formalised systems, a majority of assessments related EC in LRS opt to use a “do nothing” or null comparator. There will be few cases where there are other relevant comparators to use and this null comparison indicates a continuation of the current approach and organisation of care. Although using the null comparator approach aligns with the globally recommended strategy under the “generalised CEA approach” proposed by the WHO, it also presumes that the standard of care against which we are comparing is already cost-effective. Results only prove cost-effectiveness relative to the null comparator, and thus produce a result which cannot stand alone outside of its relativity to the given the benchmark against which we compare.⁹⁵ If the null comparator is not cost-effective to begin with, knowing that a new intervention is more cost-effective than the null is meaningless for decision making. Therefore, the affinity for evaluations in EC to select a null comparator has potential biases and may generate non-comparable ICERs since each standard of care may be different from one another.¹⁸⁶

Time horizon and discount rate

Disability and death resulting from a lack of timely and appropriate EC can lead to both short-term and life-long financial and health effects. Although selection of broader time horizons accounts for the long-term effects of EC outcomes, this choice is simultaneously at odds with the acute nature of EC which is provided within the first 48 hours of presentation. However, analyses that only consider a limited time horizon risk underestimating both the costs and benefits that might be expected in preventing premature death and disability. These benefits may only reflect as life-years at a future date. To tackle this issue, a lifetime horizon should be taken for all costs and outcomes in analyses. The duration is calculated by average life expectancy less the average age of the target population and conveyed in years.

The benefits of EC are both immediate and long-term and their value varies due to the decline in the economic value of improved health later in life. Discounting should be applied to both costs and outcomes to adequately adjust the present value of when they occur. This technique accounts for the decline in economic value of improved health later on in life and patients higher

preference for healthy years now rather than later in life.¹⁸⁷ The preference for making payments later on rather than now is accounted for by discounting costs.¹⁸⁷ While debate exists regarding the discounting of costs and outcomes equally, especially in LRS where rates of economic growth are higher than HICs, most national pharmacoeconomic guidelines recommend using an approach that applies the same margin of discount to both outcomes and costs.^{188,189} Some arguments have been made for the use of greater discounting rates on costs in LRS where there is a higher rate of economic growth exist.¹⁸⁸ Thus by using lower standard discounting rates, both health benefits and future costs may be overvalued.

Choice of health outcomes

In conducting economic evaluations, choice of health outcomes determines the measure of benefit in the evaluation. This measure must be relevant to the type of analysis being performed, yet the choice of health outcomes is not straightforward for emergency conditions. Outcome measures must seek to account for a range of both short-term and long-term consequences that can develop from each cause of illness. Although many efforts have been made to quantify the burden of acute conditions, consensus regarding the science and measurement has yet to be reached. EC services are often measured by service utilisation or system capacity rather than health outcome indicators. Recent attempts to resolve this issue adopt a proportionality approach and identify conditions in the global burden of disease that may be amenable to EC to describe the burden of disease in deaths, DALYs and YLL.¹⁹⁰

There are several direct effects which can be used as outcome measures, based on the specific emergency condition of interest. 48-hour mortality is a shared representative measure which can capture the acute nature of diverse emergency conditions. Because EC can greatly impact both mortality and long-lasting morbidity, it is important to choose a composite outcome measure that can combine the effects of both morbidity and mortality. Many economic evaluations achieve this aim with the use of DALYs which combine both YLL and years lived with disability (YLD). The use of DALYs in EC allow analysts to circumvent the lack of local, context specific health state preference values. DALYs rely primarily on epidemiological data, whereas emergency conditions are often defined by acuity related to the time and severity of any condition. Relatively little information has been published on the epidemiology of EC presentations. Furthermore, DALY estimates are influenced by the population parameter and methodology used. Although EC often results in rapid recovery, the use of prevalence-based DALYs better accounts for severe disability experienced from non-fatal acute conditions. On the other hand, incidence-based approaches to DALYs capture only the burden of new emergency conditions without fully noting the continued burden of ECs in the form of disabilities.¹⁹¹ Both YLL and DALYs averted are widely used measures in economic evaluations of health programmes in LICs which allow for comparability between various health programme investments.

Measurement of effectiveness

There are very few studies related to systematising EC in LICs from which to draw data on effectiveness.⁹⁷ Furthermore, as a result of the challenges in obtaining standard informed consent

from patients who are physically incapable of being informed of the risks and benefits of their treatment (for example if they are unconscious), randomised control trials (RCTs) in EC are extremely rare. The ethical complexities of conducting effectiveness studies in EC greatly hinder the availability of quality effectiveness data, which results in the use of single-study based-estimates or the use of observational data instead of evidence from RCTs. This introduces potential biases, by analysing a population not representative of the full patient population.¹⁹² Analysts must be very clear on the limitations and the details of which effectiveness has been demonstrated. Furthermore, methodologies should account for the effect of confounding factors when attributing health outcome changes to EC.¹⁸²

Measurement and valuation of preference-based outcomes

Preference-based instruments are not broadly used in EC, perhaps due to the urgent life-saving nature of the care and the lack of nuance of the choice between two health states of survival and mortality. The urgent nature of EC make it particularly difficult to develop a measurement of superiority of one intervention above another. In EC this measures survival and death, as well as whether or not patients sustain permanent disabilities. How these measures are generated, and whether they are country specific or used from other settings is critical to the applicability of the results. Rarely are decisions in EC made based on considerations outside of survival, so the value of measuring preference between two states is limited. Preference elicitation techniques are seldom used in LRS, leaving limited data available regarding the preference of patients in these contexts. To bypass the scarcity context specific health state preference values DALYs, which utilise universal sets of standard weights based on statistically analysed population-based choices among pairs of health conditions, are more commonly engaged in LRS settings than QALYs.¹⁹³ These methods rely on elicitation of preference-based health-related quality of life measures. The expression of ratios in similar units ensures that they are comparable when reaching determinations regarding the most efficient use of health resources.

Estimating resources and costs

Estimating the resources use associated with EC interventions requires using creative approaches. Costs associated with the delivery of EC include capital equipment and consumables, as well as training and salaries for health professionals. For essential functions provided at dedicated EUs, costed elements should include salaries of all unit staff, total BEC training, equipment for resuscitation kits, equipment for clinical assessment and monitoring, and incremental increase of medication, lab and radiology cost as a result of a dedicated EU. EC is often delivered across various departments in a range of cross-cutting and interlinked interventions. This means that it is more difficult to capture accurate data on costs of EC care than care delivered in other specialities. The lack of basic cost information poses a significant challenge to appropriately estimating resource use and costs.

Unique challenges exist in acquiring budget records for those analysts considering top-down approaches. Specifically, current systems are not established with the aim of capturing data from emergency services separately from other medical care. Without available EU budgets, dedicated

analysts must try to separate costs incurred in EC services from in or out patient division registers in hospitals. Establishing a clear boundary on what constitutes EC, and from which available reported budget resource use details can be drawn, is highly complicated in these settings and may vary considerably depending on the selected definitions of the timing or scope.

There are also costs to consider which are incurred by services currently dispersed elsewhere in the health system including certain clinical interventions, laboratory testing, and radiologic investigations. Measuring the shared resources with other hospital departments can be problematic. Lastly, any analysis taken from a societal approach must consider the additional costs borne by patients as a result of the weakened health system. These include consideration for the challenges patients may face in accessing EC where no formal system exists by including costs for transportation into their analysis, or in the purchasing cost of medicines and supplies in facilities where stockouts are frequent.

There are persistent limitations in applying economic evaluation to the EC in LRS. The paucity, and lacklustre rigor, of published cost data from LRS means modellers will have to rely on a number of assumptions that may not be robust. Expert advice may be used to guide in areas where data are especially limited, although this approach should be used sparingly. To be able to model the effect on cost and outcomes, one must make some of the assumptions based on the available routine data which may be vulnerable to the improper association for EC. At best, the use of regional data from comparable context, if available, may be considered appropriate under these circumstances. For the moment, until more systematised budgeting is done under the umbrella of EC, valuing each item and unit costs is more accurately done in this setting using bottom-up micro-costing methodologies. Improvements in costing methodologies in this arena are necessary to overcome these challenges.

Currency, price, date, and conversion

As a result of the complexities in estimating resources, it is unlikely that EC costs and prices will come from a single source budget. Unit costs are likely to be derived from different price years or be expressed in different currencies. Therefore it is necessary to adjust all data used to achieve a common currency and price year of all inputs.¹⁹⁴

Choice of model

Since EC is care delivered in the first 48 hours of the patient's presentation to care, there are typically fewer health-states to consider, and health states are often linked with the immediate previous state. The choice of a simple decision-tree analytical model is more appropriate for assessing the treatment of urgent and emergent conditions than a multistate Markov model, which depends on a sequence of stochastic events. Furthermore, a decision tree structure best reflects the nature of many interventions in EC, which may be corrective or not. Beyond this point, patients fall under the care of other departments in the hospital, such as internal medicine and therefore branching health states would be considered under the budget outcomes of another division of care.

5.2.2 Analytical challenges

Aside from methodological challenges, there are many analytical challenges in assessing EC which demand special attention. Addressing these characteristics requires the application of certain analytical techniques to account for the common issues. In this section, the common analytical issues when conducting CEAs for EC and recommend specific techniques to address each are discussed.

Characterising uncertainty

The lack of routine data collected regarding EC produces in potentially high parameter uncertainty which should be accounted for in any analyses. Using probabilistic sensitivity analysis is recommended to allow for all parameters activated in the analysis to be varied concurrently.⁵² Yet even this can pose a challenge when confidence intervals necessary to vary inputs are unknown. All economic modelling requires the analyst to make a series of assumptions, but adequately accounting for uncertainty tied to the limited amount of data available to emergency conditions and their cost can lead to imperfect or flawed results.

Methods for extrapolation

It is necessary to account for the interrelated risk factors experienced by urgent care patients who may survive with additional health complications. To accommodate this a life-time horizon microsimulation should be employed for the evaluation of emergency conditions. Doing so aggregates individual results to better represent the cohort's experience and accounts for future points where additional resources would be used long-term disability care. Examples include survivors of trauma who have undergone amputation and will require new prosthetics at intervals throughout the remainder of their lifetime, or survivors of injuries who require physical therapy rehabilitation appointments.

Unmeasured confounding

Due to the limited availability of RCTs and greater frequency of observational studies, analyses of EC interventions are susceptible to unmeasured confounding. Different characteristics of patients in each treatment group, such as prior illness, previous health state, or ability to access hospitals, can impact the observed association between the intervention and the outcomes. For example, reductions in mortality might be related to the observed intervention, or might be associated with differences in underlying behavioural risk factors or health issues between the pre and post- intervention patients which were unobserved. Analysts need to undertake a corrective course of action, such as Bayesian approaches to remedy this common issue.¹⁹⁵ This statistical analysis control has the benefit of being applied after the data collection process. Using statistical control methods allows analysts to better separate out the impact of the independent variable by identifying confounding variables. As the body of evidence continues to grow, analysts should endeavour to use RCTs to inform CEAs where possible to avoid the wide uncertainty borne by depending on observational studies.

5.3 BUDGET IMPACT ANALYSES

A compendium of issues around employing BIAs in EC are organised here using the ISPOR Principles of Good Practice for Budget Impact Analysis checklist. An overview of key issues and their recommended approach are provided in **Table 5.2**.

Table 5.2 Overview of considerations for use of budget impact analyses in emergency care

Item	Issues	Recommendation
<i>Patient Population</i>	Lack of data on the epidemiology of emergency presentations, demand for care is unpredictable and the patient population who we must calculate for is not well known	To model the cost of a scale-up scenario based on the demand of the setting we can use the current incidence of hospital visits to understand the volume of patients whose care must be budgeted
<i>Intervention mix</i>	Lack of clarity on how improved EC may impact the treatment mix in changing market share of EC in contrast to other treatments	Assume conservatively that the improvement of EC is additive to current mix rather than substitutive.
<i>Perspective</i>	No EC specific challenges identified	Follow standard BIA approaches and utilise a payer perspective to accurately reflect decision-maker
<i>Time horizon</i>	No EC specific challenges identified	Follow standard BIA approaches and use a time-period that reflects assumed national budgeting timelines
<i>Input data and sources</i>	Lack of formal EC systems leads to a scarcity of EC-specific data on resource use.	When possible collect primary data in setting or use of regional data from comparable context, if available. Otherwise, access DHIS2 data and make all assumptions and sources of data explicit.
<i>Uncertainty</i>	Need to account for uncertainty in findings	Use scenario analyses to test out best-case and worst-case scenarios

5.3.1 Methodological challenges

Epidemiology and management of health problems

Importantly, emergencies can happen to anyone at any time and the epidemiology of conditions amenable to EC are not well studied. Details of prevalence and incidence are particularly rare in LRS where routine data collection may be limited. Understanding the burden, severity of disease, and disease progression in these contexts is difficult. The impacts of undertreated cases and pertinent risk factors are also not well documented in this environment. Recent efforts have been made to define EC sensitive conditions, identifying a series of conditions such as asthma and

pneumonia.¹⁹⁶ Of those diseases reported in the global burden of disease, 31 (8.4%) have been identified as emergency medical diseases. Emergency conditions have a range of severity and most are life-threatening if left undiagnosed or untreated. Many risk factors of these conditions are endemic to life in LRS including occupational and environmental hazards, lack of immunisations, and weak road safety initiatives. Management of these conditions relies on a range of multidisciplinary clinicians depending on the condition.

Clinical impact

Acute conditions are currently managed within the existing health care system by providers without specialised training in triage and management of severe acute conditions. Patients are treated on a first-come, first serve basis rather than by severity priority. Since EC covers a wide breadth of conditions, prognosis, disease progress and treatment options vary widely. A lack of immediate medical attention can seriously jeopardise a patient's condition. Most conditions seen in the EU benefit from aggressive diagnosis and treatment to address the urgent needs. There is likely very little relevant efficacy and safety data regarding the existing treatment options. The clinical impact of improved EC has the potential to reduce morbidity and mortality as a result of timely care.

Economic impact

Cost-of-care studies in the field are extraordinarily rare even for condition-specific treatment patterns. Guidance may be drawn from similar studies conducted on the Emergency Triage, Assessment and Treatment (ETAT) course for under-5 populations in Kenya, which found scale-up costs of \$3,559,328.78 or 0.60% of the annual budget for children under five care in the setting.¹²⁵ Economic impacts of improved EC are twofold. Firstly, finances are required to implement systematic approaches to care. Secondly, improved health and wellbeing may contribute to improved economic benefits to society as a result of avoiding lost productivity.

Patient population

Emergencies can happen to anyone at any time. For this reason, the size and characteristics of the eligible population capable of benefitting from the intervention are the full population. Realistically, not everyone will need to access EC services. Most facility-based interventions do little to prevent injuries or emergencies from occurring in the first place and thus an assumption is made that there will be little change to the volume of patients presenting at hospitals with acute emergency conditions. To model the cost of a scale-up scenario based on the demand of the setting, current incidence of hospital visits can be used to estimate the volume of patients whose care must be budgeted. Quantifying the target population may be estimated based on annual numbers of patient visits to facilities for EC. This may be derived from routine data collected through Health Management Information Systems (HMIS) such as the District Health Information Software 2 (DHIS2). From such open source software systems the following routine indicators represent some of the indicators which could be to be combined to estimate the number of EU patients presenting per level of facility: admissions to the emergency ward; admissions to acute care unit; road traffic accident (cases); injuries: motorcycle (boda-boda

accidents) cases; injuries: (trauma due to other causes); medical emergencies (cerebrovascular events; cardiac arrest; gastrointestinal bleeding; respiratory distress, acute renal failure, all others); outpatient department- stroke/cardiovascular accident, outpatient department injuries (trauma due to other causes); outpatient department obstructed labour; and outpatient department haemorrhage related to pregnancy. This is likely an under estimation considering that many emergency presentations are not captured in these categories.

Intervention Mix

The current mix for EC service is based on a first come, first served basis. Changes in therapies to treat emergency conditions are expected to increase appropriate care while simultaneously decreasing some instances of inappropriate care. In the low-resource environment, it is more likely to increase rather than decrease frequency of interventions. The expected intervention mix after EC interventions is still relatively unknown. There is a chance that some EC interventions will substitute for current treatment in other areas, although there is a need for more evidence regarding exactly which market share it will take. However, there is very little empirical evidence to this point. Thus, reasonable analysts should take the most conservative approach given available evidence and presuming an additive factor of EC interventions to the current mix.

Perspective and time horizon

BIAs frequently use different time horizons and perspectives to capture the appropriate budgetary considerations, when compared to CEAs. A budget holder or payer perspective should be applied, and attention paid to aligning the time horizon to reflect assumed national budgeting timelines. Although the use of discount rates is common in CEAs, they are not particularly useful to governments in budget planning. Therefore, to best guide budgeting and forecasting, no discounting is applied to the BIA in this model.

Input data, data sources, and collection of data

Adequate country-level inputs are necessary to calculate the local BIA. Certain inputs related to the cost of care or cost of intervention may not be available on a local scale. **Table 5.3** identifies the required inputs and suggests sources where modellers might be able to draw appropriate sources of data.

Table 5.3 Examples of local inputs and suggested sources

Input required	<i>Suggested sources</i>
Total number of facilities for scale-up	<i>National guidelines</i>
Eligible population per facility	<i>DHISII data</i>
Cost of intervention per facility	<i>Pilot budgets, previous training budgets</i>
Cost of care delivered per patient (pre-intervention)	<i>Top-down from hospital budgets, or bottom-up micro-costing</i>
Cost of care delivered per patient (post-intervention)	<i>Top-down from hospital budgets, or bottom-up micro-costing</i>
Total national health budget	<i>Annual health sector report</i>
Total budget for the level of facility (e.g. district hospitals)	<i>Annual health sector report</i>

5.4 DISCUSSION

Conscious efforts to invest in EC must be supported by context-relevant evidence. Ongoing work is required to improve the quality and quantity of CEAs for EC interventions. Assessing sufficient value for money and demonstrating cost-effectiveness must be methodologically credible. Outlining the critical challenges in applying economic evaluations to EC produces a better understanding of the challenges faced in generating a body of evidence locally. Steps are taken towards building the systematic capacity to generate evidence from varying contexts.

5.4.1 Limitations of applying economic evaluation for EC

The applicability of CEAs and BIAs depends on the availability of accurate local data, which may still be challenging to obtain due to the widespread lack of routine data collection systems in LRS. Resources may not be available to undergo the costly methodologies required to collect robust economic data, such as bottom-up micro-costing or time and motion studies. Although it does not resolve all issues of poor-quality data which may persist in many LRS, efforts are made to minimise this challenge by suggesting creative and innovative solutions in obtaining this data and providing some recommended sources for relevant publicly available data sources, such as the data sets from World Bank and WHO.

5.5 CHAPTER SUMMARY

In this chapter, the challenges and considerations in applying economic evaluation methods to EC are reviewed. Guidance is provided on appropriate methodological approaches to address these concerns.

In the next chapter, a robust methodology to collect the empirical cost of care inputs in the Ugandan setting is employed to meet a central challenge of estimating local resources use and costs.

Chapter 6

THE COSTS OF DELIVERING EMERGENCY CARE AT REGIONAL REFERRAL HOSPITALS IN UGANDA: A MICRO-COSTING STUDY

In the first chapter, our systematic review identified that a lack of local and contextually relevant data is a significant challenge to CEAs. To be able to assess changes in the cost of care due to the frequency of interventions, we needed to establish the true cost of delivering EC in the context. This chapter presents a micro-costing study conducted to identify these costs and provide robust inputs for subsequent economic analysis. This study has been accepted for publication (Werner et al, 2021)¹⁹⁷. A copy of the published paper, verbatim with citations and table numbers changed to keep consistent format style with this dissertation, follows over the next 12 pages.

6.1 BACKGROUND

Emergency care (EC) encompasses a range of interventions delivered soon after the onset of acute disease or injury. Due to the time-sensitive nature of successfully managing these conditions, there is strong evidence that organised EC systems effectively reduce mortality and improve patient outcomes.^{12,198-200} Globally, emergency conditions contribute to over half of total deaths, the majority of which occur in low- and middle-income countries (LMICs) where formal emergency care systems are rare.^{5,190,201} Emergencies occur on a daily basis regardless of whether there is an organised effort to treat them, indicating that the consequences of neglecting EC systems may be disastrous.^{5,30} With 1,191 deaths from emergency conditions per 100,000 and 52,441 DALYs from emergency conditions per 100,000⁵ the burden of emergency conditions in Uganda is devastating.

There is a mounting body of evidence demonstrating the impact of emergency care in LMICs^{9,34}; however, not enough is known about the cost and resources required to achieve these gains. The existing body of cost-effectiveness literature is methodologically weak, often failing to use empirically derived local inputs, and focused on analysing single-intervention rather than the cost-effectiveness of system changes and process improvements.⁹⁷ Electronic medical records, digital billing systems, and dedicated emergency unit budgets available in high-income settings have supported efforts to evaluate the costs for many EC interventions in these settings.^{202,203} However, data from high-income settings do not accurately reflect the fiscal environment more common in LMICs. Numerous additional research challenges, including: paper-based data management systems, unreliable supply chains with frequent stockouts and highly variable accounting practices, present further challenges in assessing local costs in LMIC environments to provide context-relevant guidance.²⁹ Under these circumstances, capturing accurate figures requires resource and time intensive methods such as direct observation via time-motion methodology – a likely reason for the paucity of published data surrounding performance and capability of delivering of EC in LMICs.¹⁸³

Nevertheless, it is problematic to pledge resources to strengthen EC delivery systems without first understanding the cost. For this reason, knowing the true outlay of EC is essential to understanding the affordability or sustainability of scaling up services given already strained health care budgets in many LMICs. Hospital managers and decision makers require this information to engage in evidence-based decision making while setting priorities and improving efficiencies. While efforts have been made to quantify the pattern of resource use and procedure utilization in functional emergency units in Uganda, the actual cost of delivering these services in this setting remains unclear.²⁰⁴

In this study, we describe methods for performing an accurate costing of the provision of EC from a health care provider perspective at the facility level, illustrated through costing research performed at public facilities in Uganda. This study addresses some of the critical gaps in the economic evidence for EC in LMICs and accompanies ongoing research assessing the effectiveness of the World Health Organization (WHO) Emergency Care Toolkit in Uganda, whose methods are previously described.²⁰⁵ To offer insights into the cost of implementing EC in an LMIC, a bottom-up micro-costing methodology is used to classify all relevant cost components of EC to the most exhaustive level by gathering detailed information on the quantity of resources used and their value at a patient-specific level. Precise cost estimates, which reflect the realities of resource use as it occurs in facility-based delivery of EC in a low-resource setting, are presented. These estimates may be used to demonstrate cost-effectiveness of EC interventions in future evidence-based decision making in resource scarce contexts.

6.2 METHODS

A direct, activity-based costing was carried out over a four-week period from September 2019 to October 2019. The cost analysis was conducted from the healthcare provider perspective following published methods guidelines on costing approaches performed in LMICs.^{206,207} All costs were collected in 2017 Ugandan shillings, and later adjusted and reported in 2017 US Dollars using the annual average exchange rate (1 dollar = 3700 shillings).²⁰⁸ Ethics approvals were obtained from the institutional review board at University of Cape Town and University of Makerere, and site approval was provided by the Uganda Ministry of Health (MoH) (Reference: 549/2019 & 2019-013).

6.2.1 Setting

Data were collected by convenience sampling at five regional referral hospital sites (RRHs), which are tertiary level centres that offer both general and specialist clinical services and partake in teaching and research. The following criteria were used for site inclusion to the study: a public RRH, with an emergency/casualty/A&E unit, which had not received any of the elements of the WHO EC Toolkit. Any sites which had received previous elements of the WHO toolkit were excluded from the study. All sites are funded by the Ugandan government and deliver most services free of user charges. The five sites are geographically diverse and serve various catchment sizes. In particular, Mbale RRH and Jinja RRH receive high numbers of mass casualties from

road traffic accidents due to proximity of the nearby highway. There are currently no national guidelines for the layout of emergency units.²⁹ Consequently, each site demonstrated unique features to their physical space, staffing, equipment and supplies. A brief overview of key characteristics of each of the five sites, observed during site visits is provided in the **Table 6.1**.

Table 6.1 Key characteristics of study sites

	Jinja	Mbale	Gulu	Hoima	Kabale
Distance from Kampala (km)	80km E	224km E	333km N	200km W	426km SW
Population served	3.5 million	2 million	2 million	Over 3 million	2 million
Region	Eastern central region	Mid-eastern region	Mid-northern region	Mid-western region	Kigezi region
Districts served	Bugiri, Buyende, Iganga, Jinja, Kaliro, Kamuli, Kayunga, Luuka, Mayuge, Namutumba, Namayingo	Busia, Budaka, Bududa, Kibuku, Kapchorwa, Kween Bukwo, Butalega, Manafwa, Mbale, Pallisa Sironko, Tororo	Amuru, Gulu, Kitgum, Lamwo, Pader, Nwoya, Oyam	Hoima, Kibale, Masindi, Bulisa, Kiryandongo, Kyankwanzi, Kiboga, and Easter part of DRC	Kabale, Kisoro, Rukungiri, Kanungu and some parts of Ntungamo (as well as ppl from neighboring Rwanda and DRC)
Estimated annual number of visits to EU¹	10,788 Inpatient	9,156 Inpatient 9,540 Outpatient	4,452 Inpatient 8,172 Outpatient	2,952 Inpatient	2,076 Inpatient 3,240 Outpatient
No. of beds in hospital²	500	302	335	300	280
No. of staff in EU department over 24 hr period³	8 Nurses 2 Doctors	7 Nurses 3 Interns 4 Clinical Officers 1 Medical Officer	3 Nurses 2 interns 1 Medical Officer	6 Nurses	5 Nurses *Medical Officer as needed from Inpatient Ward

¹ Estimation taken from extrapolation of monthly registers from July 2019 site visits.

² <https://www.ubos.org/onlinefiles/uploads/ubos/pdf/20documents/PNSD/2010MOHStatAbst.pdf> and <https://health.go.ug/affiliated-institutions/hospitals>

³ Figures provided by EU staff during site visits in July 2019

6.2.2 Specifying the production process

In alignment with ongoing monitoring and evaluation by WHO and MoH, five sentinel conditions were selected by an expert panel as representative of conditions highly amenable to timely and appropriate EC.^{159,209} Conditions were process mapped to identify equipment and supplies involved in the current practice of care. For each condition, a range of likeliest treatment pathways were first identified using procedures outlined in the AFEM 2nd edition Handbook²¹⁰ and later validated in discussions with global emergency care experts, Ugandan health care providers, and during visits to the hospital sites. This process resulted in the identification of 13 crucial interventions in the delivery of care for the five sentinel conditions. A table of these

treatments processes can be found in the supplementary materials (**Appendix I**). Our expert panel identified a list of single use supplies (such as sundries and consumables), reusable supplies and capital inputs (such as medical equipment and devices), medication received, labour and diagnostic tests required for each intervention. Our approach in costing for care was to define the incremental cost associated with implementing EC described in the WHO EC Toolkit at existing hospitals. These hospitals were assumed to include some infrastructure capacities, such as building and utilities, which were not considered in our costs.

The sample population for the study was comprised of patients receiving unscheduled care for the treatment of five sentinel conditions; post-partum haemorrhage (PPH), road traffic incident (RTI), asthma, pneumonia, paediatric diarrhoea. Patients presenting to the unit with one of the selected conditions but whom did not receive one of the 13 identified treatments were excluded from the sample.

6.2.3 Enumerating inputs for each process

Each instance of resource utilization was counted at the individual patient level. Enumeration of inputs followed Hendricks et al guidelines, using the bottom-up micro-costing method.²¹¹ Study data were collected and managed using REDCap (Research Electronic Data Capture), a secure, web-based software platform designed to support data capture for research studies, hosted at the University of Cape Town.²¹²

All efforts were made to observe a minimum of 25 cases for each intervention, and data collectors were instructed to observe the same intervention at different points across the four-week period to ensure time-based data was representative of various providers. Data were largely collected from the emergency unit, although occasional cases of PPH and paediatric cases were captured in the Maternal and Children's wards respectively. Six Ugandan data collectors were on site, daily, to observe all eligible cases. Data collectors identified potential cases as they arrived on site and followed providers throughout the duration of the delivery of intervention. During observation, data collectors noted all supplies, medicines and medical devices used throughout the intervention, as well as the occurrence of any diagnostic tests. The number of medical supplies used in the delivery of the interventions were tallied on a daily basis. Data clerks either entered data directly to REDCap using tablets, or first captured data on paper tools which were later uploaded into the online system.

Although services at government facilities are free of charge, anecdotal evidence suggest that due to extreme resource constraints patients may be asked to purchase their own medical supplies in order to receive timely care. To capture instances of out-of-pocket payment for single use items, medications and diagnostic tests, data collectors were asked to indicate if the item was paid for by the patient, presumably from a nearby pharmacy or private hospital or clinic.

Time-motion methodology was used to capture the resource use of labour.²⁰⁶ Labour time was defined as hands-on time of providers in the delivery of an intervention, from the moment a

provider decides on a course of action in treatment to the completion of that action. Tablet and phone timers were used to capture time spent in delivering care. Only activities and tasks which could be observed by the data clerk were captured, including diagnosis, stabilization and treatment of patients. In addition, data collectors captured the cadre of providers and number of each cadre present while delivering the intervention.

6.2.4 Costs

Unit costs of single use supplies, medicines and diagnostic tests were obtained from the National Medical Stores (NMS) price survey report, the primary provider of medical supplies to government hospitals.²¹³ The price of any items missing from the NMS report were obtained from Joint Medical Stores (JMS) – one of the largest private medical supply providers in the country. Estimated costs for diagnostics tests were taken from the literature.²¹⁴⁻²¹⁷ Labour unit costs were expressed as cost per minute, calculated by dividing each cadre's annual salary – obtained online from Ministry of Public Service salary structure for the fiscal year 2018-2019 – by the working minutes in each year (252 working days x 8 hrs per day x 60 mins per hour = 120,960).²¹⁸

Reusable items, such as monitors and forceps, were distilled to a cost per each use. This was derived from the purchasing cost of each device, at an annualised value of the useful lifespan divided by the presumed usage of once per day. Certain high use items, such as stethoscopes, were assumed to be used fifteen times per day based on expert opinion of in-country physicians and amended accordingly. All costs were converted from Ugandan Shillings to US Dollars at annual exchange average rate for 2017 (1 dollar = 3700 shilling).²⁰⁸ Resource use and unit costs attributable the interventions are listed in **Appendix H**.

The following items were included in calculating the total direct costs; personnel time, equipment/reusable supplies, single use supplies, diagnostic tests and medications. A series of assumptions were made in our analytical approach to costing these services. Costs were calculated at patient level by multiplying the frequency of use for each item used by the unit price, added with the time spent conducting the intervention by staff multiplied by labour costs per minute, to determine the total cost. Costs were apportioned to each intervention by the average number of times consumables and drugs were utilized for each intervention. Capital costs included all reusable items and medical devices. Cost per use of reusable equipment was apportioned to each intervention by the average number of times utilized for that intervention. Salaries were proportioned by the average amount of time spent for that intervention by the care team. A table summarizing details of all sources of information, basic analysis and cost share assumption per costing area is provided in **Table 6.2**. Data was analysed for measures of central tendency for each condition and each intervention using Microsoft Excel (Microsoft Redmond, WA), and STATA 13 software (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). A Kruskal-Wallis H test was conducted to determine if total cost was different for the sentinel conditions. A post-hoc Nemenyi test was performed to make pairwise comparisons between the conditions.

Table 6.2 Costing and cost share assumptions

Costing area	Sources of Information	Basic Analysis	Cost share assumptions
Consumables (<i>Price and Quantity</i>)	Quantity: observed by on-site data collectors Prices: Market price from government distributors and where necessary other local distributors .	The expenditure on consumables was calculated from the quantity used multiplied by the unit prices.	Costs were apportioned to each intervention by average number of times utilizing the consumables for each intervention.
Medicines and Drugs (<i>Price and Quantity</i>)	Price: Market price lists were obtained from government distributors and where necessary other local distributors . Quantity: Observed by on-site data collectors	The amount spent on drugs and medicines were calculated by multiplying quantity used and unit price for each drug or medicine.	Costs were apportioned to each intervention by average number of times utilizing these drugs for each intervention.
Reusable equipment and machinery (<i>Quantity, Price and Average life</i>)	Quantity: Observed by on-site data collectors Price: Market price from government distributors, local distributors and relevant websites. Average life: literature review, interviews with staff at health facility	Cost of equipment and machinery were distilled to a cost per use. The onetime costs of purchase of reusable equipment and machinery were annualized for their average life using a discount rate of 3% and then divided by number of uses per year.	The cost per use was then apportioned to each intervention by the average number of times utilized for that intervention.
Salaries of human resource (<i>Time and Salary</i>)	Salary: Public Service salary structure for the fiscal year 2018-2019 Time: Observed to the nearest minute by data on-site data collectors.	Annual salaries of the health staff of the facility were distilled to an per minute unit cost by dividing annual salary by number of working minutes in a year (120,960) Amount spent on human resources was calculated by multiplying number of minutes in care by price for one minute of provider time.	Proportioned by the average amount of time spent for that intervention by the care team.

6.3 RESULTS

872 cases across the five sites were captured for this study. The distribution of the cases by condition and intervention, as well as the median costs of treatment, are summarised in **Table 6.3**.

Table 6.3 Cost of care per sentinel condition and intervention in 2017 US Dollars

	n	Median (IQR)	Mean (SD)	Min	Max	Kruskal Wallis H
TOTALS	872	15.53 (14.44-19.22)	19.03 (16.96)	13.66	413.11	
<i>Cost in USD by sentinel condition</i>						
RTI	371	15.96 (14.51-20.30)	21.59 (25.14)	13.71	413.11	H =92.92
PPH	59	17.25 (15.02-21.36)	19.97 (9.10)	13.75	73.79	$p < .0001$
Asthma	66	15.90 (14.76-19.30)	17.49 (3.67)	13.70	28.01	n= 872
Pneumonia	186	15.55 (14.65-20.12)	15.55 (4.39)	13.66	38.26	
Paediatric diarrhoea	190	14.61 (13.74-15.57)	15.74 (3.46)	13.66	30.31	
<i>Cost in USD by intervention</i>						
Wound closure	69	18.76 (16.63-21.79)	20.71 (8.51)	14.18	73.54	
Fracture reduction & splinting	55	27.77 (22.00-31.50)	38.2 (56.93)	14.43	413.11	
Haemorrhage Control	56	18.07 (17.10-22.83)	25.55 (19.48)	13.94	83.94	
IV fluids	178	15.79 (15.05-17.85)	18.42 (8.54)	13.96	83.89	
Oral Rehydration	91	13.74 (13.70-13.83)	14.12 (1.42)	13.66	23.57	
Antibiotics	160	15.44 (14.74-18.0)	16.92 (3.49)	13.89	38.26	
Oxygen	80	14.69 (13.91-20.00)	16.99 (4.01)	13.70	29.68	
Nebulisation	39	15.84 (15.15-18.64)	17.36 (3.50)	13.98	28.01	
Analgesia	96	14.22 (13.96-14.51)	14.71 (2.58)	13.66	37.72	
Transfusion/blood given	33	15.54 (14.68-18.31)	18.04 (9.75)	14.01	71.20	
Oral or Nasal Pharyngeal						
Airway*	2	16.73 (16.69-16.77)	16.73 (0.12)	16.64	16.82	
Needle decompression*	6	15.76 (15.60-16.02)	15.76 (0.50)	15.27	16.72	
Intubation*	7	29.31 (17.45-35.86)	27.08 (10.19)	15.24	38.42	

*Small sample size

RTI is the most common presentation observed across hospital sites accounting for over 42% of all cases captured. Delivery of IV fluids was the most commonly observed intervention (20.41%), followed by delivery of antibiotics (18.35%), analgesia (11%) and oral rehydration (10.4%). The overall median (IQR) cost of care across all conditions is \$15.53 (14.44 to 19.22). The median (IQR) cost per condition was highest for PPH at \$17.25(15.02 to 21.36), followed by \$15.96(14.51 to 20.30) for RTI, \$15.90(14.76 to 19.30) for asthma, \$15.55(14.65 to 20.12) for pneumonia, and \$14.61(13.74 to 15.57) for paediatric diarrhoea. Cost of care for a patient with RTI varied the most significantly, with a mean(SD) of \$21.59(25.14) and median(IQR) \$16.05(14.51 to 20.30) as compared to paediatric diarrhoea which varies the least, with mean(SD) \$15.74(3.46) and median(IQR) \$14.65(13.74 to 15.57). The median cost per intervention was highest for fracture reduction & splinting (\$27.77), wound closure (\$18.76) and haemorrhage control (\$18.07). Cost of care per case for these interventions varied the most significantly, fracture reduction and splinting with a mean(SD) of \$38.23(56.93) and median(IQR) \$27.77(22.00 to 31.50) as compared to paediatric diarrhoea which varies the least, with mean(SD) \$15.74(3.46) and median(IQR) \$14.65(13.74 to 15.57). A Krauskal-Wallis test yielded statistically significant difference in cost values between sentinel conditions $H=92.92$, $p=3.15E-19$. At a P value of $< .05$, the post-hoc Nemenyi test revealed paediatric diarrhoea has a statistically significant lower median cost compared to all other conditions but did not yield any significant differences in median cost between the remaining four sentinel conditions (Table 6.4).

Table 6.4 Correlation results matrix of Nemenyi test of sentinel conditions

	RTI	PPH	Asthma	Pneumonia	Paediatric diarrhoea
		$q\text{-stat} = 2.374$	$q\text{-stat} = 0.260$	$q\text{-stat} = 2.012$	$q\text{-stat} = 12.381$
RTI	-	$p = 0.448$	$p = 0.999$	$p = 0.613$	$p < 0.001^*$
			$q\text{-stat} = 2.051$	$q\text{-stat} = 3.437$	$q\text{-stat} = 9.644$
PPH		-	$p = 0.595$	$p = 0.109$	$p < 0.001^*$
				$q\text{-stat} = 1.019$	$q\text{-stat} = 7.487$
Asthma			-	$p = 0.952$	$p < 0.001^*$
					$q\text{-stat} = 8.956$
Pneumonia				-	$p < 0.001^*$
Paediatric diarrhoea					-

*significant at the 0.05 level, $q\text{-crit} = 3.875$

Single use supplies contributed considerably to the total cost of care (67%), followed by reusable supplies (16%) and diagnostic tests (8%). Medications (5%) and labour (4%) were the least significant drivers of cost (Table 6.5). This similar distribution pattern held true across most conditions and interventions with the exception of haemorrhage control, where labour costs contributed to 22% of total costs.

Table 6.5 Components of direct cost of care per sentinel condition and intervention

	Single Use Supplies	Reusable Supplies	Medications	Labour	Diagnostics
TOTALS	67%	16%	5%	4%	8%
<i>Proportion of total cost by sentinel condition</i>					
RTI	69%	14%	5%	4%	8%
PPH	64%	15%	8%	7%	6%
Asthma	62%	18%	6%	6%	8%
Pneumonia	64%	18%	3%	4%	11%
Paediatric diarrhoea	70%	19%	3%	3%	4%
<i>Proportion of total cost by intervention</i>					
Wound closure	69%	15%	3%	7%	6%
Fracture reduction & splinting	76%	8%	7%	5%	3%
Haemorrhage Control	57%	12%	5%	4%	22%
IV fluids	62%	17%	9%	4%	8%
Oral Rehydration	76%	21%	0%	1%	2%
Antibiotics	68%	18%	2%	3%	8%
Oxygen	64%	19%	1%	6%	10%
Nebulisation	62%	18%	9%	5%	6%
Analgesia	75%	21%	3%	1%	1%
Transfusion/blood given	63%	17%	0%	5%	15%
Oral or Nasal Pharyngeal Airway*	64%	18%	0%	17%	0%
Needle decompression*	70%	19%	0%	11%	0%
Intubation*	55%	12%	1%	22%	10%

¹ Single use supplies includes all supplies and equipment which are discarded after one use such as gauze.

² Reusable supplies include all supplies and equipment which are used more than once such as stethoscopes, monitors and kidney dishes.

³ Medications includes all drugs used in treatment.

⁴ Labour includes all observed time of care delivered by health care workers.

⁵ Diagnostics include all tests and procedures used in identification and treatment such as, radiology and labs.

*Small sample size, therefore results unreliable at intervention level.

Median labour time and proportional time of care by cadres is presented in **Table 6.6**. Providers spent the most time in care for patients with asthma 24.5 minutes (10 to 69) and PPH at 23 minutes (9 to 46), and the least time on interventions with patients with paediatric diarrhoea at 8 minutes (3 to 25). Labour time was highest for the intervention of fracture reduction & splinting at 42.5 minutes (21.75 to 64.25) and wound closure at 39.5 minutes (25 to 64). RTI care had a higher proportion of medical specialist time than any other condition (12%). Care for paediatric diarrhoea was almost exclusively delivered by nurses (90%). 64% of labour was provided by nurses or nursing student, which is in alignment with the literature regarding delivery of care in sub-Saharan Africa.²¹⁹

Table 6.6 Median time spent by providers and distribution by cadre

	Time Median (IQR) in minutes	Proportion of total time specialist care ¹	Proportion of total time nurse care ²	Proportion of total time medical care ³
TOTALS	15 (5- 45)	2%	64%	30%
<i>By condition</i>				
RTI	18 (7-42)	12%	53%	35%
PPH	23 (9-46)	0%	56%	43%
Asthma	24.5 (10-69)	0%	61%	38%
Pneumonia	15 (5-70)	1%	72%	26%
Paediatric diarrhoea	8 (3-25)	0%	90%	9%
<i>By intervention</i>				
Wound closure	39.5 (25-64)	2%	48%	39%
Fracture reduction & splinting	42.5 (21.75-64.25)	12%	49%	23%
Haemorrhage Control	22.5 (9.5-58.5)	0%	54%	41%
IV fluids	20 (10.25-43.5)	1%	80%	18%
Oral Rehydration	3 (2-5)	0%	92%	7%
Antibiotics	14 (8-38)	0%	85%	14%
Oxygen	15 (4-73.25)	0%	52%	45%
Nebulisation	25 (11-63)	0%	64%	36%
Intubation*	128 (68.5-295)	0%	46%	52%
Analgesia	5 (1-9.25)	4%	82%	13%
Transfusion/blood given	25 (8-45)	0%	57%	41%
Oral or Nasal Pharyngeal Airway*	83 (80-86)	0%	0%	92%
Needle decompression*	22 (16.25-25.5)	0%	0%	89%

¹ Specialist care includes all specialists including: surgical, paediatric, obstetrics, internal medicine and other

² Nurse care includes nursing students and nurses

³ Medical care includes interns, medical officers and clinical officers

*Small sample size, therefore results unreliable at intervention level.

Most supplies, medications and screening tests were provided by the hospital (94%). Only 6% of the 5490 items captured were paid for by patients. Over 50% of all screening tests (Ultrasound, X-ray, CT Scan) were paid for by patients as presented in **Table 6.7**.

Table 6.7 Proportion of out-of-pocket payment by patients for screening tests

	Ultrasound	X-ray	CT Scan	Other*
TOTALS (N)	1	79	9	123
Hospital provided (n)	0	39	0	89
Out of pocket by patient (n)	1	40	9	34
% out of pocket by patient	100%	51%	100%	28%

*Other includes complete blood counts, urine, stool and sputum tests.

6.4 DISCUSSION

This study is the first to describe the direct costs of EC in hospitals in Uganda by observing the delivery of clinical services, using robust activity-based costing and time motion methodology. The costs for EC interventions are found to be considerably lower than other health programmes in the Ugandan setting such as tuberculosis treatment (\$151), HIV anti-retroviral therapy (\$628) and obstetric fistula repair (\$378).²²⁰⁻²²² Emergency care could be highly impactful in Uganda, where injuries from trauma and road traffic incidents are a leading cause of death²²³, accounting for 7% of all mortality in public health facilities in 2017 to 2018.⁴⁹

Our methodology attempted to capture all relevant costs for implementing WHO recommended care delivery in the emergency care setting. Our analysis finds that single use supplies, as opposed to multiuse supplies, are the most important cost drivers to the total cost of EC. Reusable resources which have a cost of use and are broadly less sensitive to variations in patient load, such as reusable medical equipment and labour, contributed significantly less to the total cost. Discounting of capital costs resulted in very minimal changes to results with median economic costs being 2.4% higher than median accounting costs. This finding implies that marginal costs contribute sizeably to the total cost of EC care; as such, economies of scale – where unit cost decreases as the volume of output increases – may not be as significant to EC care interventions as previously suggested.²²⁴ This finding aligns with current evidence of the higher than expected marginal costs of outpatient EC in HIC.²⁰²

These findings hint that a further cost saving may be realised if additional reuse of supplies is promoted where reasonable. To recommend such an approach, the impact on effectiveness of patient care, which falls outside of the scope of this work, would need to be better understood. In many ways this practice of reuse is already routine in LMIC settings where supplies such as suturing tools, disposed after a single use in HIC settings, are commonly sterilised and reused in LMICs. During our study we observed the use of cardboard boxes for splints or gloves as tourniquets, further demonstrating the extreme resourcefulness of practitioners in this setting. In the absence of EC guidelines and recommendations many hospitals have improvised walls made of tarps, and IV bags zip-tied to walls rather than hanging from drip stands. Future research should endeavour to better understand the impact which operating under resource scarcity has on the delivery of EC and how local adaptations may provide further cost savings.

Although we suspected that patients would be responsible to pay for many supply items if unstocked, from our limited data we found little evidence of this practice and low frequencies of out-of-pocket payment made by patients. On the other hand, 100% of CT Scans and Ultrasounds and over 50% of X-Rays were paid for by patients, likely because almost no sites had CT Scanners at their facility, and many had limited x-ray machines or film. This pattern indicates particular challenges in diagnostic testing resources and access which could interrupt patient care.

Assessing the economic cost of EC is complex because of the heterogenous nature of EC conditions and their wide-ranging clinical features. Inconsistent cost data further convolutes the sparsity of information regarding EC in LMICs. In South Africa, a \$6,749 difference was observed between a top-down and bottom-up costing approach of the average healthcare cost per road traffic injury patient.²²⁵ While efforts have been made to quantify the pattern of resource use and procedure utilization in functional emergency units in Uganda, the actual cost of delivering these services in this setting remains unclear.²⁰⁴ As a result, we rather unconventionally approach the costing of EC services by presenting the cost of care for five sentinel conditions, as well as the cost per intervention conducted. We predicted finding a high variation in cost for each condition. Interestingly, our results show that the cost of delivering care is relatively stable across conditions, and only statistically lower for paediatric diarrhoea. As expected, costs of RTIs had the highest variability in cost, due to the wide range of injuries which fall under that condition; but overall RTI interventions do not have significantly higher costs than other conditions (except paediatric diarrhoea). This finding suggests that there may be a set of basic, low-cost, high impact, lifesaving approaches and interventions such as IV support or blood transfusion, which provide significant value for money. Benefits of economies of scope—where unit cost of production decrease as variety of products increase—may still apply to extending EC services in the context of existing health systems.²²⁶

Our time-motion study found that nurses provided most of the labour for all interventions, which is supported by their representation of 75% of the healthcare workforce.²²⁷ This pattern touches on the significance of the nursing workforce in the delivery of emergency care in LMICs, which may impact the planning of training and labour budgets for delivering EC, and aligns with broader discussions of task-shifting acute care to nursing cadres.²²⁸

This study illuminates some of the key challenges to pursuing a research agenda in cost-effectiveness research for EC in LMICs. Collecting rigorous data is costly and time consuming, and in contexts where care delivery may be fractured it can be challenging to identify the emergency centre's contributions to both the budget and patient survival of a hospital. As such, strengthening routine data collection systems to better understand supply use in public facilities could greatly aid future economic analyses and cost-effectiveness studies. Further research to better understand the impact creative material use and reuse may have on practice and budgets in a resource limited setting is also essential. Through these findings we can begin to understand what it means to operate EC services under resource scarcity.

6.4.1 Limitations

This study has potential limitations. First, free text entry of data by non-medically trained research assistants resulted in a small amount of data (0.5%) regarding medications being lost due to misspelling, incorrect transcription or unidentified unit measurements. Second, a widespread lack of basic equipment and medicines for EC has been well categorised in Uganda²⁹ and treatment decisions and resource used in the care of patients may be influenced by this scarcity. In order to appropriately represent the context, we adopted a direct observation approach using activity-based costing and time motion methodology. As a result, while accurately reflecting the actual costs of care, our findings may underestimate the costs of ideal care that is uncompromised by persistent resource limitation. Future research could examine the impact of resource scarcity on care delivery behaviour. Similarly, the full costs of EC are likely underestimated, as indirect costs are not captured in this study due to resource limitations. Nevertheless, this study provides detailed direct cost information that can inform future research which aims to consider indirect costs such as social opportunity costs and patient and caretaker time.

Additionally, restocking at hospitals occurs on a monthly basis and may impact the supply use patterns of providers where patients at the beginning of the month receive more services, or medicines and supplies are reserved for high-risk patients. To account for these variations data were collected for a full period of a month but the impacts of inventory upon patterns of resource use fall beyond the scope of this paper and should be prioritised in future research. Certain interventions, such as intubation, oral or nasal pharyngeal airway insertion and needle decompression, are extraordinarily rare in the Ugandan setting likely due to the absence of the next step in the chain of care such as intensive care units. Therefore, these interventions are under-powered in our findings. We included these interventions in our aggregated analysis to further shed light on EC healthcare utilizations but were unable to draw any conclusions at the intervention level given the small sample size.

Despite best efforts to move towards formalised EC in Uganda, there is still much to be done to systematize the approach to EC. Staffing, equipment and physical space differ greatly between hospitals. Due to the unique, country-specific characteristics of Uganda, the data and findings here reflect site-specific practices with specific patient populations within the particulars of the public Ugandan health care system and local prices. Therefore the results of our study are not generalizable to other LMICs.

6.5 CONCLUSION

This study finds that EC in Uganda is managed at considerably lower costs compared to many priority health interventions in low-resource settings. Given the prevalence of these conditions and our research findings, it is likely that allocating resources to strengthening EC may be an extremely valuable investment to the health system. The results provide evidence on the direct costs of delivering EC in LMICs, which can be further used to estimate the health care costs faced by LMICs looking to expand access to EC services. Further research assessing acute care

delivery and the impact of creative material use and reuse in resource scarce settings would be useful in planning wider health care delivery systems development.

6.6 CHAPTER SUMMARY

This chapter details a bottom-up costing analysis where all relevant cost components are classified to the most exhaustive level by gathering detailed information on the quantity of resources used and their value at a patient-specific level. Precise cost estimates, which reflect accurate resource use as it occurs in facility-based delivery of EC in an LRS, are presented for the very first time. These estimates may therefore be used broadly to demonstrate cost-effectiveness of EC interventions in future evidence-based decision-making in resource scarce contexts.

This review finds evidence that the cost of EC in RRHs compares favourably in cost to other prioritised health issues in LRS and allows us to begin to measure the significant potential value of these interventions. Moreover, this chapter substantiates the need for further research into the realities of delivering EC in low resource countries and the potential gains of economies of scale from implementing EC.

In the next chapter, applicability of the framework developed in Chapter 4 is tested using empirical cost and outcomes data obtained from a pilot study and micro-costing study conducted in Uganda to run a retrospective CEA. This illustrative example uses a decision-tree model to compare the costs and benefits of strengthening facility-based EC using various elements of the WHO toolkit within an LRS health care system.

Chapter 7

COST-EFFECTIVENESS ANALYSIS OF THE MULTI-STRATEGY WHO EMERGENCY CARE TOOLKIT IN REGIONAL REFERRAL HOSPITALS IN UGANDA

Previous chapters established robust inputs related to the cost of delivering care at RRHs in Uganda and outlined a conceptual framework to using CEAs and BIAs in EC. In this chapter a retrospective CEA is presented using the results of the previous chapter alongside health outcomes and cost data from the pilot study of the 2017 WHO Emergency Care Outcomes Project (ECOP). Details of the WHO Toolkit for Emergency Care intervention are provided and used to illustrate the application and challenges of assessing EC using economic evaluation. The impact of the toolkit implementation is measured through two outcomes; 48-hour mortality from sentinel conditions (as captured and measured by WHO), and the changes in facility expenditure. A BIA is presented which extends the cost-effectiveness results to report the affordability of the intervention under a national rollout given the current national budget and MoH budget for Uganda.

7.1 BACKGROUND

The WHO Toolkit for Emergency Care

This presented CEA was designed in response to the release of a suite of tools developed by the WHO Emergency, Trauma and Acute Care programme to support strengthening EC systems. All of these resources are available on the WHO website.²²⁹ The analysis leverages off of the recent pilot as well as ongoing monitoring and evaluation studies related to the effectiveness of the WHO toolkit for EC. This offers a genuine instance where the toolkit has been adopted to illustrate the theoretical frameworks presented earlier in this work and identify health and economic benefits.

The simple package of interventions is designed to strengthen reliable, timely, efficient and effective management of urgent patient care at facilities in LRS and was implemented as part of a pilot program at two hospitals in Uganda throughout 2015-2016. The two sites include Kawolo Hospital, a 106 bed hospital located in the Central Region of Uganda and Mubende RRH, a 175 bed hospital serving the districts of Mubende, Koboga, Mityana and some of Mpigi District MRRH. The package included a set of training and tools relevant to the provision of effective EC including; the BEC course, standardised patient charts with identified data points related to EC, a triage tool, trauma and medical checklists, and EU protocols and guidelines.

Prior to training two WHO international trainers held a two-day Training of Trainers (ToT) to train three lead staff per site (1 clinical officer 2 nursing officers) in the intervention package. Five days were then dedicated to the BEC course and two days for training on process guidance such as the triage tool and trauma and medical checklists. Sessions were led by two international trainers alongside three local site trainers. The course was made available to all interested

clinicians currently working in site EUs. Ten participants were trained at each site. 2 doctors, 1 clinical officer and 7 nurses at Kawolo, and 1 doctor, 2 clinical officers, and 7 nurses at Mubende.¹⁵⁹

A standardised tablet-based data abstraction form was used to capture primary outcome of 48-hour mortality. Given the presentation rates of sentinel conditions and a baseline fatality rate of 2.98%, a sample size of 1500 patients in both pre-and post-intervention groups was used to detect a 30% mortality reduction. No data was collected one week prior to or one week after implementation. The toolkit was implemented over a seven-day period in March 2017, during which no data was collected. Demographics of the study population are summarised in **Table 7.1**.

Table 7.1 Demographics of study population

Key emergency condition	Cases (n, %)	Age category distribution (n, %)					Gender distribution (n, %)		
		<1 yr	1 - <5 yrs	5 - <18 yrs	≥18 yrs	Missing age	Male	Female	Missing gender
Pediatric diarrhea	915 (24.8)	45 (4.9)	610 (66.7)	253 (27.7)	NA	7 (0.8)	472 (51.6)	412 (45.0)	31 (3.4)
Pediatric pneumonia	1202 (32.6)	48 (4.0)	891 (74.1)	251 (20.9)	NA	12 (1.0)	660 (54.9)	504 (41.9)	38 (3.2)
Road traffic incidents	1378 (37.4)	3 (0.2)	87 (6.3)	210 (15.2)	1068 (77.5)	10 (0.7)	1018 (73.9)	335 (24.3)	25 (1.8)
Postpartum hemorrhage	83 (2.3)	0 (0.0)	0 (0.0)	2 (2.4)	80 (96.4)	1 (1.2)	0 (0.0)	83 (100.0)	0 (0.0)
Asthma	111 (3.0)	1 (0.9)	2 (1.8)	23 (20.7)	83 (74.8)	2 (1.8)	44 (39.6)	66 (59.5)	1 (0.9)
All conditions	3689 (100.0)	97 (2.63)	1590 (43.1)	739 (20.0)	1231 (33.4)	32 (0.9)	1400 (37.9)	2194 (59.5)	95 (2.6)

Source: Reynolds et al.²⁰⁹

The implementation of this toolkit provided the chance to create the science around economic evaluation in the field of EC. The availability of data from the pilot study in Uganda presented the opportunity to run this initial CEA to gain a better understanding of the value of the toolkit. This study has been submitted for publication. A verbatim copy of the submitted manuscript, with citations and table numbers changed to keep consistent format style with this dissertation, follows over the remainder of the chapter.



7.2 INTRODUCTION

Emergency care refers to the collection of systems and interventions to address acute illness and injury, such as trauma, infections, obstetric emergencies, and sudden complications of non-communicable diseases like diabetes, asthma, and cardiovascular disease. Health emergencies occur everywhere on a daily basis, whether or not there is an organised and well-resourced system present to address them. Over half of all deaths worldwide results are conditions amenable to emergency care and the burden of these conditions is nearly 60% higher in low-income countries (LICs) than middle or high-income settings.^{1,5}

In Uganda a lack of organised emergency care services likely contributes to excess morbidity and mortality. There are several local challenges in organising emergency care (EC), including a lack of systemwide protocols, clinical documentation, equipment and regulation.²⁹ A national assessment of facility-based acute care in Uganda identified inadequate EC in urban settings, and no or minimal access to EC in rural settings.⁴⁸ Patients with emergency conditions in hospitals are commonly cared for by staff who have received no specialised training in EC and few sites have formal triage protocols to prioritise the delivery of care based on patient acuity, despite the established benefits of these features.^{230,231}

7.2.1 Description of the study

The World Health Organization (WHO) Emergency Care Outcomes Project (ECOP) was a study carried out in two Ugandan public hospital sites from 2016-2017 to assess the impact of the implementation of the WHO Emergency Care Toolkit. The interventions within the toolkit include: Basic Emergency Care (BEC) training for clinical staff, a trauma registry, standardised triage processes, trauma checklists, and reorganization of the emergency unit (without addition of resources) to facilitate resuscitation of critically ill patients. Further details how the WHO toolkit was introduced during the study have been published elsewhere.^{159,232} Both sites, Kawolo District Hospital (KDH) and Mubende Regional Referral Hospital (MRRH), are under management by the MoH, deliver services in a less formal manner than standard emergency units in HICs, and are staffed by non-rotating personnel who had not received specialised training in trauma and acute care prior to the intervention.²⁰⁵

Mortality data were collected for one year prior to (n=2,241 patients) and one year after the intervention (n=1,753) for all patients arriving with one of five sentinel conditions: road traffic injuries; paediatric pneumonia; paediatric diarrhoea; asthma, and post-partum haemorrhage. These conditions were selected due to the ease of rapidly assessing the impact of an emergency care intervention on outcomes. Findings included in **Box 7.1**.

Box 7.1. Key findings of ECOP study

Findings included:

- Across both sites, overall 48-hour mortality associated with key emergency conditions was 3.54% pre-intervention and 1.86% post-intervention, representing a significant relative reduction of 47.5%
- Paediatric cases (diarrhoea and pneumonia) had the highest admission to ward (89.2% and 87.1%, respectively).
- Most patients reach EUs via paid transportation, such as in taxis
- Less than 6% of patients were referred from other healthcare facilities

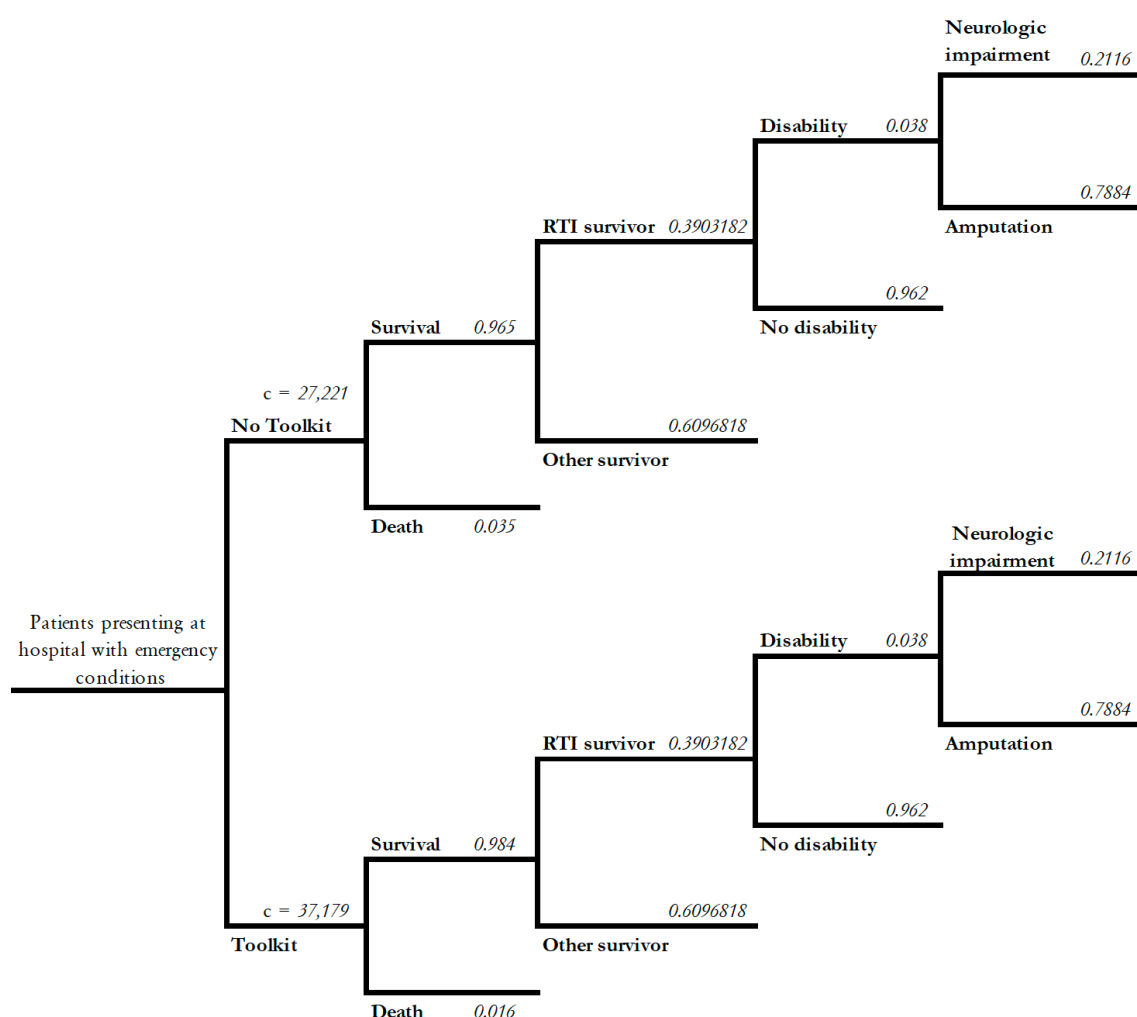
*Source: Reynolds et al*²⁰⁹

While introduction of the toolkit reveals a promising reduction in the mortality rate for patients, little is known about the intervention's cost-effectiveness and affordability.²⁰⁹ These considerations are critical to decision makers and health system planners, who are operating under tight fiscal constraints. Research in this area has been highlighted as a critical gap and a recent systematic review demonstrated the paucity of published evidence around the cost-effectiveness of emergency care, particularly regarding analyses of multi-modal interventions that impact multiple diseases.^{97,182} Although cost-effectiveness analyses (CEA) should never be the sole criteria for decision making, this information can aid in making well-informed decisions regarding resource allocation, particularly in the setting of resource scarcity. To better understand the financial implications of implementing the toolkit, ECOP study results were used to create a CEA. A budget impact analysis was also conducted to estimate the affordability of scaling this to all regional referral hospitals at the national level.

7.3 METHODS

A decision tree model was constructed to compare the costs and health outcomes of implementing the ECOP package of interventions against the pre-intervention status quo from a societal perspective. In reporting our methods and results of the analysis we adhere to the Consolidated Health Economic Evaluation Reporting Standards statement (CHEERS) and ISPOR Principles of Good Practice for Budget Impact Analysis.^{107,172} The decision analytic model was developed using Microsoft Excel software (Microsoft Corp., Redmond, WA, USA) and is shown in **Figure 7.1**.²³³

Figure 7.1 Decision Tree Model



7.3.1 Outcome measures and effectiveness

All probabilities related to clinical effectiveness were obtained from reported outcomes of the ECOP study.²⁰⁹ The study population included patients presenting to either of the two selected hospital sites in Uganda for unscheduled care with one of the five sentinel conditions. Results were reported as 48-hour case fatality rates.

We selected disability adjusted life years (DALYs) as our composite measure of effectiveness, given their wide acceptance as the primary measure for disease burden, particularly in LMICs.¹⁹³ In addition, we report incremental life-years saved (LYS) as a secondary unit of measurement to interpret effectiveness. These two measures allow us to represent the circumstances of emergency conditions, which often impact the young during the peak of their economic productivity and enumerate the economic productivity losses resulting from premature death.

Both costs and health outcomes were discounted equally at a rate of 3.5% annually. This follows standard practice and published pharmacoeconomic guidelines from Egypt, the most relevant guidelines available for our setting.²³⁴

In valuing health status, we used a human capital, rather than a preference elicitation approach. This follows prevailing practice for LMICs where health state valuation studies are uncommon.²³⁵ Following this approach, value is appointed based on the economic activity of individuals and their ability to contribute to GDP.⁷¹ Economic losses of production were estimated by the loss of income per year of life prematurely lost. The number of life years lost were enumerated by subtracting the average age of patient in the study (14 years) from the average life expectancy of the population at that age (68.6 years).²³⁶ All study parameters are outlined in **Table 7.2**.

Table 7.2 Model parameter range and distribution

Parameter	Base case	Range	Distribution	Source
<i>Costs (USD)</i>				
Intervention costs	5873.80	4992.73 – 6754.86	gamma	Project budgets
Average annual cash income	1354.68	469.16 – 3,054.55	gamma	UBOSS ²³⁷
Rehabilitation	27.03	22.97 – 31.08	gamma	Expert input
Prosthetics	672.5	400 – 945	gamma	Kenney et al ²³⁸
Hospital care of sentinel conditions	15.19	12.91 – 17.47	gamma	Werner et al
<i>Probabilities</i>				
Survival with toolkit	0.984	0.978–0.989	beta	Reynolds et al ²⁰⁹
Survival without toolkit	0.965	0.958–0.973	beta	Reynolds et al ²⁰⁹
Survival as RTI case	0.390	0.332 – 0.449	beta	Reynolds et al ²⁰⁹
Survival non RTI case	0.610	0.518 – 0.701	beta	Reynolds et al ²⁰⁹
Survive without disability	0.962	0.818 – 0.992	beta	Chalya et al ²³⁹
Survive with amputation	0.788	0.670 – 0.907	beta	Chalya et al ²³⁹
Survive with neurological deficit	0.212	0.179 – 0.243	beta	Chalya et al ²³⁹
Survive with rehab needs	0.115	0.098 – 0.133	beta	Chalya et al ²³⁹
<i>DALY weights</i>				
Amputation	0.275	0.234–0.316	beta	Global Burden of Disease ²⁴⁰
Neurological deficit	0.359	0.305–0.413	beta	Global Burden of Disease ²⁴⁰
<i>Model assumptions</i>				
Discount rate (%)	3.5	0 – 5	beta	Egyptian Pharmacoeconomic guidelines ²³⁴
Time horizon costs and outcomes	55	46.41–62.79	lognormal	Global Health Observatory ²⁴¹

7.3.2 Resource use and costs

We used a micro-costing approach to estimate the resource use associated with introducing the toolkit. In a prior study we performed an accurate costing of the provision of EC from a health care provider perspective at the facility level, illustrated through costing research performed at public facilities in Uganda. A direct, activity-based costing was carried out over a four-week period from September 2019 to October 2019. Data were collected by convenience sampling at five regional referral hospital sites (RRHs). Further details of the methods used have been published elsewhere.¹⁹⁷ Indirect and direct costs were captured in 2017 Ugandan shillings (UGX) and converted to 2020 USD for reporting (1 US Dollar = 3,675 Ugandan shilling).²⁰⁸

A societal perspective was selected to allow for broad estimation of the intervention’s economic impact. We use a standard human capital approach to capture the resulting loss to society of individual’s future production due to premature death or disability.²⁴² Consistent with this, we tabulated all costs associated with the delivery of medical care, as well as costs borne by the public owing to the loss of income as a consequence of premature death and years of life lost. The

majority of treatment costs were incurred within the first 48 hours of presentation at site, however for disabled survivors, costs and outcomes were evaluated over a lifetime horizon to capture all consequences, both financial and health related, assumed by society as a result of premature death or lifelong disability, including continued care costs for survivors with disability, and productivity losses due to premature death or disability. The time horizon of the intervention and was limited to the study cohort and period of one year.

Costs of the intervention were derived by project budgets and through interviews conducted with research team staff.¹⁵⁹ Direct costs of implementation of the toolkit include; initial start-up training costs (training of trainer sessions), training in BEC for health care providers, and printing of posters and guidebooks for the triage tool triage, and trauma care checklists. In total across the two sites, 4 trainers were trained during training of trainer sessions, 10 health care providers were subsequently trained through roll out of the BEC course to each hospital site.¹⁵⁹ Costs for trainings included venue hire, skills equipment, printing, meals, per-diem reimbursement for attendees and salaries of local trainers. Five wall charts and 20 pocket manuals were printed with the triage tool. Average overall cost of training to the site was \$1,683 for the ToT course and \$3,515 for the BEC course (a total of \$5,199 by site). All development costs of the toolkit materials, such as curriculum or checklist development, were provided in-kind by the WHO and are available free of cost for other interested countries who may seek to implement the Toolkit intervention and therefore excluded from our analysis. Implementation of the toolkit required no additional space or equipment outside of what the hospital was already provided through existing national budget and procurement. The model assumes staff trained in BEC are already employed under the national staffing levels and therefore no additional salaries or human resources scale up are incorporated in to our analysis.

Hospital unit staff who had acted as local champions during the project were interviewed in August 2019 to identify additional costs which may have occurred at the hospitals as a result of the intervention, such as continuing training or education for staff members. Although staff cited the use of a systematised approaches to onboarding new staff, no further costs were identified. Direct medical costs were enumerated by including both the costs of care in the treatment of the sentinel conditions, as well as expected medical costs of care required as a result of disability. For example, survivors of RTI with amputation included costs of immediate medical treatment, rehabilitation services and prosthetic limbs. Additional care costs resulting from disability were valued by estimating the number of patients who survived with disability and multiplying that by an annual cost of care for each condition. The average cost was calculated and multiplied by the number of admitted patients during the study period. Treatment costs for sentinel conditions were derived from an earlier micro-costing study conducted by the authors.¹⁹⁷ Medical costs of care were derived from the literature and through expert input of providers in Uganda. All costs used in the model are provided in **Table 7.3**.

Table 7.3 Summary of cost variables for the WHO Toolkit intervention during study in Uganda

Cost item	Price (2020 USD)	Source
Start-up costs (including ToT)	\$1,683	Kivelehan et al ²⁴³
BEC training	\$3,515	Kivelehan et al ²⁴³
Triage tool	\$172	Kivelehan et al ²⁴³
Checklist tool	\$503	Kivelehan et al ²⁴³
Total costs of toolkit	\$5,873	Kivelehan et al ²⁴³
Treatment cost of sentinel conditions	\$15.53	Werner et al ¹⁹⁷
Physical rehabilitation	\$27.03	Expert input
Long term TBI care	\$1354.68	Expert input
Prosthetics	\$672	Kenney et al ²³⁸
Annual salary	\$1354.68	UBOSS ²³⁷

7.3.3 Assumptions and threshold analysis

The thresholds used in this analysis makes an implicit assumption of maximizing health across entire populations rather than seek more equal health states across individuals.⁷¹ We use additional guidance from Woods et al. regarding opportunity based cost-effectiveness thresholds for LMICs to consider our results at various levels of willingness to pay between \$11 and \$289.⁸⁹

7.3.4 Analytical methods

Data collected during the study phase does not stipulate the disability status of survivors, but we can assume that not all patients who survive are able to do so free of disability. Of the five conditions assessed, most are curable with appropriate treatment with the exception of RTIs which present a possibility of survival but under health conditions requiring further resources and care. Therefore we assumed that patients surviving from all conditions, except RTIs, survive in full good health. To account for the impact of disability due to non-fatal injuries from RTIs we use published data on health outcomes for survivors of RTI to identify subgroups who would require further health costs after survival.²³⁹ We do not believe that these other conditions do not infer disability, such as sepsis from pneumonia, but the data available for this study was does not allow us to reliably account for these additional disabilities. We then simulate the following outcomes proportionately based off of the literature; neurological disability (e.g. traumatic brain injury (TBI) or spinal cord injury) and musculoskeletal disability (e.g. loss of limb function/ amputation). We assume that the probability of disability health outcome remains the same prior to and after intervention, as ECOP did not directly measure this outcome and improved care could theoretically lead to either decreased or increased cases of disabled survivors. A micro-simulation was run to account for discounted costs and health outcomes. We assume amputees require rehabilitation care services and prosthetics every five years, and survivors with neurological impairment require life-long care. This care is frequently delivered by family members, rather than employed caretakers and therefore the cost of this care was quantified at the annual salary of one individual caretaker.

It is plausible that an increase in knowledge could lead to health care providers who are either more comfortable in executing care, or who can more readily identify cases where care should be delivered. This in turn would cause an increase in the use of appropriate and timely interventions increasing the need for supplies and equipment. On the other hand, these improvements may also decrease wastage. Since data from the study was limited in regard to changes in the volume of actions or use of supplies, we integrated appropriate sensitivity analyses to test this hypothesis.

7.3.5 Scale-up and Budget impact analysis

In LRS, interventions which prove cost-effective may still be prohibitively expensive.²⁴⁴ To assess the affordability of the toolkit, we modelled a national scale up scenario to all RRHs allowing for projection of cost, impact and return on investment at a national level.

We present the impact the rollout would have on both the total health budget and the budget for RRHs following ISPOR guidelines.¹⁷² Using a payer perspective, we shift our time horizon to 5 years with no discounting to assist with budget planning and forecasting.¹⁶⁹ Although primary data were not captured on the change in process functions, training may produce a net increased use of resources by health care workers as a result of gaining new skills, and knowledge and through checklist reminders, or a net decrease due to mitigation of wastage.^{154,157} We took a conservative approach and modelled for a 15% increased utilization of resources arising from the intervention. This estimate was based on an average percentage increase of checklist adherence and intervention occurrence found in the literature. We assumed training costs that treatment costs vary based on the number of patients seen and training costs fluctuate as a result of the number of sites, and when scaled fully the intervention would be implemented in all 19 RRHs.

A Return on Investment (ROI) analysis was performed by comparing the societal economic gains from having the toolkit at all RRHs with the current investment required to treat emergency conditions.

7.4 RESULTS

Implementation of the WHO Toolkit averted 509 DALYs when compared to standard care over a one-year time horizon. The initial investment of \$5,873 saved 27 lives (1,826 life years) and avoided \$664,231 in downstream societal costs. As such the ICER is not calculable because the toolkit is both less expensive and more effective and therefore dominates the scenario of no intervention. Results are presented in **Table 7.4**.

Table 7.4 Incremental cost-effectiveness results

	Costs (USD) (95% CI)	DALYs	YLL
No toolkit	17,474,132.58	16,880	3,370
Toolkit	16,809,901	16,372	1,545
Difference	-\$664,231 (-\$658,552 to \$669,910)	509	1,826

A national scale-up of this intervention to all RRHs over a five year time horizon, would save 722 lives (39,421 life years) and 18,821 DALYs. Costs of the projected national scale-up are \$5,726,356 USD, which would increase the Ugandan MoH budget by \$1,197,862 USD over five years. This is equivalent to a 0.18% increase of the total health budget for Uganda based budgetary figures from 2018, or an increase of 3.29% of historic budgetary allotment specific to RRHs. The economic gains are estimated to be \$24,030,598 USD, the equivalent of a 418% ROI. Details are provided in **Table 7.5** and **Table 7.6**.

Table 7.5 Budget impact analysis cost of national scale up to all RRHs

Description	
<i>n</i> regional referral hospitals	19
Estimated annual EU patient population (for all RRHs)	38,000 or 2,000 per site
Deaths averted	722
LYS	39,421
DALY averted (non-discounted)	18,821
Costs of scale-up	\$5,726,356 USD
Budget impact of scale-up	\$1,197,862 USD
Health budget 2018/2019 ⁴⁹	2,363,652,000,000 UGX
	\$643,941,532.62 USD
RRH budget 2018/2019	127,637,208,000 UGX
	\$34,772,842.76 USD
Impact of scaling up on the total health budget	0.18% of total annual health budget
Impact of scaling up on the RRH budget	3.29% increase

Table 7.6 Budget impact of new treatment over five years

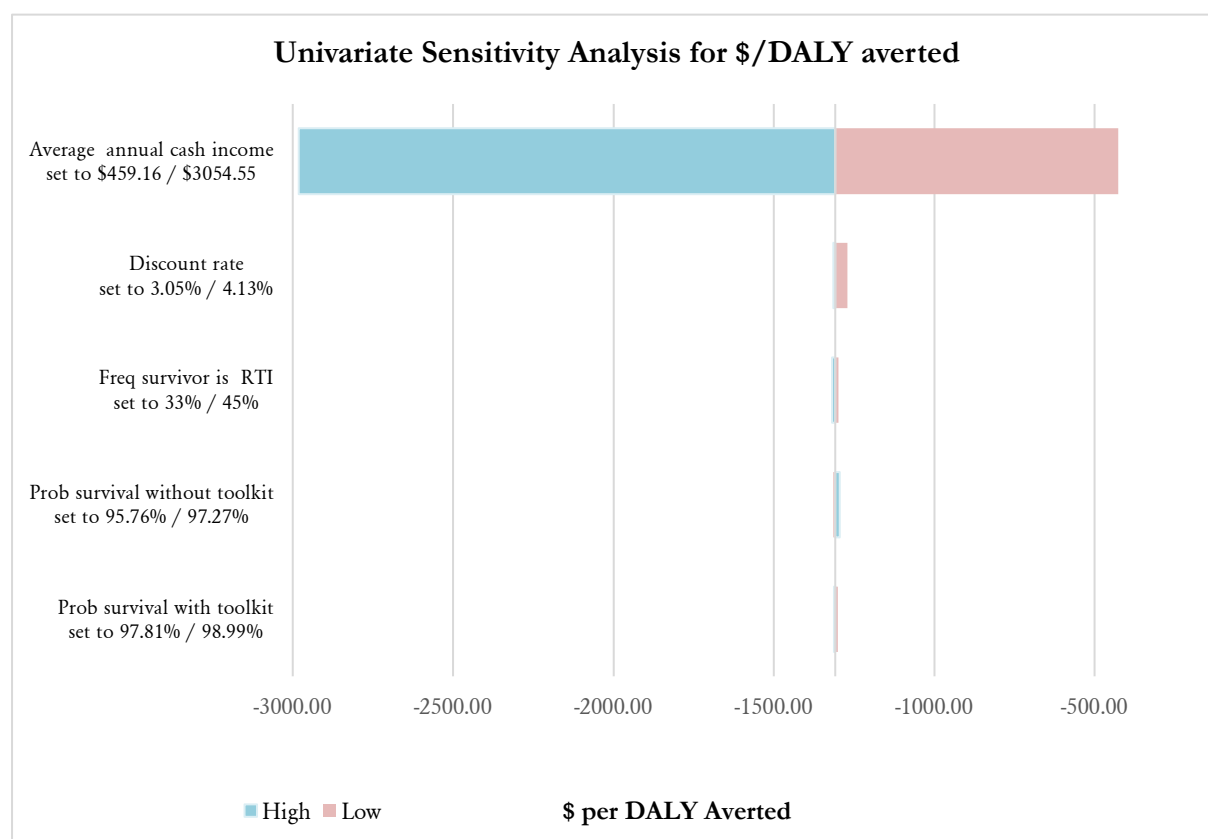
Outcome	Year 1	Year 2	Year 3	Year 4	Year 5	TOTAL
<i>Cost outcomes new treatment</i>						
Intervention costs	\$111,602	\$0	\$0	\$0	\$0	\$111,602
Treatment costs	\$1,225,387	\$1,104,248	\$1,099,591	\$1,095,013	\$1,090,513	\$5,614,753
						\$5,726,356
<i>Cost outcomes old treatment</i>						
Intervention costs	\$0	\$0	\$0	\$0	\$0	\$0
Treatment costs	\$1,126,315	\$858,753	\$854,186	\$849,696	\$845,283	\$4,534,234
						\$4,534,234
<i>Budget Impact (BI)</i>						
Intervention BI	\$112,949	-	-	-	-	
Treatment BI	\$99,072	\$245,495	\$245,405	\$245,317	\$100,559	
Total BI	\$210,674	\$245,495	\$245,405	\$245,317	\$245,230	\$1,192,122

7.4.1 Addressing uncertainty

Parameter uncertainty was handled in two ways: first, with a univariate deterministic sensitivity analysis, and second with a multivariate probabilistic analysis and Monte Carlo simulation. Probabilistic sensitivity analyses are used to address parameter uncertainty. Salaries were adapted to capture sub-regional variation from the lowest average monthly cash earnings (141,000 UGX per month or 1,692,000 UGX per annum in the Bukedi sub-region), to the highest earnings (938,000 UGX per month or 11,256,000 UGX per annum in the Kampala sub-region).²³⁷ Discounting rates were varied from 0% up to 5% to reflect current literature indicating that LMICs typically experience a higher economic growth rate and therefore require a larger

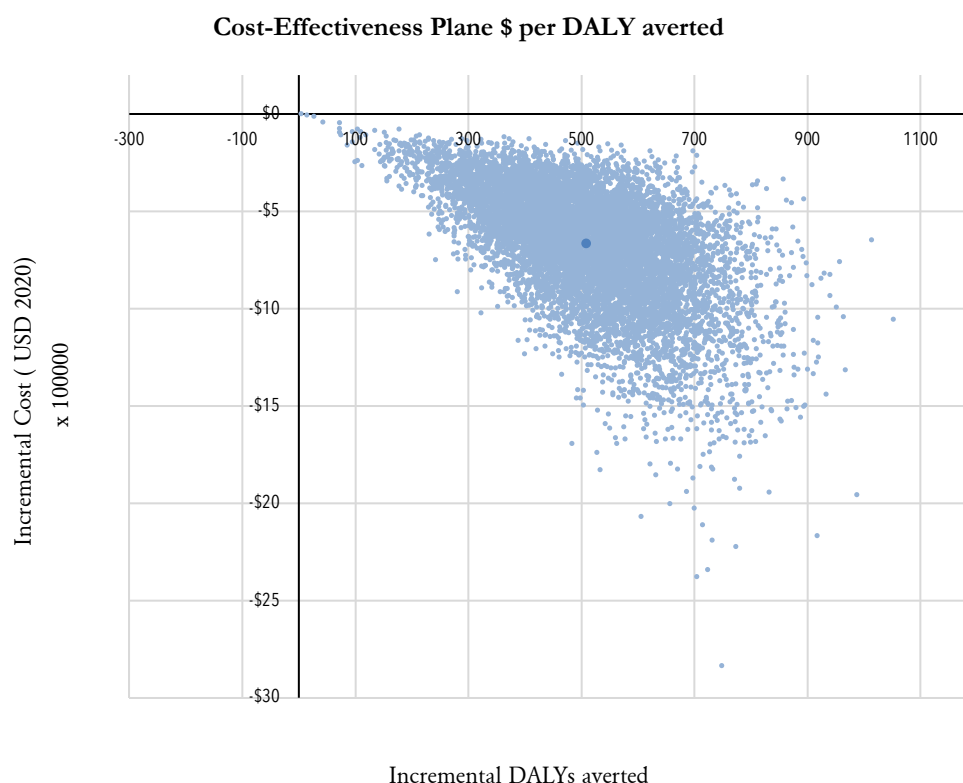
discounting figure to accurately reflect the desire to make payments later on rather than now.¹⁸⁸ Average annual cash income and discount rate and frequency survivor is an RTI survivor were the most vulnerable to changes. All other variables were highly robust. Results of the deterministic sensitivity analyses are presented in **Figure 7.2**.

Figure 7.2 Results of a univariate sensitivity analysis of key variables on cost per DALY averted



A probabilistic sensitivity analysis using Monte Carlo simulation was conducted to understand the interaction of multi-variable uncertainty. Distributions were assigned to each variable and simulations re-sampled 10000 times varying all input parameters simultaneously. Uncertainty due to costs were assumed to take on gamma distribution which adequately represents the nature of cost as a continuous positive variable with a skewed distribution.²⁴⁵ All probability parameters assumed a beta distribution.

Figure 7.3 Cost-effectiveness plane results of 10,000 samples



The use of a cost-effectiveness acceptability curve to indicate the probability the intervention is cost-effective at various values of willingness to pay was not conducted given the extreme cost savings of the intervention. To assess the robustness of our assumption regarding increased service provision as a result of training, additional one-way sensitivity analysis was conducted for our budget impact analysis which showed our analysis was most sensitive to change in intervention volume and population per site.

Structural uncertainty was assessed for the robustness of structural assumptions by using various scenarios. Given the observed structural uncertainty in areas of volume of services provided and variation in volume of patients surviving with disabilities we ran five different scenarios. The base model assumes a probable increase in service provision as a result of training. Thus the following alternative scenarios are therefore possible for the model: scenario 2 in which intervention frequency decreases from baseline as a result of more appropriate and precise care, and scenario 3 in which there are no changes to intervention frequency as a result of the intervention. In scenario 2 we test a 15% reduction in intervention frequency.

Our model further assumed that the probability of disability health outcome remains the same prior to and after the implementation of the toolkit, although improved care could theoretically lead to either a decrease or increase in cases of disabled survivors. Therefore two further alternative scenarios are possible: scenario 4 in which the effect of improved care decreases the

incidence of disability amongst patient who survive, and scenario 5 in which the number of survivors with serious disability increase, presumably due to the capacity of improved care to save more complex cases of lifelong disability which previously would have resulted in premature mortality. In scenario 4 we increase the chance survivors do so without disability to 99% and in scenario 5 we reduce the frequency of surviving without disability by 25% and increase the probability a survivor with disability experiences a neurological deficit by 35% for the intervention arm.

The results of these scenarios are presented in **Table 7.7**. Our analysis indicates the model is most sensitive to assumptions made regarding impact of the toolkit on the rate of survivors with disability. Were the toolkit to increase the rate of survivors with disabilities, both costs and total DALYs would increase, although additional lives would still be saved. However, in most scenarios the toolkit dominated over standard of care, indicating the robustness of our structural assumptions.

Table 7.7 Structural uncertainty scenario analysis

Strategy	DALYs	Costs	ICER
Scenario 1 - Base case			
Standard care	16,876	17.48 million	
WHO toolkit	16,366	16.81 million	Dominated
Scenario 2 - Reduce interventions			
Standard care	16,876	17.48 million	
WHO toolkit	16,366	16.80 million	Dominated
Scenario 3 -No change interventions			
Standard care	16,876	17.48 million	
WHO toolkit	16,366	16.80 million	Dominated
Scenario 4 - Reducing disability rate			
Standard care	16,876	17.48 million	
WHO toolkit	16,281	16.60 million	Dominated
Scenario 5 - Increasing disability rate			
Standard care	16,876	22.01 million	Dominated
WHO toolkit	17,162	22.63 million	

7.5 DISCUSSION

This is one of the first CEAs to assess a multifaceted EC strengthening intervention introduced in a LRS.⁹⁷ Based upon the results of the ECOP study, we compare the costs and effects of implementing a toolkit in RRHs in Uganda. Our results demonstrate with high certainty that the intervention is cost-saving, having a net positive health and economic impact. The intervention compares highly favourably to other common health programmes such as HIV treatment or rotavirus vaccinations (\$890/DALY averted and \$29/DALY averted respectively) which receive a substantial proportion of the current national health budget.^{246,247} Health care in Uganda faces extreme resource constraints with the country's total expenditure on health per capita (Intl \$, 2014) at \$133 and health spending comprising only 6.4% of its GDP during the

2017/2018 reported year.^{236,248} Furthermore our findings align with the growing body of literature indicating provider training and facility-based emergency care are cost-effective interventions in health.^{41,117,123,125}

It should be noted that many interventions in EC serve to benefit the young, who have the most potential for additional economic productivity throughout their lifetime. This is likely the reason our model is most sensitive to the variable of annual income. Our study population, where the average age was 14 years old and consequently premature mortality led to nearly 55 years of lost life and productivity, unmistakably demonstrates this. LICs, whose populations are younger than those in HICs, serve to benefit more significantly due to societal gains when cost analysis take this perspective approach.

The true cost of non-fatal outcomes and disability care is not well documented in LRS. Post-acute care is often provided by young family members rather than through formal or institutional caregivers. Consequently, the true costs of long-term survival of trauma and injury, and the shifting of costs to other areas of the system are not well understood. In LRS locally appropriate solutions, such as community based rehabilitation, show promise of creating a cost-effective and contextually aligned continuum of care for survivors of trauma.²⁴⁹ Despite the lack of data, we felt it was important to consider the economic burden of surviving with disability and include the losses that may be incurred in this scenario.

7.5.1 Limitations

This study sought to conduct a CEA using local or contextually relevant data and as a result, our analysis has some important limitations. Firstly, effectiveness data are derived from a single study of two sites in Uganda with a sample size of at least 1500 patients in both pre-and post-intervention groups to detect at 30% mortality reduction. Therefore, caution is warranted when generalising the findings of this study to other country contexts. Although this data represents the best available at present, they have various limitations.

Due to the design of the ECOP study, we were not able to conduct a sub-analysis of the cost-effectiveness of different elements of the toolkit. It is possible that certain elements of the toolkit are not cost-effective and others are highly cost-effective, which on balance led to our results. However, improving skills and knowledge around resuscitation and triage, for example, will benefit all patients seeking emergency care regardless of their specific disease process. For this reason, measuring costs and mortality at the aggregate level has the advantage of catching economies of scope that may be achieved through emergency care interventions.

The implied cause of a change in health outcomes, which is not directly measured in this model, is the delivery of timely and appropriate care as a result of skills and knowledge gained in training, and systematising approaches to triage. We suspect that training and the use of checklists leads to an improved knowledge and comfort with principles of emergency care. Our base analysis was limited by a lack of empirical data on the difference between the frequency of treatment before

and after the intervention, or the impact of this treatment to change survivorship with disability. It is likely that supplies are being more appropriately used after the intervention, but the balance of decreased wastage and increased appropriate use was not measured. We addressed this by using current literature on the increased probability of treatment following training and checklist interventions to create an appropriate sensitivity analysis of a possible range which this change could account for. However, as illustrated through our scenario analyses it is clear that should the toolkit lead to an increase in patients with long term disabilities, rather than a reduction, the impact could well be less cost-effective than standard of care. This raises questions of financial feasibility which should be balanced with the possibility of reduced mortality. Without appropriately robust data we were not able to capture these changes in our analysis, although future research should seek to quantify the changes in practice of providers, such as procedure frequency, which may result from the intervention.

Furthermore, assessing CEAs of interventions which target multiple diseases can be challenging. This can be particularly true in estimating staffing and resource use which may benefit from economies of scale. Our chosen measure of effectiveness may not capture the impact of indirect improvements to the hospital resulting from the intervention, such as better organization of care, enhanced triaging, or improved health outcomes outside of the EU as a result of timelier, more appropriate acute care. The impact of these changes may only be assessable in other areas of the hospital, such as inpatient care, for which health outcomes of the study were not captured. Improved EC may lead to less severe cases for other departments such as internal medicine. Due to a lack of reliable data, we were not able to capture the impact that the use of additional resources would have on the health system budget at large. Timely treatment could lead to more patients who survive their initial conditions to require further care outside of the EU, such as ICU and ventilation. Facility interventions represent only part of a the larger chain of care which is required for positive patient outcomes. In future studies, the ability to assess EC's impact on the resource use of other areas of the hospital would prove important.

Finally, there are no data available on the sustained benefits of these organisational changes. Even though acute care may be primarily concerned with immediate actions, in taking a lifetime horizon approach it is essential to understand if further costs can be expected to maintain the impact witnessed from the studies. It is clear that strengthening this body of evidence could alter the outcomes of future CEAs. Despite the challenges, this is a significant step forward in EC.

7.6 CONCLUSION

This is the first CEA to assess a multifaceted EC strengthening intervention introduced two Ugandan hospitals. The results indicate with a high level of certainty that the implementation of the WHO EC toolkit led to a net health and economic benefit. Budget impact analysis demonstrated that the small upfront investment to achieve this benefit is affordable in a LRS. These findings support the adoption and scale-up of similar intervention packages in similar settings. Future research is needed to better understand changes in supply utilization after training and process interventions as well as the relative value of different elements of the toolkit.

7.7 CHAPTER SUMMARY

This chapter produced the first country-specific estimates for the implementation of scalable interventions in strengthening EC. As one of few decision-analytic models for EC tailored to LRS, and the first as far as we know to assess a multipart intervention in the field, these results validate the practicality of the frameworks outlined in Chapter 4. Results supply specific and contextualised variables of cost and mortality to ensure accurate analysis for the country of interest. The excel based model demonstrates the feasibility of using a decision analytic tools to estimate the cost-effectiveness of scalable investments in facility-based EC. The full excel-based model is provided in **Appendix K**.

The next chapter explores the implications of the cost saving outcomes of this work, the contribution of this research to the existing literature, and make recommendations for future research.

Chapter 8

IMPLICATIONS OF THE RESEARCH

The cost effective and cost saving effect of implementing the WHO toolkit in Ugandan RRHs is substantiated by the empirical analyses in this dissertation. Though the transferability of these findings is limited, they demonstrate a prospect that comparable or additional gains could be realised in further LRS. There is clear potential for these improvements to transform the notoriety of systematising EC within the context of severe resource constraints.

8.1 INTRODUCTION

The primary aim of this dissertation was to investigate the cost-effectiveness of interventions that create a systematic approach to emergency care in health facilities in low-resource settings. This was achieved by accomplishing the following objectives:

1. Synthesising evidence relating to the cost-effectiveness of emergency care in low-resource settings.
2. Enumerating the context specific costs of delivering facility-based emergency care.
3. Retrospectively evaluating the impact of implementing a low-cost set of emergency care interventions in low resource emergency care naïve health facilities on cost and outcome (mortality), deriving a measure of cost-effectiveness.

Insights are gained from an economic perspective into the value of organised EC in areas where resources are limited. First, the body of available evidence was thoroughly reviewed, pointing to a paucity of robust CEA literature regarding EC in LRS. Outcome measures were rarely reported in conventional comparable units such as QALYs or DALYs, making it difficult to use what little evidence does exist to inform rational planning.

Efforts to develop a set of context specific costs showed delivering care in a variety of EC interventions to be reasonably unchanging in cost and proved less expensive than other priority health issues. Using study data, we were able to derive a measure of cost-effectiveness which showed that scalable interventions to improve the organisation of EC in LRS are indeed cost saving. Together these results culminated in a better understanding of the true cost of EC and acknowledgement of reasonably low-cost interventions which can achieve significant societal benefits. In doing so this work advances the research agenda needed to identify the “value for money” of EC that is of particular relevance to decision makers in resource limited settings.

8.2 CONTRIBUTIONS TO THE LITERATURE

This work primarily advocates the use of economic models to measure the delivery of EC in LRS. Insights, methodology and technical guidance are provided to illustrate the feasibility of applying critical economic value assessments in the field of EC. This dissertation makes important conceptual, analytical and empirical contributions to the body of literature. Doing so generates an organised approach towards assessing EC which clearly establishes the economic and social value of rationalising EC in LRS.

8.2.1 Conceptual contributions

Conceptual contributions include a synopsis and assessment of the existing body of knowledge and the development of a guiding framework to recognise the cost-effectiveness of EC in LRS. The systematic review in Chapter 3 successfully characterises the existing knowledge around the costs and benefits of delivering EC in these settings. Here, CHEERS checklists are used to examine and summarise the quality of the literature at an economic standard. As part of the process, and despite previous ambiguity, EC interventions are successfully labelled for searchability for the first time. Another contribution includes the proposal of a new framework for establishing the correlation between the investments in EC and the societal gains from an economic perspective. This framework was based on the discussions outlined in Chapters 4 and 5 on the appropriate application of principles of economic evaluation to EC. This has relevance to defining an approach to questions of economic value in EC and facilitate the capacity development and expansion of technical analysis to address unmet EC needs. These are the key conceptual contributions of the study.

8.2.2 Empirical contributions

Empirical contributions are made concerning the previously undetermined knowledge of the costs of delivering EC in LRS, and the incremental cost-effectiveness of implementing a scalable bundle of interventions to strengthen EC. In Chapters 6 for the first time, rigorous cost data were collected on EC interventions across five conditions representative of a wider body of those amenable to EC. Surprisingly, it appears cost does not vary significantly across a variety of conditions. The earlier presented framework was then tested against this empirical data.

Chapter 7 then presented the first CEA of systematic improvements of EC to be conducted in a LRS based on primary data. For the first time the cost of EC delivered in contexts of significant resource constraints is known. We were able to quantify that these efforts are not only cost-effective but in-fact a cost saving proposition for LRS where the greatest benefit may be realised. This dissertation therefore made significant contributions to the empirical knowledge about the cost of delivering and strengthening EC.

8.2.3 Analytical contributions

Analytical contributions were made by applying prevailing economic evaluation tools, such as micro-costing and CEAs, to issues of EC in LRS. Chapter 6 illustrates the methodology to collect rigorous cost data using a bottom-up micro-costing approach. With few electronic records available in LRS, this is data urgently needed.

In Chapter 7 a CEA model is developed to assess the efficiency of making investments into EC and calculate the incremental cost-effectiveness. The presentation and use of methods based on CHEERS standards improves comparability of the value of EC and contributes to better decision making in resource allocation. This finding suggests that important gains could be realised by increasing investment in facility-based EC to address unmet needs. Furthermore, the success in deriving the ICER illustrates the feasibility of using economic models for matters of EC. A copy of the CEA model is included as additional support for this dissertation in **Appendix K**.

Findings of this dissertation appeal to policymakers, health care administrators and researchers, by enabling them to better understand the financial implications of strengthening EC to care for their populations. Considering the growing burden of conditions attended to by EC this insight is critical.

Findings of this study can be used to develop policies that more effectively address the mounting challenge. By supplying technical guidance for difficult decision-making, the research develops a platform for further development of evidence related to the value of EC and advances the research agenda needed to identify the “value for money” of EC.

These results answer questions regarding the value of EC in LRS by considering the unique challenges and applying methods of economic evaluation to facility-based EC. Even though equity is not explicitly stated as a value in this work, it is important to consider the breadth of the impact of these findings to reduce inequitable health delivery. This work justifies the pursuit of a strategy of EC investment in LRS, putting numbers and figures to many years of anecdotal belief in the value of EC. Providing this measure of true value of EC and the opportunity costs of investment is better understood. The sample excel-based analytical tool provides a framework for decision makers to conduct further analyses appropriate to their context.

The merit of this work lies in the foundation for applying crucial economic evidence to issues of EC. In critically examining the unique features and challenges, and recognising the value these services bring, this work offers a platform for decision-makers to better understand the role of EC in the growth of national health care initiatives under a limited budget.

8.3 LIMITATIONS

There are several shortcomings of this research that deserve consideration. Most significantly, reliance on available literature restricts the transferability of the study’s findings. Ordinarily CEAs in other disease areas, or contexts with strong research capacity, are able to draw from a

much more extensive collection of available literature for appropriate effectiveness or cost variables. Due to the novelty of this work, very few reliable resources exist.

We were determined to remain as precise and relevant to the setting, and thus great efforts had to be made to capture data which could be deemed accurate enough to use in our CEA. Although we aimed to remark on the broader level of all LRS, limited funding and capacity meant it was only feasible to capture robust inputs in a single country. Despite demonstrating the cost saving impact of facility-based EC in the Ugandan setting, we are unable to extend these findings broadly to other LRS. It would therefore be inappropriate to apply these results broadly to other countries with similar environments. However, EC delivery in Uganda does showcase many commonly held characteristics in other LRS such as a tiered hospital-care delivery system, lack of electronic records, constrained human resources for health, periodic stockouts and a young population. Thus by being clear about the circumstance of our analyses, the results still reasonably estimate the likely cost-effectiveness of providing improvements to facility-based EC across LRS.

Early assessments of the programme were conducted at a tertiary hospital level and therefore the appropriateness of this structure to lower-level hospitals, which may in fact be the first point of access or care for most of the population, may be limited. Without reliable data it is difficult to isolate the impact of each element of the toolkit. Although there is supportive literature to believe each of these elements would make an impact on their own, due to a lack of certainty on the degree to which how each element is responsible for change the full toolkit was analysed together.

Although our approach focused on hospital-based care within a 48-hour window, facility-based EC is part of the larger continuum of care and is interdependent on the success of other functions of the system including but not limited to pre-hospital care, internal medicine and ICUs. Outcomes, both in terms of health and costs are reliant on care delivered across these areas. Cost shifting to other areas, such as resources for long term survivors of critical care, are pertinent expenses not well captured in these analyses. The primary data collection of the analyses did not capture some of these more complex inter-connections in other parts of the hospital. The parameters of our research limits our ability to draw conclusions about shifts in costs and the impacts on other areas of the hospital and health system.

If health systems are unable to provide further treatment to stabilised patients, the benefits of EC may become stifled. For example, in many LRS, ICU availability is highly limited. Effective EC might be able to provide definitive care which can reduce mortality in the first 72 hours, but if patients require intensive care afterwards, the lack of a continuum of care could mean poor outcomes. The glaring reality that EC works in harmony with the wider system cannot be overlooked. While we were not able to assess where shifts in spending may occur across the health system, such as increases in intensive or long-term care as a result of improved EC, the strengthening of these links remains important. This limitation was tackled through our use of additional branches in our CEA which identified costs of continued disability care. Despite our attempts to wrestle with this issue, our approach may still overlook costs shifted to other areas of the hospital such as in-patient care.

In addition, analyses presented here do not capture the impact which saving more complex cases might have on the longer-term hospital costs, such as patients who are able to be initially resuscitated and subsequently require ICU care for an extended period of time. For example, it is possible that cost savings gained through efficient EC simply shift costs to other functions of the hospital, such as the ICU or in-patient care. Capturing primary data on continued care within another ward in the hospital is resource intensive, especially in a setting where electronic records are unavailable. This was not feasible for our study period. Rather, efforts were made to capture all long-term costs where feasible, such as for survivors with disabilities discharged from the EU. Using this method captures some continued care costs directly related to EU care. The shift of such costs should be considered in future analyses as well as exploring the potential economies of scope which may exist as a result of strengthening EC. Evidence supporting the influence of these secondary outcomes on patient outcomes is limited. These issues are critically important and deserve further scholarly attention.

Finally, costs are only one of several considerations that must be addressed when deciding policies, albeit an incredibly important one in context of extreme resource constraints. In pursuing an assessment of value that relies heavily on an economic basis, other considerations focusing more explicitly on issues such as equity may be underestimated.

This limitation means guideline benefit of our analysis is narrower than alternative approaches. Whilst there are many other important considerations which are not assessed in this thesis, understanding the cost of EC and budget implications of projects that saves lives will contribute to a richer representation for decisions-makers and advocates to use in their work.

Chapter 9

CONCLUSIONS

Although evidence is sparse, there are several promising interventions for strengthening EC. Moreover, independent of cost considerations, the positive impact of effective EC has been widely acknowledged in both contemporary literature and policy circles. Commitments have been made formally through high-level global dialogs such as WHA Resolution 72.16 *Emergency care systems for universal health coverage: ensuring timely care for the acutely ill and injured* adopted at the 2019 World Health Assembly. Many LRS are vulnerable to the troubles of weak ECS. Given the potential of such health gains and the importance of using data which reflects the values of the decision-makers' population, it is important that further analysis be carried out in additional contexts which could also benefit from such interventions.

There is an imminent need by leaders in LRS to find ways to finance essential urgent care services in fulfilling commitments to UHC. Results of this work substantiate earlier assertions of the importance of EC, and for the first time measure this value in economic terms. Better organised urgent care systems are shown to be affordable and even cost saving in LRS. The benefits for strained health budgets are both direct in reducing immediate costs and indirect in creating efficiencies which could free up necessary resources for other areas of the health system. This dissertation corroborates that unrealised health and economic gains in LRS could be achieved if action to address unmet EC needs were further prioritised.

9.1 RECOMMENDATIONS FOR FURTHER RESEARCH

Some remaining considerations fall beyond the scope of this dissertation. Equally, many new research questions arose through the pursuit of this work. This section outlines key areas that should be prioritised in future research, including the development of widely available user-friendly analytic tools, understanding the impact of scarcity on practice, and assessing the potential economies of scale and interactions of EC with the broader health system.

9.1.1 Developing widely available user-friendly tools

It became evident throughout this research that although there is growing enthusiasm for the advancement of EC related CEAs in LRS, serious limitations exist in regard to analytic capacity. A pressing need exists to advance decision models that can illustrate the value of scalable investments in facility-based EC. Throughout our exploration of the literature, and despite the fact that results of CEAs are not transferrable to other settings, rarely were the underlying analytical models of the literature obtainable. Limited model accessibility severely restricts the ability for decision-makers, working under different health care systems, to consider how the conclusions might apply to the parameters of their own contexts. Model sharing could minimise wasteful duplication of efforts and streamline the growth of the body of evidence related to scalable investments in facility-based EC in LRS. This is achievable through effort towards user-

friendly open-source tools, such as excel-based decision-analytic models that have the capacity to incorporate local inputs. This would also allow stakeholders to gain a richer understanding of the value of investments into EC and the implications in their specific context.

In furthering the systematic capacity of these analyses to be conducted locally, a widely available tool could improve the quality and comparability of assessments between settings and interventions to generate a cohesive body of evidence. Standardising the calculation of EC value enhances the comparability of studies and improves the overall value of study results to guide priority setting. Efforts should be made that promote analyses to develop a model structure with the flexibility for users to vary the inputs and apply the parameters of their setting with locally relevant data. This will result in measures of cost-effectiveness that are pertinent to their setting and reflective of their needs and context. Developing a more complete understanding of the implications of strengthening EC in LRS is dependent on this.

9.1.2 Understanding the impact of scarcity on practice

Collecting empirical data provided the opportunity to observe current realities of supplying EC in LRS. It became apparent that the delivery of EC continues with or without the systems or supplies normally needed to succeed. Providers continue to care for patients even under extreme resource constraints, without the essential supplies, equipment or human resources normally considered indispensable. The results are habitually resourceful actions in the form of unexpected or creative approaches to care.

Assessments conducted in this dissertation were bound to a normative approach rather than a positive approach. Thus, measures were based on providers' actions given the resources they *ought* to have rather than those which they do have. There is significant scope for future research to better understand the impacts scarcity has on the provider's choices. Developing a better understanding the effect these adjustments have on both outcomes and costs could reveal further areas of efficiency. This is particularly relevant in LRS where locally tailored solutions could make more sense both culturally and economically. More robust studies should be conducted to understand the impact of scarcity upon the practice of EC and identify how secondary outcomes, such as process improvements, may impact patient outcomes.

9.1.3 Health system interactions and economies of scale

EC complements broader health system goals and strengthens core elements of care delivery. In some cases, EC acts as a safeguard for vulnerable populations who may not otherwise have access to the health care system. While our efforts concentrated on cost and outcomes within parameters of an EUs, as set in the ECS framework, there are larger health system interactions which fell beyond the scope of this work. The benefits gained from improved EC interact with numerous elements of the broader health care system. For example, streamlined EC could help realise cost savings for the entire health system by achieving economies of scale that result from reducing a per unit fixed cost through generating higher quantities of a good. Conversely, effective EC may prolong the life of patients creating a need for costly higher-level care through ICUs. The

literature on this issue is sparse, but future research should endeavour to better understand how systematised emergency care may lead to savings in some areas of the hospital, which increase costs in others.²²⁶ Researchers should endeavour to develop precise measurements of the impacts of effective EC with the wider health care system, especially in the capacity to either further harmonise or fracture limited resources. Future research should seek to better understand these synergies.

9.2 CONCLUSIONS

Earlier approaches to assessing the value of EC with economic evaluation have had a significant amount of ambiguity, both in the methodology and the results. The findings of this dissertation indicate that a scalable integrated model of EC delivery is not only cost-effective but could lead to significant cost savings in LRS. Quantitative analysis revealed the context specific costs of delivering facility-based EC in LRS compared favourably to other priority disease programs.

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APPENDICES

Appendix A. Study Proposal FHS015

Assessing the Cost-Effectiveness of Facility-Based Emergency Care in Low-Income Countries

STUDENT: Kalin Werner
MSc
University of Cape Town
WRNKAL001

SUPERVISOR(s): Lee Wallis
MBChB, MD, FRCM
University of Cape Town

This study is in partial fulfilment of the PhD degree.

Declaration:

I, Kalin Werner, hereby declare that the work contained in this assignment is my original work and that I have not previously submitted it, in its entirety or in part, at any university for degree purposes.

INTRODUCTION

1.1 Background and Literature Review

Traumatic injury is a substantial contributor to the global burden of disease and a key cause of disability and premature death worldwide: it already represents 11% of all global deaths per year and is forecast to account for 20% of all ill-health in the world by 2020.^{1,2} Even with such a considerable burden, trauma care garners little attention and consideration from health stakeholders worldwide, contributing to its moniker as the “neglected disease of modern society”.³ Injuries disproportionately affect low- and middle-income countries (LMICs). Over 90% of all injury-related deaths occur in LMICs.⁴ The burden of emergency conditions is nearly 60% worse in low income countries (LICs), which experience a burden of 25,186 disability-adjusted life years (DALYs) per 100,000 population, compared to the 15,691 DALYs per 100,000 in middle income countries.⁵ Death and disability resulting from trauma exact a weighty societal and economic toll. The primary victims of injury related mortality cases are young economic contributors, between the ages of 15 and 44 years old.⁶ Rapid urbanization, economic growth, and the resulting increase in the number of motorised vehicles in LMICs indicate a likeliness that the burden of trauma will only increase in the coming decade.

Much of this burden comes from life-threatening, yet treatable, sequelae that can be ameliorated by effective, timely emergency care (EC). Under emergency conditions, delays in care or delivery of inappropriate care can mean the difference between life and death. The diseases treated through EC are diverse and often unavoidable, and organized EC provides crucial access to immediate and urgent medical interventions for life threatening conditions. The timing and appropriateness of these interventions are vital to reducing the incidence of morbidity and mortality, so significantly that the Disease Control Priorities project estimates over half of deaths in LMICs could be addressed through the implementation of effective emergency care.⁷

Emergency care may be a critical component of any effective health care system, but the organization and function of EC varies considerably from country to country. In LMICs, which by definition face significant challenges, the reality of emergency care is one of extreme resource constraint coupled with high patient volumes and mortality. Treatment ability of facilities varies widely, and health systems are plagued by a scarcity of clinicians trained in emergency care. In a study of 192 facilities across 59 LMICs, only 18% had physicians on staff with specialty emergency training, and only 4% surveyed had staff with these skills available all the time.⁸ Emergency care systems in LMICs, where present, struggle to meet demand. Volumes of patient presenting for EC at these facilities are nearly ten times those of high income countries.⁹ It is a circumstance where the greatest burden injury occurs in systems least prepared to meet the challenge, a reality further confirmed by the fact that individuals with life-threatening but treatable injuries are six times more likely to die in an LMIC than in an HIC.⁴

Nevertheless, there is hope. Simple interventions in emergency care may provide a promising solution for even the most resource limited settings.⁹ This is especially true for interventions

require limited new investments in infrastructure.¹⁰ Investigations into how improved triage, patient flow, and supervision can lead to reductions in mortality are underway.¹¹ These simple interventions move beyond the myth that EC is high-technology field, and aim to prove that averting death and disability may be helped as a result of nominal new resource inputs, such as in service training of existing hospital staff.¹¹ Further low-cost interventions such as team and facility organization, communication, and protocols have also shown promise in improving access to life saving care.¹¹

Still, not enough is known about the costs of delivering emergency care in LMICs and many barriers continue to impede progress in this understanding of its fiscal impacts. This includes a lack of routine data collection systems and patient registries, meaning the costs of EC remain largely unassessed.¹² There are several studies which suggest that EC systems are likely to be cost-effective under the state of high disease burden affecting LMICs, but there is an urgent need for more robust findings.^{13,14} To make things more difficult, where research has been conducted, findings are often not reported in means which speak to the metrics used by health stakeholders, such as DALYs and YLLs.¹⁵ Perceptions of the high cost of emergency care persist only furthered by a lack of robust cost data, which impedes the ability to understand the impacts of, and plan improvements for, emergency care in LMICs.

Sound planning and organisation of health care systems in LMICs are regularly inhibited by the lack of context relevant cost analyses. Most of the existing literature is derived from HICs, which is problematic when seeking locally appropriate solutions for EC in LMICs. How emergency care is implemented and what it costs is highly reflective of the distinctive systems under which it operates, and funding and political drivers. Therefore, very few of these findings can translate to the conditions experienced by LMICs. Cost information is important in circumstances under which resource limitations necessitate tough choices.¹⁶ Global funding for emergency care is sparse, especially when contrasted to that for vertical disease programs, such as HIV/AIDs, TB or Malaria. With very few significant global donors or international organizations committed to its cause, proving the viability and impact of emergency services is imperative. Likewise, governments are confronted with determining how and where to prioritize interventions in health.⁹ Financial constraints and concerns of cost are frequently mentioned as the motivation behind the lack of investment in emergency care. Robust cost-effectiveness research and findings are necessary to reveal the true impact of EC and to guide decision makers towards a better understanding of the value of emergency care; one which fits the urgent needs of both their citizens and their budgets.

Based on the recently developed WHO model of emergency care delivery in the Emergency Care Systems (ECS) Framework the essential functional components of emergency care include interventions at the scene, during transport and in facilities.¹⁷ In analysing which of these components is likely to yield cost-effective solutions, one must consider where infrastructure already exists. In many LMICs, communities and facilities already exist, even where transport is absent. In reply, improved methods for providing scene care through low-cost interventions have launched in many LMICs. Research in this area indicates positive results the implementation of lay person first aid responder programmes.^{18,19} These interventions work with existing networks of transportation to enhance the delivery of

emergency care in a locally appropriate, resource-relevant solution. Likewise, facility-based interventions may be able tap into the existing but fragile health systems, most especially in LICs. The realisation of simple interventions to improve facility-based care has the potential to tackle key bottlenecks in EC while contributing significantly to the strengthening of health systems as a whole.

1.2 Motivation

Distinguishing the "value for money" of emergency care is critical, especially for LICs. Developing robust data on the cost of implementing emergency care within low-income contexts will greatly aid in sound planning and priority setting of countries carrying some of the highest burdens of morbidity and mortality related to emergency care treatable disease. Interest in developing better facility-based emergency care is expanding rapidly, and there is a significant gap in the cost-effectiveness literature in this area.

The WHO has developed a simple package of interventions designed to strengthen facility-based emergency care in low resource settings, and is implementing it in facilities across Uganda. The package includes a set of training and tools including the Basic Emergency Care course, standardized patient charts with identified data points related to emergency care, a triage tool, trauma and medical checklists, and emergency unit protocols and guidelines.

The time-sensitive ability to assess ongoing implementation of the WHO package presents a unique opportunity to contribute robust evidence to the cost-effectiveness of facility-based interventions. While clinical effectiveness has been assessed (and is currently being prepared for publication), cost-effectiveness of this EC package – or indeed of any EC intervention in LICs – has never been assessed. It is rational to consider that the implementation of an emergency care package would realise further facility efficiencies rather than drain resources.

1.3 Research Question

We hypothesize that the implementation of the WHO bundle of facility-based emergency care interventions will provide a cost-effective intervention in LICs. Our research questions are:

- What does the current literature say about the cost-effectiveness of emergency care in LMICs?
- Is the implementation of a low-cost bundle of emergency care interventions facilities cost-effective in LIC settings?

1.4 Aim

The primary aim of this research is to investigate the cost-effectiveness of implementing the WHO emergency care intervention bundle in health facilities in a low-income country.

1.5 Objectives

To achieve this aim, we have the following objectives:

1. Systematically review published evidence surrounding the cost-effectiveness of emergency care in LMICs.
2. Prospectively study the impact of implementing a low-cost set of emergency care interventions in low resource emergency care naïve health facilities on cost and outcome (mortality), to derive a measure of cost effectiveness.

METHODOLOGY

2.1 Study 1- Study Design

In order to achieve the first objective, a systematic review of published articles will be conducted to identify and assess all available data on the cost-effectiveness of emergency care interventions in LMICs.

2.1.1 Inclusion and exclusion criteria

Studies will be assessed for inclusion using four main criteria:

- Study describes an emergency care intervention
- Study takes place in a LMIC (according to the World Bank classification), or analyses costing data from an LMIC.
- Study undertakes a full economic evaluation (either a cost-effectiveness analysis, cost-utility analysis or cost-benefit analysis).
- Study is published in English.

2.1.2 Research procedures and data collection methods

A PRISMA Systematic review will be conducted of published articles in 5 databases including: PubMed, Scopus, EMBASE, Cochrane, and Web of Science, applying Cochrane LMIC filter to search results. A search strategy was developed in coordination with librarians at the research institution of the co-reviewer, Johns Hopkins University (see **Appendix 1**).

After running the search, all studies will be uploaded onto Covidence, a web-based screening and data extraction software platform. All voting by reviewers is blinded when conducted in Covidence to minimise bias. The initial screening of title and abstracts will involve two reviewers, requiring two votes in order to move on in the review. Full text reviews will be conducted by same two reviewers, with an optional third reviewer for any conflicts which cannot be resolved.

2.1.3 Data analysis

A validated tool, the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Checklist, will be used to grade quality of available evidence (see **Appendix 2**).²⁰ Summary statistics and descriptive analysis will be produced regarding the findings of the review.

2.1.4 Ethical Considerations

Multiple reviewers with no conflict of interest will participate in undertaking this review. There are no ethical considerations or concerns related to this study.

2.1.5 Strengths and limitations

This exercise is highly valuable to determine what is currently known, and unknown, about cost-effectiveness of EC interventions in LMICs. The findings of this work will provide a critical starting point for further investigations into the cost-effectiveness of emergency care in LMICs.

The review may be limited by the paucity of data which utilizes economic evaluations for emergency care in LMICs. Further, generalizability of findings may be difficult if there is dissimilarity in the cost variables used across studies or heterogeneity in care interventions.

2.1.6 Dissemination plan

Findings from this study will be shared in the hope of contributing to the setting of priorities for research on EC, especially in low resources settings. Reports on the findings will be shared with key stakeholders (the WHO) and the study will be disseminated through publishing in a pertinent peer-reviewed journal.

2.1.7 Project Timeline

2018 / 2019	AUG	SEPT	OCT	NOV	DEC	JAN	FEB
EM-DRC	X						
Ethics (UCT)		X					
Data collection			X				
Data Analysis			X	X			
Compilation of Final Report					X	X	
Submission							X

2.1.8 Resources and budget

Resources that require no budget but will be utilised in the pursuit of this study. These include the researcher's personal laptop computer and access to Covidence software (provided in-kind by the WHO). Further in-kind support will be provided from researchers at the WHO in the form of personal time. No further anticipated resources or budget are required for this study.

2.2 Study 2- Study Design

In order to achieve the second objective, a prospective study will be conducted assessing the cost impact and mortality outcomes of implementing the EC intervention package in five regional hospitals in Uganda.

In 2016-17, the WHO piloted the implementation of toolkit designed to strengthen emergency care in LICs. Effectiveness of the package was tested by assessing mortality related to patients presenting with five sentinel conditions at two sites in Uganda and two in Tanzania. Unpublished findings from the pilot study show a composite 48-hour mortality decrease of 45% across the selected sentinel conditions.²¹ Under guidance from a biostatistician, to power to detect a mortality reduction of 45% requires a sample size of 1,500 patients per arm of the study (pre and post implementation). However, we have taken a more conservative approach and aimed at a sample of 30%, requiring about 3500 patients per arm.

Ugandan data suggest that the typical rate of patients presenting with the five sentinel conditions at regional hospitals is approximately 1,500 patients per year; 7500 in a year at five sites.²¹ Therefore, a sampling of five sites over the course of six months will accomplish the required number of patients in our sample population for each arm of the study. The same period of time and number of sites will be used to achieve the same for post- intervention data. This timeframe accounts for collection of data on 3,500 patients per arm.

In 2018 and 2019, the WHO will implement the emergency care intervention package in 14 regional hospitals across Uganda. As part of an ongoing quality improvement initiative, both pre and the post-intervention mortality will be recorded. After baseline data are collected, implementation of the WHO EC bundle will occur. The WHO package includes the following components: 1) the standardized chart for emergency care (SCEC), a paper-based medical chart with embedded emergency care data points to ensure consistently and reliably captured across all patient encounters; 2) the Basic Emergency Care course, designed to teach frontline providers in low resource settings the fundamentals of emergency resuscitation and stabilization of critically ill patients; 3) a triage tool tailored to a low resource environment; 4) medical/trauma patient checklists designed to aid providers during the real-time resuscitation of a critically ill patient; and 5) guidance on key emergency unit processes. Directly afterward, post-intervention data will be collected for six months.

The impact of a package of EC systems interventions will be measured on the basis of two outcomes; 48 hour mortality from sentinel conditions (as captured and measured by WHO), and the changes in facility expenditure (the additional data captured for this study). The fiscal impact of the package will be captured through data from hospital budget reports.

2.2.1 Characteristics of the study population and sampling

The study population will consist of patients presenting with the five sentinel conditions in study hospitals. The following inclusion criteria will be used for patients:

- Presenting at one of the five regional health hospital sites in Uganda.

- Presenting with one of the following five WHO-determined sentinel conditions: asthma, pneumonia, paediatric diarrhoea, road traffic injury, or postpartum haemorrhage.
- Presenting either in the six months prior to the implementation of the package, or six months post implementation.

2.2.2 Recruitment and enrolment

The WHO currently collects data on mortality for the purposes of quality improvement activities. 48-hour mortality rates will be collected pre- and post-intervention for the five sentinel conditions. The conditions were identified as being representative of emergency care in LICs due to their high volume and responsiveness to proper identification and resuscitation in an emergency care setting. Records will be accessed from the REDCap database entries completed by research assistants at each site and included in the study on a continuous basis as patients present to one of the facilities with a sentinel condition.

2.2.3 Research procedures and data collection methods

Pre-intervention data will be collected across all sites on mortality outcomes for six months prior to the intervention. The data will be populated by WHO research assistants at selected sites will collect information on all eligible patients who present with the sentinel conditions. Data collection will continue for six months. Directly following the implementation of the package, collection of post-intervention data will commence, and will continue for six months. The same team of research assistants will be engaged to collect this data.

While clinical data collection is ongoing through the WHO quality improvement measures, supplementary cost data related to the expenditure of the facilities will be prospectively recorded. The following costs will be collected on a monthly basis by research assistants at the sites and entered into an excel document. These will be derived from the expenditure reports from the hospitals.

- Fixed costs indicators: staff salaries, training of staff, and all necessary medical equipment for EC.
- Variable costs indicators: expenditure associated with labs, medicines and supplies.

2.2.4 Data safety and monitoring

All data related to mortality and expenditures will be collected and stored via REDcap, a secure encrypted database platform hosted on UCSF servers. To protect participants and ensure anonymity, all patient data is de-identified prior to storage on the REDcap database collection system (which will be a secure and encrypted platform). Exported data files will be encrypted and stored on a password-protected laptop.

2.2.5 Data analysis

Analysis of the pre and post intervention samples will be undertaken to assess the cost effectiveness of the WHO emergency care package. This analysis will be achieved through a multi-step process. First descriptive statistics will be generated regarding the cost and outcome

indicators for the pre and post- intervention data. Then a comparative analysis will be conducted between the post-intervention data and baseline data collected prior to the implementation of the emergency care intervention package to measure reductions in mortality and differences in expenditures. These findings of these principal analyses will be used to derive the cost per life saved of implementing the WHO toolkit.

The primary analysis involves assessing the association between mortality and cost as recognised through a general Incremental Cost Effectiveness Ratio (ICER) measuring the relative value of implementing of the WHO facility-based emergency care package in emergency naïve facilities. This cost-effectiveness measure is calculated by dividing the number of lives saved by the cost of the implementation of the package.

Secondary analysis will include a budget impact analysis and cost impact analysis will be conducted in order to provide an understanding of the affordability and financial consequences of the intervention. These additional analyse will better inform resource allocation.

2.2.6 Ethical Considerations

Ethics approval for this project is first being sought from the University of Cape Town. Once provisional approval is granted, we will seek ethics from Makerere University and obtain permission letters from the Ministry of Health of Uganda.

Only data relevant to mortality and expenditures will be collected. To protect participants and ensure anonymity, all patient data will be de-identified prior to storage on the REDcap database collection system (which will be a secure and encrypted platform). Exported data files will be encrypted and stored on a password-protected laptop of secure server.

Informed consent process

This research involves a secondary analysis of routinely collected clinical outcomes data by the WHO, therefore consent related to clinical outcomes data is not necessary for this study. However data related to cost, which is not collected routinely by the WHO, will involve approval for access received from the Ministry of Health Uganda.

Privacy and confidentiality

All personal-identified information will be removed from the records during data collection, eliminating any risk and ensuring protection of privacy and confidentiality.

Reimbursement for participation

There is no patient participation. Data collectors are remunerated for their activities through Emergency Medicine Uganda.

2.2.7 Risks and benefits

This analysis utilizes data that will be de-identified by the WHO prior to data analysis by UCT researchers. There are no anticipated risks.

There are many benefits to analysing changes in patient outcomes and the associated cost prior to and after implementation of the EC package. Although efficacy of the package has been tested, collecting outcomes and cost data allows for a measure of cost-effectiveness and confirmation of these results across new settings, which may strengthen overall conclusions of the program.

2.2.8 Limitations

Data will be collected by many research assistants, which invites the possibility of inconsistencies. Quality assurance activities will be taken for the duration of the data collection. Data cleaning will be undertaken to control for these inconsistencies.

The costs collected in this study are limited to expenditure data within activities undertaken at the hospital. Indirect costs such as costs to caretakers and relatives will not be included. Therefore, it is anticipated that the estimate of the cost per life saved may underestimate the true impact of the intervention.

All data will be collected from sites with a distinctive feature of being regional hospitals in Uganda. For this reason, the sites may share many similarities in capacity, existing infrastructure, and budget size prior to the implementation of the package. Therefore, the findings cannot be assumed to transfer to other levels of care facilities (such as district hospitals), or other countries.

2.2.9 Dissemination Plan

Results from this study will primarily be used to fill the long-standing knowledge gap related to the cost-effectiveness of providing emergency care in LMICS. Equally, results will further validate the WHO EC package as an intervention suitable in contexts of severe resource constraints and provide recommendations and insights into the development of emergency care in Uganda. Findings will be disseminated to all stakeholders as reports, including WHO project leads at implementing hospitals and the Ugandan Ministry of Health. The study will also be disseminated through publishing in a pertinent peer-reviewed journal. The WHO will use the findings to inform their program activities and contribute to ongoing quality improvement processes.

2.2.10 Project Timeline

2018/2019	AUG	SEPT	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN
EM-DRC	X										
Ethics (UCT)		X									
Ethics (Makerere)		X	X	X							
Pre-intervention data collection				X	X	X	X	X	X		
Pre-intervention data analysis								X	X	X	
WHO package intervention										X	X
2019/2020	JUL	AUG	SEPT	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY

Post intervention data collection	X	X	X	X	X	X	
Post intervention data analysis				X	X	X	X
Comparative Data Analysis						X	X
Compilation of Final Report						X	X
Submission							X

2.2.11 Resources and Budget

Resources have already been dedicated to host sites for in-country activities for the implementation of the WHO EC package. Data collectors for pre-post intervention data collection will be needed for a time period of approximately 12 months. Further in-kind support will be provided from in-country partners in Uganda. The WHO will be covering expenses of the study.

August 2018-March 2020				
Item	Description	Unit cost	N° of Units	Total cost
Consumables				
1. office supplies, printing & reproduction for data collection	Misc. printing for data collection and surveys at each site, pre and post data collection.	\$200	10	\$2000
2. Tablet for data collection	1 tablet per research assistant for collection of data and data entry into the REDCap encrypted database	\$500	5	\$2500
3. office supplies, printing & reproduction for reports	Printing of reports distributed to key stakeholders	\$200	1	\$200
4. Implementation costs	Training; Monitoring and evaluation – 5 sites	\$800	5	\$4000
Research travel				
1. Airfare and visa	Cape Town – Kampala return trip	\$650	2	\$1300
2. Entry visa	Entry visa	\$50	2	\$100
3. Lodging	Lodging near study sites	\$350/ week	4	\$1400
4. In country travel	In country transportation to visit sites	\$500	2	\$1000
Personnel				
2. Research assistants	5 research assistants to contribute to the collection of data at sites across Uganda at cost of \$200/ month for a total of 12 months	\$2,400	5	\$12000
Total				\$24,500

AGGREGATED TIMELINE

	2018					2019								2020							
	AUG	SEPT	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEPT	OCT	NOV	DEC	JAN	FEB	MAR	APR
EM-DRC	X																				
Ethics (HREC)		X																			
Ethics (Makerere)		X	X	X																	
Study 1 Data Collection			X																		
Study 1 Data Analysis			X	X																	
Study 1 Compilation of Final Report					X	X															
Study 1 Submission						X															
Study 2 Pre-intervention data collection			X	X	X	X	X	X													
Study 2 Pre-intervention data analysis							X	X	X												
WHO Package intervention									X	X											
Study 2 Post-intervention data collection											X	X	X	X	X	X					
Study 2 Post intervention data analysis														X	X	X	X				
Study 1 Compilation of Final Report																X	X	X	X		
Submission Study 2																					X

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APPENDICES

Appendix 1: Search strategy

Appendix 2: CHEERS Checklist

Appendix 1: Systematic Review Search Strategy

Pubmed

("Cost-Benefit Analysis"[mh] OR "cost benefit" OR "cost effective" OR "cost effectiveness" OR "cost utility")

AND

("Emergency Service, Hospital"[mh] OR "Emergency Medicine"[mh] OR "Emergency medicine"[TW] OR "Emergency services"[TW] OR "Emergency department"[TW] OR "Emergency service"[TW] OR "Emergency departments"[TW] OR "Emergency room"[TW] OR "Emergency rooms"[TW] OR "Emergency ward"[TW] OR "Emergency Unit"[TW] OR "Trauma Centers"[mh] OR "Trauma Center"[TW] OR "Trauma Centers"[TW] OR "emergency health service"[tw] OR "emergency health services"[tw] OR "emergency medical services"[tw] OR "emergency medical service"[tw] OR "accident and emergency"[tw] OR "accident & emergency"[tw] OR "a&e"[tw] OR "A & E"[tw] OR "prehospital"[tw] OR "ambulance"[tw])

AND

#10 Search #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9

#9 Search "developing country"[tiab] OR "developing countries"[tiab] OR "developing nation"[tiab] OR "developing nations"[tiab] OR "developing population"[tiab] OR "developing populations"[tiab] OR "developing world"[tiab] OR "less developed country"[tiab] OR "less developed countries"[tiab] OR "less developed nation"[tiab] OR "less developed nations"[tiab] OR "less developed population"[tiab] OR "less developed populations"[tiab] OR "less developed world"[tiab] OR "lesser developed country"[tiab] OR "lesser developed countries"[tiab] OR "lesser developed nation"[tiab] OR "lesser developed nations"[tiab] OR "lesser developed population"[tiab] OR "lesser developed populations"[tiab] OR "lesser developed world"[tiab] OR "under developed country"[tiab] OR "under developed countries"[tiab] OR "under developed nation"[tiab] OR "under developed nations"[tiab] OR "under developed population"[tiab] OR "under developed populations"[tiab] OR "under developed world"[tiab] OR "underdeveloped country"[tiab] OR "underdeveloped countries"[tiab] OR "underdeveloped nation"[tiab] OR "underdeveloped nations"[tiab] OR "underdeveloped population"[tiab] OR "underdeveloped populations"[tiab] OR "underdeveloped world"[tiab] OR "middle income country"[tiab] OR "middle income countries"[tiab] OR "middle income nation"[tiab] OR "middle income nations"[tiab] OR "middle income population"[tiab] OR "middle income populations"[tiab] OR "low income country"[tiab] OR "low income countries"[tiab] OR "low income nation"[tiab] OR "low income nations"[tiab] OR "low income population"[tiab] OR "low income populations"[tiab] OR "lower income country"[tiab] OR "lower income countries"[tiab] OR "lower income nation"[tiab] OR "lower income nations"[tiab] OR "lower income population"[tiab] OR "lower income populations"[tiab] OR "underserved country"[tiab] OR "underserved countries"[tiab] OR "underserved nation"[tiab] OR "underserved nations"[tiab] OR "underserved population"[tiab] OR "underserved populations"[tiab] OR "underserved world"[tiab] OR "under served country"[tiab] OR "under served countries"[tiab] OR "under served nation"[tiab] OR "under served nations"[tiab] OR "under served population"[tiab] OR "under served populations"[tiab] OR "under served world"[tiab] OR "deprived country"[tiab] OR "deprived countries"[tiab] OR "deprived nation"[tiab] OR "deprived nations"[tiab] OR "deprived population"[tiab] OR "deprived populations"[tiab] OR "deprived world"[tiab] OR "poor country"[tiab] OR "poor countries"[tiab] OR "poor nation"[tiab] OR "poor nations"[tiab] OR "poor population"[tiab] OR "poor populations"[tiab] OR "poor world"[tiab] OR "poorer country"[tiab] OR "poorer countries"[tiab] OR "poorer nation"[tiab] OR "poorer nations"[tiab] OR "poorer population"[tiab] OR "poorer populations"[tiab] OR "poorer world"[tiab] OR "developing economy"[tiab] OR "developing economies"[tiab] OR "less developed economy"[tiab] OR "less developed economies"[tiab] OR "lesser developed economy"[tiab] OR "lesser developed economies"[tiab] OR "under developed economy"[tiab] OR "under developed economies"[tiab] OR "underdeveloped economy"[tiab] OR

"underdeveloped economies"[tiab] OR "middle income economy"[tiab] OR "middle income economies"[tiab] OR "low income economy"[tiab] OR "low income economies"[tiab] OR "lower income economy"[tiab] OR "lower income economies"[tiab] OR "low gdp"[tiab] OR "low gnp"[tiab] OR "low gross domestic"[tiab] OR "low gross national"[tiab] OR "lower gdp"[tiab] OR "lower gnp"[tiab] OR "lower gross domestic"[tiab] OR "lower gross national"[tiab] OR lmic[tiab] OR lmic[tiab] OR "third world"[tiab] OR "lami country"[tiab] OR "lami countries"[tiab] OR "transitional country"[tiab] OR "transitional countries"[tiab]

#8 Search "developing country"[ot] OR "developing countries"[ot] OR "developing nation"[ot] OR "developing nations"[ot] OR "developing population"[ot] OR "developing populations"[ot] OR "developing world"[ot] OR "less developed country"[ot] OR "less developed countries"[ot] OR "less developed nation"[ot] OR "less developed nations"[ot] OR "less developed population"[ot] OR "less developed populations"[ot] OR "less developed world"[ot] OR "lesser developed country"[ot] OR "lesser developed countries"[ot] OR "lesser developed nation"[ot] OR "lesser developed nations"[ot] OR "lesser developed population"[ot] OR "lesser developed populations"[ot] OR "lesser developed world"[ot] OR "under developed country"[ot] OR "under developed countries"[ot] OR "under developed nation"[ot] OR "under developed nations"[ot] OR "under developed population"[ot] OR "under developed populations"[ot] OR "under developed world"[ot] OR "underdeveloped country"[ot] OR "underdeveloped countries"[ot] OR "underdeveloped nation"[ot] OR "underdeveloped nations"[ot] OR "underdeveloped population"[ot] OR "underdeveloped populations"[ot] OR "underdeveloped world"[ot] OR "middle income country"[ot] OR "middle income countries"[ot] OR "middle income nation"[ot] OR "middle income nations"[ot] OR "middle income population"[ot] OR "middle income populations"[ot] OR "low income country"[ot] OR "low income countries"[ot] OR "low income nation"[ot] OR "low income nations"[ot] OR "low income population"[ot] OR "low income populations"[ot] OR "lower income country"[ot] OR "lower income countries"[ot] OR "lower income nation"[ot] OR "lower income nations"[ot] OR "lower income population"[ot] OR "lower income populations"[ot] OR "underserved country"[ot] OR "underserved countries"[ot] OR "underserved nation"[ot] OR "underserved nations"[ot] OR "underserved population"[ot] OR "underserved populations"[ot] OR "underserved world"[ot] OR "under served country"[ot] OR "under served countries"[ot] OR "under served nation"[ot] OR "under served nations"[ot] OR "under served population"[ot] OR "under served populations"[ot] OR "under served world"[ot] OR "deprived country"[ot] OR "deprived countries"[ot] OR "deprived nation"[ot] OR "deprived nations"[ot] OR "deprived population"[ot] OR "deprived populations"[ot] OR "deprived world"[ot] OR "poor country"[ot] OR "poor countries"[ot] OR "poor nation"[ot] OR "poor nations"[ot] OR "poor population"[ot] OR "poor populations"[ot] OR "poor world"[ot] OR "poorer country"[ot] OR "poorer countries"[ot] OR "poorer nation"[ot] OR "poorer nations"[ot] OR "poorer population"[ot] OR "poorer populations"[ot] OR "poorer world"[ot] OR "developing economy"[ot] OR "developing economies"[ot] OR "less developed economy"[ot] OR "less developed economies"[ot] OR "lesser developed economy"[ot] OR "lesser developed economies"[ot] OR "under developed economy"[ot] OR "under developed economies"[ot] OR "underdeveloped economy"[ot] OR "underdeveloped economies"[ot] OR "middle income economy"[ot] OR "middle income economies"[ot] OR "low income economy"[ot] OR "low income economies"[ot] OR "lower income economy"[ot] OR "lower income economies"[ot] OR "low gdp"[ot] OR "low gnp"[ot] OR "low gross domestic"[ot] OR "low gross national"[ot] OR "lower gdp"[ot] OR "lower gnp"[ot] OR "lower gross domestic"[ot] OR "lower gross national"[ot] OR lmic[ot] OR lmic[ot] OR "third world"[ot] OR "lami country"[ot] OR "lami countries"[ot] OR "transitional country"[ot] OR "transitional countries"[ot]

#7 Search Africa[pl] OR Asia[pl] OR Caribbean[pl] OR West Indies[pl] OR South America[pl] OR Latin America[pl] OR Central America[pl] OR Afghanistan[pl] OR Albania[pl] OR Algeria[pl] OR Angola[pl] OR Antigua[pl] OR Barbuda[pl] OR Argentina[pl] OR Armenia[pl] OR Armenian[pl] OR Aruba[pl] OR Azerbaijan[pl] OR Bahrain[pl] OR Bangladesh[pl] OR Barbados[pl] OR Benin[pl] OR Byelarus[pl] OR Byelorussian[pl] OR Belarus[pl] OR Belorussian[pl] OR Belorussia[pl] OR Belize[pl] OR Bhutan[pl] OR

Bolivia[pl] OR Bosnia[pl] OR Herzegovina[pl] OR Hercegovina[pl] OR Botswana[pl] OR Brasil[pl] OR Brazil[pl] OR Bulgaria[pl] OR Burkina Faso[pl] OR Burkina Fasso[pl] OR Upper Volta[pl] OR Burundi[pl] OR Urundi[pl] OR Cambodia[pl] OR Khmer Republic[pl] OR Kampuchea[pl] OR Cameroon[pl] OR Cameroons[pl] OR Cameron[pl] OR Camerons[pl] OR Cape Verde[pl] OR Central African Republic[pl] OR Chad[pl] OR Chile[pl] OR China[pl] OR Colombia[pl] OR Comoros[pl] OR Comoro Islands[pl] OR Comores[pl] OR Mayotte[pl] OR Congo[pl] OR Zaire[pl] OR Costa Rica[pl] OR Cote d'Ivoire[pl] OR Ivory Coast[pl] OR Croatia[pl] OR Cuba[pl] OR Cyprus[pl] OR Czechoslovakia[pl] OR Czech Republic[pl] OR Slovakia[pl] OR Slovak Republic[pl] OR Djibouti[pl] OR French Somaliland[pl] OR Dominica[pl] OR Dominican Republic[pl] OR East Timor[pl] OR East Timur[pl] OR Timor Leste[pl] OR Ecuador[pl] OR Egypt[pl] OR United Arab Republic[pl] OR El Salvador[pl] OR Eritrea[pl] OR Estonia[pl] OR Ethiopia[pl] OR Fiji[pl] OR Gabon[pl] OR Gabonese Republic[pl] OR Gambia[pl] OR Gaza[pl] OR Georgia Republic[pl] OR Georgian Republic[pl] OR Ghana[pl] OR Gold Coast[pl] OR Greece[pl] OR Grenada[pl] OR Guatemala[pl] OR Guinea[pl] OR Guam[pl] OR Guiana[pl] OR Guyana[pl] OR Haiti[pl] OR Honduras[pl] OR Hungary[pl] OR India[pl] OR Maldives[pl] OR Indonesia[pl] OR Iran[pl] OR Iraq[pl] OR Isle of Man[pl] OR Jamaica[pl] OR Jordan[pl] OR Kazakhstan[pl] OR Kazakh[pl] OR Kenya[pl] OR Kiribati[pl] OR Korea[pl] OR Kosovo[pl] OR Kyrgyzstan[pl] OR Kirghizia[pl] OR Kyrgyz Republic[pl] OR Kirghiz[pl] OR Kirgizstan[pl] OR "Lao PDR"[pl] OR Laos[pl] OR Latvia[pl] OR Lebanon[pl] OR Lesotho[pl] OR Basutoland[pl] OR Liberia[pl] OR Libya[pl] OR Lithuania[pl]

#6 Search Macedonia[pl] OR Madagascar[pl] OR Malagasy Republic[pl] OR Malaysia[pl] OR Malaya[pl] OR Malay[pl] OR Sabah[pl] OR Sarawak[pl] OR Malawi[pl] OR Nyasaland[pl] OR Mali[pl] OR Malta[pl] OR Marshall Islands[pl] OR Mauritania[pl] OR Mauritius[pl] OR Agalega Islands[pl] OR Mexico[pl] OR Micronesia[pl] OR Middle East[pl] OR Moldova[pl] OR Moldovia[pl] OR Moldovian[pl] OR Mongolia[pl] OR Montenegro[pl] OR Morocco[pl] OR Ifni[pl] OR Mozambique[pl] OR Myanmar[pl] OR Myanma[pl] OR Burma[pl] OR Namibia[pl] OR Nepal[pl] OR Netherlands Antilles[pl] OR New Caledonia[pl] OR Nicaragua[pl] OR Niger[pl] OR Nigeria[pl] OR Northern Mariana Islands[pl] OR Oman[pl] OR Muscat[pl] OR Pakistan[pl] OR Palau[pl] OR Palestine[pl] OR Panama[pl] OR Paraguay[pl] OR Peru[pl] OR Philippines[pl] OR Philipines[pl] OR Phillipines[pl] OR Phillippines[pl] OR Poland[pl] OR Portugal[pl] OR Puerto Rico[pl] OR Romania[pl] OR Rumania[pl] OR Roumania[pl] OR Russia[pl] OR Russian[pl] OR Rwanda[pl] OR Ruanda[pl] OR Saint Kitts[pl] OR St Kitts[pl] OR Nevis[pl] OR Saint Lucia[pl] OR St Lucia[pl] OR Saint Vincent[pl] OR St Vincent[pl] OR Grenadines[pl] OR Samoa[pl] OR Samoan Islands[pl] OR Navigator Island[pl] OR Navigator Islands[pl] OR Sao Tome[pl] OR Saudi Arabia[pl] OR Senegal[pl] OR Serbia[pl] OR Montenegro[pl] OR Seychelles[pl] OR Sierra Leone[pl] OR Slovenia[pl] OR Sri Lanka[pl] OR Ceylon[pl] OR Solomon Islands[pl] OR Somalia[pl] OR South Africa[pl] OR Sudan[pl] OR Suriname[pl] OR Surinam[pl] OR Swaziland[pl] OR Syria[pl] OR Tajikistan[pl] OR Tadjhikistan[pl] OR Tadjikistan[pl] OR Tadjhik[pl] OR Tanzania[pl] OR Thailand[pl] OR Togo[pl] OR Togolese Republic[pl] OR Tonga[pl] OR Trinidad[pl] OR Tobago[pl] OR Tunisia[pl] OR Turkey[pl] OR Turkmenistan[pl] OR Turkmen[pl] OR Uganda[pl] OR Ukraine[pl] OR Uruguay[pl] OR USSR[pl] OR Soviet Union[pl] OR Union of Soviet Socialist Republics[pl] OR Uzbekistan[pl] OR Uzbek OR Vanuatu[pl] OR New Hebrides[pl] OR Venezuela[pl] OR Vietnam[pl] OR Viet Nam[pl] OR West Bank[pl] OR Yemen[pl] OR Yugoslavia[pl] OR Zambia[pl] OR Zimbabwe[pl] OR Rhodesia[pl]

#5 Search Africa[tiab] OR Asia[tiab] OR Caribbean[tiab] OR West Indies[tiab] OR South America[tiab] OR Latin America[tiab] OR Central America[tiab] OR Afghanistan[tiab] OR Albania[tiab] OR Algeria[tiab] OR Angola[tiab] OR Antigua[tiab] OR Barbuda[tiab] OR Argentina[tiab] OR Armenia[tiab] OR Armenian[tiab] OR Aruba[tiab] OR Azerbaijan[tiab] OR Bahrain[tiab] OR Bangladesh[tiab] OR Barbados[tiab] OR Benin[tiab] OR Byelarus[tiab] OR Byelorussian[tiab] OR Belarus[tiab] OR Belorussian[tiab] OR Belorussia[tiab] OR Belize[tiab] OR Bhutan[tiab] OR Bolivia[tiab] OR Bosnia[tiab] OR Herzegovina[tiab] OR Hercegovina[tiab] OR Botswana[tiab] OR Brasil[tiab] OR Brazil[tiab] OR Bulgaria[tiab] OR Burkina Faso[tiab] OR Burkina Fasso[tiab] OR Upper Volta[tiab] OR Burundi[tiab] OR Urundi[tiab] OR Cambodia[tiab] OR Khmer Republic[tiab] OR Kampuchea[tiab] OR Cameroon[tiab] OR

Cameroons[tiab] OR Cameron[tiab] OR Camerons[tiab] OR Cape Verde[tiab] OR Central African Republic[tiab] OR Chad[tiab] OR Chile[tiab] OR China[tiab] OR Colombia[tiab] OR Comoros[tiab] OR Comoro Islands[tiab] OR Comores[tiab] OR Mayotte[tiab] OR Congo[tiab] OR Zaire[tiab] OR Costa Rica[tiab] OR Cote d'Ivoire[tiab] OR Ivory Coast[tiab] OR Croatia[tiab] OR Cuba[tiab] OR Cyprus[tiab] OR Czechoslovakia[tiab] OR Czech Republic[tiab] OR Slovakia[tiab] OR Slovak Republic[tiab] OR Djibouti[tiab] OR French Somaliland[tiab] OR Dominica[tiab] OR Dominican Republic[tiab] OR East Timor[tiab] OR East Timur[tiab] OR Timor Leste[tiab] OR Ecuador[tiab] OR Egypt[tiab] OR United Arab Republic[tiab] OR El Salvador[tiab] OR Eritrea[tiab] OR Estonia[tiab] OR Ethiopia[tiab] OR Fiji[tiab] OR Gabon[tiab] OR Gabonese Republic[tiab] OR Gambia[tiab] OR Gaza[tiab] OR Georgia Republic[tiab] OR Georgian Republic[tiab] OR Ghana[tiab] OR Gold Coast[tiab] OR Greece[tiab] OR Grenada[tiab] OR Guatemala[tiab] OR Guinea[tiab] OR Guam[tiab] OR Guiana[tiab] OR Guyana[tiab] OR Haiti[tiab] OR Honduras[tiab] OR Hungary[tiab] OR India[tiab] OR Maldives[tiab] OR Indonesia[tiab] OR Iran[tiab] OR Iraq[tiab] OR Isle of Man[tiab] OR Jamaica[tiab] OR Jordan[tiab] OR Kazakhstan[tiab] OR Kazakh[tiab] OR Kenya[tiab] OR Kiribati[tiab] OR Korea[tiab] OR Kosovo[tiab] OR Kyrgyzstan[tiab] OR Kirghizia[tiab] OR Kyrgyz Republic[tiab] OR Kirghiz[tiab] OR Kirgizstan[tiab] OR "Lao PDR"[tiab] OR Laos[tiab] OR Latvia[tiab] OR Lebanon[tiab] OR Lesotho[tiab] OR Basutoland[tiab] OR Liberia[tiab] OR Libya[tiab] OR Lithuania[tiab]

#4 Search Macedonia[tiab] OR Madagascar[tiab] OR Malagasy Republic[tiab] OR Malaysia[tiab] OR Malaya[tiab] OR Malay[tiab] OR Sabah[tiab] OR Sarawak[tiab] OR Malawi[tiab] OR Nyasaland[tiab] OR Mali[tiab] OR Malta[tiab] OR Marshall Islands[tiab] OR Mauritania[tiab] OR Mauritius[tiab] OR Agalega Islands[tiab] OR Mexico[tiab] OR Micronesia[tiab] OR Middle East[tiab] OR Moldova[tiab] OR Moldovia[tiab] OR Moldovian[tiab] OR Mongolia[tiab] OR Montenegro[tiab] OR Morocco[tiab] OR Ifni[tiab] OR Mozambique[tiab] OR Myanmar[tiab] OR Myanma[tiab] OR Burma[tiab] OR Namibia[tiab] OR Nepal[tiab] OR Netherlands Antilles[tiab] OR New Caledonia[tiab] OR Nicaragua[tiab] OR Niger[tiab] OR Nigeria[tiab] OR Northern Mariana Islands[tiab] OR Oman[tiab] OR Muscat[tiab] OR Pakistan[tiab] OR Palau[tiab] OR Palestine[tiab] OR Panama[tiab] OR Paraguay[tiab] OR Peru[tiab] OR Philippines[tiab] OR Philipines[tiab] OR Phillipines[tiab] OR Phillippines[tiab] OR Poland[tiab] OR Portugal[tiab] OR Puerto Rico[tiab] OR Romania[tiab] OR Rumania[tiab] OR Roumania[tiab] OR Russia[tiab] OR Russian[tiab] OR Rwanda[tiab] OR Ruanda[tiab] OR Saint Kitts[tiab] OR St Kitts[tiab] OR Nevis[tiab] OR Saint Lucia[tiab] OR St Lucia[tiab] OR Saint Vincent[tiab] OR St Vincent[tiab] OR Grenadines[tiab] OR Samoa[tiab] OR Samoan Islands[tiab] OR Navigator Island[tiab] OR Navigator Islands[tiab] OR Sao Tome[tiab] OR Saudi Arabia[tiab] OR Senegal[tiab] OR Serbia[tiab] OR Montenegro[tiab] OR Seychelles[tiab] OR Sierra Leone[tiab] OR Slovenia[tiab] OR Sri Lanka[tiab] OR Ceylon[tiab] OR Solomon Islands[tiab] OR Somalia[tiab] OR Sudan[tiab] OR Suriname[tiab] OR Surinam[tiab] OR Swaziland[tiab] OR Syria[tiab] OR Tajikistan[tiab] OR Tadzhikistan[tiab] OR Tadjikistan[tiab] OR Tadjhik[tiab] OR Tanzania[tiab] OR Thailand[tiab] OR Togo[tiab] OR Togolese Republic[tiab] OR Tonga[tiab] OR Trinidad[tiab] OR Tobago[tiab] OR Tunisia[tiab] OR Turkey[tiab] OR Turkmenistan[tiab] OR Turkmen[tiab] OR Uganda[tiab] OR Ukraine[tiab] OR Uruguay[tiab] OR USSR[tiab] OR Soviet Union[tiab] OR Union of Soviet Socialist Republics[tiab] OR Uzbekistan[tiab] OR Uzbek OR Vanuatu[tiab] OR New Hebrides[tiab] OR Venezuela[tiab] OR Vietnam[tiab] OR Viet Nam[tiab] OR West Bank[tiab] OR Yemen[tiab] OR Yugoslavia[tiab] OR Zambia[tiab] OR Zimbabwe[tiab] OR Rhodesia[tiab]

#3 Search Africa[ot] OR Asia[ot] OR Caribbean[ot] OR West Indies[ot] OR South America[ot] OR Latin America[ot] OR Central America[ot] OR Afghanistan[ot] OR Albania[ot] OR Algeria[ot] OR Angola[ot] OR Antigua[ot] OR Barbuda[ot] OR Argentina[ot] OR Armenia[ot] OR Armenian[ot] OR Aruba[ot] OR Azerbaijan[ot] OR Bahrain[ot] OR Bangladesh[ot] OR Barbados[ot] OR Benin[ot] OR Byelarus[ot] OR Byelorussian[ot] OR Belarus[ot] OR Belorussian[ot] OR Belorussia[ot] OR Belize[ot] OR Bhutan[ot] OR Bolivia[ot] OR Bosnia[ot] OR Herzegovina[ot] OR Hercegovina[ot] OR Botswana[ot] OR Brasil[ot] OR Brazil[ot] OR Bulgaria[ot] OR Burkina Faso[ot] OR Burkina Fasso[ot] OR Upper Volta[ot] OR Burundi[ot]

OR Urundi[ot] OR Cambodia[ot] OR Khmer Republic[ot] OR Kampuchea[ot] OR Cameroon[ot] OR Cameroons[ot] OR Cameron[ot] OR Camerons[ot] OR Cape Verde[ot] OR Central African Republic[ot] OR Chad[ot] OR Chile[ot] OR China[ot] OR Colombia[ot] OR Comoros[ot] OR Comoro Islands[ot] OR Comores[ot] OR Mayotte[ot] OR Congo[ot] OR Zaire[ot] OR Costa Rica[ot] OR Cote d'Ivoire[ot] OR Ivory Coast[ot] OR Croatia[ot] OR Cuba[ot] OR Cyprus[ot] OR Czechoslovakia[ot] OR Czech Republic[ot] OR Slovakia[ot] OR Slovak Republic[ot] OR Djibouti[ot] OR French Somaliland[ot] OR Dominica[ot] OR Dominican Republic[ot] OR East Timor[ot] OR East Timur[ot] OR Timor Leste[ot] OR Ecuador[ot] OR Egypt[ot] OR United Arab Republic[ot] OR El Salvador[ot] OR Eritrea[ot] OR Estonia[ot] OR Ethiopia[ot] OR Fiji[ot] OR Gabon[ot] OR Gabonese Republic[ot] OR Gambia[ot] OR Gaza[ot] OR "Georgia Republic"[ot] OR "Georgian Republic"[ot] OR Ghana[ot] OR Gold Coast[ot] OR Greece[ot] OR Grenada[ot] OR Guatemala[ot] OR Guinea[ot] OR Guam[ot] OR Guiana[ot] OR Guyana[ot] OR Haiti[ot] OR Honduras[ot] OR Hungary[ot] OR India[ot] OR Maldives[ot] OR Indonesia[ot] OR Iran[ot] OR Iraq[ot] OR Isle of Man[ot] OR Jamaica[ot] OR Jordan[ot] OR Kazakhstan[ot] OR Kazakh[ot] OR Kenya[ot] OR Kiribati[ot] OR Korea[ot] OR Kosovo[ot] OR Kyrgyzstan[ot] OR Kirghizia[ot] OR Kyrgyz Republic[ot] OR Kirghiz[ot] OR Kirgizstan[ot] OR "Lao PDR"[ot] OR Laos[ot] OR Latvia[ot] OR Lebanon[ot] OR Lesotho[ot] OR Basutoland[ot] OR Liberia[ot] OR Libya[ot] OR Lithuania[ot]

#2 Search Macedonia[ot] OR Madagascar[ot] OR Malagasy Republic[ot] OR Malaysia[ot] OR Malaya[ot] OR Malay[ot] OR Sabah[ot] OR Sarawak[ot] OR Malawi[ot] OR Nyasaland[ot] OR Mali[ot] OR Malta[ot] OR Marshall Islands[ot] OR Mauritania[ot] OR Mauritius[ot] OR Agalega Islands[ot] OR Mexico[ot] OR Micronesia[ot] OR Middle East[ot] OR Moldova[ot] OR Moldovia[ot] OR Moldovan[ot] OR Mongolia[ot] OR Montenegro[ot] OR Morocco[ot] OR Ifni[ot] OR Mozambique[ot] OR Myanmar[ot] OR Myanma[ot] OR Burma[ot] OR Namibia[ot] OR Nepal[ot] OR Netherlands Antilles[ot] OR New Caledonia[ot] OR Nicaragua[ot] OR Niger[ot] OR Nigeria[ot] OR Northern Mariana Islands[ot] OR Oman[ot] OR Muscat[ot] OR Pakistan[ot] OR Palau[ot] OR Palestine[ot] OR Panama[ot] OR Paraguay[ot] OR Peru[ot] OR Philippines[ot] OR Philipines[ot] OR Phillipines[ot] OR Phillipines[ot] OR Poland[ot] OR Portugal[ot] OR Puerto Rico[ot] OR Romania[ot] OR Rumania[ot] OR Roumania[ot] OR Russia[ot] OR Russian[ot] OR Rwanda[ot] OR Ruanda[ot] OR Saint Kitts[ot] OR St Kitts[ot] OR Nevis[ot] OR Saint Lucia[ot] OR St Lucia[ot] OR Saint Vincent[ot] OR St Vincent[ot] OR Grenadines[ot] OR Samoa[ot] OR Samoan Islands[ot] OR Navigator Island[ot] OR Navigator Islands[ot] OR Sao Tome[ot] OR Saudi Arabia[ot] OR Senegal[ot] OR Serbia[ot] OR Montenegro[ot] OR Seychelles[ot] OR Sierra Leone[ot] OR Slovenia[ot] OR Sri Lanka[ot] OR Ceylon[ot] OR Solomon Islands[ot] OR Somalia[ot] OR Sudan[ot] OR Suriname[ot] OR Surinam[ot] OR Swaziland[ot] OR Syria[ot] OR Tajikistan[ot] OR Tadjhikistan[ot] OR Tadjikistan[ot] OR Tadjhik[ot] OR Tanzania[ot] OR Thailand[ot] OR Togo[ot] OR Togolese Republic[ot] OR Tonga[ot] OR Trinidad[ot] OR Tobago[ot] OR Tunisia[ot] OR Turkey[ot] OR Turkmenistan[ot] OR Turkmen[ot] OR Uganda[ot] OR Ukraine[ot] OR Uruguay[ot] OR USSR[ot] OR Soviet Union[ot] OR Union of Soviet Socialist Republics[ot] OR Uzbekistan[ot] OR Uzbek OR Vanuatu[ot] OR New Hebrides[ot] OR Venezuela[ot] OR Vietnam[ot] OR Viet Nam[ot] OR West Bank[ot] OR Yemen[ot] OR Yugoslavia[ot] OR Zambia[ot] OR Zimbabwe[ot] OR Rhodesia[ot]

#1 Search Developing Countries[Mesh:noexp] OR Africa[Mesh:noexp] OR Africa, Northern[Mesh:noexp] OR Africa South of the Sahara[Mesh:noexp] OR Africa, Central[Mesh:noexp] OR Africa, Eastern[Mesh:noexp] OR Africa, Southern[Mesh:noexp] OR Africa, Western[Mesh:noexp] OR Asia[Mesh:noexp] OR Asia, Central[Mesh:noexp] OR Asia, Southeastern[Mesh:noexp] OR Asia, Western[Mesh:noexp] OR Caribbean Region[Mesh:noexp] OR West Indies[Mesh:noexp] OR South America[Mesh:noexp] OR Latin America[Mesh:noexp] OR Central America[Mesh:noexp] OR Afghanistan[Mesh:noexp] OR Albania[Mesh:noexp] OR Algeria[Mesh:noexp] OR American Samoa[Mesh:noexp] OR Angola[Mesh:noexp] OR "Antigua and Barbuda"[Mesh:noexp] OR Argentina[Mesh:noexp] OR Armenia[Mesh:noexp] OR Azerbaijan[Mesh:noexp] OR Bahrain[Mesh:noexp] OR Bangladesh[Mesh:noexp] OR Barbados[Mesh:noexp] OR Benin[Mesh:noexp] OR Byelarus[Mesh:noexp] OR Belize[Mesh:noexp] OR Bhutan[Mesh:noexp] OR

Bolivia[Mesh:noexp] OR Bosnia-Herzegovina[Mesh:noexp] OR Botswana[Mesh:noexp] OR Brazil[Mesh:noexp] OR Bulgaria[Mesh:noexp] OR Burkina Faso[Mesh:noexp] OR Burundi[Mesh:noexp] OR Cambodia[Mesh:noexp] OR Cameroon[Mesh:noexp] OR Cape Verde[Mesh:noexp] OR Central African Republic[Mesh:noexp] OR Chad[Mesh:noexp] OR Chile[Mesh:noexp] OR China[Mesh:noexp] OR Colombia[Mesh:noexp] OR Comoros[Mesh:noexp] OR Congo[Mesh:noexp] OR Costa Rica[Mesh:noexp] OR Cote d'Ivoire[Mesh:noexp] OR Croatia[Mesh:noexp] OR Cuba[Mesh:noexp] OR Cyprus[Mesh:noexp] OR Czechoslovakia[Mesh:noexp] OR Czech Republic[Mesh:noexp] OR Slovakia[Mesh:noexp] OR Djibouti[Mesh:noexp] OR "Democratic Republic of the Congo"[Mesh:noexp] OR Dominica[Mesh:noexp] OR Dominican Republic[Mesh:noexp] OR East Timor[Mesh:noexp] OR Ecuador[Mesh:noexp] OR Egypt[Mesh:noexp] OR El Salvador[Mesh:noexp] OR Eritrea[Mesh:noexp] OR Estonia[Mesh:noexp] OR Ethiopia[Mesh:noexp] OR Fiji[Mesh:noexp] OR Gabon[Mesh:noexp] OR Gambia[Mesh:noexp] OR "Georgia (Republic)"[Mesh:noexp] OR Ghana[Mesh:noexp] OR Greece[Mesh:noexp] OR Grenada[Mesh:noexp] OR Guatemala[Mesh:noexp] OR Guinea[Mesh:noexp] OR Guinea-Bissau[Mesh:noexp] OR Guam[Mesh:noexp] OR Guyana[Mesh:noexp] OR Haiti[Mesh:noexp] OR Honduras[Mesh:noexp] OR Hungary[Mesh:noexp] OR India[Mesh:noexp] OR Indonesia[Mesh:noexp] OR Iran[Mesh:noexp] OR Iraq[Mesh:noexp] OR Jamaica[Mesh:noexp] OR Jordan[Mesh:noexp] OR Kazakhstan[Mesh:noexp] OR Kenya[Mesh:noexp] OR Korea[Mesh:noexp] OR Kosovo[Mesh:noexp] OR Kyrgyzstan[Mesh:noexp] OR Laos[Mesh:noexp] OR Latvia[Mesh:noexp] OR Lebanon[Mesh:noexp] OR Lesotho[Mesh:noexp] OR Liberia[Mesh:noexp] OR Libya[Mesh:noexp] OR Lithuania[Mesh:noexp] OR Macedonia[Mesh:noexp] OR Madagascar[Mesh:noexp] OR Malaysia[Mesh:noexp] OR Malawi[Mesh:noexp] OR Mali[Mesh:noexp] OR Malta[Mesh:noexp] OR Mauritania[Mesh:noexp] OR Mauritius[Mesh:noexp] OR Mexico[Mesh:noexp] OR Micronesia[Mesh:noexp] OR Middle East[Mesh:noexp] OR Moldova[Mesh:noexp] OR Mongolia[Mesh:noexp] OR Montenegro[Mesh:noexp] OR Morocco[Mesh:noexp] OR Mozambique[Mesh:noexp] OR Myanmar[Mesh:noexp] OR Namibia[Mesh:noexp] OR Nepal[Mesh:noexp] OR Netherlands Antilles[Mesh:noexp] OR New Caledonia[Mesh:noexp] OR Nicaragua[Mesh:noexp] OR Niger[Mesh:noexp] OR Nigeria[Mesh:noexp] OR Oman[Mesh:noexp] OR Pakistan[Mesh:noexp] OR Palau[Mesh:noexp] OR Panama[Mesh:noexp] OR Papua New Guinea[Mesh:noexp] OR Paraguay[Mesh:noexp] OR Peru[Mesh:noexp] OR Philippines[Mesh:noexp] OR Poland[Mesh:noexp] OR Portugal[Mesh:noexp] OR Puerto Rico[Mesh:noexp] OR Romania[Mesh:noexp] OR Russia[Mesh:noexp] OR "Russia (Pre-1917)"[Mesh:noexp] OR Rwanda[Mesh:noexp] OR "Saint Kitts and Nevis"[Mesh:noexp] OR Saint Lucia[Mesh:noexp] OR "Saint Vincent and the Grenadines"[Mesh:noexp] OR Samoa[Mesh:noexp] OR Saudi Arabia[Mesh:noexp] OR Senegal[Mesh:noexp] OR Serbia[Mesh:noexp] OR Montenegro[Mesh:noexp] OR Seychelles[Mesh:noexp] OR Sierra Leone[Mesh:noexp] OR Slovenia[Mesh:noexp] OR Sri Lanka[Mesh:noexp] OR Somalia[Mesh:noexp] OR South Africa[Mesh:noexp] OR Sudan[Mesh:noexp] OR Suriname[Mesh:noexp] OR Swaziland[Mesh:noexp] OR Syria[Mesh:noexp] OR Tajikistan[Mesh:noexp] OR Tanzania[Mesh:noexp] OR Thailand[Mesh:noexp] OR Togo[Mesh:noexp] OR Tonga[Mesh:noexp] OR "Trinidad and Tobago"[Mesh:noexp] OR Tunisia[Mesh:noexp] OR Turkey[Mesh:noexp] OR Turkmenistan[Mesh:noexp] OR Uganda[Mesh:noexp] OR Ukraine[Mesh:noexp] OR Uruguay[Mesh:noexp] OR USSR[Mesh:noexp] OR Uzbekistan[Mesh:noexp] OR Vanuatu[Mesh:noexp] OR Venezuela[Mesh:noexp] OR Vietnam[Mesh:noexp] OR Yemen[Mesh:noexp] OR Yugoslavia[Mesh:noexp] OR Zambia[Mesh:noexp] OR Zimbabwe[Mesh:noexp]

Embase:

('cost benefit analysis'/exp OR 'cost benefit' OR 'cost effective' OR 'cost effectiveness' OR 'cost utility')
AND ('emergency health service'/exp OR 'emergency medicine'/exp OR 'emergency ward'/exp OR

'emergency health service' OR 'emergency medicine':ab,ti,de,au,lnk OR 'emergency services' OR 'emergency department':ab,ti,de,au,lnk OR 'emergency service' OR 'emergency departments' OR 'emergency room' OR 'emergency rooms' OR 'emergency ward' OR 'emergency unit' OR 'trauma centers' OR 'trauma center' OR 'emergency health services' OR 'emergency medical services' OR 'emergency medical service' OR 'accident & emergency' OR 'accident and emergency' OR 'A&E' OR 'A & E')

AND

Combine: (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)

#1 Search 'developing country':ab,ti OR 'developing countries':ab,ti OR 'developing nation':ab,ti OR 'developing nations':ab,ti OR 'developing population':ab,ti OR 'developing populations':ab,ti OR 'developing world':ab,ti OR 'less developed country':ab,ti OR 'less developed countries':ab,ti OR 'less developed nation':ab,ti OR 'less developed nations':ab,ti OR 'less developed population':ab,ti OR 'less developed populations':ab,ti OR 'less developed world':ab,ti OR 'lesser developed country':ab,ti OR 'lesser developed countries':ab,ti OR 'lesser developed nation':ab,ti OR 'lesser developed nations':ab,ti OR 'lesser developed population':ab,ti OR 'lesser developed populations':ab,ti OR 'lesser developed world':ab,ti OR 'under developed country':ab,ti OR 'under developed countries':ab,ti OR 'under developed nation':ab,ti OR 'under developed nations':ab,ti OR 'under developed population':ab,ti OR 'under developed populations':ab,ti OR 'under developed world':ab,ti OR 'underdeveloped country':ab,ti OR 'underdeveloped countries':ab,ti OR 'underdeveloped nation':ab,ti OR 'underdeveloped nations':ab,ti OR 'underdeveloped population':ab,ti OR 'underdeveloped populations':ab,ti OR 'underdeveloped world':ab,ti OR 'middle income country':ab,ti OR 'middle income countries':ab,ti OR 'middle income nation':ab,ti OR 'middle income nations':ab,ti OR 'middle income population':ab,ti OR 'middle income populations':ab,ti OR 'low income country':ab,ti OR 'low income countries':ab,ti OR 'low income nation':ab,ti OR 'low income nations':ab,ti OR 'low income population':ab,ti OR 'low income populations':ab,ti OR 'lower income country':ab,ti OR 'lower income countries':ab,ti OR 'lower income nation':ab,ti OR 'lower income nations':ab,ti OR 'lower income population':ab,ti OR 'lower income populations':ab,ti OR 'underserved country':ab,ti OR 'underserved countries':ab,ti OR 'underserved nation':ab,ti OR 'underserved nations':ab,ti OR 'underserved population':ab,ti OR 'underserved populations':ab,ti OR 'underserved world':ab,ti OR 'under served country':ab,ti OR 'under served countries':ab,ti OR 'under served nation':ab,ti OR 'under served nations':ab,ti OR 'under served population':ab,ti OR 'under served populations':ab,ti OR 'under served world':ab,ti OR 'deprived country':ab,ti OR 'deprived countries':ab,ti OR 'deprived nation':ab,ti OR 'deprived nations':ab,ti OR 'deprived population':ab,ti OR 'deprived populations':ab,ti OR 'deprived world':ab,ti OR 'poor country':ab,ti OR 'poor countries':ab,ti OR 'poor nation':ab,ti OR 'poor nations':ab,ti OR 'poor population':ab,ti OR 'poor populations':ab,ti OR 'poor world':ab,ti OR 'poorer country':ab,ti OR 'poorer countries':ab,ti OR 'poorer nation':ab,ti OR 'poorer nations':ab,ti OR 'poorer population':ab,ti OR 'poorer populations':ab,ti OR 'poorer world':ab,ti OR 'developing economy':ab,ti OR 'developing economies':ab,ti OR 'less developed economy':ab,ti OR 'less developed economies':ab,ti OR 'lesser developed economy':ab,ti OR 'lesser developed economies':ab,ti OR 'under developed economy':ab,ti OR 'under developed economies':ab,ti OR 'underdeveloped economy':ab,ti OR 'underdeveloped economies':ab,ti OR 'middle income economy':ab,ti OR 'middle income economies':ab,ti OR 'low income economy':ab,ti OR 'low income economies':ab,ti OR 'lower income economy':ab,ti OR 'lower income economies':ab,ti OR 'low gdp':ab,ti OR 'low gnp':ab,ti OR 'low gross domestic':ab,ti OR 'low gross national':ab,ti OR 'lower gdp':ab,ti OR 'lower gnp':ab,ti OR 'lower gross domestic':ab,ti OR 'lower gross national':ab,ti OR 'lamic':ab,ti OR 'lamics':ab,ti OR 'third world':ab,ti OR 'lami country':ab,ti OR 'lami countries':ab,ti OR 'transitional country':ab,ti OR 'transitional countries':ab,ti

#2 Search Africa:ti,ab OR Asia:ti,ab OR Caribbean:ti,ab OR 'West Indies':ti,ab OR 'South America':ti,ab OR 'Latin America':ti,ab OR 'Central America':ti,ab OR 'atlantic islands':ab,ti OR 'commonwealth of

independent states':ab,ti OR 'pacific islands':ab,ti OR 'indian ocean islands':ab,ti OR 'eastern europe':ab,ti

#3 Search Afghanistan:ti,ab OR Albania:ti,ab OR Algeria:ti,ab OR Angola:ti,ab OR Antigua:ti,ab OR Barbuda:ti,ab OR Argentina:ti,ab OR Armenia:ti,ab OR Armenian:ti,ab OR Aruba:ti,ab OR Azerbaijan:ti,ab OR Bahrain:ti,ab OR Bangladesh:ti,ab OR Barbados:ti,ab OR Benin:ti,ab OR Byelarus:ti,ab OR Byelorussian:ti,ab OR Belarus:ti,ab OR Belorussian:ti,ab OR Belorussia:ti,ab OR Belize:ti,ab OR Bhutan:ti,ab OR Bolivia:ti,ab OR Bosnia:ti,ab OR Herzegovina:ti,ab OR Hercegovina:ti,ab OR Botswana:ti,ab OR Brasil:ti,ab OR Brazil:ti,ab OR Bulgaria:ti,ab OR 'Burkina Faso':ti,ab OR 'Burkina Fasso':ti,ab OR 'Upper Volta':ti,ab OR Burundi:ti,ab OR Urundi:ti,ab OR Cambodia:ti,ab OR 'Khmer Republic':ti,ab OR Kampuchea:ti,ab OR Cameroon:ti,ab OR Cameroons:ti,ab OR Cameron:ti,ab OR Camerons:ti,ab OR 'Cape Verde':ti,ab OR 'Central African Republic':ti,ab OR Chad:ti,ab OR Chile:ti,ab OR China:ti,ab OR Colombia:ti,ab OR Comoros:ti,ab OR 'Comoro Islands':ti,ab OR Comores:ti,ab OR Mayotte:ti,ab OR Congo:ti,ab OR Zaire:ti,ab OR 'Costa Rica':ti,ab OR 'Cote d'Ivoire' OR 'Ivory Coast':ti,ab OR Croatia:ti,ab OR Cuba:ti,ab OR Cyprus:ti,ab OR Czechoslovakia:ti,ab OR 'Czech Republic':ti,ab OR Slovakia:ti,ab OR 'Slovak Republic':ti,ab OR Djibouti:ti,ab OR 'French Somaliland':ti,ab OR Dominica:ti,ab OR 'Dominican Republic':ti,ab OR 'East Timor':ti,ab OR 'East Timur':ti,ab OR 'Timor Leste':ti,ab OR Ecuador:ti,ab OR Egypt:ti,ab OR 'United Arab Republic':ti,ab OR El Salvador:ti,ab OR Eritrea:ti,ab OR Estonia:ti,ab OR Ethiopia:ti,ab OR Fiji:ti,ab OR Gabon:ti,ab OR 'Gabonese Republic':ti,ab OR Gambia:ti,ab OR Gaza:ti,ab OR 'Georgia Republic':ti,ab OR 'Georgian Republic':ti,ab OR Ghana:ti,ab OR 'Gold Coast':ti,ab OR Greece:ti,ab OR Grenada:ti,ab OR Guatemala:ti,ab OR Guinea:ti,ab OR Guam:ti,ab OR Guiana:ti,ab OR Guyana:ti,ab OR Haiti:ti,ab OR Honduras:ti,ab OR Hungary:ti,ab OR India:ti,ab OR Maldives:ti,ab OR Indonesia:ti,ab OR Iran:ti,ab OR Iraq:ti,ab OR 'Isle of Man':ti,ab OR Jamaica:ti,ab OR Jordan:ti,ab OR Kazakhstan:ti,ab OR Kazakh:ti,ab OR Kenya:ti,ab OR Kiribati:ti,ab OR Korea:ti,ab OR Kosovo:ti,ab OR Kyrgyzstan:ti,ab OR Kirghizia:ti,ab OR 'Kyrgyz Republic':ti,ab OR Kirghiz:ti,ab OR Kirgizstan:ti,ab OR 'Lao PDR':ti,ab OR Laos:ti,ab OR Latvia:ti,ab OR Lebanon:ti,ab OR Lesotho:ti,ab OR Basutoland:ti,ab OR Liberia:ti,ab OR Libya:ti,ab OR Lithuania:ti,ab

#4 Search Macedonia:ti,ab OR Madagascar:ti,ab OR 'Malagasy Republic':ti,ab OR Malaysia:ti,ab OR Malaya:ti,ab OR Malay:ti,ab OR Sabah:ti,ab OR Sarawak:ti,ab OR Malawi:ti,ab OR Nyasaland:ti,ab OR Mali:ti,ab OR Malta:ti,ab OR 'Marshall Islands':ti,ab OR Mauritania:ti,ab OR Mauritius:ti,ab OR **melanesia:ab,ti** OR 'Agalega Islands':ti,ab OR Mexico:ti,ab OR Micronesia:ti,ab OR 'Middle East':ti,ab OR Moldova:ti,ab OR Moldovia:ti,ab OR Moldovian:ti,ab OR Mongolia:ti,ab OR Montenegro:ti,ab OR Morocco:ti,ab OR Ifni:ti,ab OR Mozambique:ti,ab OR Myanmar:ti,ab OR Myanma:ti,ab OR Burma:ti,ab OR Namibia:ti,ab OR Nepal:ti,ab OR 'Netherlands Antilles':ti,ab OR 'New Caledonia':ti,ab OR Nicaragua:ti,ab OR Niger:ti,ab OR Nigeria:ti,ab OR 'Northern Mariana Islands':ti,ab OR Oman:ti,ab OR Muscat:ti,ab OR Pakistan:ti,ab OR Palau:ti,ab OR Palestine:ti,ab OR Panama:ti,ab OR Paraguay:ti,ab OR Peru:ti,ab OR Philippines:ti,ab OR Philipines:ti,ab OR Phillipines:ti,ab OR Phillipines:ti,ab OR Poland:ti,ab OR Portugal:ti,ab OR 'Puerto Rico':ti,ab OR Romania:ti,ab OR Rumania:ti,ab OR Roumania:ti,ab OR Russia:ti,ab OR Russian:ti,ab OR Rwanda:ti,ab OR Ruanda:ti,ab OR 'Saint Kitts':ti,ab OR 'St Kitts':ti,ab OR Nevis:ti,ab OR 'Saint Lucia':ti,ab OR 'St Lucia':ti,ab OR 'Saint Vincent':ti,ab OR 'St Vincent':ti,ab OR Grenadines:ti,ab OR Samoa:ti,ab OR 'Samoan Islands':ti,ab OR 'Navigator Island':ti,ab OR 'Navigator Islands':ti,ab OR 'Sao Tome':ti,ab OR 'Saudi Arabia':ti,ab OR Senegal:ti,ab OR Serbia:ti,ab OR Montenegro:ti,ab OR Seychelles:ti,ab OR 'Sierra Leone':ti,ab OR Slovenia:ti,ab OR 'Sri Lanka':ti,ab OR Ceylon:ti,ab OR 'Solomon Islands':ti,ab OR Somalia:ti,ab OR Sudan:ti,ab OR Suriname:ti,ab OR Surinam:ti,ab OR Swaziland:ti,ab OR Syria:ti,ab OR Syrian:ti,ab OR Tajikistan:ti,ab OR Tadzhhikistan:ti,ab OR Tadjikistan:ti,ab OR Tadzhhik:ti,ab OR Tanzania:ti,ab OR Thailand:ti,ab OR Togo:ti,ab OR 'Togolese Republic':ti,ab OR Tonga:ti,ab OR Trinidad:ti,ab OR Tobago:ti,ab OR Tunisia:ti,ab OR Turkey:ti,ab OR Turkmenistan:ti,ab OR Turkmen:ti,ab OR Tuvalu:ti,ab OR Uganda:ti,ab OR Ukraine:ti,ab OR Uruguay:ti,ab OR USSR:ti,ab OR 'Soviet

Union':ti,ab OR 'Union of Soviet Socialist Republics':ti,ab OR Uzbekistan:ti,ab OR Uzbek OR Vanuatu:ti,ab OR 'New Hebrides':ti,ab OR Venezuela:ti,ab OR Vietnam:ti,ab OR 'Viet Nam':ti,ab OR 'West Bank':ti,ab OR Yemen:ti,ab OR Yugoslavia:ti,ab OR Zambia:ti,ab OR Zimbabwe:ti,ab OR Rhodesia:ti,ab

#5 Search: 'developing country'/exp OR 'Africa'/de OR 'Africa south of the Sahara'/de OR 'North Africa'/de OR 'Central Africa'/de OR 'Asia'/de OR 'South Asia'/de OR 'Southeast Asia'/de OR 'South America'/de OR 'Central America'/de OR 'South and Central America'/de OR 'Atlantic islands'/de OR 'Caribbean Islands'/de OR 'Pacific islands'/de OR 'Indian Ocean'/de OR 'Eastern Europe'/de

#6 Search Afghanistan/exp OR Albania/exp OR Algeria/exp OR 'American Samoa'/exp OR Angola/exp OR 'Antigua and Barbuda'/exp OR Argentina/exp OR Armenia/exp OR Azerbaijan/exp OR Bahrain/exp OR Bangladesh/exp OR Barbados/exp OR Benin/exp OR 'Belarus'/exp OR 'Baltic States'/exp OR Belize/exp OR Bhutan/exp OR Bolivia/exp OR 'Bosnia and Herzegovina'/exp OR Botswana/exp OR Brazil/exp OR Bulgaria/exp OR 'Burkina Faso'/exp OR Burundi/exp OR Cambodia/exp OR Cameroon/exp OR 'Cape Verde'/exp OR 'Central African Republic'/exp OR Chad/exp OR Chile/exp OR China/exp OR Colombia/exp OR Comoros/exp OR Congo/exp OR 'Costa Rica'/exp OR 'Cote d'Ivoire'/exp OR Croatia/exp OR Cuba/exp OR Cyprus/exp OR Czechoslovakia/exp OR 'Czech Republic'/exp OR Slovakia/exp OR Djibouti/exp OR 'Democratic Republic Congo'/exp OR Dominica/exp OR 'Dominican Republic'/exp OR 'Timor-Leste'/exp OR Ecuador/exp OR Egypt/exp OR 'El Salvador'/exp OR Eritrea/exp OR Estonia/exp OR Ethiopia/exp OR 'French Guiana'/exp OR Fiji/exp OR Gabon/exp OR Gambia/exp OR 'Georgia (Republic) '/exp OR Ghana/exp OR Greece/exp OR Grenada/exp OR Guatemala/exp OR Guinea/exp OR Guinea-Bissau/exp OR Guam/exp OR Guyana/exp OR Haiti/exp OR Honduras/exp OR Hungary/exp OR India/exp OR Indonesia/exp OR Iran/exp OR Iraq/exp OR Jamaica/exp OR Jordan/exp OR Kazakhstan/exp OR Kenya/exp OR Korea/exp OR Kyrgyzstan/exp OR Laos/exp OR Latvia/exp OR Lebanon/exp OR Lesotho/exp OR Liberia/exp OR 'Libyan Arab Jamahiriya'/exp OR Lithuania/exp OR 'Macedonia (republic)'/exp OR Madagascar/exp OR Malaysia/exp OR Malawi/exp OR Mali/exp OR Malta/exp OR Mauritania/exp OR Mauritius/exp OR "Melanesia"/exp

#7 Search Mexico/exp OR 'Federated States of Micronesia'/exp OR 'Middle East'/de OR Moldova/exp OR Mongolia/exp OR Montenegro/exp OR Morocco/exp OR Mozambique/exp OR Myanmar/exp OR Namibia/exp OR Nepal/exp OR 'Netherlands Antilles'/exp OR 'New Caledonia'/exp OR Nicaragua/exp OR Niger/exp OR Nigeria/exp OR 'North Korea'/exp OR Oman/exp OR Pakistan/exp OR Palau/exp OR Panama/exp OR 'Papua New Guinea'/exp OR Paraguay/exp OR Peru/exp OR Philippines/exp OR Poland/exp OR Portugal/exp OR 'Puerto Rico'/exp OR Romania/exp OR 'Russian Federation'/exp OR Rwanda/exp OR 'Saint Kitts and Nevis'/exp OR 'Saint Lucia'/exp OR 'Saint Vincent and the Grenadines'/exp OR 'Samoan Islands'/exp OR Samoa/exp OR 'Saudi Arabia'/exp OR Senegal/exp OR Serbia/exp OR 'Montenegro (republic)'/exp OR Seychelles/exp OR 'Sierra Leone'/exp OR Slovenia/exp OR 'Sri Lanka'/exp OR Somalia/exp OR 'South Korea'/exp OR 'South Africa'/exp OR Sudan/exp OR Suriname/exp OR Swaziland/exp OR 'Syrian Arab Republic'/exp OR Tajikistan/exp OR Tanzania/exp OR Thailand/exp OR Togo/exp OR Tonga/exp OR 'Trinidad and Tobago'/exp OR Tunisia/exp OR 'Turkey (republic)'/exp OR Turkmenistan/exp OR Uganda/exp OR Ukraine/exp OR Uruguay/exp OR USSR/exp OR Uzbekistan/exp OR Vanuatu/exp OR Venezuela/exp OR 'Viet Nam'/exp OR Yemen/exp OR Yugoslavia/exp OR 'Yugoslavia (pre-1992)'/exp OR Zambia/exp OR Zimbabwe/exp

Scopus:

TITLE-ABS-KEY({cost benefit} OR {cost effectiveness} OR {cost effective} OR {cost utility}) AND TITLE-ABS-KEY({Emergency medicine} OR {Emergency services} OR {Emergency department} OR {Emergency service} OR {Emergency departments} OR {Emergency room} OR {Emergency rooms} OR {Emergency ward} OR {Emergency Unit} OR {Trauma Center} OR {Trauma Centers} OR {emergency health service} OR {emergency health services} OR {emergency medical services} OR

{emergency medical service} OR {accident and emergency} OR {accident & emergency} OR {a&e} OR {A & E})

AND

#1 Search TITLE-ABS-KEY(({developing country} OR {developing countries} OR {developing nation} OR {developing nations} OR {developing population} OR {developing populations} OR {developing world} OR {less developed country} OR {less developed countries} OR {less developed nation} OR {less developed nations} OR {less developed population} OR {less developed populations} OR {less developed world} OR {lesser developed country} OR {lesser developed countries} OR {lesser developed nation} OR {lesser developed nations} OR {lesser developed population} OR {lesser developed populations} OR {lesser developed world} OR {under developed country} OR {under developed countries} OR {under developed nation} OR {under developed nations} OR {under developed population} OR {under developed populations} OR {under developed world} OR {underdeveloped country} OR {underdeveloped countries} OR {underdeveloped nation} OR {underdeveloped nations} OR {underdeveloped population} OR {underdeveloped populations} OR {underdeveloped world} OR {middle income country} OR {middle income countries} OR {middle income nation} OR {middle income nations} OR {middle income population} OR {middle income populations} OR {low income country} OR {low income countries} OR {low income nation} OR {low income nations} OR {low income population} OR {low income populations} OR {lower income country} OR {lower income countries} OR {lower income nation} OR {lower income nations} OR {lower income population} OR {lower income populations} OR {underserved country} OR {underserved countries} OR {underserved nation} OR {underserved nations} OR {underserved population} OR {underserved populations} OR {underserved world} OR {under served country} OR {under served countries} OR {under served nation} OR {under served nations} OR {under served population} OR {under served populations} OR {under served world} OR {deprived country} OR {deprived countries} OR {deprived nation} OR {deprived nations} OR {deprived population} OR {deprived populations} OR {deprived world})

#2 Search TITLE-ABS-KEY({poor country} OR {poor countries} OR {poor nation} OR {poor nations} OR {poor population} OR {poor populations} OR {poor world} OR {poorer country} OR {poorer countries} OR {poorer nation} OR {poorer nations} OR {poorer population} OR {poorer populations} OR {poorer world} OR {developing economy} OR {developing economies} OR {less developed economy} OR {less developed economies} OR {lesser developed economy} OR {lesser developed economies} OR {under developed economy} OR {under developed economies} OR {underdeveloped economy} OR {underdeveloped economies} OR {middle income economy} OR {middle income economies} OR {low income economy} OR {low income economies} OR {lower income economy} OR {lower income economies} OR {low gdp} OR {low gnp} OR {low gross domestic} OR {low gross national} OR {lower gdp} OR {lower gnp} OR {lower gross domestic} OR {lower gross national} OR lmic OR lmic OR {third world} OR {lami country} OR {lami countries} OR {transitional country} OR {transitional countries})

#3 Search TITLE-ABS-KEY(Africa OR Asia OR Caribbean OR {West Indies} OR {South America} OR {Latin America} OR {Central America} OR {Atlantic Islands} OR {Commonwealth of Independent States} OR {Pacific Islands} OR {Indian Ocean Islands} OR {Eastern Europe} OR Afghanistan OR Albania OR Algeria OR Angola OR Antigua OR Barbuda OR Argentina OR Armenia OR Armenian OR Aruba OR Azerbaijan OR Bahrain OR Bangladesh OR Barbados OR Benin OR Byelarus OR Byelorussian OR Belarus OR Belorussian OR Belorussia OR Belize OR Bhutan OR Bolivia OR Bosnia OR Herzegovina OR Hercegovina OR Botswana OR Brasil OR Brazil OR Bulgaria OR {Burkina Faso} OR {Burkina Fasso} OR {Upper Volta} OR Burundi OR Urundi OR Cambodia OR {Khmer Republic} OR Kampuchea OR Cameroon OR Cameroons OR Cameron OR Camerons OR {Cape Verde} OR {Central African Republic} OR Chad OR Chile OR China OR Colombia OR Comoros OR {Comoro Islands} OR Comores OR Mayotte OR Congo OR Zaire OR {Costa Rica} OR {Cote d'Ivoire} OR {Ivory Coast} OR Croatia OR Cuba OR Cyprus OR Czechoslovakia OR {Czech Republic} OR Slovakia OR {Slovak Republic} OR Djibouti OR {French Somaliland} OR Dominica OR {Dominican Republic} OR {East Timor} OR {East

Timur} OR {Timor Leste} OR Ecuador OR Egypt OR {United Arab Republic} OR {El Salvador} OR Eritrea OR Estonia OR Ethiopia OR Fiji OR Gabon OR {Gabonese Republic} OR Gambia OR Gaza OR {Georgia Republic} OR {Georgian Republic} OR Ghana OR {Gold Coast} OR Greece OR Grenada OR Guatemala OR Guinea OR Guam OR Guiana OR Guyana OR Haiti OR Honduras OR Hungary OR India OR Maldives OR Indonesia OR Iran OR Iraq OR {Isle of Man} OR Jamaica OR Jordan OR Kazakhstan OR Kazakh OR Kenya OR Kiribati OR Korea OR Kosovo OR Kyrgyzstan OR Kirghizia OR {Kyrgyz Republic} OR Kirghiz OR Kirgizstan OR {Lao PDR} OR Laos OR Latvia OR Lebanon OR Lesotho OR Basutoland OR Liberia OR Libya OR Lithuania)

#4 Search TITLE-ABS-KEY(Macedonia OR Madagascar OR {Malagasy Republic} OR Malaysia OR Malaya OR Malay OR Sabah OR Sarawak OR Malawi OR Nyasaland OR Mali OR Malta OR {Marshall Islands} OR Mauritania OR Mauritius OR {Agalega Islands} OR {Melanesia} OR Mexico OR Micronesia OR {Middle East} OR Moldova OR Moldavia OR Moldovan OR Mongolia OR Montenegro OR Morocco OR Ifni OR Mozambique OR Myanmar OR Myanma OR Burma OR Namibia OR Nepal OR {Netherlands Antilles} OR {New Caledonia} OR Nicaragua OR Niger OR Nigeria OR {Northern Mariana Islands} OR Oman OR Muscat OR Pakistan OR Palau OR Palestine OR Panama OR Paraguay OR Peru OR Philippines OR Philipines OR Phillipines OR Phillippines OR Poland OR Portugal OR {Puerto Rico} OR Romania OR Rumania OR Roumania OR Russia OR Russian OR Rwanda OR Ruanda OR {Saint Kitts} OR {St Kitts} OR Nevis OR {Saint Lucia} OR {St Lucia} OR {Saint Vincent} OR {St Vincent} OR Grenadines OR Samoa OR {Samoan Islands} OR {Navigator Island} OR {Navigator Islands} OR {Sao Tome} OR {Saudi Arabia} OR Senegal OR Serbia OR Montenegro OR Seychelles OR {Sierra Leone} OR Slovenia OR {Sri Lanka} OR Ceylon OR {Solomon Islands} OR Somalia OR Sudan OR Suriname OR Surinam OR Swaziland OR Syria OR Syrian OR Tajikistan OR Tadjikistan OR Tadjikistan OR Tadjhik OR Tanzania OR Thailand OR Togo OR {Togolese Republic} OR Tonga OR Trinidad OR Tobago OR Tunisia OR Turkey OR Turkmenistan OR Turkmen OR Tuvalu OR Uganda OR Ukraine OR Uruguay OR USSR OR {Soviet Union} OR {Union of Soviet Socialist Republics} OR Uzbekistan OR Uzbek OR Vanuatu OR {New Hebrides} OR Venezuela OR Vietnam OR {Viet Nam} OR {West Bank} OR Yemen OR Yugoslavia OR Zambia OR Zimbabwe OR Rhodesia)

Web of Science:

TS=("cost benefit" OR "cost effectiveness" OR "cost effective" OR "cost utility") AND

TS=("Emergency medicine" OR "Emergency services" OR "Emergency department" OR "Emergency service" OR "Emergency departments" OR "Emergency room" OR "Emergency rooms" OR "Emergency ward" OR "Emergency Unit" OR "Trauma Center" OR "Trauma Centers" OR "emergency health service" OR "emergency health services" OR "emergency medical services" OR "emergency medical service" OR "accident and emergency" OR "accident & emergency" OR "a&e" OR "A & E")

AND

Combine: (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)

#1 Search TS=("developing country" OR "developing countries" OR "developing nation" OR "developing nations" OR "developing population" OR "developing populations" OR "developing world" OR "less developed country" OR "less developed countries" OR "less developed nation" OR "less developed nations" OR "less developed population" OR "less developed populations" OR "less developed world" OR "lesser developed country" OR "lesser developed countries" OR "lesser developed nation" OR "lesser developed nations" OR "lesser developed population" OR "lesser developed populations" OR "lesser developed world" OR "under developed country" OR "under developed countries" OR "under developed nation" OR "under developed nations" OR "under developed population" OR "under developed populations" OR "under developed world" OR "underdeveloped country" OR "underdeveloped countries" OR "underdeveloped nation" OR "underdeveloped nations" OR "underdeveloped population" OR "underdeveloped populations" OR "underdeveloped world" OR "middle income country" OR "middle income countries" OR "middle income

nation" OR "middle income nations" OR "middle income population" OR "middle income populations" OR "low income country" OR "low income countries" OR "low income nation" OR "low income nations" OR "low income population" OR "low income populations" OR "lower income country" OR "lower income countries" OR "lower income nation" OR "lower income nations" OR "lower income population" OR "lower income populations" OR "underserved country" OR "underserved countries" OR "underserved nation" OR "underserved nations" OR "underserved population" OR "underserved populations" OR "underserved world" OR "under served country" OR "under served countries" OR "under served nation" OR "under served nations" OR "under served population" OR "under served populations" OR "under served world" OR "deprived country" OR "deprived countries" OR "deprived nation" OR "deprived nations" OR "deprived population" OR "deprived populations" OR "deprived world")

#2 Search TS=("poor country" OR "poor countries" OR "poor nation" OR "poor nations" OR "poor population" OR "poor populations" OR "poor world" OR "poorer country" OR "poorer countries" OR "poorer nation" OR "poorer nations" OR "poorer population" OR "poorer populations" OR "poorer world" OR "developing economy" OR "developing economies" OR "less developed economy" OR "less developed economies" OR "lesser developed economy" OR "lesser developed economies" OR "under developed economy" OR "under developed economies" OR "underdeveloped economy" OR "underdeveloped economies" OR "middle income economy" OR "middle income economies" OR "low income economy" OR "low income economies" OR "lower income economy" OR "lower income economies" OR "low gdp" OR "low gnp" OR "low gross domestic" OR "low gross national" OR "lower gdp" OR "lower gnp" OR "lower gross domestic" OR "lower gross national" OR lmic OR lmic OR "third world" OR "lami country" OR "lami countries" OR "transitional country" OR "transitional countries")

#3 Search TS=(Africa OR Asia OR Caribbean OR "West Indies" OR "South America" OR "Latin America" OR "Central America" OR "Atlantic Islands" OR "Commonwealth of Independent States" OR "Pacific Islands" OR "Indian Ocean Islands" OR "Eastern Europe" OR Afghanistan OR Albania OR Algeria OR Angola OR Antigua OR Barbuda OR Argentina OR Armenia OR Armenian OR Aruba OR Azerbaijan OR Bahrain OR Bangladesh OR Barbados OR Benin OR Byelarus OR Byelorussian OR Belarus OR Belorussian OR Belorussia OR Belize OR Bhutan OR Bolivia OR Bosnia OR Herzegovina OR Hercegovina OR Botswana OR Brasil OR Brazil OR Bulgaria OR "Burkina Faso" OR "Burkina Fasso" OR "Upper Volta" OR Burundi OR Urundi OR Cambodia OR "Khmer Republic" OR Kampuchea OR Cameroon OR Cameroons OR Cameron OR Camerons OR "Cape Verde" OR "Central African Republic" OR Chad OR Chile OR China OR Colombia OR Comoros OR "Comoro Islands" OR Comores OR Mayotte OR Congo OR Zaire OR "Costa Rica" OR "Cote d'Ivoire" OR "Ivory Coast" OR Croatia OR Cuba OR Cyprus OR Czechoslovakia OR "Czech Republic" OR Slovakia OR "Slovak Republic" OR Djibouti OR "French Somaliland" OR Dominica OR "Dominican Republic" OR "East Timor" OR "East Timur" OR "Timor Leste" OR Ecuador OR Egypt OR "United Arab Republic" OR "El Salvador" OR Eritrea OR Estonia OR Ethiopia OR Fiji OR Gabon OR "Gabonese Republic" OR Gambia OR Gaza OR "Georgia Republic" OR "Georgian Republic" OR Ghana OR "Gold Coast" OR Greece OR Grenada OR Guatemala OR Guinea OR Guam OR Guiana OR Guyana OR Haiti OR Honduras OR Hungary OR India OR Maldives OR Indonesia OR Iran OR Iraq OR "Isle of Man" OR Jamaica OR Jordan OR Kazakhstan OR Kazakh OR Kenya OR Kiribati OR Korea OR Kosovo OR Kyrgyzstan OR Kirghizia OR "Kyrgyz Republic" OR Kirghiz OR Kirgizstan OR "Lao PDR" OR Laos OR Latvia OR Lebanon OR Lesotho OR Basutoland OR Liberia OR Libya OR Lithuania)

#4 Search TS=(Macedonia OR Madagascar OR "Malagasy Republic" OR Malaysia OR Malaya OR Malay OR Sabah OR Sarawak OR Malawi OR Nyasaland OR Mali OR Malta OR "Marshall Islands" OR Mauritania OR Mauritius OR "Agalega Islands" OR "Melanesia" OR Mexico OR Micronesia OR "Middle East" OR Moldova OR Moldovia OR Moldovan OR Mongolia OR Montenegro OR Morocco OR Ifni OR Mozambique OR Myanmar OR Myanma OR Burma OR Namibia OR Nepal OR "Netherlands Antilles" OR "New Caledonia" OR Nicaragua OR Niger OR Nigeria OR "Northern Mariana Islands" OR Oman

OR Muscat OR Pakistan OR Palau OR Palestine OR Panama OR Paraguay OR Peru OR Philippines
 OR Philipines OR Phillipines OR Phillippines OR Poland OR Portugal OR "Puerto Rico" OR Romania
 OR Rumania OR Roumania OR Russia OR Russian OR Rwanda OR Ruanda OR "Saint Kitts" OR "St
 Kitts" OR Nevis OR "Saint Lucia" OR "St Lucia" OR "Saint Vincent" OR "St Vincent" OR Grenadines
 OR Samoa OR "Samoan Islands" OR "Navigator Island" OR "Navigator Islands" OR "Sao Tome" OR
 "Saudi Arabia" OR Senegal OR Serbia OR Montenegro OR Seychelles OR "Sierra Leone" OR Slovenia
 OR "Sri Lanka" OR Ceylon OR "Solomon Islands" OR Somalia OR Sudan OR Suriname OR Surinam
 OR Swaziland OR Syria OR Syrian OR Tajikistan OR Tadjhikistan OR Tadjikistan OR Tadjhik OR
 Tanzania OR Thailand OR Togo OR "Togolese Republic" OR Tonga OR Trinidad OR Tobago OR
 Tunisia OR Turkey OR Turkmenistan OR Turkmen OR Tuvalu OR Uganda OR Ukraine OR Uruguay
 OR USSR OR "Soviet Union" OR "Union of Soviet Socialist Republics" OR Uzbekistan OR Uzbek OR
 Vanuatu OR "New Hebrides" OR Venezuela OR Vietnam OR "Viet Nam" OR "West Bank" OR Yemen
 OR Yugoslavia OR Zambia OR Zimbabwe OR Rhodesia)

Cochrane:

MeSH:

Cost-Benefit Analysis

Keywords:

"cost benefit":ti,ab,kw OR "cost effective":ti,ab,kw OR "cost effectiveness":ti,ab,kw OR "cost
 utility":ti,ab,kw

MeSH:

Emergency Service, Hospital

Emergency Medicine

Trauma Centers

Keywords:

"Emergency medicine":ti,ab,kw OR "Emergency services":ti,ab,kw OR "Emergency
 department":ti,ab,kw OR "Emergency service":ti,ab,kw OR "Emergency departments":ti,ab,kw OR
 "Emergency room":ti,ab,kw OR "Emergency rooms":ti,ab,kw OR "Emergency ward":ti,ab,kw OR
 "Emergency Unit":ti,ab,kw OR "Trauma Center":ti,ab,kw OR "Trauma Centers":ti,ab,kw OR "emergency
 health service":ti,ab,kw OR "emergency health services":ti,ab,kw OR "emergency medical
 services":ti,ab,kw OR "emergency medical service":ti,ab,kw OR "accident & emergency":ti,ab,kw OR
 "accident and emergency":ti,ab,kw OR "A&E":ti,ab,kw OR "A & E":ti,ab,kw

#1 (Africa or Asia or Caribbean or "West Indies" or "South America" or "Latin America" or "Central
 America"):ti,ab,kw

#2 (Afghanistan or Albania or Algeria or Angola or Antigua or Barbuda or Argentina or Armenia or
 Armenian or Aruba or Azerbaijan or Bahrain or Bangladesh or Barbados or Benin or Byelarus
 or Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia
 or Herzegovina or Hercegovina or Botswana or Brasil or Brazil or Bulgaria or "Burkina Faso" or
 "Burkina Fasso" or "Upper Volta" or Burundi or Urundi or Cambodia or "Khmer Republic" or
 Kampuchea or Cameroon or Cameroons or Cameron or Camerons or "Cape Verde" or "Central
 African Republic" or Chad or Chile or China or Colombia or Comoros or "Comoro Islands" or
 Comores or Mayotte or Congo or Zaire or "Costa Rica" or "Cote d'Ivoire" or "Ivory Coast" or
 Croatia or Cuba or Cyprus or Czechoslovakia or "Czech Republic" or Slovakia or "Slovak
 Republic"):ti,ab,kw

#3 (Djibouti or "French Somaliland" or Dominica or "Dominican Republic" or "East Timor" or "East
 Timur" or "Timor Leste" or Ecuador or Egypt or "United Arab Republic" or "El Salvador" or
 Eritrea or Estonia or Ethiopia or Fiji or Gabon or "Gabonese Republic" or Gambia or Gaza or

- Georgia or Georgian or Ghana or "Gold Coast" or Greece or Grenada or Guatemala or Guinea or Guam or Guiana or Guyana or Haiti or Honduras or Hungary or India or Maldives or Indonesia or Iran or Iraq or "Isle of Man" or Jamaica or Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Korea or Kosovo or Kyrgyzstan or Kirghizia or "Kyrgyz Republic" or Kirghiz or Kirgizstan or "Lao PDR" or Laos or Latvia or Lebanon or Lesotho or Basutoland or Liberia or Libya or Lithuania):**ti,ab,kw**
- #4** (Macedonia or Madagascar or "Malagasy Republic" or Malaysia or Malaya or Malay or Sabah or Sarawak or Malawi or Nyasaland or Mali or Malta or "Marshall Islands" or Mauritania or Mauritius or "Agalega Islands" or Mexico or Micronesia or "Middle East" or Moldova or Moldavia or Moldovan or Mongolia or Montenegro or Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or Namibia or Nepal or "Netherlands Antilles" or "New Caledonia" or Nicaragua or Niger or Nigeria or "Northern Mariana Islands" or Oman or Muscat or Pakistan or Palau or Palestine or Panama or Paraguay or Peru or Philippines or Philipines or Phillipines or Phillippines or Poland or Portugal or "Puerto Rico"):**ti,ab,kw**
- #5** (Romania or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or "Saint Kitts" or "St Kitts" or Nevis or "Saint Lucia" or "St Lucia" or "Saint Vincent" or "St Vincent" or Grenadines or Samoa or "Samoan Islands" or "Navigator Island" or "Navigator Islands" or "Sao Tome" or "Saudi Arabia" or Senegal or Serbia or Montenegro or Seychelles or "Sierra Leone" or Slovenia or "Sri Lanka" or Ceylon or "Solomon Islands" or Somalia or Sudan or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadzhikistan or Tadjikistan or Tadjhik or Tanzania or Thailand or Togo or "Togolese Republic" or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Turkmen or Uganda or Ukraine or Uruguay or USSR or "Soviet Union" or "Union of Soviet Socialist Republics" or Uzbekistan or Uzbek or Vanuatu or "New Hebrides" or Venezuela or Vietnam or "Viet Nam" or "West Bank" or Yemen or Yugoslavia or Zambia or Zimbabwe or Rhodesia):**ti,ab,kw**
- #6** (developing or less* NEXT developed or "under developed" or underdeveloped or "middle income" or low* NEXT income or underserved or "under served" or deprived or poor*) NEXT (countr* or nation* or population* or world):**ti,ab,kw**
- #7** (developing or less* NEXT developed or "under developed" or underdeveloped or "middle income" or low* NEXT income) NEXT (economy or economies):**ti,ab,kw**
- #8** low* NEXT (gdp or gnp or "gross domestic" or "gross national"): **ti,ab,kw**
- #9** (low NEAR/3 middle NEAR/3 countr*):**ti,ab,kw**
- #10** (Imic or Imics or "third world" or "lami country" or "lami countries"): **ti,ab,kw**
- #11** ("transitional country" or "transitional countries"): **ti,ab,kw**
- #12** (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11)

Appendix 2: Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Checklist

Consolidated Health Economic Evaluation Reporting Standards – CHEERS Checklist 1

CHEERS Checklist

Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force*, provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: <http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp>

Section/item	Item No	Recommendation	Reported on page No/line 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.	_____
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.	_____
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.	_____
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	_____
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	_____
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	_____
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	_____
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	_____
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	_____
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.	_____
Measurement of effectiveness	11a	<i>Single study-based estimates:</i> Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	_____



	11b	<i>Synthesis-based estimates:</i> Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	
Estimating resources and costs	13a	<i>Single study-based economic evaluation:</i> 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.	
	13b	<i>Model-based economic evaluation:</i> 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.	
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.	
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.	
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	
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.	
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.	
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.	
Characterising uncertainty	20a	<i>Single study-based economic evaluation:</i> 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).	_____
	20b	<i>Model-based economic evaluation:</i> Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	_____
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.	_____
Discussion			
Study findings, limitations, generalisability, 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.	_____
Other			
Source 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.	_____
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.	_____

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: <http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp>

The citation for the CHEERS Task Force Report is:
Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—Explanation and elaboration: A report of the ISPOR health economic evaluations publication guidelines good reporting practices task force. *Value Health* 2013;16:231-50.



Appendix B. University of Cape Town HREC Ethics Review Approval Letter



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



Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: sumayah.aries@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

28 September 2018

HREC REF: 549/2018

Prof L Wallis
Division of Emergency Medicine
F-51
OMB

Dear Prof Wallis

PROJECT TITLE: ASSESSING THE COST-EFFECTIVENESS OF FACILITY-BASED EMERGENCY CARE IN LOW-INCOME COUNTRIES (PhD Candidate - Kalin Werner)

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

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study, subject to approval from local Ugandan research ethics.

Approval is granted for one year until the 30 September 2019.

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

We acknowledge that the student: Kalin Werner will also be involved in this study.

Please quote the HREC REF in all your correspondence.

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

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

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001637

Appendix C. University of Makerere Institutional Review Board Approval Letter



COLLEGE OF HEALTH SCIENCES SCHOOL OF MEDICINE

RESEARCH ETHICS COMMITTEE

February 28th 2019

Ms. Kalin Werner
University of Cape Town

Category of Review

- ☒ Initial review
- ☒ Full board review
- ☐ Expedited review
- ☐ Continuing review
- ☐ Amendment
- ☐ Termination of study
- ☐ SAEs

Dear Ms. Kalin,

Re: Approval of proposal #REC REF 2019-035

“Assessing the cost-effectiveness of facility based emergency care in low-income countries”

Thank you for submitting an application for approval of the above – referenced **proposal**. The committee reviewed it and granted approval for one year, effective February 28th, 2019. Approval will expire on February 27th, 2020.

Continuing Review

In order to continue work on this study (including data analysis) beyond the expiration date, the School of Medicine Research and Ethics Committee must reapprove the protocol after conducting a substantive, meaningful, continuing review. This means that you must submit a continuing report form as a request for continuing review. To best avoid a lapse, you should submit the request six (6) weeks before the lapse date. Please use the forms supplied by our office.

Amendments

During the approval period, if you propose any change to the protocol such as its funding source, recruiting materials, or consent documents, you must seek School of Medicine Research and Ethics Committee approval before implementing it.

Please summarize the proposed change and the rationale for it in a letter to the School of Medicine Research and Ethics Committee. In addition, submit three (3) copies of an updated version of your original protocol application- one showing all proposed changes in bold or ‘track changes,’ and the other without bold or track changes.

Page 1 of 2

Reporting

Other events which must be reported promptly in writing to the School of Medicine Research and Ethics Committee include:

Suspension or termination of the protocol by you or the grantor
Unexpected problems involving risk to participants or others

Adverse events, including unanticipated or anticipated but severe physical harm to participants.

Do not hesitate to contact us if you have any questions. Thank you for your cooperation and commitment to the protection of human subjects in research.

Documents approved for use along with protocol:

- Waiver of consent
- Data collection tools

Please Note:

1. Final approval is to be granted by Uganda National Council for Science and Technology.
2. All the study documents including the revised proposal, Informed Consent Forms, Data Collection Tools and any other study documents should be stamped by the REC.
3. Approval from National Drug Authority should be sought where applicable.
4. Approval for use of research devices should be sought from the Ministry of Health/Uganda National Council for Science and Technology where applicable.
5. Administrative clearance should be sought from the various study sites.
6. This study will be monitored by the School of Medicine Research Ethics Committee to assess for compliance to both national and international research guidelines for protecting the rights and welfare of research participants.
7. The REC should be involved in the dissemination of study findings to the different stakeholders. (This applies to staff research, collaborative research and PhD students).
8. The REC should be informed and involved in the process of study closure.

Yours sincerely,

Assoc. Prof. Ponsiano Ocama
Chairperson School of Medicine Research and Ethics Committee



Appendix D. Ugandan Ministry of Health Approval Letter

Telephone: General Lines: 256 – 417 – 712260
Permanent Secretary's Office: 256 – 417 – 712221
Toll Free 0800100066

E-mail: ps@health.go.ug

Website: www.health.go.ug

ADM. 130/313/05



Ministry of Health
P. O. Box 7272
Plot 6, Lourdel Road,
Wandegeya
KAMPALA
UGANDA

27th September 2018

To whom it may concern

Dear Sir/ Madam,

ASSESSING THE COST-EFFECTIVENESS OF FACILITY-BASED EMERGENCY CARE

The Ministry of Health of Uganda, in collaboration with the World Health Organization, is implementing a simple package of emergency care interventions at regional hospitals throughout Uganda during 2018/19. Alongside implementation, the WHO, together with UCT PhD student Kalin Werner, will be carrying out an evaluation of the package to assess its cost-effectiveness.

The Ministry **approves and authorises collection of pre- and post-intervention data related to the health outcomes at the following regional hospitals:**

- Arua Regional Referral Hospital
- Fort Portal Regional Referral Hospital
- Gulu Regional Referral Hospital
- Hoima Regional Referral Hospital
- Jinja Regional Referral Hospital
- Kabale Regional Referral Hospital
- Kampala Regional Referral Hospital
- Lira Regional Referral Hospital
- Masaka Regional Referral Hospital
- Mbale Regional Referral Hospital
- Mbarara Regional Referral Hospital
- Moroto Regional Referral Hospital
- Mubende Regional Referral Hospital
- Soroti Regional Referral Hospital

Results from the assessment will distinguish the “value for money” of emergency care, guiding the prioritization of funding and developing the capacity of health facilities across Uganda.

Sincerely,

Dr. Otaro Charles
For. **DIRECTOR GENERAL HEALTH SERVICES**

Cc: Permanent Secretary

Signatures Removed on Appendices

Appendix E. Systematic Review Search Strategy

Pubmed

("Cost-Benefit Analysis"[mh] OR "cost benefit" OR "cost effective" OR "cost effectiveness" OR "cost utility")

AND

("Emergency Service, Hospital"[mh] OR "Emergency Medicine"[mh] OR "Emergency medicine"[TW] OR "Emergency services"[TW] OR "Emergency department"[TW] OR "Emergency service"[TW] OR "Emergency departments"[TW] OR "Emergency room"[TW] OR "Emergency rooms"[TW] OR "Emergency ward"[TW] OR "Emergency Unit"[TW] OR "Trauma Centers"[mh] OR "Trauma Center"[TW] OR "Trauma Centers"[TW] OR "emergency health service"[tw] OR "emergency health services"[tw] OR "emergency medical services"[tw] OR "emergency medical service"[tw] OR "accident and emergency"[tw] OR "accident & emergency"[tw] OR "a&e"[tw] OR "A & E"[tw] OR "prehospital"[tw] OR "ambulance"[tw])

AND

#10 Search #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9

#9 Search "developing country"[tiab] OR "developing countries"[tiab] OR "developing nation"[tiab] OR "developing nations"[tiab] OR "developing population"[tiab] OR "developing populations"[tiab] OR "developing world"[tiab] OR "less developed country"[tiab] OR "less developed countries"[tiab] OR "less developed nation"[tiab] OR "less developed nations"[tiab] OR "less developed population"[tiab] OR "less developed populations"[tiab] OR "less developed world"[tiab] OR "lesser developed country"[tiab] OR "lesser developed countries"[tiab] OR "lesser developed nation"[tiab] OR "lesser developed nations"[tiab] OR "lesser developed population"[tiab] OR "lesser developed populations"[tiab] OR "lesser developed world"[tiab] OR "under developed country"[tiab] OR "under developed countries"[tiab] OR "under developed nation"[tiab] OR "under developed nations"[tiab] OR "under developed population"[tiab] OR "under developed populations"[tiab] OR "under developed world"[tiab] OR "underdeveloped country"[tiab] OR "underdeveloped countries"[tiab] OR "underdeveloped nation"[tiab] OR "underdeveloped nations"[tiab] OR "underdeveloped population"[tiab] OR "underdeveloped populations"[tiab] OR "underdeveloped world"[tiab] OR "middle income country"[tiab] OR "middle income countries"[tiab] OR "middle income nation"[tiab] OR "middle income nations"[tiab] OR "middle income population"[tiab] OR "middle income populations"[tiab] OR "low income country"[tiab] OR "low income countries"[tiab] OR "low income nation"[tiab] OR "low income nations"[tiab] OR "low income population"[tiab] OR "low income populations"[tiab] OR "lower income country"[tiab] OR "lower income countries"[tiab] OR "lower income nation"[tiab] OR "lower income nations"[tiab] OR "lower income population"[tiab] OR "lower income populations"[tiab] OR "underserved country"[tiab] OR "underserved countries"[tiab] OR "underserved nation"[tiab] OR "underserved nations"[tiab] OR "underserved population"[tiab] OR "underserved populations"[tiab] OR "underserved world"[tiab] OR "under served country"[tiab] OR "under served countries"[tiab] OR "under served nation"[tiab] OR "under served nations"[tiab] OR "under served population"[tiab] OR "under served populations"[tiab] OR "under served world"[tiab] OR "deprived country"[tiab] OR "deprived countries"[tiab] OR "deprived nation"[tiab] OR "deprived nations"[tiab] OR "deprived population"[tiab] OR "deprived populations"[tiab] OR "deprived world"[tiab] OR "poor country"[tiab] OR "poor countries"[tiab] OR "poor nation"[tiab] OR "poor nations"[tiab] OR "poor population"[tiab] OR "poor populations"[tiab] OR "poor world"[tiab] OR "poorer country"[tiab] OR "poorer countries"[tiab] OR "poorer nation"[tiab] OR "poorer nations"[tiab] OR "poorer population"[tiab] OR "poorer populations"[tiab] OR "poorer world"[tiab] OR "developing economy"[tiab] OR "developing economies"[tiab] OR "less developed economy"[tiab] OR "less developed economies"[tiab] OR "lesser developed economy"[tiab] OR "lesser developed economies"[tiab] OR "under developed economy"[tiab] OR "under developed economies"[tiab] OR "underdeveloped economy"[tiab] OR "underdeveloped economies"[tiab] OR "middle income economy"[tiab] OR "middle income economies"[tiab] OR "low income economy"[tiab] OR "low income economies"[tiab] OR "lower income economy"[tiab] OR "lower income economies"[tiab] OR "low gdp"[tiab] OR "low gnp"[tiab] OR "low gross domestic"[tiab] OR "low gross

national"[tiab] OR "lower gdp"[tiab] OR "lower gnp"[tiab] OR "lower gross domestic"[tiab] OR "lower gross national"[tiab] OR lmic[tiab] OR lmic[tiab] OR "third world"[tiab] OR "lami country"[tiab] OR "lami countries"[tiab] OR "transitional country"[tiab] OR "transitional countries"[tiab]

#8 Search "developing country"[ot] OR "developing countries"[ot] OR "developing nation"[ot] OR "developing nations"[ot] OR "developing population"[ot] OR "developing populations"[ot] OR "developing world"[ot] OR "less developed country"[ot] OR "less developed countries"[ot] OR "less developed nation"[ot] OR "less developed nations"[ot] OR "less developed population"[ot] OR "less developed populations"[ot] OR "less developed world"[ot] OR "lesser developed country"[ot] OR "lesser developed countries"[ot] OR "lesser developed nation"[ot] OR "lesser developed nations"[ot] OR "lesser developed population"[ot] OR "lesser developed populations"[ot] OR "lesser developed world"[ot] OR "under developed country"[ot] OR "under developed countries"[ot] OR "under developed nation"[ot] OR "under developed nations"[ot] OR "under developed population"[ot] OR "under developed populations"[ot] OR "under developed world"[ot] OR "underdeveloped country"[ot] OR "underdeveloped countries"[ot] OR "underdeveloped nation"[ot] OR "underdeveloped nations"[ot] OR "underdeveloped population"[ot] OR "underdeveloped populations"[ot] OR "underdeveloped world"[ot] OR "middle income country"[ot] OR "middle income countries"[ot] OR "middle income nation"[ot] OR "middle income nations"[ot] OR "middle income population"[ot] OR "middle income populations"[ot] OR "low income country"[ot] OR "low income countries"[ot] OR "low income nation"[ot] OR "low income nations"[ot] OR "low income population"[ot] OR "low income populations"[ot] OR "lower income country"[ot] OR "lower income countries"[ot] OR "lower income nation"[ot] OR "lower income nations"[ot] OR "lower income population"[ot] OR "lower income populations"[ot] OR "underserved country"[ot] OR "underserved countries"[ot] OR "underserved nation"[ot] OR "underserved nations"[ot] OR "underserved population"[ot] OR "underserved populations"[ot] OR "underserved world"[ot] OR "under served country"[ot] OR "under served countries"[ot] OR "under served nation"[ot] OR "under served nations"[ot] OR "under served population"[ot] OR "under served populations"[ot] OR "under served world"[ot] OR "deprived country"[ot] OR "deprived countries"[ot] OR "deprived nation"[ot] OR "deprived nations"[ot] OR "deprived population"[ot] OR "deprived populations"[ot] OR "deprived world"[ot] OR "poor country"[ot] OR "poor countries"[ot] OR "poor nation"[ot] OR "poor nations"[ot] OR "poor population"[ot] OR "poor populations"[ot] OR "poor world"[ot] OR "poorer country"[ot] OR "poorer countries"[ot] OR "poorer nation"[ot] OR "poorer nations"[ot] OR "poorer population"[ot] OR "poorer populations"[ot] OR "poorer world"[ot] OR "developing economy"[ot] OR "developing economies"[ot] OR "less developed economy"[ot] OR "less developed economies"[ot] OR "lesser developed economy"[ot] OR "lesser developed economies"[ot] OR "under developed economy"[ot] OR "under developed economies"[ot] OR "underdeveloped economy"[ot] OR "underdeveloped economies"[ot] OR "middle income economy"[ot] OR "middle income economies"[ot] OR "low income economy"[ot] OR "low income economies"[ot] OR "lower income economy"[ot] OR "lower income economies"[ot] OR "low gdp"[ot] OR "low gnp"[ot] OR "low gross domestic"[ot] OR "low gross national"[ot] OR "lower gdp"[ot] OR "lower gnp"[ot] OR "lower gross domestic"[ot] OR "lower gross national"[ot] OR lmic[ot] OR lmic[ot] OR "third world"[ot] OR "lami country"[ot] OR "lami countries"[ot] OR "transitional country"[ot] OR "transitional countries"[ot]

#7 Search Africa[pl] OR Asia[pl] OR Caribbean[pl] OR West Indies[pl] OR South America[pl] OR Latin America[pl] OR Central America[pl] OR Afghanistan[pl] OR Albania[pl] OR Algeria[pl] OR Angola[pl] OR Antigua[pl] OR Barbuda[pl] OR Argentina[pl] OR Armenia[pl] OR Armenian[pl] OR Aruba[pl] OR Azerbaijan[pl] OR Bahrain[pl] OR Bangladesh[pl] OR Barbados[pl] OR Benin[pl] OR Belarus[pl] OR Byelorussian[pl] OR Belarus[pl] OR Belorussian[pl] OR Belorussia[pl] OR Belize[pl] OR Bhutan[pl] OR Bolivia[pl] OR Bosnia[pl] OR Herzegovina[pl] OR Hercegovina[pl] OR Botswana[pl] OR Brasil[pl] OR Brazil[pl] OR Bulgaria[pl] OR Burkina Faso[pl] OR Burkina Fasso[pl] OR Upper Volta[pl] OR Burundi[pl] OR Urundi[pl] OR Cambodia[pl] OR Khmer Republic[pl] OR Kampuchea[pl] OR Cameroon[pl] OR Cameroons[pl] OR Cameron[pl] OR Camerons[pl] OR Cape Verde[pl] OR Central African Republic[pl] OR Chad[pl] OR Chile[pl] OR China[pl] OR Colombia[pl] OR Comoros[pl] OR Comoro Islands[pl] OR Comores[pl] OR Mayotte[pl] OR Congo[pl] OR Zaire[pl] OR Costa Rica[pl] OR Cote d'Ivoire[pl] OR Ivory Coast[pl] OR Croatia[pl] OR Cuba[pl] OR Cyprus[pl] OR Czechoslovakia[pl] OR Czech Republic[pl] OR Slovakia[pl] OR Slovak Republic[pl] OR Djibouti[pl] OR French Somaliland[pl] OR Dominica[pl] OR Dominican Republic[pl] OR East Timor[pl] OR East Timur[pl] OR Timor Leste[pl] OR Ecuador[pl] OR Egypt[pl] OR United Arab Republic[pl] OR El Salvador[pl] OR Eritrea[pl] OR

Estonia[pl] OR Ethiopia[pl] OR Fiji[pl] OR Gabon[pl] OR Gabonese Republic[pl] OR Gambia[pl] OR Gaza[pl] OR Georgia Republic[pl] OR Georgian Republic[pl] OR Ghana[pl] OR Gold Coast[pl] OR Greece[pl] OR Grenada[pl] OR Guatemala[pl] OR Guinea[pl] OR Guam[pl] OR Guiana[pl] OR Guyana[pl] OR Haiti[pl] OR Honduras[pl] OR Hungary[pl] OR India[pl] OR Maldives[pl] OR Indonesia[pl] OR Iran[pl] OR Iraq[pl] OR Isle of Man[pl] OR Jamaica[pl] OR Jordan[pl] OR Kazakhstan[pl] OR Kazakh[pl] OR Kenya[pl] OR Kiribati[pl] OR Korea[pl] OR Kosovo[pl] OR Kyrgyzstan[pl] OR Kirghizia[pl] OR Kyrgyz Republic[pl] OR Kirghiz[pl] OR Kirgizstan[pl] OR "Lao PDR"[pl] OR Laos[pl] OR Latvia[pl] OR Lebanon[pl] OR Lesotho[pl] OR Basutoland[pl] OR Liberia[pl] OR Libya[pl] OR Lithuania[pl]

#6 Search Macedonia[pl] OR Madagascar[pl] OR Malagasy Republic[pl] OR Malaysia[pl] OR Malaya[pl] OR Malay[pl] OR Sabah[pl] OR Sarawak[pl] OR Malawi[pl] OR Nyasaland[pl] OR Mali[pl] OR Malta[pl] OR Marshall Islands[pl] OR Mauritania[pl] OR Mauritius[pl] OR Agalega Islands[pl] OR Mexico[pl] OR Micronesia[pl] OR Middle East[pl] OR Moldova[pl] OR Moldavia[pl] OR Moldovan[pl] OR Mongolia[pl] OR Montenegro[pl] OR Morocco[pl] OR Ifni[pl] OR Mozambique[pl] OR Myanmar[pl] OR Myanma[pl] OR Burma[pl] OR Namibia[pl] OR Nepal[pl] OR Netherlands Antilles[pl] OR New Caledonia[pl] OR Nicaragua[pl] OR Niger[pl] OR Nigeria[pl] OR Northern Mariana Islands[pl] OR Oman[pl] OR Muscat[pl] OR Pakistan[pl] OR Palau[pl] OR Palestine[pl] OR Panama[pl] OR Paraguay[pl] OR Peru[pl] OR Philippines[pl] OR Philipines[pl] OR Phillipines[pl] OR Phillippines[pl] OR Poland[pl] OR Portugal[pl] OR Puerto Rico[pl] OR Romania[pl] OR Rumania[pl] OR Roumania[pl] OR Russia[pl] OR Russian[pl] OR Rwanda[pl] OR Ruanda[pl] OR Saint Kitts[pl] OR St Kitts[pl] OR Nevis[pl] OR Saint Lucia[pl] OR St Lucia[pl] OR Saint Vincent[pl] OR St Vincent[pl] OR Grenadines[pl] OR Samoa[pl] OR Samoan Islands[pl] OR Navigator Island[pl] OR Navigator Islands[pl] OR Sao Tome[pl] OR Saudi Arabia[pl] OR Senegal[pl] OR Serbia[pl] OR Montenegro[pl] OR Seychelles[pl] OR Sierra Leone[pl] OR Slovenia[pl] OR Sri Lanka[pl] OR Ceylon[pl] OR Solomon Islands[pl] OR Somalia[pl] OR South Africa[pl] OR Sudan[pl] OR Suriname[pl] OR Surinam[pl] OR Swaziland[pl] OR Syria[pl] OR Tajikistan[pl] OR Tadjhikistan[pl] OR Tadjikistan[pl] OR Tadjhik[pl] OR Tanzania[pl] OR Thailand[pl] OR Togo[pl] OR Togolese Republic[pl] OR Tonga[pl] OR Trinidad[pl] OR Tobago[pl] OR Tunisia[pl] OR Turkey[pl] OR Turkmenistan[pl] OR Turkmen[pl] OR Uganda[pl] OR Ukraine[pl] OR Uruguay[pl] OR USSR[pl] OR Soviet Union[pl] OR Union of Soviet Socialist Republics[pl] OR Uzbekistan[pl] OR Uzbek OR Vanuatu[pl] OR New Hebrides[pl] OR Venezuela[pl] OR Vietnam[pl] OR Viet Nam[pl] OR West Bank[pl] OR Yemen[pl] OR Yugoslavia[pl] OR Zambia[pl] OR Zimbabwe[pl] OR Rhodesia[pl]

#5 Search Africa[tiab] OR Asia[tiab] OR Caribbean[tiab] OR West Indies[tiab] OR South America[tiab] OR Latin America[tiab] OR Central America[tiab] OR Afghanistan[tiab] OR Albania[tiab] OR Algeria[tiab] OR Angola[tiab] OR Antigua[tiab] OR Barbuda[tiab] OR Argentina[tiab] OR Armenia[tiab] OR Armenian[tiab] OR Aruba[tiab] OR Azerbaijan[tiab] OR Bahrain[tiab] OR Bangladesh[tiab] OR Barbados[tiab] OR Benin[tiab] OR Byelarus[tiab] OR Byelorussian[tiab] OR Belarus[tiab] OR Belorussian[tiab] OR Belorussia[tiab] OR Belize[tiab] OR Bhutan[tiab] OR Bolivia[tiab] OR Bosnia[tiab] OR Herzegovina[tiab] OR Hercegovina[tiab] OR Botswana[tiab] OR Brasil[tiab] OR Brazil[tiab] OR Bulgaria[tiab] OR Burkina Faso[tiab] OR Burkina Fasso[tiab] OR Upper Volta[tiab] OR Burundi[tiab] OR Urundi[tiab] OR Cambodia[tiab] OR Khmer Republic[tiab] OR Kampuchea[tiab] OR Cameroon[tiab] OR Cameroons[tiab] OR Cameron[tiab] OR Camerons[tiab] OR Cape Verde[tiab] OR Central African Republic[tiab] OR Chad[tiab] OR Chile[tiab] OR China[tiab] OR Colombia[tiab] OR Comoros[tiab] OR Comoro Islands[tiab] OR Comores[tiab] OR Mayotte[tiab] OR Congo[tiab] OR Zaire[tiab] OR Costa Rica[tiab] OR Cote d'Ivoire[tiab] OR Ivory Coast[tiab] OR Croatia[tiab] OR Cuba[tiab] OR Cyprus[tiab] OR Czechoslovakia[tiab] OR Czech Republic[tiab] OR Slovakia[tiab] OR Slovak Republic[tiab] OR Djibouti[tiab] OR French Somaliland[tiab] OR Dominica[tiab] OR Dominican Republic[tiab] OR East Timor[tiab] OR East Timur[tiab] OR Timor Leste[tiab] OR Ecuador[tiab] OR Egypt[tiab] OR United Arab Republic[tiab] OR El Salvador[tiab] OR Eritrea[tiab] OR Estonia[tiab] OR Ethiopia[tiab] OR Fiji[tiab] OR Gabon[tiab] OR Gabonese Republic[tiab] OR Gambia[tiab] OR Gaza[tiab] OR Georgia Republic[tiab] OR Georgian Republic[tiab] OR Ghana[tiab] OR Gold Coast[tiab] OR Greece[tiab] OR Grenada[tiab] OR Guatemala[tiab] OR Guinea[tiab] OR Guam[tiab] OR Guiana[tiab] OR Guyana[tiab] OR Haiti[tiab] OR Honduras[tiab] OR Hungary[tiab] OR India[tiab] OR Maldives[tiab] OR Indonesia[tiab] OR Iran[tiab] OR Iraq[tiab] OR Isle of Man[tiab] OR Jamaica[tiab] OR Jordan[tiab] OR Kazakhstan[tiab] OR Kazakh[tiab] OR Kenya[tiab] OR Kiribati[tiab] OR Korea[tiab] OR Kosovo[tiab] OR Kyrgyzstan[tiab] OR Kirghizia[tiab] OR Kyrgyz Republic[tiab] OR Kirghiz[tiab]

OR Kirgizstan[tiab] OR "Lao PDR"[tiab] OR Laos[tiab] OR Latvia[tiab] OR Lebanon[tiab] OR Lesotho[tiab] OR Basutoland[tiab] OR Liberia[tiab] OR Libya[tiab] OR Lithuania[tiab]

#4 Search Macedonia[tiab] OR Madagascar[tiab] OR Malagasy Republic[tiab] OR Malaysia[tiab] OR Malaya[tiab] OR Malay[tiab] OR Sabah[tiab] OR Sarawak[tiab] OR Malawi[tiab] OR Nyasaland[tiab] OR Mali[tiab] OR Malta[tiab] OR Marshall Islands[tiab] OR Mauritania[tiab] OR Mauritius[tiab] OR Agalega Islands[tiab] OR Mexico[tiab] OR Micronesia[tiab] OR Middle East[tiab] OR Moldova[tiab] OR Moldovia[tiab] OR Moldovian[tiab] OR Mongolia[tiab] OR Montenegro[tiab] OR Morocco[tiab] OR Ifni[tiab] OR Mozambique[tiab] OR Myanmar[tiab] OR Myanma[tiab] OR Burma[tiab] OR Namibia[tiab] OR Nepal[tiab] OR Netherlands Antilles[tiab] OR New Caledonia[tiab] OR Nicaragua[tiab] OR Niger[tiab] OR Nigeria[tiab] OR Northern Mariana Islands[tiab] OR Oman[tiab] OR Muscat[tiab] OR Pakistan[tiab] OR Palau[tiab] OR Palestine[tiab] OR Panama[tiab] OR Paraguay[tiab] OR Peru[tiab] OR Philippines[tiab] OR Philipines[tiab] OR Phillipines[tiab] OR Phillippines[tiab] OR Poland[tiab] OR Portugal[tiab] OR Puerto Rico[tiab] OR Romania[tiab] OR Rumania[tiab] OR Roumania[tiab] OR Russia[tiab] OR Russian[tiab] OR Rwanda[tiab] OR Ruanda[tiab] OR Saint Kitts[tiab] OR St Kitts[tiab] OR Nevis[tiab] OR Saint Lucia[tiab] OR St Lucia[tiab] OR Saint Vincent[tiab] OR St Vincent[tiab] OR Grenadines[tiab] OR Samoa[tiab] OR Samoan Islands[tiab] OR Navigator Island[tiab] OR Navigator Islands[tiab] OR Sao Tome[tiab] OR Saudi Arabia[tiab] OR Senegal[tiab] OR Serbia[tiab] OR Montenegro[tiab] OR Seychelles[tiab] OR Sierra Leone[tiab] OR Slovenia[tiab] OR Sri Lanka[tiab] OR Ceylon[tiab] OR Solomon Islands[tiab] OR Somalia[tiab] OR Sudan[tiab] OR Suriname[tiab] OR Surinam[tiab] OR Swaziland[tiab] OR Syria[tiab] OR Tajikistan[tiab] OR Tadjhikistan[tiab] OR Tadjikistan[tiab] OR Tadjhik[tiab] OR Tanzania[tiab] OR Thailand[tiab] OR Togo[tiab] OR Togolese Republic[tiab] OR Tonga[tiab] OR Trinidad[tiab] OR Tobago[tiab] OR Tunisia[tiab] OR Turkey[tiab] OR Turkmenistan[tiab] OR Turkmen[tiab] OR Uganda[tiab] OR Ukraine[tiab] OR Uruguay[tiab] OR USSR[tiab] OR Soviet Union[tiab] OR Union of Soviet Socialist Republics[tiab] OR Uzbekistan[tiab] OR Uzbek OR Vanuatu[tiab] OR New Hebrides[tiab] OR Venezuela[tiab] OR Vietnam[tiab] OR Viet Nam[tiab] OR West Bank[tiab] OR Yemen[tiab] OR Yugoslavia[tiab] OR Zambia[tiab] OR Zimbabwe[tiab] OR Rhodesia[tiab]

#3 Search Africa[ot] OR Asia[ot] OR Caribbean[ot] OR West Indies[ot] OR South America[ot] OR Latin America[ot] OR Central America[ot] OR Afghanistan[ot] OR Albania[ot] OR Algeria[ot] OR Angola[ot] OR Antigua[ot] OR Barbuda[ot] OR Argentina[ot] OR Armenia[ot] OR Armenian[ot] OR Aruba[ot] OR Azerbaijan[ot] OR Bahrain[ot] OR Bangladesh[ot] OR Barbados[ot] OR Benin[ot] OR Byelarus[ot] OR Byelorussian[ot] OR Belarus[ot] OR Belorussian[ot] OR Belorussia[ot] OR Belize[ot] OR Bhutan[ot] OR Bolivia[ot] OR Bosnia[ot] OR Herzegovina[ot] OR Hercegovina[ot] OR Botswana[ot] OR Brasil[ot] OR Brazil[ot] OR Bulgaria[ot] OR Burkina Faso[ot] OR Burkina Fasso[ot] OR Upper Volta[ot] OR Burundi[ot] OR Urundi[ot] OR Cambodia[ot] OR Khmer Republic[ot] OR Kampuchea[ot] OR Cameroon[ot] OR Cameroons[ot] OR Cameron[ot] OR Camerons[ot] OR Cape Verde[ot] OR Central African Republic[ot] OR Chad[ot] OR Chile[ot] OR China[ot] OR Colombia[ot] OR Comoros[ot] OR Comoro Islands[ot] OR Comores[ot] OR Mayotte[ot] OR Congo[ot] OR Zaire[ot] OR Costa Rica[ot] OR Cote d'Ivoire[ot] OR Ivory Coast[ot] OR Croatia[ot] OR Cuba[ot] OR Cyprus[ot] OR Czechoslovakia[ot] OR Czech Republic[ot] OR Slovakia[ot] OR Slovak Republic[ot] OR Djibouti[ot] OR French Somaliland[ot] OR Dominica[ot] OR Dominican Republic[ot] OR East Timor[ot] OR East Timur[ot] OR Timor Leste[ot] OR Ecuador[ot] OR Egypt[ot] OR United Arab Republic[ot] OR El Salvador[ot] OR Eritrea[ot] OR Estonia[ot] OR Ethiopia[ot] OR Fiji[ot] OR Gabon[ot] OR Gabonese Republic[ot] OR Gambia[ot] OR Gaza[ot] OR "Georgia Republic"[ot] OR "Georgian Republic"[ot] OR Ghana[ot] OR Gold Coast[ot] OR Greece[ot] OR Grenada[ot] OR Guatemala[ot] OR Guinea[ot] OR Guam[ot] OR Guiana[ot] OR Guyana[ot] OR Haiti[ot] OR Honduras[ot] OR Hungary[ot] OR India[ot] OR Maldives[ot] OR Indonesia[ot] OR Iran[ot] OR Iraq[ot] OR Isle of Man[ot] OR Jamaica[ot] OR Jordan[ot] OR Kazakhstan[ot] OR Kazakh[ot] OR Kenya[ot] OR Kiribati[ot] OR Korea[ot] OR Kosovo[ot] OR Kyrgyzstan[ot] OR Kirghizia[ot] OR Kyrgyz Republic[ot] OR Kirghiz[ot] OR Kirgizstan[ot] OR "Lao PDR"[ot] OR Laos[ot] OR Latvia[ot] OR Lebanon[ot] OR Lesotho[ot] OR Basutoland[ot] OR Liberia[ot] OR Libya[ot] OR Lithuania[ot]

#2 Search Macedonia[ot] OR Madagascar[ot] OR Malagasy Republic[ot] OR Malaysia[ot] OR Malaya[ot] OR Malay[ot] OR Sabah[ot] OR Sarawak[ot] OR Malawi[ot] OR Nyasaland[ot] OR Mali[ot] OR Malta[ot] OR Marshall Islands[ot] OR Mauritania[ot] OR Mauritius[ot] OR Agalega Islands[ot] OR Mexico[ot] OR Micronesia[ot] OR Middle East[ot] OR Moldova[ot] OR Moldovia[ot] OR Moldovian[ot] OR Mongolia[ot] OR Montenegro[ot] OR

Morocco[ot] OR Ifni[ot] OR Mozambique[ot] OR Myanmar[ot] OR Myanma[ot] OR Burma[ot] OR Namibia[ot] OR Nepal[ot] OR Netherlands Antilles[ot] OR New Caledonia[ot] OR Nicaragua[ot] OR Niger[ot] OR Nigeria[ot] OR Northern Mariana Islands[ot] OR Oman[ot] OR Muscat[ot] OR Pakistan[ot] OR Palau[ot] OR Palestine[ot] OR Panama[ot] OR Paraguay[ot] OR Peru[ot] OR Philippines[ot] OR Philipines[ot] OR Phillipines[ot] OR Phillippines[ot] OR Poland[ot] OR Portugal[ot] OR Puerto Rico[ot] OR Romania[ot] OR Rumania[ot] OR Roumania[ot] OR Russia[ot] OR Russian[ot] OR Rwanda[ot] OR Ruanda[ot] OR Saint Kitts[ot] OR St Kitts[ot] OR Nevis[ot] OR Saint Lucia[ot] OR St Lucia[ot] OR Saint Vincent[ot] OR St Vincent[ot] OR Grenadines[ot] OR Samoa[ot] OR Samoan Islands[ot] OR Navigator Island[ot] OR Navigator Islands[ot] OR Sao Tome[ot] OR Saudi Arabia[ot] OR Senegal[ot] OR Serbia[ot] OR Montenegro[ot] OR Seychelles[ot] OR Sierra Leone[ot] OR Slovenia[ot] OR Sri Lanka[ot] OR Ceylon[ot] OR Solomon Islands[ot] OR Somalia[ot] OR Sudan[ot] OR Suriname[ot] OR Surinam[ot] OR Swaziland[ot] OR Syria[ot] OR Tajikistan[ot] OR Tadjikistan[ot] OR Tadjikistan[ot] OR Tadjhik[ot] OR Tanzania[ot] OR Thailand[ot] OR Togo[ot] OR Togolese Republic[ot] OR Tonga[ot] OR Trinidad[ot] OR Tobago[ot] OR Tunisia[ot] OR Turkey[ot] OR Turkmenistan[ot] OR Turkmen[ot] OR Uganda[ot] OR Ukraine[ot] OR Uruguay[ot] OR USSR[ot] OR Soviet Union[ot] OR Union of Soviet Socialist Republics[ot] OR Uzbekistan[ot] OR Uzbek OR Vanuatu[ot] OR New Hebrides[ot] OR Venezuela[ot] OR Vietnam[ot] OR Viet Nam[ot] OR West Bank[ot] OR Yemen[ot] OR Yugoslavia[ot] OR Zambia[ot] OR Zimbabwe[ot] OR Rhodesia[ot]

#1 Search Developing Countries[Mesh:noexp] OR Africa[Mesh:noexp] OR Africa, Northern[Mesh:noexp] OR Africa South of the Sahara[Mesh:noexp] OR Africa, Central[Mesh:noexp] OR Africa, Eastern[Mesh:noexp] OR Africa, Southern[Mesh:noexp] OR Africa, Western[Mesh:noexp] OR Asia[Mesh:noexp] OR Asia, Central[Mesh:noexp] OR Asia, Southeastern[Mesh:noexp] OR Asia, Western[Mesh:noexp] OR Caribbean Region[Mesh:noexp] OR West Indies[Mesh:noexp] OR South America[Mesh:noexp] OR Latin America[Mesh:noexp] OR Central America[Mesh:noexp] OR Afghanistan[Mesh:noexp] OR Albania[Mesh:noexp] OR Algeria[Mesh:noexp] OR American Samoa[Mesh:noexp] OR Angola[Mesh:noexp] OR "Antigua and Barbuda"[Mesh:noexp] OR Argentina[Mesh:noexp] OR Armenia[Mesh:noexp] OR Azerbaijan[Mesh:noexp] OR Bahrain[Mesh:noexp] OR Bangladesh[Mesh:noexp] OR Barbados[Mesh:noexp] OR Benin[Mesh:noexp] OR Byelarus[Mesh:noexp] OR Belize[Mesh:noexp] OR Bhutan[Mesh:noexp] OR Bolivia[Mesh:noexp] OR Bosnia-Herzegovina[Mesh:noexp] OR Botswana[Mesh:noexp] OR Brazil[Mesh:noexp] OR Bulgaria[Mesh:noexp] OR Burkina Faso[Mesh:noexp] OR Burundi[Mesh:noexp] OR Cambodia[Mesh:noexp] OR Cameroon[Mesh:noexp] OR Cape Verde[Mesh:noexp] OR Central African Republic[Mesh:noexp] OR Chad[Mesh:noexp] OR Chile[Mesh:noexp] OR China[Mesh:noexp] OR Colombia[Mesh:noexp] OR Comoros[Mesh:noexp] OR Congo[Mesh:noexp] OR Costa Rica[Mesh:noexp] OR Cote d'Ivoire[Mesh:noexp] OR Croatia[Mesh:noexp] OR Cuba[Mesh:noexp] OR Cyprus[Mesh:noexp] OR Czechoslovakia[Mesh:noexp] OR Czech Republic[Mesh:noexp] OR Slovakia[Mesh:noexp] OR Djibouti[Mesh:noexp] OR "Democratic Republic of the Congo"[Mesh:noexp] OR Dominica[Mesh:noexp] OR Dominican Republic[Mesh:noexp] OR East Timor[Mesh:noexp] OR Ecuador[Mesh:noexp] OR Egypt[Mesh:noexp] OR El Salvador[Mesh:noexp] OR Eritrea[Mesh:noexp] OR Estonia[Mesh:noexp] OR Ethiopia[Mesh:noexp] OR Fiji[Mesh:noexp] OR Gabon[Mesh:noexp] OR Gambia[Mesh:noexp] OR "Georgia (Republic)"[Mesh:noexp] OR Ghana[Mesh:noexp] OR Greece[Mesh:noexp] OR Grenada[Mesh:noexp] OR Guatemala[Mesh:noexp] OR Guinea[Mesh:noexp] OR Guinea-Bissau[Mesh:noexp] OR Guam[Mesh:noexp] OR Guyana[Mesh:noexp] OR Haiti[Mesh:noexp] OR Honduras[Mesh:noexp] OR Hungary[Mesh:noexp] OR India[Mesh:noexp] OR Indonesia[Mesh:noexp] OR Iran[Mesh:noexp] OR Iraq[Mesh:noexp] OR Jamaica[Mesh:noexp] OR Jordan[Mesh:noexp] OR Kazakhstan[Mesh:noexp] OR Kenya[Mesh:noexp] OR Korea[Mesh:noexp] OR Kosovo[Mesh:noexp] OR Kyrgyzstan[Mesh:noexp] OR Laos[Mesh:noexp] OR Latvia[Mesh:noexp] OR Lebanon[Mesh:noexp] OR Lesotho[Mesh:noexp] OR Liberia[Mesh:noexp] OR Libya[Mesh:noexp] OR Lithuania[Mesh:noexp] OR Macedonia[Mesh:noexp] OR Madagascar[Mesh:noexp] OR Malaysia[Mesh:noexp] OR Malawi[Mesh:noexp] OR Mali[Mesh:noexp] OR Malta[Mesh:noexp] OR Mauritania[Mesh:noexp] OR Mauritius[Mesh:noexp] OR Mexico[Mesh:noexp] OR Micronesia[Mesh:noexp] OR Middle East[Mesh:noexp] OR Moldova[Mesh:noexp] OR Mongolia[Mesh:noexp] OR Montenegro[Mesh:noexp] OR Morocco[Mesh:noexp] OR Mozambique[Mesh:noexp] OR Myanmar[Mesh:noexp] OR Namibia[Mesh:noexp] OR Nepal[Mesh:noexp] OR Netherlands Antilles[Mesh:noexp] OR New Caledonia[Mesh:noexp] OR Nicaragua[Mesh:noexp] OR Niger[Mesh:noexp] OR Nigeria[Mesh:noexp] OR

Oman[Mesh:noexp] OR Pakistan[Mesh:noexp] OR Palau[Mesh:noexp] OR Panama[Mesh:noexp] OR Papua New Guinea[Mesh:noexp] OR Paraguay[Mesh:noexp] OR Peru[Mesh:noexp] OR Philippines[Mesh:noexp] OR Poland[Mesh:noexp] OR Portugal[Mesh:noexp] OR Puerto Rico[Mesh:noexp] OR Romania[Mesh:noexp] OR Russia[Mesh:noexp] OR "Russia (Pre-1917)"[Mesh:noexp] OR Rwanda[Mesh:noexp] OR "Saint Kitts and Nevis"[Mesh:noexp] OR Saint Lucia[Mesh:noexp] OR "Saint Vincent and the Grenadines"[Mesh:noexp] OR Samoa[Mesh:noexp] OR Saudi Arabia[Mesh:noexp] OR Senegal[Mesh:noexp] OR Serbia[Mesh:noexp] OR Montenegro[Mesh:noexp] OR Seychelles[Mesh:noexp] OR Sierra Leone[Mesh:noexp] OR Slovenia[Mesh:noexp] OR Sri Lanka[Mesh:noexp] OR Somalia[Mesh:noexp] OR South Africa[Mesh:noexp] OR Sudan[Mesh:noexp] OR Suriname[Mesh:noexp] OR Swaziland[Mesh:noexp] OR Syria[Mesh:noexp] OR Tajikistan[Mesh:noexp] OR Tanzania[Mesh:noexp] OR Thailand[Mesh:noexp] OR Togo[Mesh:noexp] OR Tonga[Mesh:noexp] OR "Trinidad and Tobago"[Mesh:noexp] OR Tunisia[Mesh:noexp] OR Turkey[Mesh:noexp] OR Turkmenistan[Mesh:noexp] OR Uganda[Mesh:noexp] OR Ukraine[Mesh:noexp] OR Uruguay[Mesh:noexp] OR USSR[Mesh:noexp] OR Uzbekistan[Mesh:noexp] OR Vanuatu[Mesh:noexp] OR Venezuela[Mesh:noexp] OR Vietnam[Mesh:noexp] OR Yemen[Mesh:noexp] OR Yugoslavia[Mesh:noexp] OR Zambia[Mesh:noexp] OR Zimbabwe[Mesh:noexp]

Embase:

('cost benefit analysis'/exp OR 'cost benefit' OR 'cost effective' OR 'cost effectiveness' OR 'cost utility') AND ('emergency health service'/exp OR 'emergency medicine'/exp OR 'emergency ward'/exp OR 'emergency health service' OR 'emergency medicine':ab,ti,de,au,lnk OR 'emergency services' OR 'emergency department':ab,ti,de,au,lnk OR 'emergency service' OR 'emergency departments' OR 'emergency room' OR 'emergency rooms' OR 'emergency ward' OR 'emergency unit' OR 'trauma centers' OR 'trauma center' OR 'emergency health services' OR 'emergency medical services' OR 'emergency medical service' OR 'accident & emergency' OR 'accident and emergency' OR 'A&E' OR 'A & E')

AND

Combine: (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)

#1 Search 'developing country':ab,ti OR 'developing countries':ab,ti OR 'developing nation':ab,ti OR 'developing nations':ab,ti OR 'developing population':ab,ti OR 'developing populations':ab,ti OR 'developing world':ab,ti OR 'less developed country':ab,ti OR 'less developed countries':ab,ti OR 'less developed nation':ab,ti OR 'less developed nations':ab,ti OR 'less developed population':ab,ti OR 'less developed populations':ab,ti OR 'less developed world':ab,ti OR 'lesser developed country':ab,ti OR 'lesser developed countries':ab,ti OR 'lesser developed nation':ab,ti OR 'lesser developed nations':ab,ti OR 'lesser developed population':ab,ti OR 'lesser developed populations':ab,ti OR 'lesser developed world':ab,ti OR 'under developed country':ab,ti OR 'under developed countries':ab,ti OR 'under developed nation':ab,ti OR 'under developed nations':ab,ti OR 'under developed population':ab,ti OR 'under developed populations':ab,ti OR 'under developed world':ab,ti OR 'underdeveloped country':ab,ti OR 'underdeveloped countries':ab,ti OR 'underdeveloped nation':ab,ti OR 'underdeveloped nations':ab,ti OR 'underdeveloped population':ab,ti OR 'underdeveloped populations':ab,ti OR 'underdeveloped world':ab,ti OR 'middle income country':ab,ti OR 'middle income countries':ab,ti OR 'middle income nation':ab,ti OR 'middle income nations':ab,ti OR 'middle income population':ab,ti OR 'middle income populations':ab,ti OR 'low income country':ab,ti OR 'low income countries':ab,ti OR 'low income nation':ab,ti OR 'low income nations':ab,ti OR 'low income population':ab,ti OR 'low income populations':ab,ti OR 'lower income country':ab,ti OR 'lower income countries':ab,ti OR 'lower income nation':ab,ti OR 'lower income nations':ab,ti OR 'lower income population':ab,ti OR 'lower income populations':ab,ti OR 'underserved country':ab,ti OR 'underserved countries':ab,ti OR 'underserved nation':ab,ti OR 'underserved nations':ab,ti OR 'underserved population':ab,ti OR 'underserved populations':ab,ti OR 'underserved world':ab,ti OR 'under served country':ab,ti OR 'under served countries':ab,ti OR 'under served nation':ab,ti OR 'under served nations':ab,ti OR 'under served population':ab,ti OR 'under served populations':ab,ti OR 'under served world':ab,ti OR 'deprived country':ab,ti OR 'deprived countries':ab,ti OR 'deprived nation':ab,ti OR 'deprived nations':ab,ti OR 'deprived population':ab,ti OR 'deprived populations':ab,ti OR 'deprived world':ab,ti OR 'poor country':ab,ti OR 'poor countries':ab,ti OR 'poor nation':ab,ti OR 'poor nations':ab,ti OR 'poor population':ab,ti OR 'poor populations':ab,ti OR 'poor world':ab,ti OR 'poorer country':ab,ti OR 'poorer countries':ab,ti OR 'poorer nation':ab,ti OR 'poorer nations':ab,ti OR 'poorer population':ab,ti OR 'poorer populations':ab,ti OR 'poorer world':ab,ti OR 'developing economy':ab,ti OR

'developing economies':ab,ti OR 'less developed economy':ab,ti OR 'less developed economies':ab,ti OR 'lesser developed economy':ab,ti OR 'lesser developed economies':ab,ti OR 'under developed economy':ab,ti OR 'under developed economies':ab,ti OR 'underdeveloped economy':ab,ti OR 'underdeveloped economies':ab,ti OR 'middle income economy':ab,ti OR 'middle income economies':ab,ti OR 'low income economy':ab,ti OR 'low income economies':ab,ti OR 'lower income economy':ab,ti OR 'lower income economies':ab,ti OR 'low gdp':ab,ti OR 'low gnp':ab,ti OR 'low gross domestic':ab,ti OR 'low gross national':ab,ti OR 'lower gdp':ab,ti OR 'lower gnp':ab,ti OR 'lower gross domestic':ab,ti OR 'lower gross national':ab,ti OR 'lami':ab,ti OR 'lami countries':ab,ti OR 'lami countries':ab,ti OR 'third world':ab,ti OR 'lami country':ab,ti OR 'lami countries':ab,ti OR 'transitional country':ab,ti OR 'transitional countries':ab,ti

#2 Search Africa:ti,ab OR Asia:ti,ab OR Caribbean:ti,ab OR 'West Indies':ti,ab OR 'South America':ti,ab OR 'Latin America':ti,ab OR 'Central America':ti,ab OR 'atlantic islands':ab,ti OR 'commonwealth of independent states':ab,ti OR 'pacific islands':ab,ti OR 'indian ocean islands':ab,ti OR 'eastern europe':ab,ti

#3 Search Afghanistan:ti,ab OR Albania:ti,ab OR Algeria:ti,ab OR Angola:ti,ab OR Antigua:ti,ab OR Barbuda:ti,ab OR Argentina:ti,ab OR Armenia:ti,ab OR Armenian:ti,ab OR Aruba:ti,ab OR Azerbaijan:ti,ab OR Bahrain:ti,ab OR Bangladesh:ti,ab OR Barbados:ti,ab OR Benin:ti,ab OR Byelarus:ti,ab OR Byelorussian:ti,ab OR Belarus:ti,ab OR Belorussian:ti,ab OR Belorussia:ti,ab OR Belize:ti,ab OR Bhutan:ti,ab OR Bolivia:ti,ab OR Bosnia:ti,ab OR Herzegovina:ti,ab OR Hercegovina:ti,ab OR Botswana:ti,ab OR Brasil:ti,ab OR Brazil:ti,ab OR Bulgaria:ti,ab OR 'Burkina Faso':ti,ab OR 'Burkina Fasso':ti,ab OR 'Upper Volta':ti,ab OR Burundi:ti,ab OR Urundi:ti,ab OR Cambodia:ti,ab OR 'Khmer Republic':ti,ab OR Kampuchea:ti,ab OR Cameroon:ti,ab OR Cameroons:ti,ab OR Cameron:ti,ab OR Camerons:ti,ab OR 'Cape Verde':ti,ab OR 'Central African Republic':ti,ab OR Chad:ti,ab OR Chile:ti,ab OR China:ti,ab OR Colombia:ti,ab OR Comoros:ti,ab OR 'Comoro Islands':ti,ab OR Comores:ti,ab OR Mayotte:ti,ab OR Congo:ti,ab OR Zaire:ti,ab OR 'Costa Rica':ti,ab OR 'Cote d'Ivoire' OR 'Ivory Coast':ti,ab OR Croatia:ti,ab OR Cuba:ti,ab OR Cyprus:ti,ab OR Czechoslovakia:ti,ab OR 'Czech Republic':ti,ab OR Slovakia:ti,ab OR 'Slovak Republic':ti,ab OR Djibouti:ti,ab OR 'French Somaliland':ti,ab OR Dominica:ti,ab OR 'Dominican Republic':ti,ab OR 'East Timor':ti,ab OR 'East Timur':ti,ab OR 'Timor Leste':ti,ab OR Ecuador:ti,ab OR Egypt:ti,ab OR 'United Arab Republic':ti,ab OR El Salvador:ti,ab OR Eritrea:ti,ab OR Estonia:ti,ab OR Ethiopia:ti,ab OR Fiji:ti,ab OR Gabon:ti,ab OR 'Gabonese Republic':ti,ab OR Gambia:ti,ab OR Gaza:ti,ab OR 'Georgia Republic':ti,ab OR 'Georgian Republic':ti,ab OR Ghana:ti,ab OR 'Gold Coast':ti,ab OR Greece:ti,ab OR Grenada:ti,ab OR Guatemala:ti,ab OR Guinea:ti,ab OR Guam:ti,ab OR Guiana:ti,ab OR Guyana:ti,ab OR Haiti:ti,ab OR Honduras:ti,ab OR Hungary:ti,ab OR India:ti,ab OR Maldives:ti,ab OR Indonesia:ti,ab OR Iran:ti,ab OR Iraq:ti,ab OR 'Isle of Man':ti,ab OR Jamaica:ti,ab OR Jordan:ti,ab OR Kazakhstan:ti,ab OR Kazakh:ti,ab OR Kenya:ti,ab OR Kiribati:ti,ab OR Korea:ti,ab OR Kosovo:ti,ab OR Kyrgyzstan:ti,ab OR Kirghizia:ti,ab OR 'Kyrgyz Republic':ti,ab OR Kirghiz:ti,ab OR Kirgizstan:ti,ab OR 'Lao PDR':ti,ab OR Laos:ti,ab OR Latvia:ti,ab OR Lebanon:ti,ab OR Lesotho:ti,ab OR Basutoland:ti,ab OR Liberia:ti,ab OR Libya:ti,ab OR Lithuania:ti,ab

#4 Search Macedonia:ti,ab OR Madagascar:ti,ab OR 'Malagasy Republic':ti,ab OR Malaysia:ti,ab OR Malaya:ti,ab OR Malay:ti,ab OR Sabah:ti,ab OR Sarawak:ti,ab OR Malawi:ti,ab OR Nyasaland:ti,ab OR Mali:ti,ab OR Malta:ti,ab OR 'Marshall Islands':ti,ab OR Mauritania:ti,ab OR Mauritius:ti,ab OR melanesia:ab,ti OR 'Agalega Islands':ti,ab OR Mexico:ti,ab OR Micronesia:ti,ab OR 'Middle East':ti,ab OR Moldova:ti,ab OR Moldovia:ti,ab OR Moldovian:ti,ab OR Mongolia:ti,ab OR Montenegro:ti,ab OR Morocco:ti,ab OR Ifni:ti,ab OR Mozambique:ti,ab OR Myanmar:ti,ab OR Myanma:ti,ab OR Burma:ti,ab OR Namibia:ti,ab OR Nepal:ti,ab OR 'Netherlands Antilles':ti,ab OR 'New Caledonia':ti,ab OR Nicaragua:ti,ab OR Niger:ti,ab OR Nigeria:ti,ab OR 'Northern Mariana Islands':ti,ab OR Oman:ti,ab OR Muscat:ti,ab OR Pakistan:ti,ab OR Palau:ti,ab OR Palestine:ti,ab OR Panama:ti,ab OR Paraguay:ti,ab OR Peru:ti,ab OR Philippines:ti,ab OR Philipines:ti,ab OR Phillipines:ti,ab OR Phillipines:ti,ab OR Poland:ti,ab OR Portugal:ti,ab OR 'Puerto Rico':ti,ab OR Romania:ti,ab OR Rumania:ti,ab OR Roumania:ti,ab OR Russia:ti,ab OR Russian:ti,ab OR Rwanda:ti,ab OR Ruanda:ti,ab OR 'Saint Kitts':ti,ab OR 'St Kitts':ti,ab OR Nevis:ti,ab OR 'Saint Lucia':ti,ab OR 'St Lucia':ti,ab OR 'Saint Vincent':ti,ab OR 'St Vincent':ti,ab OR Grenadines:ti,ab OR Samoa:ti,ab OR 'Samoa Islands':ti,ab OR 'Navigator Island':ti,ab OR 'Navigator Islands':ti,ab OR 'Sao Tome':ti,ab OR 'Saudi Arabia':ti,ab OR Senegal:ti,ab OR Serbia:ti,ab OR Montenegro:ti,ab OR Seychelles:ti,ab OR 'Sierra Leone':ti,ab OR Slovenia:ti,ab OR 'Sri Lanka':ti,ab OR Ceylon:ti,ab OR 'Solomon Islands':ti,ab OR Somalia:ti,ab OR Sudan:ti,ab OR Suriname:ti,ab OR Surinam:ti,ab OR Swaziland:ti,ab OR Syria:ti,ab OR Syrian:ti,ab OR Tajikistan:ti,ab OR Tadjikistan:ti,ab OR Tadjikistan:ti,ab OR Tadjik:ti,ab OR Tanzania:ti,ab OR Thailand:ti,ab OR Togo:ti,ab OR 'Togolese Republic':ti,ab OR Tonga:ti,ab OR Trinidad:ti,ab

OR Tobago:ti,ab OR Tunisia:ti,ab OR Turkey:ti,ab OR Turkmenistan:ti,ab OR Turkmen:ti,ab OR Tuvalu:ti,ab OR Uganda:ti,ab OR Ukraine:ti,ab OR Uruguay:ti,ab OR USSR:ti,ab OR 'Soviet Union':ti,ab OR 'Union of Soviet Socialist Republics':ti,ab OR Uzbekistan:ti,ab OR Uzbek OR Vanuatu:ti,ab OR 'New Hebrides':ti,ab OR Venezuela:ti,ab OR Vietnam:ti,ab OR 'Viet Nam':ti,ab OR 'West Bank':ti,ab OR Yemen:ti,ab OR Yugoslavia:ti,ab OR Zambia:ti,ab OR Zimbabwe:ti,ab OR Rhodesia:ti,ab

#5 Search: 'developing country'/exp OR 'Africa'/de OR 'Africa south of the Sahara'/de OR 'North Africa'/de OR 'Central Africa'/de OR 'Asia'/de OR 'South Asia'/de OR 'Southeast Asia'/de OR 'South America'/de OR 'Central America'/de OR 'South and Central America'/de OR 'Atlantic islands'/de OR 'Caribbean Islands'/de OR 'Pacific islands'/de OR 'Indian Ocean'/de OR 'Eastern Europe'/de

#6 Search Afghanistan/exp OR Albania/exp OR Algeria/exp OR 'American Samoa'/exp OR Angola/exp OR 'Antigua and Barbuda'/exp OR Argentina/exp OR Armenia/exp OR Azerbaijan/exp OR Bahrain/exp OR Bangladesh/exp OR Barbados/exp OR Benin/exp OR 'Belarus'/exp OR 'Baltic States'/exp OR Belize/exp OR Bhutan/exp OR Bolivia/exp OR 'Bosnia and Herzegovina'/exp OR Botswana/exp OR Brazil/exp OR Bulgaria/exp OR 'Burkina Faso'/exp OR Burundi/exp OR Cambodia/exp OR Cameroon/exp OR 'Cape Verde'/exp OR 'Central African Republic'/exp OR Chad/exp OR Chile/exp OR China/exp OR Colombia/exp OR Comoros/exp OR Congo/exp OR 'Costa Rica'/exp OR 'Cote d'Ivoire'/exp OR Croatia/exp OR Cuba/exp OR Cyprus/exp OR Czechoslovakia/exp OR 'Czech Republic'/exp OR Slovakia/exp OR Djibouti/exp OR 'Democratic Republic Congo'/exp OR Dominica/exp OR 'Dominican Republic'/exp OR 'Timor-Leste'/exp OR Ecuador/exp OR Egypt/exp OR 'El Salvador'/exp OR Eritrea/exp OR Estonia/exp OR Ethiopia/exp OR 'French Guiana'/exp OR Fiji/exp OR Gabon/exp OR Gambia/exp OR 'Georgia (Republic) '/exp OR Ghana/exp OR Greece/exp OR Grenada/exp OR Guatemala/exp OR Guinea/exp OR Guinea-Bissau/exp OR Guam/exp OR Guyana/exp OR Haiti/exp OR Honduras/exp OR Hungary/exp OR India/exp OR Indonesia/exp OR Iran/exp OR Iraq/exp OR Jamaica/exp OR Jordan/exp OR Kazakhstan/exp OR Kenya/exp OR Korea/exp OR Kyrgyzstan/exp OR Laos/exp OR Latvia/exp OR Lebanon/exp OR Lesotho/exp OR Liberia/exp OR 'Libyan Arab Jamahiriya'/exp OR Lithuania/exp OR 'Macedonia (republic)'/exp OR Madagascar/exp OR Malaysia/exp OR Malawi/exp OR Mali/exp OR Malta/exp OR Mauritania/exp OR Mauritius/exp OR "Melanesia"/exp

#7 Search Mexico/exp OR 'Federated States of Micronesia'/exp OR 'Middle East'/de OR Moldova/exp OR Mongolia/exp OR Montenegro/exp OR Morocco/exp OR Mozambique/exp OR Myanmar/exp OR Namibia/exp OR Nepal/exp OR 'Netherlands Antilles'/exp OR 'New Caledonia'/exp OR Nicaragua/exp OR Niger/exp OR Nigeria/exp OR 'North Korea'/exp OR Oman/exp OR Pakistan/exp OR Palau/exp OR Panama/exp OR 'Papua New Guinea'/exp OR Paraguay/exp OR Peru/exp OR Philippines/exp OR Poland/exp OR Portugal/exp OR 'Puerto Rico'/exp OR Romania/exp OR 'Russian Federation'/exp OR Rwanda/exp OR 'Saint Kitts and Nevis'/exp OR 'Saint Lucia'/exp OR 'Saint Vincent and the Grenadines'/exp OR 'Samoa Islands'/exp OR Samoa/exp OR 'Saudi Arabia'/exp OR Senegal/exp OR Serbia/exp OR 'Montenegro (republic)'/exp OR Seychelles/exp OR 'Sierra Leone'/exp OR Slovenia/exp OR 'Sri Lanka'/exp OR Somalia/exp OR 'South Korea'/exp OR 'South Africa'/exp OR Sudan/exp OR Suriname/exp OR Swaziland/exp OR 'Syrian Arab Republic'/exp OR Tajikistan/exp OR Tanzania/exp OR Thailand/exp OR Togo/exp OR Tonga/exp OR 'Trinidad and Tobago'/exp OR Tunisia/exp OR 'Turkey (republic)'/exp OR Turkmenistan/exp OR Uganda/exp OR Ukraine/exp OR Uruguay/exp OR USSR/exp OR Uzbekistan/exp OR Vanuatu/exp OR Venezuela/exp OR 'Viet Nam'/exp OR Yemen/exp OR Yugoslavia/exp OR 'Yugoslavia (pre-1992)'/exp OR Zambia/exp OR Zimbabwe/exp

Scopus:

TITLE-ABS-KEY({cost benefit} OR {cost effectiveness} OR {cost effective} OR {cost utility}) AND
TITLE-ABS-KEY({Emergency medicine} OR {Emergency services} OR {Emergency department} OR {Emergency service} OR {Emergency departments} OR {Emergency room} OR {Emergency rooms} OR {Emergency ward} OR {Emergency Unit} OR {Trauma Center} OR {Trauma Centers} OR {emergency health service} OR {emergency health services} OR {emergency medical services} OR {emergency medical service} OR {accident and emergency} OR {accident & emergency} OR {a&e} OR {A & E})

AND

#1 Search TITLE-ABS-KEY({developing country} OR {developing countries} OR {developing nation} OR {developing nations} OR {developing population} OR {developing populations} OR {developing world} OR

{less developed country} OR {less developed countries} OR {less developed nation} OR {less developed nations} OR {less developed population} OR {less developed populations} OR {less developed world} OR {lesser developed country} OR {lesser developed countries} OR {lesser developed nation} OR {lesser developed nations} OR {lesser developed population} OR {lesser developed populations} OR {lesser developed world} OR {under developed country} OR {under developed countries} OR {under developed nation} OR {under developed nations} OR {under developed population} OR {under developed populations} OR {under developed world} OR {underdeveloped country} OR {underdeveloped countries} OR {underdeveloped nation} OR {underdeveloped nations} OR {underdeveloped population} OR {underdeveloped populations} OR {underdeveloped world} OR {middle income country} OR {middle income countries} OR {middle income nation} OR {middle income nations} OR {middle income population} OR {middle income populations} OR {low income country} OR {low income countries} OR {low income nation} OR {low income nations} OR {low income population} OR {low income populations} OR {lower income country} OR {lower income countries} OR {lower income nation} OR {lower income nations} OR {lower income population} OR {lower income populations} OR {underserved country} OR {underserved countries} OR {underserved nation} OR {underserved nations} OR {underserved population} OR {underserved populations} OR {underserved world} OR {under served country} OR {under served countries} OR {under served nation} OR {under served nations} OR {under served population} OR {under served populations} OR {under served world} OR {deprived country} OR {deprived countries} OR {deprived nation} OR {deprived nations} OR {deprived population} OR {deprived populations} OR {deprived world})

#2 Search TITLE-ABS-KEY({poor country} OR {poor countries} OR {poor nation} OR {poor nations} OR {poor population} OR {poor populations} OR {poor world} OR {poorer country} OR {poorer countries} OR {poorer nation} OR {poorer nations} OR {poorer population} OR {poorer populations} OR {poorer world} OR {developing economy} OR {developing economies} OR {less developed economy} OR {less developed economies} OR {lesser developed economy} OR {lesser developed economies} OR {under developed economy} OR {under developed economies} OR {underdeveloped economy} OR {underdeveloped economies} OR {middle income economy} OR {middle income economies} OR {low income economy} OR {low income economies} OR {lower income economy} OR {lower income economies} OR {low gdp} OR {low gnp} OR {low gross domestic} OR {low gross national} OR {lower gdp} OR {lower gnp} OR {lower gross domestic} OR {lower gross national} OR lmic OR lmics OR {third world} OR {lami country} OR {lami countries} OR {transitional country} OR {transitional countries})

#3 Search TITLE-ABS-KEY(Africa OR Asia OR Caribbean OR {West Indies} OR {South America} OR {Latin America} OR {Central America} OR {Atlantic Islands} OR {Commonwealth of Independent States} OR {Pacific Islands} OR {Indian Ocean Islands} OR {Eastern Europe} OR Afghanistan OR Albania OR Algeria OR Angola OR Antigua OR Barbuda OR Argentina OR Armenia OR Armenian OR Aruba OR Azerbaijan OR Bahrain OR Bangladesh OR Barbados OR Benin OR Byelarus OR Byelorussian OR Belarus OR Belorussian OR Belorussia OR Belize OR Bhutan OR Bolivia OR Bosnia OR Herzegovina OR Hercegovina OR Botswana OR Brasil OR Brazil OR Bulgaria OR {Burkina Faso} OR {Burkina Fasso} OR {Upper Volta} OR Burundi OR Urundi OR Cambodia OR {Khmer Republic} OR Kampuchea OR Cameroon OR Cameroons OR Cameron OR Camerons OR {Cape Verde} OR {Central African Republic} OR Chad OR Chile OR China OR Colombia OR Comoros OR {Comoro Islands} OR Comores OR Mayotte OR Congo OR Zaire OR {Costa Rica} OR {Cote d'Ivoire} OR {Ivory Coast} OR Croatia OR Cuba OR Cyprus OR Czechoslovakia OR {Czech Republic} OR Slovakia OR {Slovak Republic} OR Djibouti OR {French Somaliland} OR Dominica OR {Dominican Republic} OR {East Timor} OR {East Timur} OR {Timor Leste} OR Ecuador OR Egypt OR {United Arab Republic} OR {El Salvador} OR Eritrea OR Estonia OR Ethiopia OR Fiji OR Gabon OR {Gabonese Republic} OR Gambia OR Gaza OR {Georgia Republic} OR {Georgian Republic} OR Ghana OR {Gold Coast} OR Greece OR Grenada OR Guatemala OR Guinea OR Guam OR Guiana OR Guyana OR Haiti OR Honduras OR Hungary OR India OR Maldives OR Indonesia OR Iran OR Iraq OR {Isle of Man} OR Jamaica OR Jordan OR Kazakhstan OR Kazakh OR Kenya OR Kiribati OR Korea OR Kosovo OR Kyrgyzstan OR Kirghizia OR {Kyrgyz Republic} OR Kirghiz OR Kirgizstan OR {Lao PDR} OR Laos OR Latvia OR Lebanon OR Lesotho OR Basutoland OR Liberia OR Libya OR Lithuania)

#4 Search TITLE-ABS-KEY(Macedonia OR Madagascar OR {Malagasy Republic} OR Malaysia OR Malaya OR Malay OR Sabah OR Sarawak OR Malawi OR Nyasaland OR Mali OR Malta OR {Marshall Islands} OR

Mauritania OR Mauritius OR {Agalega Islands} OR {Melanesia} OR Mexico OR Micronesia OR {Middle East} OR Moldova OR Moldavia OR Moldovan OR Mongolia OR Montenegro OR Morocco OR Ifni OR Mozambique OR Myanmar OR Myanma OR Burma OR Namibia OR Nepal OR {Netherlands Antilles} OR {New Caledonia} OR Nicaragua OR Niger OR Nigeria OR {Northern Mariana Islands} OR Oman OR Muscat OR Pakistan OR Palau OR Palestine OR Panama OR Paraguay OR Peru OR Philippines OR Philipines OR Phillipines OR Phillippines OR Poland OR Portugal OR {Puerto Rico} OR Romania OR Rumania OR Roumania OR Russia OR Russian OR Rwanda OR Ruanda OR {Saint Kitts} OR {St Kitts} OR Nevis OR {Saint Lucia} OR {St Lucia} OR {Saint Vincent} OR {St Vincent} OR Grenadines OR Samoa OR {Samoan Islands} OR {Navigator Island} OR {Navigator Islands} OR {Sao Tome} OR {Saudi Arabia} OR Senegal OR Serbia OR Montenegro OR Seychelles OR {Sierra Leone} OR Slovenia OR {Sri Lanka} OR Ceylon OR {Solomon Islands} OR Somalia OR Sudan OR Suriname OR Surinam OR Swaziland OR Syria OR Syrian OR Tajikistan OR Tadjikistan OR Tadjikistan OR Tadjhik OR Tanzania OR Thailand OR Togo OR {Togolese Republic} OR Tonga OR Trinidad OR Tobago OR Tunisia OR Turkey OR Turkmenistan OR Turkmen OR Tuvalu OR Uganda OR Ukraine OR Uruguay OR USSR OR {Soviet Union} OR {Union of Soviet Socialist Republics} OR Uzbekistan OR Uzbek OR Vanuatu OR {New Hebrides} OR Venezuela OR Vietnam OR {Viet Nam} OR {West Bank} OR Yemen OR Yugoslavia OR Zambia OR Zimbabwe OR Rhodesia)

Web of Science:

TS=("cost benefit" OR "cost effectiveness" OR "cost effective" OR "cost utility") AND

TS=("Emergency medicine" OR "Emergency services" OR "Emergency department" OR "Emergency service" OR "Emergency departments" OR "Emergency room" OR "Emergency rooms" OR "Emergency ward" OR "Emergency Unit" OR "Trauma Center" OR "Trauma Centers" OR "emergency health service" OR "emergency health services" OR "emergency medical services" OR "emergency medical service" OR "accident and emergency" OR "accident & emergency" OR "a&e" OR "A & E")

AND

Combine: (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)

#1 Search TS=("developing country" OR "developing countries" OR "developing nation" OR "developing nations" OR "developing population" OR "developing populations" OR "developing world" OR "less developed country" OR "less developed countries" OR "less developed nation" OR "less developed nations" OR "less developed population" OR "less developed populations" OR "less developed world" OR "lesser developed country" OR "lesser developed countries" OR "lesser developed nation" OR "lesser developed nations" OR "lesser developed population" OR "lesser developed populations" OR "lesser developed world" OR "under developed country" OR "under developed countries" OR "under developed nation" OR "under developed nations" OR "under developed population" OR "under developed populations" OR "under developed world" OR "underdeveloped country" OR "underdeveloped countries" OR "underdeveloped nation" OR "underdeveloped nations" OR "underdeveloped population" OR "underdeveloped populations" OR "underdeveloped world" OR "middle income country" OR "middle income countries" OR "middle income nation" OR "middle income nations" OR "middle income population" OR "middle income populations" OR "low income country" OR "low income countries" OR "low income nation" OR "low income nations" OR "low income population" OR "low income populations" OR "lower income country" OR "lower income countries" OR "lower income nation" OR "lower income nations" OR "lower income population" OR "lower income populations" OR "underserved country" OR "underserved countries" OR "underserved nation" OR "underserved nations" OR "underserved population" OR "underserved populations" OR "underserved world" OR "under served country" OR "under served countries" OR "under served nation" OR "under served nations" OR "under served population" OR "under served populations" OR "under served world" OR "deprived country" OR "deprived countries" OR "deprived nation" OR "deprived nations" OR "deprived population" OR "deprived populations" OR "deprived world")

#2 Search TS=("poor country" OR "poor countries" OR "poor nation" OR "poor nations" OR "poor population" OR "poor populations" OR "poor world" OR "poorer country" OR "poorer countries" OR "poorer nation" OR "poorer nations" OR "poorer population" OR "poorer populations" OR "poorer world" OR "developing economy" OR "developing economies" OR "less developed economy" OR "less developed economies" OR "lesser developed economy" OR "lesser developed economies" OR "under developed economy" OR "under developed economies" OR

"underdeveloped economy" OR "underdeveloped economies" OR "middle income economy" OR "middle income economies" OR "low income economy" OR "low income economies" OR "lower income economy" OR "lower income economies" OR "low gdp" OR "low gnp" OR "low gross domestic" OR "low gross national" OR "lower gdp" OR "lower gnp" OR "lower gross domestic" OR "lower gross national" OR "lami country" OR "lami countries" OR "transitional country" OR "transitional countries")

#3 Search TS=(Africa OR Asia OR Caribbean OR "West Indies" OR "South America" OR "Latin America" OR "Central America" OR "Atlantic Islands" OR "Commonwealth of Independent States" OR "Pacific Islands" OR "Indian Ocean Islands" OR "Eastern Europe" OR Afghanistan OR Albania OR Algeria OR Angola OR Antigua OR Barbuda OR Argentina OR Armenia OR Armenian OR Aruba OR Azerbaijan OR Bahrain OR Bangladesh OR Barbados OR Benin OR Byelarus OR Byelorussian OR Belarus OR Belorussian OR Belorussia OR Belize OR Bhutan OR Bolivia OR Bosnia OR Herzegovina OR Hercegovina OR Botswana OR Brasil OR Brazil OR Bulgaria OR "Burkina Faso" OR "Burkina Fasso" OR "Upper Volta" OR Burundi OR Urundi OR Cambodia OR "Khmer Republic" OR Kampuchea OR Cameroon OR Cameroons OR Cameron OR Camerons OR "Cape Verde" OR "Central African Republic" OR Chad OR Chile OR China OR Colombia OR Comoros OR "Comoro Islands" OR Comores OR Mayotte OR Congo OR Zaire OR "Costa Rica" OR "Cote d'Ivoire" OR "Ivory Coast" OR Croatia OR Cuba OR Cyprus OR Czechoslovakia OR "Czech Republic" OR Slovakia OR "Slovak Republic" OR Djibouti OR "French Somaliland" OR Dominica OR "Dominican Republic" OR "East Timor" OR "East Timur" OR "Timor Leste" OR Ecuador OR Egypt OR "United Arab Republic" OR "El Salvador" OR Eritrea OR Estonia OR Ethiopia OR Fiji OR Gabon OR "Gabonese Republic" OR Gambia OR Gaza OR "Georgia Republic" OR "Georgian Republic" OR Ghana OR "Gold Coast" OR Greece OR Grenada OR Guatemala OR Guinea OR Guam OR Guiana OR Guyana OR Haiti OR Honduras OR Hungary OR India OR Maldives OR Indonesia OR Iran OR Iraq OR "Isle of Man" OR Jamaica OR Jordan OR Kazakhstan OR Kazakh OR Kenya OR Kiribati OR Korea OR Kosovo OR Kyrgyzstan OR Kirghizia OR "Kyrgyz Republic" OR Kirghiz OR Kirgizstan OR "Lao PDR" OR Laos OR Latvia OR Lebanon OR Lesotho OR Basutoland OR Liberia OR Libya OR Lithuania)

#4 Search TS=(Macedonia OR Madagascar OR "Malagasy Republic" OR Malaysia OR Malaya OR Malay OR Sabah OR Sarawak OR Malawi OR Nyasaland OR Mali OR Malta OR "Marshall Islands" OR Mauritania OR Mauritius OR "Agalega Islands" OR "Melanesia" OR Mexico OR Micronesia OR "Middle East" OR Moldova OR Moldovia OR Moldovian OR Mongolia OR Montenegro OR Morocco OR Ifni OR Mozambique OR Myanmar OR Myanma OR Burma OR Namibia OR Nepal OR "Netherlands Antilles" OR "New Caledonia" OR Nicaragua OR Niger OR Nigeria OR "Northern Mariana Islands" OR Oman OR Muscat OR Pakistan OR Palau OR Palestine OR Panama OR Paraguay OR Peru OR Philippines OR Philipines OR Phillipines OR Phillippines OR Poland OR Portugal OR "Puerto Rico" OR Romania OR Rumania OR Roumania OR Russia OR Russian OR Rwanda OR Ruanda OR "Saint Kitts" OR "St Kitts" OR Nevis OR "Saint Lucia" OR "St Lucia" OR "Saint Vincent" OR "St Vincent" OR Grenadines OR Samoa OR "Samoan Islands" OR "Navigator Island" OR "Navigator Islands" OR "Sao Tome" OR "Saudi Arabia" OR Senegal OR Serbia OR Montenegro OR Seychelles OR "Sierra Leone" OR Slovenia OR "Sri Lanka" OR Ceylon OR "Solomon Islands" OR Somalia OR Sudan OR Suriname OR Surinam OR Swaziland OR Syria OR Syrian OR Tajikistan OR Tadjhikistan OR Tadjikistan OR Tadjhik OR Tanzania OR Thailand OR Togo OR "Togolese Republic" OR Tonga OR Trinidad OR Tobago OR Tunisia OR Turkey OR Turkmenistan OR Turkmen OR Tuvalu OR Uganda OR Ukraine OR Uruguay OR USSR OR "Soviet Union" OR "Union of Soviet Socialist Republics" OR Uzbekistan OR Uzbek OR Vanuatu OR "New Hebrides" OR Venezuela OR Vietnam OR "Viet Nam" OR "West Bank" OR Yemen OR Yugoslavia OR Zambia OR Zimbabwe OR Rhodesia)

Cochrane:

MeSH:

Cost-Benefit Analysis

Keywords:

"cost benefit":ti,ab,kw OR "cost effective":ti,ab,kw OR "cost effectiveness":ti,ab,kw OR "cost utility":ti,ab,kw

MeSH:

Emergency Service, Hospital

Emergency Medicine

Trauma Centers

Keywords:

"Emergency medicine":ti,ab,kw OR "Emergency services":ti,ab,kw OR "Emergency department":ti,ab,kw OR "Emergency service":ti,ab,kw OR "Emergency departments":ti,ab,kw OR "Emergency room":ti,ab,kw OR "Emergency rooms":ti,ab,kw OR "Emergency ward":ti,ab,kw OR "Emergency Unit":ti,ab,kw OR "Trauma Center":ti,ab,kw OR "Trauma Centers":ti,ab,kw OR "emergency health service":ti,ab,kw OR "emergency health services":ti,ab,kw OR "emergency medical services":ti,ab,kw OR "emergency medical service":ti,ab,kw OR "accident & emergency":ti,ab,kw OR "accident and emergency":ti,ab,kw OR "A&E":ti,ab,kw OR "A & E":ti,ab,kw

#1 (Africa or Asia or Caribbean or "West Indies" or "South America" or "Latin America" or "Central America"):ti,ab,kw

#2 (Afghanistan or Albania or Algeria or Angola or Antigua or Barbuda or Argentina or Armenia or Armenian or Aruba or Azerbaijan or Bahrain or Bangladesh or Barbados or Benin or Byelarus or Byelorussian or Belarus or Belorussian or Belorussia or Belize or Bhutan or Bolivia or Bosnia or Herzegovina or Hercegovina or Botswana or Brasil or Brazil or Bulgaria or "Burkina Faso" or "Burkina Fasso" or "Upper Volta" or Burundi or Urundi or Cambodia or "Khmer Republic" or Kampuchea or Cameroon or Cameroons or Cameron or Camerons or "Cape Verde" or "Central African Republic" or Chad or Chile or China or Colombia or Comoros or "Comoro Islands" or Comores or Mayotte or Congo or Zaire or "Costa Rica" or "Cote d'Ivoire" or "Ivory Coast" or Croatia or Cuba or Cyprus or Czechoslovakia or "Czech Republic" or Slovakia or "Slovak Republic"):ti,ab,kw

#3 (Djibouti or "French Somaliland" or Dominica or "Dominican Republic" or "East Timor" or "East Timur" or "Timor Leste" or Ecuador or Egypt or "United Arab Republic" or "El Salvador" or Eritrea or Estonia or Ethiopia or Fiji or Gabon or "Gabonese Republic" or Gambia or Gaza or Georgia or Georgian or Ghana or "Gold Coast" or Greece or Grenada or Guatemala or Guinea or Guam or Guiana or Guyana or Haiti or Honduras or Hungary or India or Maldives or Indonesia or Iran or Iraq or "Isle of Man" or Jamaica or Jordan or Kazakhstan or Kazakh or Kenya or Kiribati or Korea or Kosovo or Kyrgyzstan or Kirghizia or "Kyrgyz Republic" or Kirghiz or Kirgizstan or "Lao PDR" or Laos or Latvia or Lebanon or Lesotho or Basutoland or Liberia or Libya or Lithuania):ti,ab,kw

#4 (Macedonia or Madagascar or "Malagasy Republic" or Malaysia or Malaya or Malay or Sabah or Sarawak or Malawi or Nyasaland or Mali or Malta or "Marshall Islands" or Mauritania or Mauritius or "Agalega Islands" or Mexico or Micronesia or "Middle East" or Moldova or Moldovia or Moldovan or Mongolia or Montenegro or Morocco or Ifni or Mozambique or Myanmar or Myanma or Burma or Namibia or Nepal or "Netherlands Antilles" or "New Caledonia" or Nicaragua or Niger or Nigeria or "Northern Mariana Islands" or Oman or Muscat or Pakistan or Palau or Palestine or Panama or Paraguay or Peru or Philippines or Philipines or Phillipines or Phillippines or Poland or Portugal or "Puerto Rico"):ti,ab,kw

#5 (Romania or Rumania or Roumania or Russia or Russian or Rwanda or Ruanda or "Saint Kitts" or "St Kitts" or Nevis or "Saint Lucia" or "St Lucia" or "Saint Vincent" or "St Vincent" or Grenadines or Samoa or "Samoan Islands" or "Navigator Island" or "Navigator Islands" or "Sao Tome" or "Saudi Arabia" or Senegal or Serbia or Montenegro or Seychelles or "Sierra Leone" or Slovenia or "Sri Lanka" or Ceylon or "Solomon Islands" or Somalia or Sudan or Suriname or Surinam or Swaziland or Syria or Tajikistan or Tadjhikistan or Tadjikistan or Tadjhik or Tanzania or Thailand or Togo or "Togolese Republic" or Tonga or Trinidad or Tobago or Tunisia or Turkey or Turkmenistan or Turkmen or Uganda or Ukraine or Uruguay or USSR or "Soviet Union" or "Union of Soviet Socialist Republics" or Uzbekistan or Uzbek or Vanuatu or "New Hebrides" or Venezuela or Vietnam or "Viet Nam" or "West Bank" or Yemen or Yugoslavia or Zambia or Zimbabwe or Rhodesia):ti,ab,kw

#6 (developing or less* NEXT developed or "under developed" or underdeveloped or "middle income" or low* NEXT income or underserved or "under served" or deprived or poor*) NEXT (countr* or nation* or population* or world):ti,ab,kw

#7 (developing or less* NEXT developed or "under developed" or underdeveloped or "middle income" or low* NEXT income) NEXT (economy or economies):ti,ab,kw

#8 low* NEXT (gdp or gnp or "gross domestic" or "gross national"):ti,ab,kw

- #9** (low NEAR/3 middle NEAR/3 countr*):**ti,ab,kw**
- #10** (lmic or lmics or "third world" or "lami country" or "lami countries"): **ti,ab,kw**
- #11** ("transitional country" or "transitional countries"): **ti,ab,kw**
- #12** (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11)

Appendix F. Findings of the Included Studies

Author, Reference	Location	Intervention	Findings (adjusted to 2019 USD)	CHEERS Score
<i>Prehospital services</i>				
Accorsi (2017) ¹⁹	Ethiopia	Establishing ambulance service dedicated to EMOC	\$26.66 per life year saved	17
Jaldell (2014) ²¹	Thailand	Decreasing EMS response time by 1 minute nationally	Savings of \$425 million to \$850 million	12
Somigliana (2011) ²⁰	Uganda	Implementing an ambulance service for reproductive health in a remote setting	\$17.97 per year of life saved	13
deRamirez (2014) ¹³⁸	Uganda	Establishing EMS response system	\$97.10 per life saved	9
Hauswald (1997) ¹¹²	Malaysia	Establishing an EMS system responding to OHCA	\$568,642/life saved	6
<i>Training</i>				
Arreola-Risa (2004) ¹²²	Mexico	Basic trauma training for ambulance personnel	8.2% to 4.7% in patients at a cost of \$258 per medic trained. Increase in site dispatch and prehospital training increased use of prehospital interventions, decreased percentage of patients who died in transport, and cost approximately 16% of ambulance budget	12
Arreola-Risa (2000) ¹²¹	Mexico	Prehospital trauma life support course and increased number of ambulance dispatch centres	\$123,555 to improve ambulance response time in an urban setting and provide a prehospital trauma course yielded decline in prehospital mortality after medic arrival on scene from 8.2% to 4.7%	9
Jayaraman (2009) ¹⁷	Uganda	Lay first-responder trauma course	\$30-\$89 per life year saved	14
Carlson (2012) ¹²³	Haiti	2 year orthopaedic trauma residency	\$149.11+/- \$38.63 per DALY averted	17
Clark (2012) ⁴¹	Sierra Leone	ETAT training, triage implementation, and designation of space for emergency room	\$165 per paediatric death averted	14
Willcox (2017) ¹¹⁷	Ghana	Training in basic emergency obstetric and newborn care	\$57.34 per DALY averted	22
<i>Treatment interventions</i>				
Jaramillo (2016) ¹²⁷	Colombia	On demand use of Factor VIII for significant bleeding in haemophilia A	\$60,557 per QALY gained	23
Kortz (2017) ¹²⁴	Malawi	Bubble CPAP for paediatric severe pneumonia	\$13.89 per DALY averted	22
Gregorio (2007) ¹³⁷	Philippines	Zinc supplement for children with diarrhoea	\$3.33 for each day that diarrhoea is averted <4 days from consult, spending \$.04 for each case of diarrhoea <4 days from consult	14

Guerriero (2011) ¹²⁹	Tanzania, India & UK	TXA for bleeding trauma patients within 3 hours	Incremental cost per LY gained \$57, \$79 and \$76 PPP, in Tanzania, India and UK	22
Wang (2014) ¹²⁶	China	Increasing treatment for AMI	Aspirin/Statin/B-blocker/ACE,ARB and Heparin for NSTEMI \$3,291 per QALY saved. For STEMI addition of PCI in tertiary hospitals and streptokinase in secondary hospital \$13,054 per QALY saved	22
Ozelo (2007) ¹³⁶	Brazil	rFVIIa as first-line treatment for bleeding	rFVIIa more effective and less expensive than aPCC when used as first-line treatment for mild-to-moderate bleeding episodes in patients with haemophilia and inhibitors in Brazil (effectiveness: 100% (rFVIIa) vs 56.7%(aPCC), costs: (\$7,490 rFVIIa vs \$13,500 aPCC).	15
Pinto (2016) ¹⁰⁹	Brazil	TXA in trauma patients	\$17 per life year saved	15
Champunot (2014) ¹³⁰	Thailand	Emergency Dept resuscitation and early ICU admission for severe sepsis/septic shock	\$1,671 per life saved	17
Dayananda (2017) ¹¹¹	South Africa	Selective non-operative management of penetrating abdominal trauma	Managing abdominal wounds with select-non operation is effective and cost saving	11
Turhan (2009) ¹¹⁶	Turkey	Non-operative management of acute appendicitis	\$580 to \$731 per case Mortality reduced from 57% to 38%. Managed protocol for sepsis resulted in a reduction of ICU costs (\$162,005 +/- \$237,221 to \$100,181 +/- \$149,388) and an average gain of 3.2 life-years after discharge	6
Assuncao (2014) ¹¹⁹	Brazil	Standardised protocol for severe sepsis		14
Irazuzta (2016) ¹¹⁵	Paraguay	High dose prolonged magnesium sulphate infusion for severe asthma	Cost per treatment \$761-\$1,014 in Paraguay. HDMI expedites discharge which leads to a cost saving in LoS	8
Tigabu (2019) ¹³¹	Iran	Treatment of severe sepsis and septic shock	\$11,344 to \$11,898 per life year gained	15
Dwommoh (2018) ¹³⁴	South Africa	Motivational interviewing and problem solving therapy interventions to reduce substance abuse	\$4.46 - \$19.98 per patient yields improvement in mental health	18
Yang (2018) ¹¹⁸	China	Protocolised treatment for acute stroke	Protocolised treatment for acute stroke dominated usual care	9
Emergency Diagnostic tools				
Bogavac-Stanojevic (2013) ¹³³	Serbia	D-dimer testing for DVT	\$0.30 vs \$1.58 per one additional DVT positive patient (without PTP), \$0.72 vs \$1.19 per one DVT positive patient (with PTP)	18
Schulman-Marcus (2010) ¹²⁸	India	ECG for patients presenting at GP with acute chest pain	\$15.59 per QALY gained	24
Facilities and Packages of Care				
Gosselin (2008) ¹⁴⁰	Cambodia	District trauma hospital	\$98.11 per DALY averted	14

McCord (2003) ¹⁴¹	Bangladesh	Acute care facility providing package of emergency services including early access to surgical and obstetric care	\$18.33 per DALY	13
Gosselin (2010) ¹³⁹	Nigeria & Haiti	Emergency surgical and trauma care facilities	\$204 (Nigeria) and \$265 (Haiti) per DALY averted.	12
Horton (1983) ¹⁴²	Bangladesh	Stand-alone diarrheal treatment centre	Cost per death averted: large centre \$4,032, +\$1,116 if patient came by ambulance compared to \$589 at small centre	11
Kotagal (2014) ⁷⁰	LMICs	Reducing injury mortality rates in LMICs to HIC rates	2,117,500 lives could be saved per year with economic benefit ranges from \$245-261 billion (using a human capital approach) and \$758-786 billion per year (using a statistical life approach)	17
Barasa (2012) ¹²⁵	Kenya	Full ETAT guidelines implementation	\$0.94 per child admitted to achieve one percentage point improvement in quality measure	
			\$47.41-\$474.44 per DALY averted for national scale up in Kenya	23
Hu (2007) ¹¹⁴	Mexico	Increasing access to comprehensive EMOC and upgrading coverage levels in the MBP standard of care	Increasing access \$380 per DALY averted, upgrading coverage \$697 per life year saved and \$494 per DALY averted.	20

Appendix G. Quality assessment of included studies using CHEERS checklist

Author, Reference	Title, Abstract & Intro	METHODS: Target pop	Settings	Perspective	Comparators	Horizon	Discount Rate	Health outcomes	Effectiveness	Valuation	Costs	Currency	Model	Assumptions	Analysis	RESULTS: Parameters	ICER	Uncertainty	Heterogeneity	Discussion, Funding & COI	Overall CHEERS score (max 24)
Accorsi (2017) ¹⁹	3	1	1	1	0	0	1	1	1	1	1	1	0	0	0	0	1	1	0	3	17
Arreola-Risa (2000) ¹²¹	2	1	1	0	1	0	0	0	1	0	0	1	0	0	0	0	0	0	0	2	9
Arreola-Risa (2004) ¹²²	3	1	1	0	1	0	0	0	1	0	1	1	0	0	0	0	0	0	1	2	12
Assuncao (2014) ¹¹⁹	3	1	1	0	1	0	0	1	1	0	1	1	0	0	0	1	1	0	0	2	14
Barasa (2012) ¹²⁵	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	3	23
Bogavac-Stanojevic (2013) ¹³³	3	1	1	1	1	0	0	0	0	0	1	1	1	1	1	1	1	1	0	3	18
Carlson (2012) ¹²³	3	1	1	0	1	1	1	1	0	1	1	0	0	1	0	1	1	1	0	2	17
Champunot (2014) ¹³⁰	3	1	1	1	1	0	1	1	1	0	1	1	1	0	0	1	1	0	0	2	17
Clark (2012) ⁴¹	2	1	1	0	1	0	0	1	1	0	1	1	0	0	1	0	1	0	0	3	14
Dayananda (2017) ¹¹¹	3	1	1	0	1	0	0	0	0	0	1	1	1	0	0	0	0	0	0	2	11
Dwommoh (2019) ¹³⁴	3	1	1	1	1	0	1	1	1	0	0	1	1	0	0	1	1	1	0	3	18
de Ramirez (2014) ¹³⁸	2	1	1	0	0	0	0	1	0	0	1	0	0	0	0	0	1	0	1	1	9
Gosselin (2008) ¹⁴⁰	3	1	0	0	0	1	1	1	1	1	1	1	0	0	0	0	1	0	1	1	14
Gosselin (2010) ¹³⁹	3	1	1	0	0	0	0	1	1	1	1	1	0	0	0	0	1	0	0	1	12
Gregorio (2007) ¹³⁷	3	1	1	1	1	0	0	1	0	0	1	1	0	0	1	0	1	0	0	2	14
Guerriero (2011) ¹²⁹	3	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	0	3	22
Hauswald (1997) ¹¹²	3	1	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	6
Horton (1983) ¹⁴²	3	1	1	0	1	0	0	1	0	0	1	1	0	0	0	0	1	0	0	1	11
Hu (2007) ¹¹⁴	3	1	1	0	1	1	0	1	1	0	1	1	1	1	1	1	1	1	0	3	20
Irazuzta (2016) ¹¹⁵	2	1	1	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	2	8
Jaldell (2014) ²¹	3	1	1	0	0	0	0	0	1	0	1	1	1	1	0	0	0	0	0	2	12
Jaramillo (2016) ¹²⁷	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	3	23

Jayaraman (2009) ¹⁷	2	1	1	0	1	0	0	1	1	1	1	0	0	0	0	0	1	1	0	3	14
Kortz (2017) ¹²⁴	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	2	22
Kotagal (2014) ⁷⁰	3	1	1	0	0	0	1	1	1	1	1	1	1	1	1	0	0	0	0	3	17
McCord (2003) ¹⁴¹	3	0	1	0	0	1	1	1	1	1	1	1	0	0	0	0	1	0	0	1	13
Ozelo (2007) ¹³⁶	3	1	1	1	1	0	0	0	1	0	1	1	1	0	0	1	0	1	0	2	15
Pinto (2016) ¹⁰⁹	3	1	1	0	0	0	0	1	1	0	1	0	0	0	0	0	1	0	0	3	12
Schulman-Marcus (2010) ¹²⁸	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	3	24
Somigliana (2011) ²⁰	3	1	1	1	0	0	1	1	1	0	1	0	0	0	0	0	1	1	0	1	13
Tigabu (2019) ¹³¹	3	1	1	1	1	0	0	1	1	0	1	1	1	0	0	0	1	1	0	1	15
Turhan (2009) ¹¹⁶	1	1	1	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	6
Wang (2014) ¹²⁶	3	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	3	22
Willcox (2019) ¹¹⁷	3	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	3	22
Yang (2019) ¹²⁶	1	1	1	0	1	0	0	1	1	0	1	0	0	0	0	0	0	0	0	2	9

Appendix H. Resource unit costs

Items	Unit	Cost per unit (Ugandan Shilling)	Cost per unit (USD)	Source
Labour				
Nursing Student (U8)	minute	22	0.01	FY 2018-19 Salary Structure ³⁰
Nurse (U5)	minute	79	0.02	FY 2018-19 Salary Structure ³⁰
Interns (U5)	minute	79	0.02	FY 2018-19 Salary Structure ³⁰
Medical Officer (U4- Med 1)	minute	292	0.08	FY 2018-19 Salary Structure ³⁰
Clinical Officer (U4- Med 2)	minute	93	0.03	FY 2018-19 Salary Structure ³⁰
Single use supplies				
Adhesive tape	roll	39183	10.59	Joint Medical Stores
Endotracheal tube 3MM	each	1300	0.35	National Medical Stores ²⁵
Alcohol swabs	each	113.53	0.03	Estimate
Antiseptic solution (iodine)	200ml	3240	0.88	National Medical Stores ²⁵
Nebulizer mask	each	38394	10.38	Joint Medical Stores
Cotton roll	500g roll	8590	2.32	National Medical Stores ²⁵
Compression bandage	each	1412	0.38	National Medical Stores ²⁵
Non sterile gloves	pair	105.53	0.03	National Medical Stores ²⁵
Sterile gloves	pair	691.1	0.19	National Medical Stores ²⁵
Gauze dressing	90cm x 90m	41346	11.17	National Medical Stores ²⁵
Crepe bandage 4in	roll	954	0.26	National Medical Stores ²⁵
Crepe bandage 6in	roll	1702	0.46	National Medical Stores ²⁵
Blood transfusion giving set	each	615	0.17	National Medical Stores ²⁵
IV giving set	each	502.93	0.14	National Medical Stores ²⁵
Suction catheter (FG 16)	each	361	0.10	National Medical Stores ²⁵
Non adhesive dressing	90cm x91m	36492	9.86	National Medical Stores ²⁵
Plaster of Paris 6in	roll	3559	0.96	National Medical Stores ²⁵
Plaster of Paris 8in	roll	3559	0.96	National Medical Stores ²⁵
Gauze roll	roll	783.75	0.21	National Medical Stores ²⁵
Nonrebreather mask	each	12199	3.30	Joint Medical Stores
Lubricant (KY jelly)	42g tube	3770	1.02	National Medical Stores ²⁵
NG tube size 10	each	908	0.25	National Medical Stores ²⁵
NG tube size 14	each	489	0.13	National Medical Stores ²⁵
NG tube size 16	each	454	0.12	National Medical Stores ²⁵
Average NG tube	each	617	0.17	National Medical Stores ²⁵
Tongue depressor	each	50	0.01	National Medical Stores ²⁵
Water for injection	10ml vial	80	0.02	National Medical Stores ²⁵
Surgical blade average	each	237.81	0.06	National Medical Stores ²⁵
Average IV Cannula	each	366.29	0.10	National Medical Stores ²⁵
Average Syringe	each	232.83	0.06	National Medical Stores ²⁵
<i>Useful life</i>				
Reusable supplies				
	<i>years</i>	<i>Economic costs (accounting costs)</i>		
Cervical collar	5	53.87 (49.35)	53.87 (49.35)	Joint Medical Stores
Bucket	2	13.25 (12.67)	13.25 (12.67)	Joint Medical Stores
Artery forceps	7	6.08 (6.06)	6.08 (6.06)	Joint Medical Stores
Needle holder	7	4.12 (3.67)	4.12 (3.67)	Joint Medical Stores
Laryngoscope	7	42.34 (37.69)	42.34 (37.69)	Joint Medical Stores
Kidney dish	10	2.44 (2.08)	2.44 (2.08)	Joint Medical Stores
Bag valve mask	5	30.50 (27.94)	30.50 (27.94)	Joint Medical Stores
O2 cylinder	5	11.96(10.96)	11.96(10.96)	National Medical Stores ²⁵
Scalpels	5	0.07 (0.07)	0.07 (0.07)	National Medical Stores ²⁵
Scissors	10	2.75 (2.34)	2.75 (2.34)	Joint Medical Stores
O2 concentrator	10	638.22 (544.40)	638.22 (544.40)	Joint Medical Stores
Thermometer	10	1.50 (1.28)	1.50 (1.28)	Joint Medical Stores
ECG	7	1007.41 (896.59)	1007.41 (896.59)	Joint Medical Stores
Nebulizer machine	10	146.98(125.38)	146.98(125.38)	Joint Medical Stores
Mechanical ventilator	7	12136.33 (10801.34)	12136.33 (10801.34)	Joint Medical Stores
Stethoscope	5	13.64 (12.49)	13.64 (12.49)	Joint Medical Stores
Blood pressure cuff	2	31.03 (29.68)	31.03 (29.68)	Joint Medical Stores
IV infusion pump	10	589.03 (502.44)	589.03 (502.44)	Joint Medical Stores

Cardiac monitor	10	361 (307.74)	361 (307.74)	Joint Medical Stores
Glucometer	7	23.75 (21.14)	23.75 (21.14)	Joint Medical Stores
Vital signs monitor	10	361 (307.74)	361 (307.74)	Joint Medical Stores
Defibrillator	7	3089.85 (2749.97)	3089.85 (2749.97)	Joint Medical Stores
Portable ultrasound	10	8497.48 (7248.35)	8497.48 (7248.35)	Joint Medical Stores
Pulse Oximeter	7	767.50 (683.08)	767.50 (683.08)	Joint Medical Stores
Suction device	10	456.75 (389.61)	456.75 (389.61)	Joint Medical Stores
Medicines	Unit			
Iodine	200ml	3240	0.88	National Medical Stores ²⁵
Misoprostol	200mcg	360.08	0.10	National Medical Stores ²⁵
Oxytocin	10IU	194.05	0.05	National Medical Stores ²⁵
Tranexamic acid	500mg	3600	0.97	Joint Medical Stores
Diazepam	5mg tab	4.5	0.00	National Medical Stores ²⁵
Hydrocortisone	100mg	1224.32	0.33	National Medical Stores ²⁵
Salbutamol	2.5ml vial	2559.8	0.69	National Medical Stores ²⁵
Aminophylline	250mg/10ml	700	0.19	National Medical Stores ²⁵
Atropine	1mg/1ml	126.62	0.03	National Medical Stores ²⁵
Diazepam Injection	10mg/2ml	296.16	0.08	National Medical Stores ²⁵
Diclofenac Tab	tab	9.58	0.00	National Medical Stores ²⁵
Diclofenac injection	75mg/3ml	117.72	0.03	National Medical Stores ²⁵
Bupivacaine	4ml amp	5940	1.61	National Medical Stores ²⁵
Trap	325mcg tab	323.78	0.09	Joint Medical Stores
Zinc sulphite tablet	20mg tablet	31.2	0.01	National Medical Stores ²⁵
Lidocaine injection	5ml	2318	0.63	National Medical Stores ²⁵
Lignocaine injection	20ml	3536	0.96	National Medical Stores ²⁵
Misoprostol tablet	200mcg	255.54	0.07	National Medical Stores ²⁵
Paracetamol tablets	500mg tab	11.5	0.00	National Medical Stores ²⁵
Paracetamol syrup	125mg	1363	0.37	National Medical Stores ²⁵
Paracetamol vial	100ml	7233	1.95	Joint Medical Stores
Paracetamol suppository	125mg	960	0.26	National Medical Stores ²⁵
Tramadol ampoule	100mg/2ml	897.8	0.24	National Medical Stores ²⁵
Tolfree	100mcg tab	348	0.09	Joint Medical Stores
Pethidine	100mg/2ml	2257.8	0.61	National Medical Stores ²⁵
Ampiclox tab	250mg	95	0.03	National Medical Stores ²⁵
Ampiclox IV	250mg	634.43	0.17	National Medical Stores ²⁵
Ampicillin	500mg	376.12	0.10	National Medical Stores ²⁵
Aminophylline IV	250mg/10ml	700	0.19	Joint Medical Stores
Amoxycillin tab	tab	78	0.02	Joint Medical Stores
Amoxycillin syrup	100ml	3765	1.02	National Medical Stores ²⁵
Ascoril Syrup	100ml	5033	1.36	National Medical Stores ²⁵
Azithromycin tab	500mg	614.67	0.17	National Medical Stores ²⁵
Cloxacillin IV	500mg	396.88	0.11	National Medical Stores ²⁵
Cefotaxime	1g	11971	3.24	National Medical Stores ²⁵
Ceftriaxone	1g	973	0.26	National Medical Stores ²⁵
Cefixime tabs	200mg	1576	0.43	Joint Medical Stores
Cefixime syrup	50mg/5ml	1200	0.32	Joint Medical Stores
Ciprofloxacin tab	500mg	84.79	0.02	National Medical Stores ²⁵
Folic Acid pill	5mg	500	0.14	National Medical Stores ²⁵
Gentamycin	80mg/2ml	127.44	0.03	National Medical Stores ²⁵
Hydrocortisone	100mg	1224.32	0.33	National Medical Stores ²⁵
Ibuprofen Syrup		1257	0.34	National Medical Stores ²⁵
Metronidazole tab	200mg	13.5	0.00	National Medical Stores ²⁵
Metronidazole IV	500mg/100ml	794	0.21	National Medical Stores ²⁵
Metronidazole Suspension	100mg	1322	0.36	National Medical Stores ²⁵
Penicillin	600mg	270	0.07	National Medical Stores ²⁵
Phenobarbiton	30mg tab	32.22	0.01	Joint Medical Stores
D5	250ml	137.5	0.04	National Medical Stores ²⁵
D10	250ml	1200	0.32	Joint Medical Stores
D50	100ml	1397	0.38	National Medical Stores ²⁵
Dextrose	5% 500ml	1375	0.37	National Medical Stores ²⁵
Fenobabitone (Phenobarbital)	200mg/2ml	12100	3.27	National Medical Stores ²⁵
Manitol	100ml	2800	0.76	National Medical Stores ²⁵
Normal saline	250ml	1100	0.30	National Medical Stores ²⁵
Ringers Lactate	250ml	1000	0.27	National Medical Stores ²⁵

Tranexamic acid	500mg inj	3600	0.97	Joint Medical Stores
Diagnostic tests				
Complete Blood Count		14763	3.99	Amukele et al. ²⁶
Malaria test		6253	1.69	Schroeder et al. ²⁷
Stool		8880	2.40	Schroeder et al. ²⁷
Urine sample		9657	2.61	Schroeder et al. ²⁷
Sputum		7770	2.10	Whitelaw et al. ²⁸
Gene Xpert		77700	21.00	Hsiang et al. ²⁹
Cross matching		9324	2.52	Schroeder et al. ²⁷
Typhoid test		12543	3.39	Schroeder et al. ²⁷
Ultrasound		15000	4.05	Expert estimation
X-ray		10000	2.70	Expert estimation
CT Scan		200000	54.05	Expert estimation

Appendix I. Treatment processes for five sentinel conditions

Condition	Possible common treatments	Diagnostics
RTI	Antibiotics	X-ray
	Analgesia	CT Scan
	Chest Drain	Blood transfusion
	Wound Closure	Blood test
	Fracture reduction & splinting	
	Needle decompression	
	Oral or Nasal Pharyngeal Airway	
	Oxygen	
	IV Fluids	
	Transfusion/ blood given	
	Haemorrhage control	
	Intubation	
PPH	Oral or Nasal Pharyngeal Airway	Blood transfusion
	Oxygen	Blood test
	IV Fluids	X-ray
	Transfusion/ blood given	
	Haemorrhage control	
Asthma	Intubation	
	Oral or Nasal Pharyngeal Airway	X-ray
	Antibiotics	
	Nebulisation	
	Oxygen	
Pneumonia	Antibiotics	Blood test
	Chest drain	X-ray
	Oral or Nasal Pharyngeal Airway	
	IV fluids	
	Oxygen	
Paediatric diarrhoea	Oral rehydration	Blood test
	IV fluids	

Appendix J. Paper version of the micro-costing study data collection tool

Micro-costing Data Collection

Hospital Site: ☐ Hoima ☐ Kabale ☐ Gulu ☐ Mbale ☐ Jinja					Date: (DD/MM/YY)		Time (HH:MM)	
Location of intervention if not at default location (EU) tick and write in: ☐ Other: _____								
Sentinel condition: ☐ Pneumonia ☐ Paediatric diarrhoea ☐ RTI ☐ Asthma ☐ PPH ☐ Other: _____								
Intervention observed (check ONLY one) ☐ Antibiotics ☐ Haemorrhage Control ☐ IV Fluids ☐ Oxygen ☐ Oral or Nasal Pharyngeal Airway ☐ Needle decompression ☐ Oral Rehydration ☐ Nebulisation ☐ Chest drain ☐ Fracture reduction & splinting ☐ Wound closure ☐ Transfusion/ blood given ☐ Analgesia ☐ Intubation								

SINGLE USE SUPPLIES USED PER PATIENT											
Item & Unit/size	OPP?	Count	Total #	Item & Unit/size	OPP?	Count	Total #	Item & Unit/size	OPP?	Count	Total #
Adhesive tape <i>Fraction of roll, or rolls</i>	☐			Non rebreather mask	☐			Suction catheter <i>Write size:</i>	☐		
Airway <i>by piece</i>	☐			Gloves (by pair) <i>Surgical</i>	☐			Sutures <i>Write size:</i>	☐		
Oral Nasal Endotracheal				<i>Non sterile</i>	☐			Syringes <i>Write size:</i>	☐		
Alcohol swabs <i>per piece</i>	☐			Tourniquet	☐			Surgical blade <i>Write size:</i>	☐		
Antiseptic solution	☐			IV cannula <i>Write in size:</i>	☐			Tongue Depressor	☐		
Nebulizer mask	☐			IV tubing "giving set"	☐			Crepe bandage <i>Rolls 6 or 8 inch (circle one)</i>	☐		
Cotton roll <i>roll</i>	☐			Lubricant (KY jelly) <i>Estimated portion of tube</i>	☐			Non adhesive dressing	☐		
Clean water <i>ml</i>	☐			Nasal Cannula/ Prongs <i>Write in size:</i>	☐			DIAGNOSTICS (check all that apply) ☐ Ultrasound ☐ OPP? ☐ X-Ray ☐ Size of x-ray film _____ ☐ CT Scan ☐ ☐ Other _____			
Clotting agents <i>e.g TXA vials</i>	☐			Needle <i>Write in size:</i>	☐						
Compression bandage <i>Rolls</i>	☐			NG tube <i>Write in size:</i>	☐						
Chest tube <i>Write size:</i>	☐			Plaster of paris <i>Rolls 6 or 8 inch (circle one)</i>	☐						
Gauze dressing <i>pieces</i>	☐			Water for injection <i>ml</i>	☐						
Blood transfusion giving set	☐			Box splints	☐						

REUSABLE SUPPLIES include number used (Write H if hospital paid and O if patient paid) ☐ O2 cylinder # _____			
☐ Cervical collars # _____	☐ Needle holder # _____	☐ Kidney dish # _____	☐ Scalpel # _____
☐ Bucket # _____	☐ Laryngoscope # _____	☐ Tourniquet # _____	☐ Scissor # _____
☐ Artery Forceps # _____	☐ Dissecting forceps # _____	☐ Bag valve mask # _____	

MEDICATIONS USED PER PATIENT (Write amount & circle or write in unit)					
Item	OPP	Unit	Count	Total	
<i>(include name or type in space below—check box if patient paid)</i>					
Beta-agonist	☐	Mg or vial			
Analgesic	☐	Mg or vial or pills			
Antibiotics	☐	Mg or vial or pills			
Blood units	☐	o neg or cross matched			

Item	OPP	Unit	Count	Total
<i>(include name or type in space below—check box if patient paid)</i>				
ORS fluid	☐	ml		
Oxygen (flow rate)	☐	mls/minute		
IV fluids	☐	L		
Other:	☐			

MEDICAL DEVICES (check all that apply)	
☐ O2 concentrator	☐ IV infusion pump
☐ Thermometer	☐ Cardiac monitor
☐ ECG	☐ Glucometer
☐ Nebulizer machine	☐ Vital signs monitor
☐ Mechanical Ventilator	☐ Defibrillator
☐ Capnograph	☐ Portable ultrasound
☐ Stethoscope	☐ Pulse Oximeter
☐ Blood pressure cuff	☐ Suction device

Appendix K. Excel-based cost-effectiveness analysis decision analytic model

The full excel-based tool used in the analysis of Chapter 7 is available via the link below.

<https://www.dropbox.com/sh/k7bvqmkndfkval8/AADqfL9euHxVp8ZwmCCQbVv5a?dl=0>