

Evaluation of interventions to prevent surgical site infections

A case study on caesarean sections in sub-Saharan Africa guided by the *International Classification of Patient Safety* framework

Literature review

B.P. Waalewijn

The Netherlands

Master of International Health
12 September 2016 – 8 September 2017

Declaration

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A case study on caesarean sections in sub-Saharan Africa guided by the *International Classification of Patient Safety* framework

A thesis submitted in partial fulfilment of the requirement for the degree of

Master in International Health

by

Bart Waalewijn

The Netherlands

Declaration:

Where other people's work has been used (either from a printed source, internet or any other source) this has been carefully acknowledged and referenced in accordance with departmental requirements.

The thesis "Evaluation of interventions to prevent surgical site infections, A case study on caesarean sections in sub-Saharan Africa guided by the International Classification of Patient Safety framework" is my own work.

Signature:



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Table of contents

Table of contents		III
List of Tables		IV
List of Figures and Flow-chart		V
Acknowledgements		VI
Abstract		VII
List of Abbreviations		VIII
Preface		IX
Chapter 1	Background	1
Chapter 2	a. Problem statement	3
	b. Justification	4
	c. Objectives	5
	d. Methodology	6
Chapter 3	Results	
	3.1 Incident type, Patient outcome, Organisation outcome	13
	3.2 Contributing factors, Patient and Incident characteristics	15
	3.3 Prevention, Recovery and Resilience	18
	3.4 Implementation Challenges	27
Chapter 4	Discussion	29
Chapter 5	Conclusion and recommendations	33
References		34
Annexes	1. Definitions: surgical site infection and epidemiological terms	41
	2. Search keywords and yield	46
	3. Data collection grid for literature search	48
	4. Key concept terms and classes ICPS framework	49

List of Tables

Table 1	Epidemiology summary of three review articles on surgical site infections	3
Table 2	CDC definition of surgical site infection	7
Table 3	Yield of literature search for prevention strategies (#5 and #6)	18
Table 4	Summary on four C-section surgical site infection prevention strategies based on single versus multiple dose antibiotics regimens	20
Table 5	Summary on four C-section surgical site infection prevention strategies based on other antibiotics-related strategies	21
Table 6	Summary on four non-antibiotic C-section surgical site infection prevention strategies	23
Table 7	Force field analysis of infection prevention strategy implementation in sub-Saharan Africa	27
Text-box 1	Recommendations for good practice to prevent surgical site infections after caesarean sections	29

List of Figures and Flow-Chart

Figure 1	Different levels of quality of care within patient safety domain	2
Figure 2	Six WHO dimensions of quality	9
Figure 3	International Classification of Patient Safety (ICPS) conceptual framework	12
Figure 4	Contributing factors for surgical site infections	15
Figure 5	Topics intervention studies	19
Figure 6	Countries were C-section SSI prevention studies were conducted	19
Flow-chart 1	Search strategy	8

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Abstract

Background

Surgical site infections are a universal public health problem with serious impact on patient and organisational outcomes. Actions taken to reduce the risk of surgical site infections and to strengthen the system resilience are highly needed.

Thesis research objective

The aim of this thesis is to describe the burden and analyse determining factors of surgical site infections at first referral level in sub-Saharan Africa after caesarean sections. Preventive intervention strategies are critically appraised.

Methodology

A systemized literature review was conducted in three online databases (PubMed, Cochrane library and Google Scholar). Key-words, inclusion and exclusion criteria were defined. The international classification of patient safety (ICPS) conceptual framework was used as conceptual model for this thesis.

Results

Notwithstanding underreporting and publication bias towards higher level hospitals, the burden of surgical site infections in sub-Saharan Africa is probably considerably high. Incident characteristics and patient characteristics were clearly defined, and contributing factors were grouped in human, system and external factors. Twelve studies on preventive interventions were identified, topics covered antibiotic prophylaxis (N=8), surgical safety checklists (N=2), locally produced hand rub (N=1) and surgical techniques (N=1). The ICPS framework scope was broader than medical/technical interventions only, however publication bias might have resulted in limited system-related interventions.

Conclusion and recommendations

Innovative strategies are needed to mitigate the risks of surgical site infections. At intervention level, gaps were identified which suggested to shift attention from antibiotic-related strategies *only* to system interventions. More research of better quality is needed, to ensure successful implementation of such interventions.

Keywords: healthcare, infection, prevention, surgery, caesarean section, sub-Saharan Africa

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List of abbreviations

C-section	Caesarean section
CDC	Centre for Disease Control and Prevention
EVD	Ebola virus disease
HIV	human immunodeficiency virus
IPC	infection prevention and control
ICPS	International Classification for Patient Safety
LMIC	low- and middle-income country
RCT	randomised controlled trial
sSA	sub-Saharan Africa
SSI	surgical site infection
WAPS	World Alliance for Patient Safety
WHO	World Health Organisation

Preface

The topic of this thesis originates from my working experience in Sierra Leone (2013 – 2016). I was employed as medical doctor and coordinator of a surgical training programme. A large portion of my time was spent with clinical duties in a rural district teaching hospital. From the moment I started to work in this hospital I was fascinated by the complexity of infection prevention and control (IPC).

First of all, infection prevention was not only my own struggle. Getting to know other district hospitals, I realized that the challenges I faced were common or even worse in other health facilities; high numbers of surgical site infections (SSI), lack of running water and cleaning equipment, poor hospital waste management, insufficient personal protective equipment, little support from national health authorities, no infection prevention team, limited funds, few human resources, no written policies and no hepatitis B vaccines for health care workers are just a few examples I encountered during my professional life in an African district hospital. Clearly, this topic is a major public health problem which needs attention.

Secondly, the unprecedented West-African outbreak of Ebola virus disease (EVD) in 2014-2015 further inspired me to select IPC for my thesis. The epidemic caused a global threat, many health care workers died and patients avoided health facilities. I personally experienced fear of infection, the struggle to maintain routine hospital activities amid a crisis, lack of communication from health authorities and the loss of colleagues. The IPC opportunities learnt during the EVD outbreak and the surgical training programme are uncountable. Awareness and the constant process to improve quality of care, including *prevention of health-care-associated infections*, became embedded in my day-to-day work.

This brings me to the third, and probably most important reason to study infection prevention strategies in sub-Saharan Africa (sSA). Quality of care and patient safety are key components of health care provision. Health-care-associated infections are a fundamental patient safety element, which should receive attention. Patients have the right to receive the best possible care. Patient factors, disease dynamics, intervention-related factors, health system factors and environmental factors all contribute to health-care-associated infections. With this thesis I would like to explore the burden of post-operative infections in the sSA context, and use SSIs after caesarean sections (C-sections) as proxy procedure among many other surgical procedures. Critical analysis of published strategies to prevent SSIs after C-sections and similar major surgeries has been undertaken in order to make recommendations for action, further research and agenda setting by clinicians and public health policymakers.

I have learnt many lessons during my position in West Africa. Lack of understanding will often result in suboptimal implementation of new strategies. With this thesis, I hope to contribute to the body of knowledge by systematically analysing existing literature in order to identify challenges and opportunities for optimal implementation of evidence based SSI prevention strategies in hospitals. In my new position as project manager and medical doctor in rural Lesotho I attempt to apply my new insights in this field, but also profit from the academic skills acquired. Public health lessons learnt in sSA must not be wasted, but should help to make health care safer.

Bart Waalewijn

May 2017

1. BACKGROUND

Context of sub-Saharan Africa healthcare system

Providing affordable and effective healthcare to their people is a struggle in many African countries. Low-income and middle-income countries (LMICs) differ significantly from high-income countries on different levels. Obviously, the financial and human resources for health are more restricted and often maldistributed within countries.¹ Rural populations are frequently underserved, with limited access to healthcare services.¹ Besides financial and human resource constraints, national healthcare systems in sSA face a wide range of weaknesses: insufficient preparedness or responsiveness to epidemics², inadequate risk pooling for patients and catastrophic out of pocket payments³, poor dissemination and training of latest developments/guidelines to relevant health workers^{4,5}, infrastructural challenges, limited policies or strategies (e.g. national policy on patient safety)^{5,6} and incapability to enforce and monitor regulations.⁷

Facility context and C-section

In order to understand the scope of work and resources at district facility level, a description of a typical sub-Saharan hospital performing C-sections is important. The third edition of disease control priorities defines first-level hospitals as “*fairly well-developed surgical capabilities with doctors with surgical expertise*” corresponding with Level 2 district or provincial hospitals in the World Health Organisation (WHO) Guidelines for Safe Surgery 2009.^{8,9} Generally this facility would be a small hospital, with only few general medical officers¹ and possibly some surgically trained non-physician assistants (e.g. clinical officers, surgical assistant health officers).¹⁰ Foetal monitoring with ultrasound scanning and foetal doppler is normally available, but cardiotocographyⁱⁱ is mostly not. Small district facilities usually refer complex surgical cases, however basic skills and equipment to perform C-sections is commonly available.⁸ Problematic is the absence of anaesthetic providers in up to half of the hospitals offering C-section services.⁸ Operative vaginal deliveries (e.g. vacuum extractions) and continuous blood transfusion services are generally lacking or poorly available.⁸ Rural women face increased risks of dying during pregnancy and childbirth, related to poor access of facilities, lack of quality care and high costs of institutional deliveries.¹¹

C-sections are part of the essential surgery list, and a recognized cost-effective, feasible life-saving comprehensive emergency obstetric care service. C-section rates and related complications are rising, also in sSA, which is most pronounced for the urban and richer women.¹¹ While improving access and provision of C-sections to all women who *need* them, it is good to monitor inequalities in access, and the quality of service.¹² SSIs and administration of prophylactic antibiotics have been identified as proxy indicators for quality in relationship to C-sections.¹¹

Prevention of surgical site infections

This thesis builds on *Fig. 1*, where the interlinkages of the various levels of quality of care within the patient safety domain are presented. The broad concept of quality of care has been defined by the WHO and Maxwell with the following domains; *effectiveness, acceptability, efficiency, accessibility, equity, relevance* and *safety*.¹³ In the *Methods* chapter we will discuss these dimensions and focus on patient safety, health-care-associated infections and specifically SSIs in the sub-Saharan context.

ⁱ Medical doctors without further specialisation

ⁱⁱ Electronically recording of the fetal heartbeat and the uterine contractions during pregnancy



Figure 1. Different levels of quality of care within patient safety domain

International campaigns

“Clean Care is Safer Care” and “Safe Surgery Saves Lives” are two global patient safety challenges launched in 2005 and 2008 respectively, by the WHO patient safety and quality improvement unit.¹⁴ The latest challenge, formally announced in March 2017, is called “Medication Without Harm” and again broadly addresses public health preventive issues related to health-care-associated infections. These campaigns create platforms for patient engagement, sharing of materials and resources, working group meetings and technical research. Improving patient safety globally, especially in developing countries, is a continuous learning process which requires dialogue, engagement and advocacy. The latest versions of guidelines and technical reports on prevention and management of health-care-associated infections are published amongst others by the Institute for Healthcare Improvement (IHI, 2012)¹⁵, the National institute for Health and Care Excellence (NICE, 2014)¹⁶, WHO (2016)^{17,18} and the European Centre for Disease Prevention and Control (ECDC, 2017).¹⁹

Without doubt health-care-associated infections, including SSIs, receive a lot of international attention. This health topic is very important in sSA, where limited resources force health authorities to prioritize strategies. With this thesis, we systematically studied the burden of SSIs in sSA, described determining/contributing factors among the women undergoing C-sections, and critically analysed prevention strategies and implementation challenges which finally led to best practice recommendations. The results could be used as guidance for further research and help to prioritise specific implementation strategies, taking the resource-limited setting into account. Ultimately, it aims to support clinicians and health policy makers to minimize the risks of SSIs and make hospital services safer.

2. Problem statement, Justification, Objectives and Methodology

A. PROBLEM STATEMENT

Health-care-associated infections have great impact on the outcome of patients, health facilities and healthcare systems. The public health threat in sSA imposed by SSIs, especially after C-sections, will be the focus of this thesis. Clinically meaningful categoriesⁱⁱⁱ like incident type, patient outcomes and organisational outcomes could be used to describe the burden of SSIs and their public health consequences. These categories are derived from the International Classification of Patient Safety (ICPS).²⁰

Incident type – surgical site infection after caesarean section

Three review papers have been published between 2011 and 2013, assessing the burden of health-care-associated infections, including SSIs, in sSA.^{6,21,22} *Table 1* presents a summary of aggregated SSI data. This thesis will *only* study SSIs post C-section, as the scope of any health-care-associated infection is too broad. Data on, for example, bloodstream infections, pneumonia and urinary tract infections will not be presented.

The choice to select C-sections as tracer procedure for SSIs is based on the widespread availability and high volume of this type of surgical procedure at district level across sSA.^{23–25} C-sections are common in most hospitals and trends indicate increasing rates across sSA.¹¹ The international attention on maternal mortality also allows for sufficient information on this procedure, which is highly standardized and with clear procedures.^{11,12,26}

Table 1: Epidemiology summary of three review articles on surgical site infections

	Review Allegranzi ²²	Review Rothe ²¹	Review Nejad ²⁷
Incidence	Pooled 2.9 – 10.5 per 100 surgeries Pooled cumulative incidence 8.6 – 16.0 per 100 surgical patients Pooled cumulative incidence in high risk-patients 23.6 – 47.7 per 100 patients	NA	2.5 – 30.9 per 100 patients undergoing surgery
Prevalence	NA	6.8 – 26%	NA
Case fatality	NA	NA	10.8% (vs 3.9 % without SSI) in single study

Note: Original sources of pooled data can be accessed in review articles, which includes also non-C-section procedures. NA=not available

Patient outcome

The high incidence and potential severe degree of harm resulting into death, also justify the study of this public health problem. Not all SSIs cause severe impact on patients, but even moderate and mild impact can eventually accumulate to significant consequences for the patient. Permanent or long-term harm,

ⁱⁱⁱ Categories are derived from the ICPS framework, which will be explained in detail under the *Conceptual Framework*

which could also relate to psychological distress and altered health seeking behaviour should not be underestimated.²⁰

Organisational outcome

SSIs also affect healthcare organisations, where the impact upon a facility can relate to extra costs, increased length of stay, additional interventions or tests, disrupted workflow, media attention etcetera.^{21,28,29} A more in-depth analysis will explain the burden in more detail, however it is evident that the weak and poorly resourced health systems in many sSA countries would benefit from innovative and cost-effective strategies to prevent SSIs.

B. JUSTIFICATION

Knowledge gap

Within the sSA region poorer countries provide less data on health-care-associated infections leading to major knowledge gaps.²¹ There is an urgent need for more complete and reliable data on SSIs, with validated definitions and standardized reporting. In recent years, landmark publications have again pointed towards the need for more research, especially from low- and middle-income countries.^{17,18,30,31}

It is surprising to realize how few studies have been able to describe this important public health problem in a much wider perspective, systematically looking at hospital organisation, management and structure elements for the prevention of SSIs.^{4,5} At the same time, many single-site low-quality studies have been published on detailed epidemiology of specific hospital acquired pathogens and resistance patterns (data not shown). Although these latter studies are important for local and context specific hospital-based surveillance programmes, the wider studies are better able to depict the complexity of this biomedical problem within the broader healthcare system. Both perspectives (biomedical infection transmission, and health system arrangements) are important and should be incorporated as core components of IPC programmes at national and facility-level.¹⁸

Structure, process, outcome

In line with these different perspectives, the evaluation of interventional studies for the prevention of SSIs should cover different dimensions and not only describe host, pathogen and environmental factors. In 1966 Donabedian suggested to evaluate medical care structures and processes, rather than only assessing outcomes.³² This approach seems still relevant, also for the evaluation of SSIs in this thesis. Bad outcomes can be compatible with good quality of care, whereas bad quality of care sometimes results in good outcomes. The correlation between quality of care and outcome is therefore not consistent, although one can say that good quality of care increases *the chances* for good outcomes. The *process* of care itself may be more relevant, and demonstrates the extent to which care is provided properly, appropriately, competently and with respect to patients. Finally, when assessing SSI prevention strategies, we should examine the structure or instrumentalities which are needed as inputs for the prevention process.³²

This thesis will first describe the *incident type* 'SSIs in C-section patients' and associated *patient and organisational outcomes* in sSA. Studies until April 2017 are included. Next, an in-depth analysis of *determining factors* related to C-section-associated SSIs is presented, comprising of *patient characteristics, incident characteristics and contributing factors*. Following this analysis, major attention has been placed on the critical appraisal of *intervention strategies* which focus on *prevention of SSIs, incident recovery and system resilience*. Finally, a description of *implementation challenges* in relation to these intervention strategies is presented. A discussion considering trends, knowledge gaps and potential fields for research has resulted in recommendations and suggestions for further research.

A systematic review synthesized findings from 1995 to 2010 on prevention strategies for SSIs in sSA, in majority non-C-sections procedures.⁴ This research compared various interventions and summarized them broadly into antibiotic prophylaxis, pre-operative interventions, intra-operative interventions and post-operative interventions. Without doubt, these research findings have highlighted the need for standardized methodological approaches and consistent definitions.⁴

The topic for this thesis and a renewed literature review in this field is urgently required to capture the latest SSI intervention studies related to C-sections. In addition to the previous general SSI prevention review⁴, the findings in this thesis will be presented with and systematically analysed by the use of a conceptual patient safety framework (ICPS framework).²⁰ This conceptual framework has been successfully applied for the first time to a surgical population in 2016, which involved transplant patients in a developed setting.³³ To my knowledge, this will be the first time to apply the ICPS framework in a sub-Saharan population, which might help to contribute in the reduction of SSIs.

C. OBJECTIVES

1. To describe the burden of surgical site infections in district hospitals in sub-Saharan Africa, in terms of incident type, patient - and organisational outcomes
2. To analyse determining factors related to caesarean section-associated surgical site infections in sub-Saharan Africa, patient characteristics, incident characteristics and contributing factors/hazards
3. To critically appraise intervention strategies (best practices) which focus on prevention, incident recovery and system resilience in relation to caesarean section-associated surgical site infections
4. To describe implementation challenges to the intervention strategies studied under *objective three*

The objectives are formulated in a logical sequence and provide sufficient background information to allow space for best practice recommendations and advice on implementation arrangements in low- and middle-income countries. C-sections serve as tracer procedure, and recommendations could also be applied to other similar essential clean-contaminated surgical interventions.

D. METHODOLOGY

In this section, we will explore definitions and concepts applied in this thesis. The research method and supporting analytical framework will be explained. Finally, potential limitations in design and methodological weaknesses will be addressed.

DEFINITIONS

The Centre for Disease Control and Prevention (CDC) definition of SSIs is most commonly accepted and adopted.^{9,17,18,34–37} *Table 2* summarizes the definition. As it falls under the health-care-associated infections, SSIs are typically registered from 48 hours after surgery, and often occur after hospital discharge or transfer.³⁶ SSIs can be subdivided by type of surgery, degree of harm (e.g. superficial/deep) and pathogen.

The CDC definition of SSIs has been modified over the years. In 1992, “surgical wound infection” was removed, because it suggested only superficial to deep tissues at the wound site.³⁴ “Organ/space” was introduced as new term to represent the anatomy other than the incision.³⁴ Recently, CDC decided to shorten post-operative surveillance period after certain procedures to 90 days, instead of one year.³⁷ The complete CDC SSI definition, which is also adopted in this thesis, and some common epidemiological definitions, like prevalence and cumulative incidence are presented in *Annex 1*. It should be acknowledged that researchers often present their own definition of SSIs. This practice makes it difficult to compare different studies. SSIs may rely on clinical judgement from the physician only, and do not always require culture-positive results.³⁷

Defining *levels of hospital services, expertise and capabilities* in sSA, one can categorize first, second and third level hospitals.^{8,9} The first level of hospitals includes small hospitals or health centres with sparsely equipped operating rooms for ‘minor’ procedures only. Patients with obstructed labour will be referred to a level 2 hospital, which is commonly the district or provincial hospital with an adequately equipped operating room. Level 3 hospitals are referral hospitals, often academic centres with more specialised care.^{8,9} This thesis will put special attention to *level 2 district hospitals*, as these are the most common places for patients to receive operative care, including C-sections.¹¹

In the results and discussion section this thesis will refer to a *patient* as a person who receives healthcare. Healthcare is defined as *services received by individuals or communities to promote, maintain, monitor or restore health*. Health is defined as *a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity*. These definitions are in line with the WHO definitions.²⁰ Following the WHO led ICPS, this thesis will not refer to clients or consumers but to patients, although it is widely recognized that healthy pregnant women may not be considered patients.²⁰

Prior to surgery, cleanliness of tissue might be classified expressing the intensity of contamination.⁹ With the range from clean wounds, clean-contaminated wounds, contaminated wounds to dirty or infected wounds, C-sections are typically referred to as *clean* or *clean-contaminated* wounds.⁹

Table 2. CDC definition of surgical site infection (Source: 34,38)

	Superficial incisional	Deep incisional	Organ/ space
SSI: "An infection of the incision or organ/space operated on during a surgical procedure in the past 30 (or 90) days surveillance." ^{34,38} The signs and symptoms below characterise the distinct features of the three SSI classes (superficial/deep/organ)			
Purulent discharge	✓	✓	
Purulent drainage from a drain placed through a stab wound into the organ/space			✓
Organisms isolated from fluid or tissue from the wound	✓		
Organisms isolated from fluid or tissue in the organ/space			✓
Surgeon/physician diagnosis	✓	✓	✓
Surgeon deliberately opens wound, unless wound is culture-negative	✓	✓	
Wound spontaneously dehisces	✓	✓	
Pain	✓	✓	
Tenderness		✓	
Fever (>38 C)		✓	
Localized swelling (oedema)	✓		
Redness or extending margin or erythema	✓		
Heat	✓		
Skin and subcutaneous tissues involved	✓		
Involves deep soft tissues (e.g. fascia)		✓	
Abscess or other evidence of infection found on direct examination		✓	✓
Within follow-up time after procedure date (days)	30	30*	30*
* exception follow-up of 90 days after specific procedures (e.g. cardiac surgery, craniotomy)			

LITERATURE REVIEW

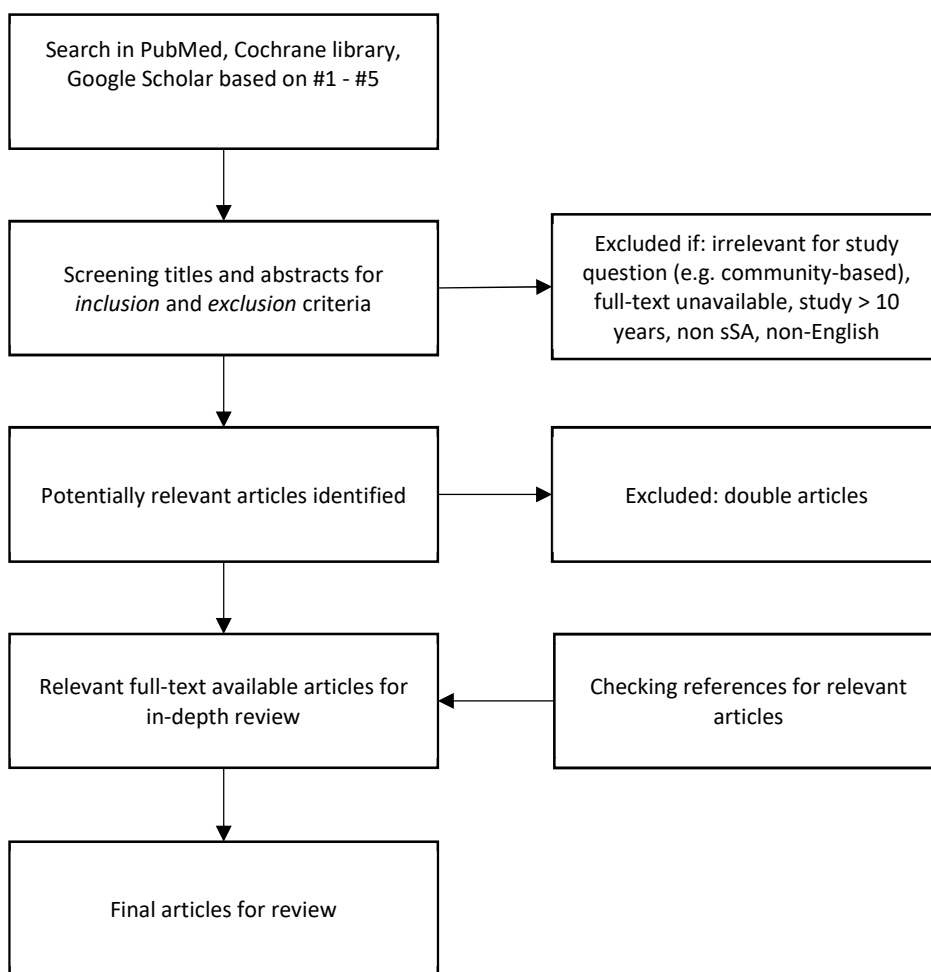
A literature search and systemized review was conducted on published data available from PubMed, Cochrane Library and Google Scholar.³⁹ The search period covered articles published during the past 10 years for the first two databases, but was more restricted for Google Scholar (2012 – 2017), in order to find the most recent information without disproportionately increasing the yield. Selected literature was inputted into an Excel® data collection sheet with 22 parameters, including year of publication, type of literature (e.g. peer reviewed article, guideline), country of study, study undertaken in district hospital, incidence, prevalence and patient population. The applied database grid is presented in *Annex 3*.

The approach to systematically study the different objectives was identical, but distinct keywords were applied for the various objectives. With each search, titles and abstracts were screened by a single person (thesis author) following predetermined criteria to identify relevant articles. Studies were included if they were relevant to the objective, full-text available from the online Free University of Amsterdam library and published within the last ten years (2007-2017). References of selected articles were assessed for additional relevant studies (*Flow-chart 1*).^{iv} Detailed information on search keywords and search yields

^{iv} For numbers of the different searches #1 - #5, full details can be found in the *Annex 2* as these are too complex to capture in a single flow-chart

are listed in *Annex 2*. Few landmark papers published before 2007 were accepted for further analysis by discretion of the thesis researcher.

Non-English language articles, studies on specialised technical procedures undertaken in academic tertiary hospitals (e.g. neurosurgery, cardiac surgery), community-based studies and duplicate references were excluded. Experimental studies solely focussing on laboratory data without clinical relevance were also excluded. Studies performed outside sSA were excluded, except in cases where authors also referred to the African context or results were deemed relevant and applicable in sSA (e.g. universal surgical techniques). No studies were rejected based on quality criteria.



Flow-chart 1: Search strategy. SSA: sub-Saharan Africa^v

CONCEPTUAL FRAMEWORK

The ICPS framework, applied in this thesis, is a model for “*patient safety concepts and their interrelationships*”.²⁰ This framework is designed to facilitate description, comparison, monitoring, analysis and interpretation of patient safety information based on standardized concepts and agreed definitions. The use of this framework in the context of SSIs, might become hypothesis generating as it potentially points out areas under-studied, and thus in need of more attention. New research gaps might be identified.

Balancing scope of framework

Patient safety is a dimension of quality of care (*Fig. 1, Fig. 2*). An overarching quality of care conceptual framework as proposed by Donabedian integrates patient safety, but it is too generic for the purpose of this thesis as it discusses many other aspects.^{32,40} Health-care-associated infections, like SSIs, represent

one single aspect of patient safety, and could be studied by a narrower framework presented by Rothe and colleagues in 2013.²¹ This framework, mainly focussing on contributing factors, was adapted by Dramowski and colleagues in 2017 who put emphasis on *prevention* of health-care-associated infections.⁴¹ The inter-relationships between these different levels is illustrated in *Fig. 1*.

The ideal conceptual framework for this thesis is the *ICPS patient safety framework*. The ICPS framework is beneficial for several reasons: First, it provides an appropriate and validated framework which is developed through a comprehensive, collaborative, in-depth process. This was not the case for the health-care-associated infection frameworks.^{21,41} Secondly, this classification is less specific for health-care-associated or SSIs only, which might generate innovative ideas for future research by allowing an open-minded approach. Finally, the ICPS framework provides a robust structure for analysis of SSI preventive interventions, following universal patient safety basics.

Starting point of the patient safety framework

From the time Dr. Ignaz Semmelweis discovered tremendous reductions of puerperal fever after the introduction of hand washing in 1847, until now major steps have been made in patient safety.⁴² To support this, the World Alliance for Patient Safety (WAPS) has moved forward to draft an internationally agreed and harmonized classification on patient safety concepts.²⁰ The African Partnerships for Patient Safety (APPS) has adopted health-care-associated infections and safe surgical care in the WHO African region, as its first priority area.⁴³

In 2009 the final technical report (version 1.1) of the ICPS conceptual framework was published.²⁰ A multidisciplinary group of experts drafted the report, and followed a set of principles to develop concepts for the full spectrum of healthcare settings based on existing patient safety classifications.²⁰ The ICPS framework is not yet a mature classification, but merely the “*starting point of an on-going process to better understand the sphere of patient safety*” according to the authors.²⁰ Three years of development thru web-based modified Delphi surveys and in-depth analysis resulted in this culturally and linguistically appropriate model (*Fig. 3*).



Figure 2. WHO six dimensions of quality. Equitable: health service does not vary in quality depending on personal characteristics, acceptable: patient-centred, taking individual preferences and cultures into account, effective: healthcare that is evidence based and based on needs, efficient: avoids waste and maximises resource use, accessible: timely delivery of appropriate care, geographically

ICPS classification 'building blocks'

The conceptual framework comprises of *ten high level* classes, each with subdivisions which allow space for regional dialects and preferences (*Fig. 3*).²⁰

Classes *incident type* and *patient outcomes* contain clinically meaningful categories which are grouped because of shared elements. For this thesis, and the description of the SSI burden, organisational outcomes are also included in this section. This is slightly *different* from the original framework, where organisational outcomes are considered as descriptive context information.

Classes *patient characteristics*, *incident characteristics* and *contributing factors/hazards* provide descriptive information on the context. The same circumstance or incident could be perceived as contributing factor or an incident.

The classes *detection*, *mitigating factors*, *ameliorating actions* and *actions taken to reduce risk* offer information relevant for prevention, recovery and system resilience and the ability to “bounce back” to initial core tasks.²⁰

Forty-eight key concepts are selected as building blocks to facilitate understanding of the classes and to disentangle interrelationships. Brief, simple and “fit-for-purpose” definitions are explained in detail. To give an example, the following six key concepts are explained in detail for patient outcomes: harm, disease, injury, suffering, disability and degree of harm. Most key concepts will be applied in the analysis, and a full description and reproduction of these terms can be found in *Annex 4*.

Linking objectives to conceptual framework

The different objectives and respective search terms follow the description of the conceptual framework. Details on these search terms and related yields can be found in *Annex 2*.

Incident type and outcome (First objective)

This thesis starts with describing the public health problem, that is the incident type (SSIs) which will be addressed and its (patient and organisational) outcomes. This demonstrates the impact of SSIs in sSA. In a logical sequence, aligned with the ICPS framework, the structure of this thesis will gradually be build up. The impact of SSIs is described from different perspectives, including patient outcomes (mortality and morbidity), and organisational outcomes (economic and social, e.g. acceptability, trust). Comprehensive understanding of the incident type is necessary to better grasp potential interventions.

Determining factors (Second objective)

This objective aims to analyse determining factors related to caesarean section-associated SSIs in sSA. Information on contributing factors, patient characteristics and incident characteristics published in literature from sSA will be described. Details on the literature search strategy conducted for this objective are presented in *Annex 2*. The purpose of this objective was to provide a scoping overview of the broad spectrum of contributing factors/hazards, rather than an all-inclusive systematic review.

Interventions for prevention, recovery and resilience (Third objective)

Analysis and critical appraisal of C-section-associated SSI preventive interventions in sSA will be undertaken. The ICPS conceptual framework leads as guiding framework, and critically addresses other actions taken to reduce the risk of SSIs, including incident recovery, ameliorating actions and system resilience.

Objective three is the *core part* of this thesis, the search strategy was adopted with the same inclusion and exclusion criteria as described in *Flow-chart 1*. Technique related interventions^v from non-African

^v Interventions related to the type of surgical technique used for the caesarean section

countries were accepted in the analysis, but not primarily searched for (*Annex 2*). Interventional studies were defined as describing at least two patient groups with different management styles or interventions like for example comparative studies, randomized controlled trials and “before-after” studies.

For the purpose of this thesis C-sections were classified as clean/clean-contaminated abdominal procedures without contamination, as the internal genital tract was opened under relatively controlled circumstances. Similar major abdominal procedures in sSA, with an equivalent wound class category, were also accepted for analysis as they could provide useful insight for interventions and incident recovery, relevant for C-sections.

Implementation challenges (Fourth objective)

This section describes implementation challenges (restraining forces), and critically analyses opportunities (driving forces) for effective application of SSI preventive interventions in sub-Saharan African. This topic is not specifically addressed in the ICPS framework. However, its description helps to translate the results of the preceding objective into best practice recommendations and implementation arrangements. Challenges and opportunities are retrieved from relevant articles found within the described searches (*Annex 2*). Findings are presented with a force field analysis.

Fig. 3 presents the ICPS conceptual framework, with indications linking the objectives of this thesis to the concepts and classes of the ICPS framework.

ASSESSMENT OF STUDY QUALITY

A standardised quality criteria list was used to evaluate studies selected under *objective 3*. These integrated quality criteria for the review of multiple study designs (ICROMS) were designed to facilitate the review of public health studies with a validated scoring tool and decision matrix.⁴⁴ This comprehensive tool is feasible for the appraisal of a large range of study designs, and sufficiently flexible to be applied in different contexts.

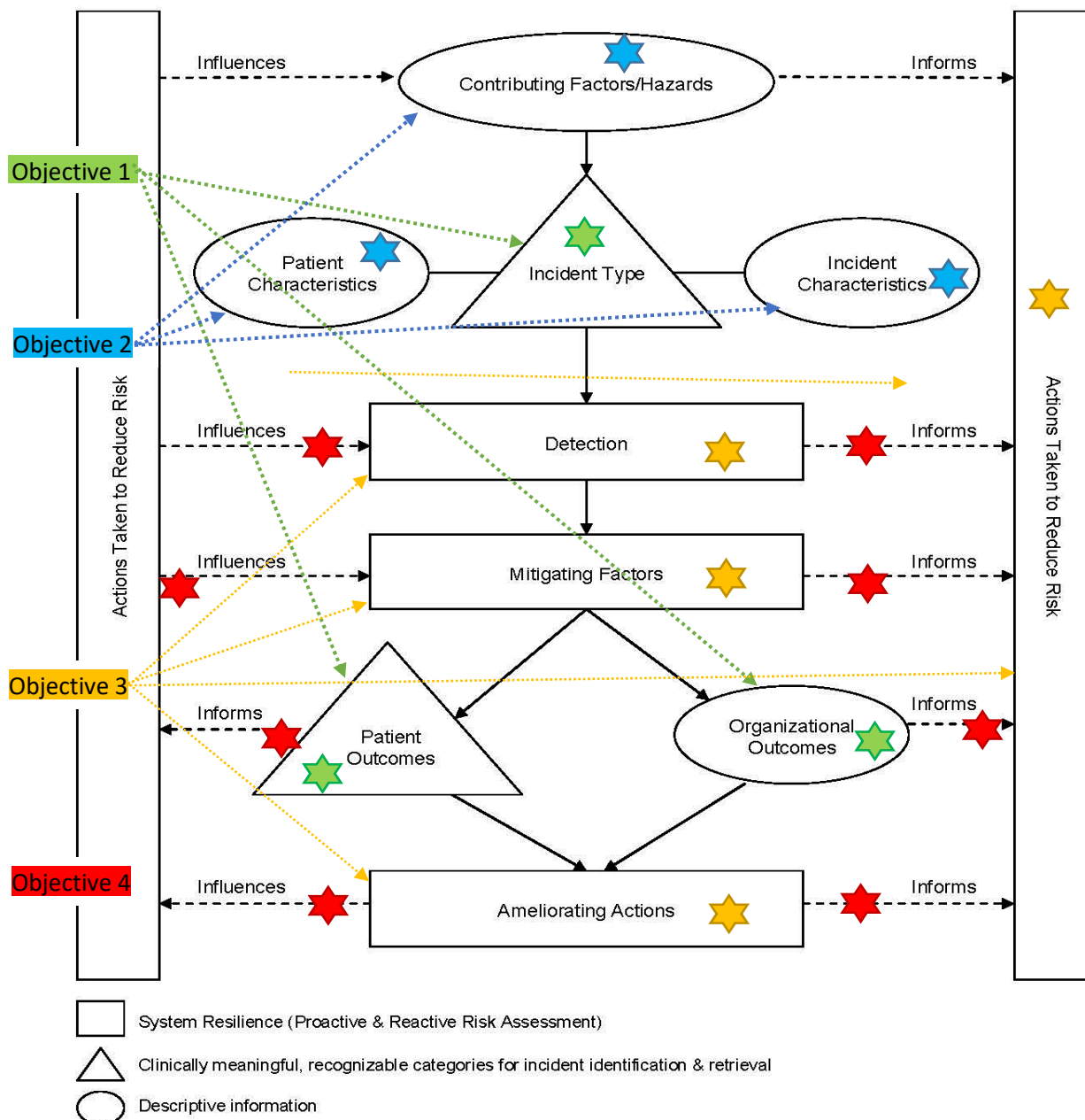
LIMITATIONS

Major limitations of the applied research method encompass the literature search itself, excluding non-English articles, which potentially excluded relevant publications, especially on SSI prevention strategies and trials in sSA. *Secondly*, only *one* researcher was involved in the screening of articles and abstracts, which could have introduced some degree of selection and information bias as there was no internal debate. It should be acknowledged that robust and strict inclusion/exclusion criteria have been put in place to minimize this bias, but more co-workers could have improved the scientific basis of this process by seeking consensus if needed. *Thirdly*, a limitation on the description of the burden of SSIs (*objective 1*) is the tremendous scope of these infections. It was not possible to capture in-depth the full impact of all C-section SSIs in the whole of sSA. Time was limited for this study and this has been addressed by explaining the restrained span of this section. *Fourthly*, definitions on SSIs are not uniformly applied and there is a tendency of slightly better hospitals being able to publish their data. Potentially these hospitals represent better practices and quality of care, which might cause publication bias.

Lastly, discussions and recommendations will be based on the academic research and findings in this thesis, rather than on practical actions as the geographical scope of this thesis covers the whole of sSA. No country-specific information has been looked for in this thesis. This limitation could also be seen as strength, as it provides a general statement on this topic.

FINAL CONSIDERATIONS

Permission for WHO copyrighted materials was requested and approved. Mendeley software (version 1.17.9) was used to organize articles and cite references. The thinkbeforeprinting.org campaign principles were applied for this thesis, none of the manuscripts were printed on paper. There is no external funding or conflict of interest to be declared. Ethics approval was not sought for this thesis. This literature review was based on published articles and no new data were collected on respondents.



The solid lines represent the semantic relationships between the classes. The dotted lines represent the flow of information.

Figure 3. International Classification of Patient Safety (ICPS) conceptual framework 2009 version 1.1. In coloured textboxes and coloured stars in framework the thesis objectives 1 – 4 are linked with framework components. Source: 20

3. Results

In this section, results will be analysed and described, following the sequence provided previously (objective 1 first etc.). These results will finally guide the discussion and recommendations in the last section.

3.1 INCIDENT TYPE, PATIENT OUTCOME, ORGANISATION OUTCOME

Incident type

This concept describes the distinct features of a patient safety category, namely SSIs after C-sections. The literature search (*Annex 2*) resulted in 3,065 articles on health-care-associated infections across sSA. Many studies were excluded as they were irrelevant for this thesis, focussing on non-SSIs or other operative procedures. Background reading on patient safety and SSIs in sSA resulted in 41 articles, technical reports and guidelines for the stated period.

Several good quality review studies have published epidemiology data on SSIs in sSA.^{21,22,27} These reviews cover relevant literature from 1995 to 2013 and suggest a high burden of this incident type. *Table 1* provides relevant data from these reviews, which clearly overlap although not all information was available and use of standardised definitions was limited. SSIs are distinct from other health-care-associated infections, as they develop after *surgery*. Other common incident types found within the health-care-associated infection group are (ventilator-associated) pneumonia, bloodstream infections and urinary tract infections. These do not necessarily involve a surgical incision, although they may be associated with the circumstances leading to or resulting from a surgical intervention.

Most studies in sSA focus on SSIs, which is recognized as the most common health-care-associated infection at the moment, accounting for approximately 30% of the health-care-associated infections in LMICs.^{21,27} Whether this truly reflects the leading position of SSIs is a point of discussion, as the diagnosis can be made much more easily compared to other infections possibly leading to information and publication bias.²¹ Compared to other surgical procedures, the percentage of SSIs seemed slightly lower among C-sections.^{45,46} Nigeria was most represented in the published literature for this incident type, with 7/41 (17%) studies on SSIs.⁴⁷⁻⁵³

The majority of this incident type SSIs are caused by incisional contamination with microorganisms from the patient's own body.⁵⁴ External infectious sources following surgery are less common. More details on incident characteristics, C-sections and contributing factors will be discussed in following sections.

Incident outcomes for patient and health facilities

C-section related SSIs can result in harm for patients. Here we present the type and degree of harm for the patient. Harm is defined as any impairment of structure and function of the body, which may be psychological, physical or social.²⁰ Organisational impact and consequences following SSIs are also discussed (*Fig. 3*).

Type and degree of patient harm

SSIs are recognized as the second major cause of morbidity and mortality among women undergoing a C-section, with haemorrhage being the leading cause of mortality.^{29,46,55} SSIs, endometritis and sepsis have been reported between 6 - 62%, 15 - 24% and 0.6 - 1.1% respectively.⁵⁶⁻⁵⁹ Unfortunately, the definition of SSIs was not uniformly applied, which might have caused some classification bias. Terms often mixed up, with wound sepsis, wound abscesses or febrile morbidity.^{56,60} One multicentre study found over 90% of the C-section SSIs being superficial, and more than half only receiving antibiotics.²⁹ Observation

(without intervening), opening of the wound and re-operation was applied in 7.5%, 30% and 6.5% respectively.²⁹ Others found much more deep incisional SSIs.⁴⁵

There is limited data on *maternal deaths* due to surgical-site infections, many deaths occur in the first 48 hours after C-section, too soon for a SSI to develop.²⁹ The NICE 2011 guideline presents conflicting data from studies, showing a non-calculable absolute risk of maternal deaths and an odds ratio of 2.28 (1.11 – 4.65) comparing planned C-sections with planned vaginal deliveries.⁶¹ Careful interpretation of these results might suggest selection bias, which makes it difficult to understand this data. Others provide postoperative data on mortality, but fail to disaggregate SSIs as cause.^{11,58}

Prolonged hospitalisation (although not significantly), stress, adverse neonatal outcomes and increased costs have all been related to women with C-section-associated infections.^{56,62,63} No studies were found on suffering, altered breast feeding practices, agitation, pain or grief following SSIs, but one can imagine that it can be frustrating for the mother to recover from a procedure and simultaneously take care for the new-born.

Organisational impact

Little is published about fear and distrust in relation to SSIs. Millar reports on societal consequences, like fear, blame, shame or loss of public confidence in health providers and institutions as justification for resource allocation towards infection prevention and control programmes.⁶⁴

In general, the mean hospital stay was prolonged after SSIs (13 versus 5.4 days) or overall health-care-associated infections (+10 days).²⁷ Many studies across sSA confirm these prolonged hospitalization or readmission findings, which in itself can be a risk factor for health-care-associated infections by increasing the exposure time in a pathogenic environment.^{29,46,51,65–68} Cost analysis of health-care-associated infections, including SSIs, should be based on excess length of stay, excess investigations (laboratory, radiology), pharmacy costs and working days lost. In South Africa, direct hospital costs suffered by any health-care-associated infection ranged from US\$ 326 – 1,471 per patient, which is far less than the US\$ 1,087-29,443 in the USA.^{17,28}

Only fragmented data was available from sSA and none of the reviews addressed the economic burden systematically.^{21,22,27} Damaged reputations, legal ramifications, media attention and disrupted workflows were not mentioned in the publications found.

3.2 CONTRIBUTING FACTORS, PATIENT AND INCIDENT CHARACTERISTICS

This section analyses determining factors related to C-section associated SSIs. Descriptive information provides context on patient demographics, circumstances surrounding the incident and influences that have played a role in the development of the SSI.

Contributing factors

Multiple influences which are thought to play a part in the development of SSIs are listed in literature and summarized in *Fig. 4*. These factors are grouped according to the ICPS framework in (1) *human factors* which could be staff or patient-related (such as inadequate communication, performance, non-adherence), (2) *system factors* (e.g. unavailability of accepted protocols) and (3) *external factors* (beyond control of the organisation, e.g. natural environment or legislation).²⁰

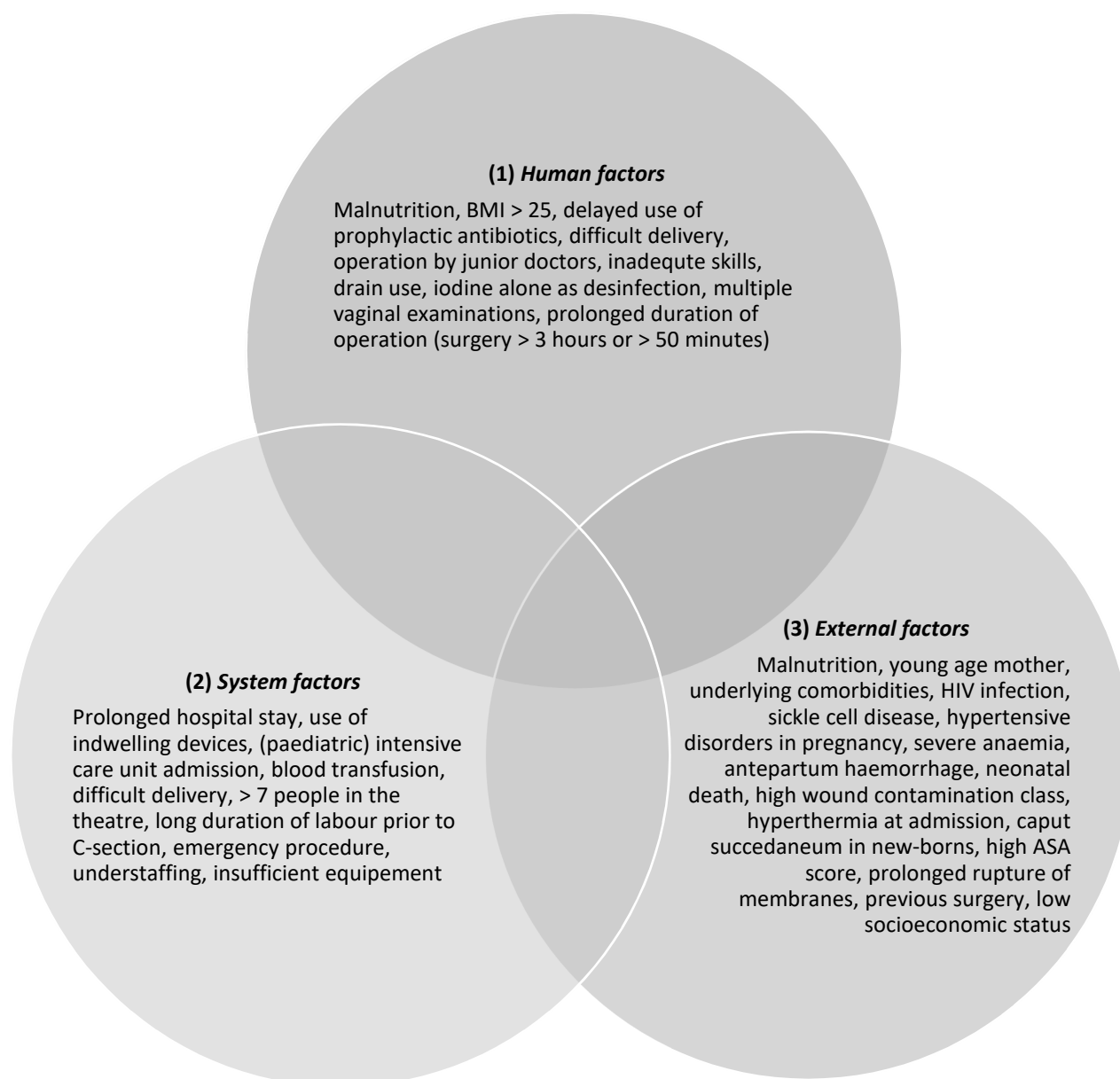


Figure 4 Contributing factors for surgical site infections, based on: 28,29,41,66,67,69–73. BMI: body mass index calculated as weight (kg) / length (m)², ASA: classification system for assessing the pre-operative fitness of patients

Literature is not consistent, and while some studies found a certain contributing factor more important (e.g. anaemia), others did not.⁷⁴ The single most discussed risk factor for the development of SSIs is wound class^{vi}. The degree of surgical wound contamination is known to be a very strong predictor for the risk of SSIs in LMICs.⁴

The groups of contributing factors overlap, as prolonged labour prior to C-section could be patient-related (choice of women to stay at home, delay to come to facility), organisational (delay in decision for C-section during admission at hospital) or even external (inadequate road or communication network) (*Fig. 4*). Some external factors, for example maternal age and low socioeconomic status, also seem to overlap with the class *patient characteristics*.

Modifiable contributing factors could be potentially addressed to reduce the risks for developing SSIs. Preventive measures and interventions will be addressed in the next section.

Incident and patient characteristics

Each type of surgical procedure has its own health-care-associated risk profile with different contributing factors. C-sections are defined as major, clean-contaminated abdominal surgery with a high proportion (>90%) unplanned procedures in sSA.^{11,29} Common indications for C-sections in sSA are obstructed labour, foetal distress, uterine rupture, cord prolapse and previous C-sections.²⁹ Indications for C-sections have expanded in recent years, leading to a call for caution from the WHO in 2015 to restrict the C-section rate.⁷⁵

Patient characteristics

The original reason for this group of women seeking care in health facilities is to receive skilled attendance during childbirth. Typically, most women are less than 30 years, self-referrals and, depending on the geographical area, human immunodeficiency virus (HIV)/hepatitis B exposed.^{29,59,66} Obesity is becoming very common, also among African women.⁶⁶

Findings from a review on C-sections in sSA show a small, but real increase in C-section rates from 1990 to 2014, with a focus on richer women in urban settings.¹¹ Potentially, this trend may cause publication bias towards women with higher social economic status, living in urbanised areas with good access. Poorer women, living in rural areas with poor access to emergency obstetric services who need a C-section are exposed to a different risk profile. These different patient profiles should be taken into consideration when analysing data.

Incident characteristics

Commonly, information collected surrounding the incident (C-section associated SSI) frequently refers to the surgery itself except for wound care and microbiological data.

Maternal characteristics (e.g. age, parity, previous C-section) and *procedural characteristics* (e.g. type of anaesthesia, wound class, emergency procedure, indication, type of skin incision, duration of procedure, type of surgical provider, estimated blood loss, suture type and use and subsequent duration of antibiotic course) at the time of C-section are frequently presented.^{29,59,66} The type of abdominal incision varies, some report most C-sections by midline (vertical) incision⁶⁶, while others promote the transverse (horizontal) approach.⁵⁹ It remains unclear what influence the abdominal incision type has on the development of SSIs.^{29,56}

^{vi} Wound contamination classification describes 4 classes: clean, clean-contaminated, contaminated and dirty wounds depending on infection and inflammation degree and entrance of anatomical tracts e.g. gastrointestinal tract. Source: 19

In most studies, it was the researcher, often supported by clinical staff, who reported SSIs during the hospital stay. From the next section it will become more clear that most infections were detected during the hospital stay only, with limited follow-up after hospital discharge.^{56,76,77} Few studies describe active surveillance, whereas most rely on passive methods expecting patients themselves to report with any signs of infection after they have left the hospital.^{56,76,77}

Minimizing the rate of C-sections will likely reduce the number of C-section related SSIs, although this depends on the background risks and indications for C-sections. If the number of C-sections reduces, but the proportion of high-risk women (anaemic / prolonged rupture of membranes etc.) increases this might still result in slightly higher risks. Like avoidance of healthcare reduces the risk of health-care-associated infections. No data was found on deliberate deviations from the standard or rule during the operative procedure or postoperative, although it should be acknowledged that if there is no standard this concept does not apply.^{45,60} The wide variation in circumstances (political fragility, economic, climate, and construction/buildings) requires careful interpretation of each specific study, although most fail to address these factors in a comprehensive way.

Finally, this section describes *microbiological pathogens* causing SSIs and their antimicrobial resistance. Two reviews report microbiological data in only 37/249 (15%) of the studies.^{22,27} Insufficient microbiological laboratory capacity constrains appropriate surveillance, and limits rational use of antibiotics or research on causes of infection.^{9,17,18,78,79} Microbiological data must be high-quality and locally relevant to guide empiric antibiotic treatment and avoid antibiotic resistance.

The most frequent single pathogen mentioned in literature is *Staphylococcus Aureus*, the leading cause of SSIs, indicating that infections acquired in hospital are caused by microorganisms which are common in the general population.²² The second most common bacterial pathogen causing SSIs is *Escherichia coli*, but it should be noted that infections are often polymicrobial in nature.⁷⁶ Antimicrobial resistance is frequently unknown, but can reach alarming rates over 90% especially for penicillin, ampicillin and chloramphenicol.^{22,80-83} Up to 54% *Staphylococcus Aureus* isolates were methicillin resistant in a review of eight studies.²²

3.3 PREVENTION, RECOVERY AND RESILIENCE

This section is the core part of the thesis, as we critically appraise intervention strategies and move towards prevention and *actions taken to avoid* these infections (*primary prevention*). *Detection* and *mitigating factors*, which are designed to timely discover and prevent/moderate the progression of SSIs after C-sections (*secondary and tertiary prevention*) will be addressed. Finally, any *ameliorating factors*, actions to compensate and avoid further harm (*tertiary prevention*) will be presented.²⁰ A methodological quality evaluation following the ICROMS assessment tool will be presented.⁴⁴

ACTIONS TAKEN TO REDUCE RISK

The review of C-section-associated SSI preventive interventions in sSA resulted in 12 relevant articles for the period 2007 to 2017 (*Annex 2*). These publications, generally focus on C-sections, although some include similar major clean to clean-contaminated surgical procedures.^{45,46,55} General characteristics of the 12 papers are presented in *Table 3*, with the studied topics and their distribution across sSA illustrated in *Fig. 5* and *Fig. 6* respectively.

Seven countries conducted research in this field, with four countries contributing with more than one publication (*Fig. 6*). Prevention strategies will be analysed and discussed in three distinct groups of actions: (1) *Single versus multiple dose antibiotic prophylaxis regimens*, (2) *Other antibiotic prophylaxis-related interventions*, (3) *Non-antibiotic-related interventions*. This last group is a heterogenous category of interventions, including multifaceted policy implementations and strategies related to C-section and surgical hand preparation technique. Summaries and quality assessments of the studies are presented in *Table 4 – 6*.

Table 3 Yield of literature search for prevention strategies (#5 and #6)

		Number of studies	Reference
Study quality [#]	High	7	46,55–57,59,62,63
	Intermediate	2	45,58
	low	3	60,76,77
Study scope	single centre	7	45,46,55,57,60,62,76
	multicentre	5	56,58,59,63,77
Setting	district hospital	2	46,58
	general hospital	4	45,56,58,60
	tertiary hospital	3	55,63,76
	academic/teaching hospital	4	57,59,62,77
Country income level [§]	low-income country	5	45,56,57,62,63
	lower-middle-income country	5	46,55,59,76,77
	higher-middle-income country	2	58,60
Geographic region [‡]	Eastern Africa	7	45,46,55–57,62,63
	Southern Africa	2	58,60
	Western Africa	3	59,76,77
Publication year	2007 – 2012	5	45,46,60,76,77
	2013 – 2017	7	55–59,62,63

[#]Study quality is based on integrated quality criteria for review of multiple study designs (ICROMS)⁴⁴,

[§]According to the World Bank classification⁸⁴, [‡]Based on United Nations Statistics Division⁸⁵. One study was an international trial including study sites outside Africa⁵⁹

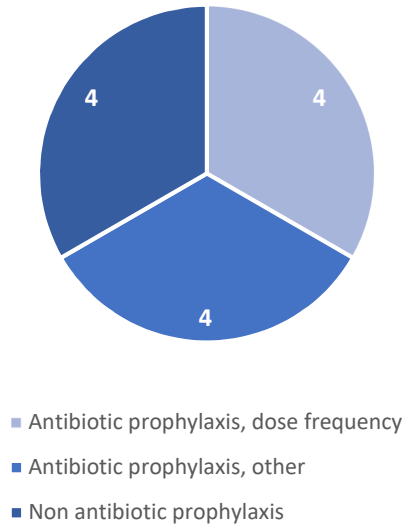


Figure 5 Topics intervention studies (N=12 articles)

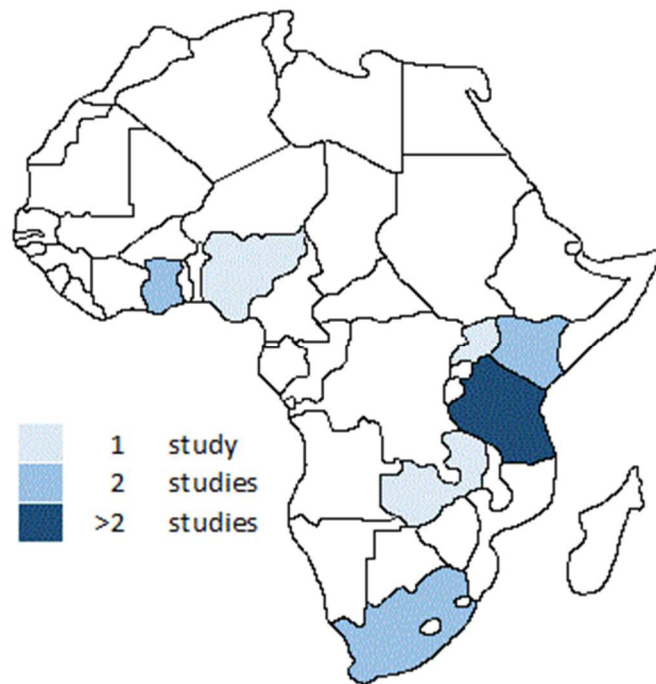


Figure 6 Countries where C-section SSI prevention studies were conducted

Single versus multiple dose antibiotic prophylaxis

Four randomised controlled trials (RCTs) compared single dose prophylactic antibiotics versus prolonged regimes (Fig. 5).^{56,62,63,77} These trials considered a wide percentage range acceptable to prove equivalence/non-inferiority between intervention and control groups (range 5 to 20%).^{56,62,77} This demonstrates that these studies used different cut-off points or criteria, some being more strict than others. Diversity in SSI definition, type of antibiotic, timing of administration and duration of multiple dose antibiotic regimes were remarkable, which makes it challenging to compare between the studies. Only one study applied standard CDC definitions⁶², others used their own definition. The nature of C-sections varied widely in terms of patient characteristics. Some studies focussed exclusively on emergency cases⁶² or elective cases⁷⁷, while others studied both.^{56,63} A Nigerian study excluded all women with ruptured membranes⁷⁷, while a Tanzanian one excluded patients with *prolonged* rupture of membranes only.⁵⁶ Lack of consistency within the same study was also detected, different types of antibiotics were compared thereby unnecessarily complicating the analysis of single dose versus multiple dose regimes.^{63,77}

Findings single versus multiple dose regimes

Despite all these quality and design differences, including lack of microbiological data, there appears to be consistent evidence that the use of single dose prophylactic antibiotics should be recommended for the prevention of SSIs in C-sections, because of equal effectiveness, reduced costs and less workload.^{56,62,63,77} A summary of the studies is presented in *Table 4*.

Other antibiotic prophylaxis related interventions

Four other antimicrobial prophylactic studies not comparing dose frequency were found, one low-quality Ghanaian RCT compared different antibiotic regimes⁷⁶, one high-quality single-blinded RCT from Uganda looked at timing of prophylaxis⁵⁷ and two East African studies investigated the introduction of an antibiotic prophylaxis policy with interrupted times series and before-after design.^{45,55} In one study, a policy was developed by multidisciplinary teams in a period of three months, and endorsed by all staff.⁵⁵ It provided rationalised recommendations on antibiotics prophylaxis for different operations, including dose timing and duration.⁵⁵ The other study on policy change was more simple, all clean-contaminated

surgeries received one single dose of amoxicillin/clavulanate prior to the incision.⁴⁵ Details on the results of these four studies are presented in *Table 5*.

Table 4 Summary on four C-section surgical site infection prevention strategies based on single versus multiple dose antibiotics regimens

<i>Year published, country, first author</i>	2008, Nigeria, Alekwe (Ref. 77)	2013, Tanzania, Lyimo (Ref. 62)	2014, Tanzania, Westen (Ref. 56)	2014, Zimbabwe, Gidiri (Ref. 63)
<i>Study design</i>	RCT (<20% difference accepted)	RCT, non-blinded equivalence (<5% difference accepted)	RCT, non-inferiority (<10% difference accepted)	RCT, non-inferiority
<i>Intervention</i>	Single dose ceftriaxone after cord clamping	Single dose gentamicin + metronidazole 30-60 min. before C-section	20 minutes pre-operatively single dose ampicillin and metronidazole	Single dose ceftriaxone iv + metronidazole iv pre-operatively only
<i>Control</i>	48 hrs multiple doses ampiclox, gentamicin, metronidazole, then 5 days ampiclox, metronidazole, 3 days gentamicine	gentamicine + metronidazole starting also pre-operatively, same dose post C-section for 24 hrs	2 doses of ampiciline + metronidazole i.v., followed by amoxicillin + metronidazole orally 2-5 days	pre-operatively benzylpen. + chloramphenicol, day 1 to 7 amoxicillin + metronidazole
<i>Size and study population</i>	N=200, elective only	N=500, emergencies only	N=181, emergencies and elective	N=280, emergencies and elective
<i>SSI definition</i>	own	CDC	own	own
<i>Follow-up period and method</i>	No follow-up defined	30 days, day 7 and 30 are post discharge, phone calls to remind patients	30 days passive follow-up (depends on patients returning)	6 weeks (42 days), method of follow-up not well described
<i>Results</i>	Single dose ceftriaxone was as effective as a combination of multiple doses of ampiclox, gentamicin, metronidazole in preventing SSIs	Single dose AB recommended, with less cost/workload and lower cumulative incidence of SSI	Single dose prophylactic ampicillin and metronidazole is equally effective as a multiple-day regimen in preventing SSIs	No statistically significant difference in the efficacies of single dose vs multiple dose antibiotics
<i>Study quality*</i>	Low quality, confusing microbiology data, protocol on timing AB not clear. Block randomization without indication of block seize, risk of predictability Follow-up not addressed, no blinding	High quality, however not clearly stated limitations. Zero loss to follow-up? Intervention effect on data collection not reported	High quality, authors mention own limitation (poor knowledge of post-discharge infections). Permuted block randomisation could introduce predictable allocation towards the end of a block	High quality, but almost 20% dropout and insufficient patients according to own power calculation. No information why participants were wrongly included, no information on limitations
<i>Patient characteristics, incident type, detection, and patient outcomes described? #</i>	Patient characteristics are well described, as well as incident type. Microbiological data missing	Yes, surgical technique and degree of harm/outcome not well addressed, diagnosis by single person, mitigating factors not discussed	Well described patient characteristics and environment context. Patient outcomes described well	Yes, well described reasons for C-section and degree of harm. Detection method not standardised nor well described
<i>Collective learning / system improvement? #</i>	Author explicitly mentions collective learning with further elaboration	Insufficient information available to make a judgement on this	Insufficient information available to make a judgement on this	Insufficient information available to make a judgement on this
<i>Notes</i>	Microbiological tests not specified, laboratory quality/accreditation not mentioned	No microbiology data, previously study published protocol well followed	No microbiological data	No microbiology data, HIV presented but unknown medication
*based on ICROMS quality appraisal tool ⁴⁴ , #elements distilled from ICPS conceptual framework ²⁰				

Table 5 Summary on four C-section surgical site infection prevention strategies based on other antibiotics-related strategies

<i>Year published, country, first author</i>	2007, Ghana, Opoku (Ref. 76)	2009, Tanzania, Saxer (Ref. 45)	2013, Kenya, Aiken (Ref. 55)	2015, Uganda, Dlamini (Ref. 57)
<i>Study design</i>	RCT	Before-after study	Interrupted times series	RCT, single-blinded
<i>Intervention</i>	amoxicillin-clav. after cord clamping and 12 hours later	amoxicillin/clavulanate, 30 min pre-operatively	Introduction of antibiotic prophylaxis policy	ceftriaxone 15 - 60 min. prior to incision
<i>Control</i>	ampicillin, metronidazole + gentamicin after clamping and 12 hours later	Normal practise, almost 90% antibiotic prophylaxis after incision and routinely for 5 days "differed depending on the surgeon"	At intervals, comparison of different measures before and after implementation new policy	ceftriaxone after incision
<i>Size and study population</i>	N=320, emergencies and elective	N=803, various operations	N=3,343 (2,594 C-section) various procedures	N=464, emergencies only
<i>SSI definition</i>	own	CDC	CDC	CDC, however no 30 days follow-up
<i>Follow-up period and method</i>	None defined	30 days, free treatment and compensation. Independent review by 2nd senior colleague.	30 days surveillance, including phone contact after discharge	10 days, first at postnatal ward and finally at postnatal check-up
<i>Results</i>	Amoxicillin/clavulanate was superior over triple therapy	Single dose of amoxicillin/clavulanate pre-operatively reduced the rate of SSI with 80%	Implementation of a locally developed policy regarding surgical antibiotic prophylaxis is an achievable quality improvement target for LMIC hospitals. After introduction, there was some evidence for a downward trend in infection risk	Prophylactic antibiotics before skin incision reduce risk of SSIs
<i>Study quality*</i>	Low quality. No blinding of outcomes, no clear follow-up, no clear description of data analysis, no limitations addressed. No ethical approval was sought.	Intermediate quality, robust assessment method of outcomes. High loss to follow-up at day 30. Conclusion slightly conflicting with other studies where amoxicillin/clavulanate was not accepted. No ethical approval sought.	High quality, intervention coincided with new junior staff starting, clear rationale for clean/clean contaminated wound groups. Timing of antibiotic dose unclear but limitations addressed.	High quality. Explicit quality control measurements, interim analysis done and rigorous protective approach for neonatal patients. Limitation briefly addressed, short period of follow-up, single blindedness.
<i>Patient characteristics, incident type, detection, and patient outcomes described? #</i>	Patient characteristics very limited described, no pre-existing comorbidities presented. Detection method not well explained. Conclusion contradicting.	Patient characteristics not well described in detail on C-sections. Detection is well described, but proportion hospital / non-hospital not addressed.	Heterogenous group of patients, not only CS patients. Not well explained characteristics. Incident type not further supported with microbiological data.	Patient characteristics generally well described. Data safety board mentioned to detect adverse events and possibly stop study prematurely. Patient SSI outcomes are very frequent.
<i>Collective learning and system improvement? #</i>	Insufficient information available to make a judgement on this	Limited sustainability, analysis in laboratory in Basel	sustained quality improvement, locally-developed, rationalised including overview of barriers and support of change	Careful consideration of the findings in light of a broader context with other approaches (adherence to aseptic procedures, quality of disinfectants etc).
<i>Notes</i>	Microbiological data mentioned, but not interpreted	Up to 60% antimicrobial resistance in control group, but no resistance in intervention group (choice of AB in intervention group based on research done in control group)		No microbiology data, study protocol well written, and also adhered to.
*based on ICROMS quality appraisal tool ⁴⁴ , # elements distilled from ICPS conceptual framework ²⁰				

Findings other antibiotic interventions (non dosing-regime studies)

Regarding prophylaxis timing, Dlamini and colleagues compared single dose ceftriaxone pre-incision with administration after incision.⁵⁷ *Preoperative administration reduced the SSI risk*, although the follow-up was only 10 days which was not in line with the statement that CDC definitions were applied.⁵⁷ The rigorous quality control measurements with interim analysis and data safety management board should be pointed out.

During 16 months SSI surveillance an antibiotic prophylaxis policy was implemented at a Kenyan government hospital.⁵⁵ *Process measures* (e.g. proportion of patients with preoperative antibiotics), *outcome measures* (risk of different SSI forms according to CDC definition) and *balancing measures* (e.g. costs and staff time requirements) were evaluated at interrupted moments. A locally developed policy on antibiotic prophylaxis appeared achievable, with some evidence of a *downward trend in risk of infection*.⁵⁵ *Organisational benefits* were reduced costs and marked reductions in time spent on injections by nurses. It should be noted that this study included a heterogenous group of surgical patients, thereby obscuring pure C-section data. This rational, locally-developed policy was studied with a different design than most other studies, but was able to demonstrate the possible impact of policy implementation.⁵⁵

The non-controlled before-after study by Saxer and colleagues compared the introduction of amoxicillin/clavulanate pre-incision with the *common practise* before this policy implementation.⁴⁵ The diverse group of 'common practise' almost exclusively consisted of antibiotic prophylaxis after incision for multiple days, but '*differed depending on the surgeon*'.⁴⁵ Like with the previous study, CDC definitions were applied but with more scrutiny using an additional independent senior evaluator.^{45,55} General clean and clean-contaminated surgeries were included in this study, which concluded that *a single dose amoxicillin/clavulanate iv was superior to 'common practise' in preventing SSIs*.⁴⁵ This same conclusion was made by Opoku, who argues that the medication costs of amoxicillin/clavulanate were four times higher.⁷⁶ Ideally, the selection of antibiotic should be based on microbiological susceptibility testing. Saxer et al. benefitted from laboratory testing and a steady medication supply from Switzerland.⁴⁵ These elements demonstrate the difficulty for a sustainable prevention intervention.

Non-antibiotic interventions

Four studies examined non-antibiotic-related strategies to prevent SSIs after C-sections. Two from South Africa looked into implementation of a modified surgical safety checklist⁵⁸ and surgical technique to close the abdomen.⁶⁰ A third study conducted in Ghana was part of a large international multi-centre trial, looking into five paired surgical technique elements of C-sections.⁵⁹ The last study was a cluster-randomised, crossover trial comparing locally produced alcohol-based hand rub with plain soap and water for surgical hand preparation.⁴⁶ The last two studies were of high quality, while the South African studies showed major drawbacks. Summary data is presented in *Table 6*

Findings of non-antibiotic interventions

Naidoo and colleagues studied 26,985 obstetric surgeries in 18 district/regional hospitals across KwaZulu-Natal province, using a stratified, cluster-RCT.⁵⁸ Blinding was not done sufficiently, with one control hospital also adopting the intervention (surgical safety checklist). Although the authors address this in their analysis with different scenarios, it is likely that this has affected the outcome. Reliability of data was not elaborated on with an internal validity test, while only *one* investigator was involved with so many patients in multiple centres. The follow-up for adverse outcomes was not clearly defined, and SSIs were not a primary or secondary outcome. Postoperative sepsis and combined overall outcome improved significantly in the intervention group.⁵⁸

Table 6 Summary on four non-antibiotic C-section surgical site infection prevention strategies

Year published, country, first author	2009, South Africa, van Bogaert (Ref. 60)	2010, Kenya, Nthumba (Ref. 46)	2013, Ghana, Brocklehurst (Ref. 59)	2017, South Africa, Naidoo (Ref. 58)
<i>Study design</i>	Unclear design, comparison between C-sections and vaginal deliveries and within various C-section techniques	RCT, cluster-randomised, crossover	RCT, fractional, factorial, unmasked	RCT, stratified, clustered
<i>Intervention</i>	None clearly described	Locally produced alcohol-based hand rub	Five elements of C-section technique studied in intervention pairs: blunt/sharp, uterus exteriorisation yes/no, single/double layer uterus closure, closure/non-closure peritoneum, chromic catgut/polyglactin-910	Modified surgical safety checklist implementation
<i>Control</i>		Soap and water for surgical hand preparation		No implementation of checklist
<i>Size and study population</i>	N=1,312 emergencies and elective	N=3,133 (18% obstetric cases)	N=15,729 emergencies and elective	N=26,985 (82% C-section)
<i>SSI definition</i>	own	CDC	own	own
<i>Follow-up period and method</i>	10 days, method of follow-up not specified	30 days, inpatients or outpatients actively called	6 weeks follow-up, by phone or home visit	unknown
<i>Results</i>	Closure or non-closure of peritoneum after C-section has no impact on sepsis or febrile morbidity	Clinically or statistically no difference in SSI rate between intervention and control group	Type of technique (based on these five pairs) has no influence on short-term outcome of complications like wound infections	Implementation of surgical safety checklist for maternity care resulted in significant improvement of combined outcomes and postoperative sepsis
<i>Study quality*</i>	Low quality. No randomisation, objective unclear. Unblinded outcomes, authors do not attempt to mitigate the effect of having no control group (vaginal deliveries are not sufficient control group). Statistical analysis unclear. Several potential sources of bias, no ethical approval	High quality. Blinded, SSI diagnosis was jointly decided and reliable. Follow-up however mostly by phone. Large number of patients not eligible, without clear reason stated. Perioperative AB prophylaxis not further defined in pre- or post-incision administration	High quality. Well described study protocol and randomisation. Robust, but limitations described like unmasked design. Possible some selection bias, with patients with greatest risk less likely to be recruited. Validation exercise done during trial, missing data corrected by more rigorous training	Intermediate quality. Blinding is not done sufficiently, reliability of data is not elaborated on. Follow-up not clearly defined, the intervention itself is likely to affect the data collection (better implementation, more data)? Limitations found in assessing compliance.
<i>Patient characteristics, incident type, detection, and patient outcomes described? #</i>	Not well described, author argues that limitations are caused by complex low-resource setting. Detection issues and patient characteristics minimally addressed	Different patient categories, each not further specified. Mitigating factors discussed in broader perspective, limitations addressed, SSI detection and outcomes addressed.	Not very detailed at individual level, data from Ghana not possible to distilled from the rest	Not much details on patient characteristics, incident type and mitigating factors. Very general article
<i>Collective learning and system improvement? #</i>	Insufficient information available to make a judgement on this	Acceptability, feasibility and affordability addressed. Locally sustainable.	Insufficient information available to make a judgement on this	Insufficient information available to make a judgement on this
<i>Notes</i>		No microbiological data	1270 C-sections (8%) done in Ghana	Primary outcomes were mortality, SSI not explicitly addressed

*based on ICROMS quality appraisal tool⁴⁴, # elements distilled from ICPS conceptual framework²⁰

Compliance of hospitals to the study protocol was judged by informal observations and through focus group discussions, which is not very objective.

The second South African study by Van Bogaert et al. was of low quality.⁶⁰ The objective was vague, and for some unclear reason a comparison between C-section and normal vaginal deliveries was introduced later in the paper. There was no randomisation, incomplete information on the rationale for the study design and no blinding of outcomes. The conclusion that closure or non-closure of peritoneum after C-sections has no impact on sepsis or febrile morbidity seemed not argued well.⁶⁰

The Ghanaian unmasked, fractional, factorial RCT was carefully planned with a previously published detailed study protocol.⁸⁶ The same patient population as studied and described in the initial trial, is followed for more long-term outcomes.^{59,87} For this thesis, long term effects of C-sections were not relevant and therefore not studied. A total of 15,729 patients at 19 sites were randomised for 5 elements of the C-section technique. None of the involved countries was low-income, five were lower-middle-income countries (including Ghana). The five elements studied in intervention pairs were: (1) blunt versus sharp abdominal entry, (2) exteriorisation of the uterus versus intraabdominal repair, (3) single-layer versus double-layer uterus closure, (4) closure versus non-closure of the peritoneum (parietal and visceral), (5) chromic catgut versus polyglactin-910 for uterine repair.⁵⁹ This rigorous study demonstrated that *type of technique had no influence on short-term outcomes like SSIs*. Limitations could be the low percentage of C-sections from Ghana (n=1,270; 8%), unmasked evaluation of the results, some limited compliance to the randomised group and selection bias asking the least risky patients to participate in this study.⁵⁹ However, the design is well thought, and most low-middle-income countries would have similar sites.

Finally, the Kenyan study by Nthumba and colleagues found that *locally made alcohol-based hand rub was not clinically and statistically different in preventing SSIs* after clean or clean-contaminated surgeries.⁴⁶ Possible unknown residual confounding factors and follow-up of patients mostly by phone were limitations. Informal analysis of acceptability, feasibility and costs suggested that this intervention was feasible, especially in places with poor water quality or unreliable supplies.⁴⁶

QUALITY OF STUDY DESIGN

The overall methodological quality of the 12 relevant articles was diverse and related to many common errors. For quality assessment, the ICROMS tool proved to be very helpful. *Table 4 - 6* present the summarized findings, based on seven dimensions: *clear aims and justification, managing bias in sampling or between groups, managing bias in outcome measurements or blinding, managing bias in follow-up, managing bias in other study aspects, analytical rigour and managing bias in reporting*.⁴⁴

Clear objectives and justification were provided in most studies, except in one.⁶⁰ Sampling was generally sufficient, with identical sealed opaque envelopes in the RCTs, but intrinsic allocation errors related to block randomisation techniques might have introduced predictable allocation towards the end of the blocks.^{56,77} One study introduced 'quasi-random allocation', allowing physicians to practice '*as they were used*'.⁶⁰ Compliance to the allocated intervention was another challenge, which some studies simply presenting it as limitation and others trying to tackle this by analysing different scenarios.^{58,59}

Generally blinding of participants or staff was often not done^{58,62,76,77}, although some key-study personnel might have been blinded.^{46,56,57} Others gave insufficient information to judge this dimension.⁶³ Some outcome variables were not completely objective (erythema, induration), and therefore detection and diagnosis by two persons was acknowledged as superior.^{45,55}

Follow-up methods and periods were highly variable, and ranged from *10 days to 6 weeks*. Most studies achieved well according to their own study protocols except for one with over 20% loss to follow-up at day 30.⁴⁵ One study achieved 100% follow-up, which also is questionable in the sub-Saharan African

context with its logistical challenges.⁶² Uniform follow-up length and intensity of outpatient follow-up efforts would greatly increase the overall quality of studies and make comparisons between them easier. The CDC definitions could serve as guide.^{34,38}

None of the authors satisfactorily reported to what extent the intervention itself influenced/affected the way of data collection. It might be possible that interventions resulted in more thorough data collection, which could increase the number of detected incidents. Statistical analysis showed wide variation, with some studies not providing clear statistical descriptions^{60,76,77} and others robustly explaining statistical tests and sample size calculations.^{45,56,57,62,63}

Vigorous study protocols were scarce, only two trials were able to publish their protocols separately.^{86,88} Frequently, lack of information made it impossible to decide if selective outcome reporting occurred. No self-reported limitations were presented by authors in three papers.^{62,63,76} Ethical clearance was not sought or reported in three studies, which is a critical omission.^{45,60,76}

A recent review and meta-analysis was undertaken by Pinto-Lopes and colleagues (2016) on single dose versus multiple dose antibiotic prophylaxis regimens.⁸⁹ Non-significant differences were observed between single and multiple dose antibiotic regimens but most articles (11/16, 69%) came from high-income countries and were published before 1995 (10/16, 63%).⁸⁹ Two studies which scored best on methodological quality have also been analysed in this thesis (published in 2013 and 2014).^{56,62} A trend with improving quality can be seen, with the more recent publications being of higher quality than the older ones (*Table 4 – 6*). This encouraging sign is also observed by others, however designing new high-quality studies remains essential and could build further on current knowledge.^{4,44,89}

CONNECTING ICPS FRAMEWORK TO INTERVENTIONS

The major classes within the ICPS analytical framework will be linked and discussed for the 12 studies presented above.²⁰ Recovery and resilience through detection, mitigating and ameliorating factors will be addressed in the final part of this section.

Incident type. The selected literature unanimously looked at SSIs. Four studies incorporated SSIs within maternal infectious morbidity, or named it differently.^{58–60,63} Only 5/12 (42%) of the papers used CDC definitions, although the correct 30 days follow-up period was not always respected.^{45,46,55,57,62}

Patient outcomes. Many studies (N=5, 42%) failed to provide information on the degree of infection^{58–60,62,77} No excess SSI attributable mortality was reported.^{56,58,63} Social impact was hardly addressed, while economic burden and cost/benefit analysis were often linked to the studied intervention.^{45,46,55,56,62,77}

Organisational outcomes. Reduced costs and less workload have been addressed as organisational benefits and justification for the prevention of SSIs.^{56,62,63,77} With regards to costs, additional hospital stay and extra money spend on antibiotics/surgery and staff were mentioned as the most important reasons for extra expenses.^{45,55,56,62,77} There was no data found in relation to fear or loss of public confidence.

Patient characteristics. Not all papers exclusively studied women undergoing C-sections (N=8, 67%), four included other (obstetric) procedures with similar wound contamination classes.^{45,46,55,58} In 5/8 (63%) of the C-section only papers, both emergency and elective procedures were accepted. One other study looked at elective cases only⁷⁷, the last two at emergencies only.^{57,62} Age and parity mostly ranged between 25 to 35 years, and one to two pregnancies respectively.^{77,81,86} Indications for C-section were generally presented, but not in studies with mixed surgical patient populations.^{45,46,55,58} The leading cause of elective C-sections was a history of C-section⁷⁷, while obstetric complications with protracted labour and foetal distress were main reason of emergency procedures.^{56,59,63} Additional patient demographics like marital status, education level, occupation and HIV status were not standard presented, and sometimes minimal data was provided.^{59,76}

Incident characteristics. Debate is ongoing about the detection timing of SSIs. One study detected over 70% of the SSIs after discharge from hospital⁴⁶, while others found the majority during hospital stay.^{29,56} Limited follow-up and passive surveillance methods seem to restrict the capacity of post-discharge SSI detection.^{56,76,77} For pragmatic reasons researchers often tended to end follow-up periods at 10 days.^{57,60} Wide variation in normal admission duration (3 – 10 days), often depending on type of abdominal incision, obviously interrelates with infection detection possibilities.^{56,57,60,62}

The type of surgical provider and wound care practitioner were only addressed in few articles, with large variation in schemes for wound inspection and care.^{45,55,76,77} Routine daily cleansing of wounds with antiseptic was promoted in a South African study⁶⁰, while others just left wounds open after initial removal of occlusive dressing.⁶² Dressings were typically removed after 24 – 48 hours, and not always replaced.^{56,62} The person reporting SSIs is not explicitly studied, as it could be a relative, home assistant, volunteer, researcher or healthcare worker.

Three (25%) papers presented microbiological test results^{45,76,77}, in which two low-quality studies failed to explain data.^{45,76,77}

Contributing factors. Factors influencing C-section-associated SSIs or implementation strategies have been distilled for presentation in the previous section (*objective two*) and next section (*objective four*), therefore they will not be discussed here.

Detection. Most SSIs were discovered by mechanisms built in by the study designs. Assessment protocols indicated certain days of inspection for SSI signs and symptoms.^{45,76} None of the studies satisfactory addressed the effect of interventions on data collection and detection, although one stated that no change to surveillance methods or staff were made.⁵⁵ Diagnosis by a single health worker was common practise, in only a few exceptions team dialogue and consensus was sought.^{45,46,55}

Mitigating factors. Actions which prevent or moderate the progression of infections harming patients are active surveillance during and after admission, prescription of antibiotics, referrals to higher levels of care, extended hospitalisation and reoperations.^{58,59,63} Some poor-quality studies failed to address any mitigating factor^{60,76,77}, although the ICPS framework shows the close relationship with patient outcomes and risk reduction.²⁰ Staff related factors such as good team work, good supervision, training, effective communication or IPC strategies are clearly undervalued in the presented papers.

Ameliorating factors. None of the articles shared information on actions taken to compensate or improve the status of patients once they became infected with a SSI. The only actions taken are often mitigating factors, which try to moderate the progression of infections.

3.4 IMPLEMENTATION CHALLENGES

Before moving to the *discussion* and *recommendations*, this last section on implementation challenges describes issues in relation to actual application of interventions in district hospitals across sSA. This contextual description might be helpful to assist with translation and planning of the described interventions into action.

Driving and restraining forces for effective implementation will be critically appraised, which might serve as ‘glue’ or ‘arrows’ connecting the different classes at the bottom of the ICPS framework (Fig. 3). These challenges/opportunities refer to *influences* and *information*, which connect *actions taken to reduce risk* with the various ICPS classes like *detection*, *mitigating factors*, *patient outcomes*, *organisational outcomes* and *ameliorating factors*.²⁰

Force field analysis

The different challenges and opportunities are presented in a *force field analysis*, with the corresponding sources listed in the adjacent column (Table 7). Data was systematically extracted from *all* the searches described earlier (Annex 2). This process was more qualitative, and searches for more challenges or restraining forces continued until saturation was reached. The validity was maximised by triangulation, having different respondents and perspectives all converging to the same driving and restraining forces. The different study types (e.g. trials, surveys, observations, interviews) which were found again add to the credibility and transferability of these findings. A weakness in the qualitative process was the limited descriptive contextual data, which makes it more difficult to interpret the forces for a specific context.

Change in practice and policy, by effective implementation of a new strategy, could start with a stakeholder analysis. All people and relevant organisations who are affected by change and with influence or power, might be good to consider before implementing a new infection prevention policy. Prioritising and understanding key stakeholders offers opportunities to engage them and communicate with them properly.

When studying forces that influence implementation and change it is important to identify as many factors as possible. Table 7 lists these variables with references, but is by no means exhaustive and may have some gaps.

Table 7 Force field analysis of infection prevention strategy implementation in sub-Saharan Africa

Driving forces →		← Restraining forces	
<i>Human forces →</i>		<i>← Human forces</i>	
90	<i>Training</i>	<i>Costs</i>	91
5	<i>Champions</i>	<i>No training</i>	92
93	<i>Role models</i>	<i>Poor payment</i>	93
58	<i>Personal motivation</i>	<i>Low motivation</i>	58
55	<i>Sensitisation of staff</i>	<i>Low risk perception</i>	91
90	<i>Adequate knowledge</i>	<i>Potential side effects</i>	91
55	<i>Personalised feedback</i>	<i>Limited health workers</i>	92
18	<i>Personal responsibility</i>	<i>Poor teamwork among staff</i>	58
93	<i>Ownership by involving stakeholders</i>	<i>Lack of knowledge and awareness</i>	94
55	<i>Multi-disciplinary policy development</i>	<i>No participation of patients or caretakers</i>	21
<i>System forces →</i>		<i>← System forces</i>	
5	<i>Auditing</i>	<i>High workload</i>	95
55	<i>Saving time</i>	<i>Lack of policies</i>	41
55	<i>Saving resources</i>	<i>Limited resources</i>	41
5	<i>Leadership support</i>	<i>Inconsistent policies</i>	91
55	<i>Upgrade of services</i>	<i>Lack of patient safety focus</i>	41

Cont. Driving forces →		← Restraining forces Cont.	
94	<i>Evaluation of strategy</i>	<i>Inadequate communication</i>	94
15	<i>Implementation strategy</i>	<i>Lack of physical infrastructure</i>	94
15	<i>Adequate communication</i>	<i>Inadequate laboratory capacity</i>	94
5	<i>Positive organisational culture</i>	<i>Limited supplies of consumables</i>	94
55	<i>Cross-departmental development</i>	<i>Lack of basic, functional equipment</i>	21
55	<i>Locally-relevant simple training material</i>	<i>Lack of support from senior health worker</i>	58
External forces →		← External forces	
55	<i>National guidelines</i>	<i>Culture</i>	94
21	<i>Political commitment</i>	<i>Climate</i>	93
94	<i>Presence of active partner</i>	<i>Poor infrastructure</i>	94
		<i>Change in governance</i>	94
		<i>Competing health priorities</i>	41
		<i>Decentralization of health services</i>	94
Other →		← Other	
55	<i>Strong evidence base</i>	...	
5	<i>Ergonomics</i>		
	...		

With a force field analysis, scores could be assigned to each individual force, based on the degree of influence of the force on the strategy implementation (weak versus strong). Based on the heterogeneous data from literature it was not possible to make a general ranking. Besides, this was not the main purpose of this thesis. This analysis could however be done for context-specific health-care-associated infection prevention strategies. Often most attention goes to challenges, rather than to supporting/driving forces.⁹⁵ Missing information could be collected by widely applied research methods such as semi-structured or in-depth interviews, focus-group discussions, surveys and observations.^{5,90,92,93,96,97} Another strategy to collect more data is by considering settings with similar external forces (e.g. climate, socio-economic development).

In conclusion, multiple driving and restraining forces play a role in change and strategy implementation. The mere absence of restraining forces, or the sole presence of driving forces does not automatically guarantee success. Understanding the complex interplay of these forces, which generally needs to be supportive, is important. Different strategies and modalities may be utilised to achieve a desired change and maintain the intervention over time.⁹⁸ Continuous refinement and improvement of the strategy implementation based on the situation is key to success.²⁰

4. Discussion

The overall results of the analysis and their connections will be discussed in this section. This thesis looked into a relevant patient safety issue, focussing on SSIs after C-sections. SSIs were used as recognized proxy indicator for quality of care, while C-sections represent a common major surgical procedure in district hospitals across sSA. C-section rates are on the rise across sSA. This is particularly true for women residing in urban areas and who come from higher social economic strata. Using the ICPS conceptual framework and classification, the results of the four objectives were systematically analysed.

The high burden of SSIs after C-sections, has great impact on patient and organisational outcomes. Excessive costs, prolonged hospitalisation, stress and need for additional treatment are related to these infections.

Among various health-care-associated infections in sSA, this type of infection is most commonly reported. Compared to developed countries, there was only scarce incidence and prevalence data available from sSA, which was mostly based on research undertaken in single hospitals or wards.²² Comparison of data from different studies and generalisability to the wider setting is challenging without standardised national or multicentre surveillance reports. Particularly data from poorer countries and rural healthcare settings is lacking.²¹ This probably leads to underreporting from these areas, which might be linked to their limited diagnostic capacities, research and publication skills.

In addition, this thesis was not able to separately judge the value of all different contributing factors. Conflicting information and the huge variation in pre- and post-operative C-section practices, made it difficult to analyse to what extent certain factors play a role in the development of SSIs, and to compare the various actions to reduce SSIs. As a result, it was difficult to come up with a well-defined research agenda, aiming to better understand these factors and to test interventions aimed at modifying them.

A comprehensive description of patient characteristics, incident characteristics and contributing factors was expected to provide a picture on the context surrounding SSIs. A total of 12 studies were identified addressing a wide range of interventions to reduce risks and prevent the occurrence of post-C-section SSIs. RCTs are often valued as ultimate study design, but in complex policy-related public health interventions other designs have also proven their value.^{45,55} Not all studies were of good quality, however, the integrated quality criteria for review of multiple study designs seemed to allow the grading of these studies in a good way. Based on analysis of the 12 articles, we can conclude that for SSI risk reduction:

- a single dose pre-incision antibiotic is sufficient
- antibiotic prophylaxis policies can be implemented with substantial benefits
- surgical safety checklists improve overall surgical outcomes including infections
- no specific surgical C-section technique is superior
- and locally produced alcohol-based hand rub is effective as surgical hand preparation

Text-box 1 Recommendations for good practice to prevent surgical site infections after caesarean sections

Sustainable and collective learning resulting in system improvement and resilience is not straightforward, and even simple SSI prevention strategies may require continuous culture or organisation improvement. Adjustment and continuous control are basic processes and part of cyclic total quality management.^{9,16,17,20,99} For unclear reasons the NICE guideline on C-sections recommends *not* to use amoxicillin-clavulanic acid prior to skin incision⁶¹, while this was done in one intervention study.⁴⁵ No supporting evidence for this discrepancy was found.

Similar to the findings in this thesis, Aiken and colleagues noticed that most studies in their review on interventions for preventing SSIs targeted antibiotic prophylaxis regimens (4/11, 36%).⁴ In addition they identified other non-antibiotic interventions, which were not found after 2007 (adhesive plastic drapes, Misgav-Ladach technique^{vii}, peritoneal non-closure, wound drainage and early discharge).⁴ No significant reduction of SSI risks was reported, except in one Misgav-Ladach study.⁴

Lack of reliable and systematic data on costs and effectiveness of potential IPC interventions is identified in recent publications^{17,30,31}, and cost-effectiveness depends on many factors such as a trained workforce of IPC practitioners with authority, time and resources (policies, financial and administrative support).¹⁰⁰ It is suggested that up to 40% of the health-care-associated infections in sSA are preventable, although limited literature was found on this topic.¹⁰⁰

Potential future research

When looking into new interventions and strategies to reduce the risk of SSIs after C-sections, patient acceptability of such interventions should be taken into account, in particular when patient rights are affected or even overruled.⁶⁴ Acceptability is often context and culture specific, and should be supported by professional opinions and consensus with patients and public.⁶⁴ Patient-centeredness and acceptability are important quality of care aspects (*Fig. 1*), but unfortunately often neglected in sSA.

The *global guidelines for the prevention of SSIs* presents 29 pre-, intra- and postoperative recommendations.¹⁷ These relate with some of the findings in this thesis (e.g. optimal timing and duration of prophylactic antibiotics), however most apply to high income countries and require (financial) resources which are often lacking in sSA. Some recommendations are formulated negatively, and recommend *against* a certain practice. Obviously, these are easier to implement, although the authors agree that more research on patient/health worker values and preferences is needed, especially from LMICs. Locally-produced alcohol-based hand rub or methods for hair removal are examples of topics which require *acceptability* before being implemented.¹⁷

Derived from this global guideline, possible areas for future targeted interventions on SSIs in sSA could look at *evidence-based revisions of antibiotic prophylaxis protocols* (preferably based on locally generated, specific microbiology data), *types of surgical hand preparation, perioperative oxygenation, antimicrobial-coated sutures and biocidal surfaces*.¹⁷

Regarding microbiology data, experiments on regional bacterial laboratories facilitating tests for multiple hospitals in their geographical proximity could inform on existing local antibiotic resistance patterns. Collaboration within regions is likely more sustainable than sending samples for culture and sensitivity testing to Europe.^{47,45} The potential research areas listed above are derived from the 29 recommendations and based on their known quality of evidence and strength of recommendation. They are, however, not yet applied in the sub-Saharan context of C-sections.¹⁷

Possible organisational factors to study could include a shift away from category 1 emergency C-sections^{viii} to less urgent C-sections, by better monitoring the normal progress and labour. Maternal

^{vii} Misgav-Ladach is a C-section related surgical technique to access the peritoneal cavity by using blunt (digital) dissection

^{viii} 'Crash' C-section with highest level of urgency

waiting homes^{ix} could contribute to reducing the likelihood of emergency C-sections, and subsequently improve the outcome of surgeries. Careful consideration should be made not to dramatically increase the C-section rate. *Staff grade/level of experience, skills mix in multidisciplinary teams* and the *availability of ongoing staff training* about C-sections and post-operative care are again interesting elements to study when looking at ways to reduce the C-section associated SSIs.⁶¹ Studies suggest that 15-20 procedures are needed to learn a C-section, although ongoing exposure further increases skills and aptitude.¹⁰¹⁻¹⁰³ It remains unclear how many C-sections are required to maintain basic skills, including proper care to prevent SSIs. *Early discharge and follow-up at home* by trained community volunteers might also be an interesting field for further research, as it minimizes the exposure to the highly pathogenic clinical environment in the hospital. Recently there has been no new insight from this approach, but it seems that early discharge (<24 hours) is not associated with more infant or maternal readmissions.⁶¹ Whether this is true in the African setting, and whether this reduces the risk of SSIs remains unclear.⁴

Another system factor which could be studied as intervention is *a standardized wound care protocol*. Dedicated wound care with removal of the dressing (> 24 hours post C-section) and gently cleaning/drying of the wound could be integrated in a study protocol on preventive interventions.⁶¹ Research on surveillance extending to the period *after* hospital discharge, possibility of *post-discharge maternity homes* to optimise hygiene and impact of patient education also deserve to be explored.

Finally, *ward occupancy and workload, identification and engagement of strategy champions* creating a *positive organisational culture* could be components that could positively influence SSI prevention strategies.⁵ All the mentioned research options could be accompanied by policy-to-practice gap studies, and cost-effectiveness studies to understand the absorption and financial consequences of these interventions.

Limitations

Major limitations related to this thesis are the wide scope of countries covered by the search. Obviously, national health systems vary significantly across sSA countries. It was impossible to address these differences, and make comparisons between specific countries. This thesis found most SSI prevention research about prophylactic antibiotics in C-sections. Whether this is a true reflection of the current situation, or simply results from the applied specific search method remains unclear. One can argue that a broader search could yield more generic interventions, which in part might also be applicable to C-sections. Nevertheless, search #4 (*Annex 2*) was undertaken with a broad scope in mind, which potentially should have discovered also other type of interventions, e.g. on cleanliness of theatres, air flow in operation rooms, number of staff present a surgery, workflow etc. There might be some degree of publication bias, related to the type of intervention people publish on. More general or organisational interventions might be found less eligible for publication. Similarly, SSI prevention interventions which apply to a wider range of surgical procedures, including C-sections, might be considered less a topic to publish on. Fragmentation and sub-specialization within the medical field tends to put less attention on day-to-day improvements, supervisions and cleaning procedures. These depend on good leadership and management of a ward, but likely do not qualify for publications, even not implementation research, whereas such practices could be extremely actionable and relevant. Contributing factors of SSIs are complex and multifactorial, and often require a multifaceted prevention strategy.¹⁰⁴ Knowing *and* eliminating all factors contributing to SSIs is impossible, as specific external factors (natural environment, e.g. humid climate, poor living conditions in LMIC) are hard to tackle. Human (behavioural) and system factors are more actionable for intervention, and likely also more published about.

^{ix} District hospitals in sub-Saharan Africa often provide accommodation to pregnant women, if access to the hospital is causing problems during the late stages of pregnancy.

Final remarks

Fundamental research on structures and processes is recommended to better understand '*why*' and '*how*' SSIs occur, rather than studying isolated outcomes only. Not only clinical staff, but also managers and patients (including caregivers) could contribute to innovative interventions and support early detection of SSIs. More distant determinants like safety culture, teamwork between doctors and nurses, support of management and personal motivation could affect many elements of the ICPS framework. Their impact is likely much broader than SSIs only, and could be strategies improving service delivery in general.^{55,58} As explained before, publication bias might have caused lack of information on these broader interventions.

A co-ordinated research agenda on the most relevant and urgent topics could increase the focus of next studies and avoid duplication and unnecessary wastage of resources. Additional studies on certain topics (e.g. single versus multiple dose regimens) seem irrational, although a recent study argues that there is insufficient evidence to make this conclusion.⁸⁹

5. Conclusions and recommendations

SSIs post C-sections are very common in sSA, and seriously impact patient and organisational outcomes resulting in high costs, prolonged admissions, excessive antibiotic use, additional re-operations and ultimately premature deaths. This public health problem is caused by many different factors, which have been studied in a systematic way using the *international classification for patient safety* framework. The lack of reliable and precise data makes it challenging to interpret data relevant for specific contexts. A comprehensive literature search on incident prevention, recovery and system resilience resulted in multiple studies targeting SSIs post C-sections.

The overall quality of evidence differed greatly, and most actions to reduce the risk of SSIs targeted purely antibiotic related interventions. Challenges to successfully implement new interventions were discussed, and intervention gaps were identified in this thesis.

Research recommendations

1. Future research should deviate from antibiotic-related protocols *only*, and evaluate other medical and organisational aspects. For example, suggestions have been made for shifting away from highly urgent C-sections and decreasing the hospital stay by early discharge and extensive community based surveillance.
2. Ideally, more research should be initiated from low-resource settings and rural district hospitals to balance the publications from sSA. Academic hospitals in urban settings are currently over represented in publications.
3. It is recommended to set regional research agendas, to list and prioritize SSI interventions within geographical areas. The wide range of research options as mentioned in the *discussion* might not be feasible or acceptable in all regions in sSA. Studies on early discharge and community follow-up might be more feasible in Southern Africa, where extensive community health systems already exist for HIV programmes.
4. To improve the quality of research, it is recommended to critically design the study according to internationally accepted standards. The ICROMS tool could serve as guidance, and ensure that international definitions on SSIs and follow-up are respected.
5. Finally, the different possible contributing factors in SSIs post C-sections should be included in future research. This enables policy makers and clinicians to understand the setting where the research is conducted. Fragmented depictions of the context lead to fragmented understanding of the problem.

Practical recommendations

6. More robust aggregated data from national level studies would be beneficial. This would make country data more reliable, and help those facilities which are not capable to conduct research themselves.
7. Stop using multiple dose antibiotic prophylaxis regimens for C-sections.
8. Start applying single dose pre-incision antibiotic prophylaxis, ideally captured in a broader prophylaxis policy which should be implemented facility wide.

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Annexes

ANNEX 1

Surgical site infection definition according to CDC's National Healthcare Safety Network 2017³⁷

Superficial incisional SSI

Must meet the following criteria:

- Date of event for infection occurs within 30 days after an operative procedure (where day 1 = the procedure date)

AND

- involves only skin and subcutaneous tissue of the incision

AND

- patient has at least **one** of the following:

a. purulent drainage from the superficial incision.

b. organisms identified from an aseptically-obtained specimen from the superficial incision or subcutaneous tissue by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not active surveillance culture/testing (ASC/AST).

c. superficial incision that is deliberately opened by a surgeon, attending physician^x or other designee and culture or non-culture based testing is not performed.

AND

patient has at least one of the following signs or symptoms: pain or tenderness; localized swelling; erythema; or heat.

d. diagnosis of a superficial incisional SSI by the surgeon or attending physician or other designee.

Comments

There are two specific types of superficial incisional SSIs:

1. Superficial Incisional Primary (SIP) – a superficial incisional SSI that is identified in the primary incision in a patient that has had an operation with one or more incisions (e.g., C-section incision or chest incision for CBGB)
2. Superficial Incisional Secondary (SIS) – a superficial incisional SSI that is identified in the secondary incision in a patient that has had an operation with more than one incision (e.g., donor site incision for CBGB)

The following do not qualify as criteria for meeting the definition of superficial SSI:

- Diagnosis/treatment of cellulitis (redness/warmth/swelling), by itself, does not meet criterion “d” for superficial incisional SSI. Conversely, an incision that is draining or that has organisms identified by culture or non-culture based testing is not considered a cellulitis.
- A stitch abscess alone (minimal inflammation and discharge confined to the points of suture penetration).
- A localized stab wound or pin site infection- Such an infection might be considered either a skin (SKIN) or soft tissue (ST) infection, depending on its depth, but not an SSI *Note:* A laparoscopic trocar site for an operative procedure is not considered a stab wound.
- Circumcision is not an operative procedure. An infected circumcision site in new-borns is classified as CIRC and is not an SSI. An infected burn wound is classified as BURN and is not an SSI.

^x The term attending physician for the purposes of application of the SSI criteria may be interpreted to mean the surgeon(s), infectious disease, other physician on the case, emergency

Deep incisional SSI

Must meet the following criteria:

- The date of event for infection occurs within 30 or 90 days after the operative procedure (where day 1 = the procedure date) according to the list in *Table 1*
AND
- involves deep soft tissues of the incision (e.g., fascial and muscle layers)
AND
- patient has at least *one* of the following:
 - a. purulent drainage from the deep incision.
 - b. a deep incision that spontaneously dehisces, or is deliberately opened or aspirated by a surgeon, attending physician** or other designee and organism is identified by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not active surveillance culture/testing (ASC/AST) or culture or non-culture based microbiologic testing method is not performed
AND
patient has at least *one* of the following signs or symptoms: fever (>38°C); localized pain or tenderness. A culture or non-culture based test that has a negative finding does not meet this criterion.
 - c. an abscess or other evidence of infection involving the deep incision that is detected on gross anatomical or histopathologic exam, or imaging test

Comments

There are two specific types of deep incisional SSIs:

1. Deep Incisional Primary (DIP) – a deep incisional SSI that is identified in a primary incision in a patient that has had an operation with one or more incisions (e.g., C-section incision or chest incision for CBGB)
2. Deep Incisional Secondary (DIS) – a deep incisional SSI that is identified in the secondary incision in a patient that has had an operation with more than one incision (e.g., donor site incision for CBGB)

Organ/Space SSI

Must meet the following criteria:

- Date of event for infection occurs within 30 or 90 days after the operative procedure (where day 1 = the procedure date) according to the list in *Table 1*.
AND
- infection involves any part of the body deeper than the fascial/muscle layers, that is opened or manipulated during the operative procedure
AND
- patient has at least one of the following:
 - a. purulent drainage from a drain that is placed into the organ/space (e.g., closed suction drainage system, open drain, T-tube drain, CT guided drainage)
 - b. organisms are identified from an aseptically-obtained fluid or tissue in the organ/space by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not active surveillance culture/testing (ASC/AST).
 - c. an abscess or other evidence of infection involving the organ/space that is detected on gross anatomical or histopathologic exam, or imaging test evidence suggestive of infection.

AND

meets at least one criterion for a specific organ/space infection site. These criteria are found in the Surveillance Definitions for Specific Types of Infections chapter.

Table 1: Surveillance periods for SSI following selected operative procedure categories. Day 1 = the date of the procedure.

30-day Surveillance Code Operative Procedure
Operative Procedure: Abdominal aortic aneurysm repair, Laminectomy, Limb amputation, Liver transplant, Appendix surgery, Neck surgery, Shunt for dialysis, Kidney surgery, Bile duct, liver or pancreatic surgery, Ovarian surgery, carotid endarterectomy, Prostate surgery, Gallbladder surgery, Rectal surgery, Colon surgery, Small bowel surgery, Caesarean section, Spleen surgery, Gastric surgery, Thoracic surgery, Heart transplant, Thyroid and/or parathyroid surgery, Abdominal hysterectomy, Vaginal hysterectomy, Kidney transplant, Exploratory Laparotomy,
90-day Surveillance
Breast surgery, Cardiac surgery, Coronary artery bypass graft with both chest and donor site incisions, Coronary artery bypass graft with chest incision only, Craniotomy, Spinal fusion, Open reduction of fracture, Herniorrhaphy, Hip prosthesis, Knee prosthesis, Pacemaker surgery, Peripheral vascular bypass surgery, Ventricular shunt
Note: Superficial incisional SSIs are only followed for a 30-day period for all procedure type

SSI Event Reporting Instructions:

1. Excluded organisms: Organisms belonging to the following genera cannot be used to meet any SSI definition: Blastomyces, Histoplasma, Coccidioides, Paracoccidioides, Cryptococcus and Pneumocystis. These organisms are typically causes of community- associated infections and are rarely known to cause healthcare-associated infections, and therefore are excluded.

2. Attributing SSI to a procedure when there is evidence of infection at the time of the primary surgery: The Present on Admission (POA) definition does not apply to the SSI protocol. If evidence of infection is present at the time of the procedure and the patient meets the SSI criteria during the SSI surveillance period, an SSI is attributed to the procedure (see PATOS below). A high wound class is not an exclusion for patient later meeting criteria for an SSI, but in most cases, is included as a risk factor for SSI in risk modelling.

3. Infection present at time of surgery (PATOS): PATOS denotes that there is evidence of an infection or abscess at the start of or during the index surgical procedure (in other words, it is present preoperatively). PATOS does not apply if there is a period of wellness between the time of a preoperative condition and surgery. The evidence of infection or abscess must be noted/documented intraoperatively in an operative note or report of surgery. The patient does not have to meet the definition of an SSI at the time of the primary procedure but there must be notation that there is evidence of an infection or abscess present at the time of surgery. PATOS is not necessarily diagnosis driven.

a. The use of the ending “itis” in an operative note/report does not necessarily meet PATOS, as it may reflect inflammation which is not infectious in nature (e.g., diverticulitis, peritonitis, and appendicitis)

b. Identification of an organism alone using culture or non-culture based microbiologic testing method or on a pathology report from a surgical specimen does not = PATOS (i.e., a positive culture/path report without surgical documentation of infection is not PATOS = yes).

c. The following verbiage alone without specific mention of infection does not meet the PATOS definition: colon perforation, necrosis, gangrene, faecal spillage, nicked bowel during procedure, or a note of inflammation.

d. Fresh trauma resulting in a contaminated case does not necessarily meet the PATOS requirement. For example, a fresh gunshot wound to the abdomen will be a trauma case with a high wound class but there would not have been time for infection to develop.

PATOS can be met when an abscess is noted, there is mention of infection in the OR note, purulence or pus is noted, or “feculent peritonitis” is noted, etc. An infected appendix that has ruptured will meet PATOS =Yes, if the patient has a subsequent intraabdominal organ space SSI.

Example:

1. Patient admitted with an acute abdomen. Sent to OR for a laparotomy where there is a finding of an abscess due to ruptured appendix and an appendectomy is performed. Patient returns two weeks later and meets criteria for an organ/space SSI. The PATOS field would be selected as YES on the SSI event since an abscess was noted at the time of surgery in the same level as the subsequent SSI.

2. Patient is admitted with a ruptured diverticulum. In the OR note the surgeon documents that there are multiple abscesses in the intraabdominal cavity. Patient returns three weeks later and meets criteria for a superficial SSI. The PATOS field would be selected as NO since there was no documentation of evidence of infection or abscess of the superficial area at the time of the procedure.

3. During an unplanned caesarean section the surgeon nicks the bowel and there is contamination of the intraabdominal cavity. One week later the patient returns and meets criteria for an organ/space SSI. The PATOS field would be selected as NO since there was no documentation of evidence of infection or abscess at the time of the caesarean section. The colon nick was a complication but there was no infection present at the time of surgery.

4. Multiple tissue levels are involved in the infection: The type of SSI (superficial incisional, deep incisional, or organ/space) reported should reflect the deepest tissue layer involved in the infection during the surveillance period. The date of event should be the date that the patient met criteria for the deepest level of infection:

a. Report infection that involves the organ/space as an organ/space SSI, whether or not it also involves the superficial or deep incision sites.

b. Report infection that involves the superficial and deep incisional sites as a deep incisional SSI.

c. If an SSI started as a deep incisional SSI on day 10 of the SSI surveillance period and then a week later, (day 17 of the SSI surveillance period) meets criteria for an organ space SSI the date of event would be the date of the organ space SSI.

5. Reporting of SSI after a non-primary closure: If a patient develops an SSI after a non- primary closure it should be attributed to that procedure if it meets criteria for an SSI within the appropriate surveillance period.

6. Attributing SSI to a procedure when several are performed on different dates: If a patient has several operative procedures performed on different dates prior to an infection, attribute the SSI to the operative procedure that was performed most closely in time prior to the infection date, unless there is evidence that the infection was associated with a different operation.

7. Attributing SSI to procedures that involve multiple primary incision sites: If multiple primary incision sites of the same operative procedure become infected, only report as a single SSI, and assign the type of SSI (superficial incisional, deep incisional, or organ/space) that represents the deepest tissue level involved at any of the infected sites. For example:

a. If one laparoscopic incision meets criteria for a superficial incisional SSI and another meets criteria for a deep incisional SSI, only report one deep incisional SSI.

b. If one or more laparoscopic incision sites meet criteria for superficial incisional SSI but the patient also has an organ/space SSI related to the laparoscopic procedure, only report one organ/space SSI.

c. If an operative procedure is limited to a single breast and involves multiple incisions in that breast that become infected, only report a single SSI.

d. In a colostomy formation or reversal (take down) procedure, the stoma and other abdominal incision sites are considered primary incisions. If both the stoma and another abdominal incision site develop superficial incisional SSI, report only as one SSI (SIP).

8. SSI detected at another facility: It is required that if an SSI is detected at a facility other than the one in which the operation was performed, the IP of the index facility will be provided with enough detail so the infection can be

reported. When reporting the SSI, the index facility should indicate that Detected = RO (Readmission to facility other than where procedure was performed).

9. SSI Attribution after Multiple types of procedures are performed during a single trip to the OR: If more than one operative procedure category was performed through a single incision/laparoscopic sites during a single trip to the operating room, attribute the SSI to the procedure that is thought to be associated with the infection. If it is not clear, as is often the case when the infection is an incisional SSI, use the Principal Operative Procedure Category Selection Lists to select the operative procedure to which the SSI should be attributed. For example, if a patient develops SSI after a single trip to the OR in which both colon and small bowel surgery were performed, and the source of the SSI is not apparent, assign the SSI to the colon procedure.

10. SSI following invasive manipulation/accession of the operative site: If during the post-operative period the surgical site has an invasive manipulation/accession for diagnostic or therapeutic purposes (e.g., needle aspiration, accession of ventricular shunts, accession of breast expanders) and there is no evidence of an infection at that time, if an SSI develops following this manipulation/accession, the infection is not attributed to the operation. This reporting instruction does NOT apply to closed manipulation (e.g., closed reduction of a dislocated hip after an orthopaedic procedure). Invasive manipulation does not include wound packing, or changing of wound packing materials as part of postoperative care.

11. Reporting instructions for specific post-operative infection scenarios: An SSI that otherwise meets the definitions should be reported without regard to post-operative accidents, falls, inappropriate showering or bathing practices, or other occurrences that may or may not be attributable to patients' intentional or unintentional postoperative actions. SSI should also be reported regardless of the presence of certain skin conditions (e.g., dermatitis, blister, impetigo) that occur near an incision, and regardless of the possible occurrence of a "seeding" event from an unrelated procedure (e.g., dental work). This instruction concerning various postoperative circumstances is necessary to reduce subjectivity and data collection burden.

Epidemiological definitions²²:

Prevalence: refers to the number of infection episodes or infected patients per 100 patients present in the hospital or ward at a given point in time

Cumulative incidence: the number of either new infection episodes or new patients acquiring an infection per 100 patients followed up for a defined period.

Incidence density: refers to the number of infection episodes per 1000 patient-days or device-days

ANNEX 2

Search keywords and yields

#1 PubMed 2007 - 2017	"Mortality" OR "morbidity" AND "Africa*" OR "Lesotho" OR "South Africa" OR "Swaziland" OR "Mozambique" OR "Zimbabwe" OR "Zambia" OR "developing country" AND "Surgical Site Infection" OR "HAI" OR "hospital acquired infect*" OR "nosocomial infection*" OR "SSI"	Search performed in April '17
#2 Cochrane 2007 – 2017	"Mortality" OR "morbidity" AND "Africa*" OR "Lesotho" OR "South Africa" OR "Swaziland" OR "Mozambique" OR "Zimbabwe" OR "Zambia" OR "developing country" AND "Surgical Site Infection" OR "HAI" OR "hospital acquired infect*" OR "nosocomial infection*" OR "SSI"	Search performed in April '17
#3 Google Scholar 2012 – 2017	At least one of the words "Africa" With the exact phrase " <i>nosocomial infection</i> "	Search performed in April '17
#4 PubMed 2007 – 2017	"surg*" OR "wound*" AND "infection*" OR "sepsis" AND "sub- Saharan Africa"	Search performed in May '17
#5 Cochrane 2007 – 2017	"caesarean section" AND "infection*" OR "sepsis" AND "Africa"	Search performed in May '17

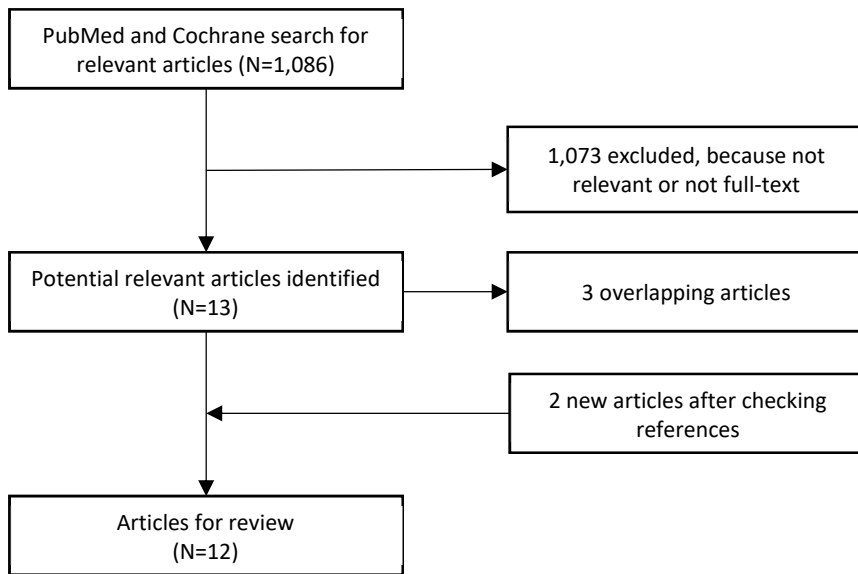
Objective 1 (incident type and outcomes): #1 - #3

Objective 2 (determining factors, characteristics and contributing factors): #1 - #5

Objective 3 (prevention, recovery, resilience): #4, #5

Objective 4 (implementation challenges): #1 - #5

Filters used for objective 3: clinical trial, classical article, clinical study, controlled clinical trial, randomized controlled trial, observational study, multicentre study, meta-analysis, review, journal article, clinical trial, clinical trial phases I – IV and comparative study



Yield search objective 3: General characteristics of included studies.

ANNEX 3

Data collection grid for literature search

1	First author	Surname
2	Material	Article / book / bulletin / clinical alert / discussion / ebook / guideline / letter / opinion / perspective / research project / series / technical report / thesis
3	Title	Full name of material
4	Publication journal	Material published
5	Publication year	e.g. 2017
6	Study type	Animal or lab study / Expert opinion / Case control study / Cohort study / Ecological study / Cross sectional study / Randomized controlled trial / Review / Systematic review / Meta-analysis / Qualitative research / Other
7	Prospective design	Yes or No
8	Level of evidence	Very low, low, moderate, high (based on design, bias, numbers)
9	District hospital	Setting of study in district hospital (WHO level 2) Yes or No
10	Country	e.g. Tanzania
11	Specific infection	No / urinary tract infection / pneumonia / bacteraemia / surgical site infection / tuberculosis / HIV / Hepatitis B / multiple infections / other
12	Number of patients	Number of patients included in study
13	Incidence density	Number of infections per 1000 patient days
14	Prevalence	Percentage infected per 100 patients (%)
15	Mortality	Percentage deaths per 100 patients (%)
16	Specific surgical procedure	e.g. caesarean section
17	Target audience	e.g. health policy makers, clinicians
18	Intervention	e.g. swabbing with alcohol 70%
19	Control	not applicable
20	Challenges	e.g. study used different definitions
21	Strengths	e.g. use of mixed methods research
22	Comments	Any other comments

ANNEX 4

Description of ICPS definitions and concepts, reproduced from the 2009 ICPS framework (version 1.1)²⁰

How the key concepts with preferred terms chosen relate to the conceptual framework for the ICPS is shown in the semantic framework diagram. The preferred terms are listed alphabetically followed by the key concepts with definitions. The semantic diagram, alphabetical list of preferred terms and conceptual definitions are at the end of this chapter.

Concepts are progressively introduced to allow understanding to be “built”, starting with the concepts in the title of the conceptual framework for the International Classification for Patient Safety (classification, patient, safety). The terms in italics have been deemed ICPS-preferred terms. Where terms have been italicized, the agreed definition for the relevant concept follows.

A *classification* is an arrangement of *concepts* (bearers or embodiments of meaning) and *classes* (groups or sets of like things, e.g., contributing factors, incident type, and patient outcomes) and their subdivision linked to express their *semantic relationships* between them (the way in which they are associated with each other based on their meanings). For example, contributing factors precede and play a role in the generation of any incident type. Similarly, detection precedes mitigating factors and is followed by outcomes; the progression of an incident cannot be limited until it has been detected and its nature determined, and outcomes cannot be described until attempts at limitation have exerted their influence.

A *patient* is a person who is a recipient of *healthcare*, itself defined as services received by individuals or communities to promote, maintain, monitor or restore health. Patients are referred to rather than clients, tenants or consumers, although it is recognized that may recipients such as a health pregnant woman or a child undergoing immunization may not be regarded, or regard themselves, as patients. Healthcare includes self-care. *Health*, as defined by the World Health Organization, is the “state of complete physical, mental and social well-being and not merely the absence of disease or infirmity”.²⁰ *Safety* is the reduction of risk of unnecessary harm to an acceptable minimum. An acceptable minimum refers to the collective notions of given current knowledge, resources available and the context in which care was delivered weighed against the risk of non-treatment or other treatment.

Hazard is a circumstance, agent or action with the potential to cause harm.

A *circumstance* is a situation or factor that may influence an event, agent or person(s).

An *event* is something that happens to or involves a patient and an *agent* is a substance, object or system that acts to produce change.

Patient safety is the reduction of risk of unnecessary harm associated with healthcare to an acceptable minimum. An acceptable minimum refers to the collective notions of given current knowledge, resources available and the context in which care was delivered weighed against the risk of non-treatment or other treatment.

Healthcare-associated harm is harm arising from or associated with plans or actions taken during the provision of healthcare, rather than an underlying disease or injury.

A *patient safety incident* is an event or circumstance that could have resulted, or did result, in unnecessary harm to a patient. In the context of the ICPS, a patient safety incident will be referred to as an incident. The use of the word “unnecessary” in this definition recognizes that errors, violation, patient abuse and deliberately unsafe acts occur in healthcare. These are considered incidents. Certain forms of harm, however, such as an incision for a laparotomy, are necessary. This is not considered an incident. Incidents arise from either unintended or intended acts. Errors are, by definition, unintentional, whereas violations are usually intentional, though rarely malicious, and may become routine and automatic in certain contexts.

An *error* is a failure to carry out a planned action as intended or application of an incorrect plan. Errors may manifest by doing the wrong thing (commission) or by failing to do the right thing (omission), at either the planning or execution phase. Thus, if screening for bowel cancer involves regular testing for occult blood, then a screening colonoscopy in the absence of prior occult blood testing comprises an error of commission (the application of an incorrect plan), whereas failure to arrange testing for occult blood would constitute an error of omission. A *violation* is a deliberate deviation from an operating procedure, standard or rule. Both errors and violations increase risk, even if an incident does not actually occur. *Risk* is the probability than an incident will occur.

An incident can be a reportable circumstance, near miss, no harm incident or harmful incident (adverse event). A *reportable circumstance* is a situation in which there was significant potential for harm, but no incident occurred (i.e., a busy intensive care unit remaining grossly understaffed for an entire shift, or taking a defibrillator to an emergency and discovery it does not work although it was not needed). A *near miss* is an incident which did not reach the patient (e.g., a unit of blood being connected to the wrong patient’s intravenous line, but the error was detected before the infusion started). A *no harm incident* is one in which an event reached a patient but no discernible harm resulted (e.g., if the unit of blood was infused, but was not incompatible). A *harmful incident (adverse event)* is an incident that results in harm to a patient (e.g., the wrong unit of blood was infused and the patient died from a haemolytic reaction).

Harm implies impairment of structure or function of the body and/or any deleterious effect arising there from, including disease, injury, suffering, disability and death, and may be physical, social or psychological. *Disease* is a physiological or psychological dysfunction. *Injury* is damage to tissues caused by an agent or event and *suffering* is the experience of anything subjectively unpleasant. Suffering includes pain, malaise, nausea, depression, agitation, alarm, fear and grief. *Disability* implies any type of impairment of body structure or function, activity limitation and/or restriction of participation in society, associated with past or present harm.

A *contributing factor* is a circumstance, action or influence (such as poor rostering or task allocation) that is thought to have played a part in the origin or development, or to increase the risk, of an incident. Contributing factors may be external (i.e., not under the control of a facility or organization), organisational (e.g., unavailability of accepted protocols), related to a staff factor (e.g., an individual cognitive or behavioural defect, poor team work or inadequate communication) or patient-related (e.g., non-adherence). A contributing factor may be a necessary precursor of an incident and may or may not be sufficient to cause the incident.

Incidents are classified into a number of different types. An *incident type* is a category made up of incidents of a common nature, grouped because of shared agreed features and is a “parent” category under which many concepts may be grouped. Incident types include clinical administration, clinical process/procedure, documentation, healthcare-associated infection, medication/IV fluids, blood/blood products, nutrition, oxygen/gas/vapour, medical device/equipment, behaviour, patient accidents, infrastructure/building/fixtures, and resources/organisational management.

Patient Characteristics are selected attributes of a patient, such as patient demographics or the reason for presentation to healthcare. *Attributes* are qualities, properties or features of someone or something.

Incident characteristics are selected attributes of an incident such as care setting, treatment status, specialties involved and date of an incident.

With reference to an agent, an *adverse reaction* is unexpected harm arising from a justified treatment. For example, unexpected neutropenia due to a drug not known to have this effect is an adverse reaction. Recurrence of a previously encountered adverse reaction may be preventable (e.g., avoiding re-exposure of a patient with a drug allergy). A *side effect* is a known effect, other than that primarily intended, related to a medicine's pharmacological properties, such as nausea after morphine has been given to alleviate pain.

Preventable is being accepted by the community as avoidable in the particular set of circumstances. *Detection* is an action or circumstance that results in the discovery of an incident (e.g., by noticing an error by a monitor or alarm, by change in patient condition, or by a risk assessment). Detection mechanisms may be part of the system, such as low pressure disconnect alarm in a breathing circuit, may result from a checking process or from vigilance and "situational awareness". A *mitigating factor* is an action or circumstances that prevents or moderates the progression of an incident towards harming a patient. The mechanism by which damage may occur is already in train, but has not yet led to either any or the maximum possible harm. The term "recovery" has been used to describe the combination of detection and mitigation; it does not refer to clinical recovery (recuperation) but to the process of recovering from an incident that has started. Reconnecting a breathing circuit after a disconnect alarm warning is an example of recovery. By collecting information about how and way "saves" are made, system design, training and education can be informed.

Patient outcome is the impact upon a patient which is wholly or partially attributable to an incident. Where harm has occurred, the *degree of harm* is the severity and duration of any harm, and any treatment implications, that result from an incident. It would seem, from the guiding principles, desirable to record the nature, severity and duration of harm separately. Whilst in pure terms one might argue for classifying each separately, most harm scales recognize these elements are conflated within the natural assessment that is made when assigning a degree of harm. Previous attempts to rank the degree of harm tend to conflate these parameters into one scale. In the context of the conceptual framework for the ICPS, the degree of harm is as follows:

- None – patient outcome is not symptomatic or no symptoms detected and no treatment is required.
 - Mild – patient outcome is symptomatic, symptoms are mild, loss of function or harm is minimal or intermediate but short term, and no or minimal intervention (e.g., extra observation, investigation, review or minor treatment) is required.
 - Moderate – patient outcome is symptomatic, requiring intervention (e.g., additional operative procedure; additional therapeutic treatment), an increased length of stay, or causing permanent or long-term harm or loss of function.
 - Severe – patient outcome is symptomatic, requiring life-saving intervention or major surgical/medical intervention, shortening life expectancy or causing major permanent or long-term harm or loss of function
 - Death – on balance of probabilities, death was caused or brought forward in the short term by the incident.
- Incidents also affect healthcare organisations. *Organisational outcome* is the impact upon an organisation that is wholly or partially attributable to an incident (e.g., adverse publicity or additional use of resources).

Ameliorating action is an action taken or circumstance altered to make better or compensate any harm after an incident. Patient ameliorating factors are actions taken or circumstances altered to make good harm to a patient, such as fixing a fracture after a fall. Whereas healthcare system ameliorating factors reduce loss or damage to an organisation, such as good public relations management after a publicized disaster to improve the effects on a facility's reputation.

Actions taken to reduce risk are actions taken to reduce, manage or control any future harm, or probability of harm, associated with an incident. Such actions can affect incidents, contributing factors, detection, mitigating factors or ameliorating actions, and can be pro-active or reactive. Pro-active actions may be identified by techniques such as failure mode and effects analysis and probabilistic risk analysis. Reactive actions are taken in response to insights gained after incidents have occurred (e.g., root causes analysis).

Resilience references to the degree to which a system continuously prevents, detects, mitigates or ameliorates hazards or incidents. Resilience allows an organisation to "bounce back" to its original ability to provide care functions as soon as possible after incurring damage.

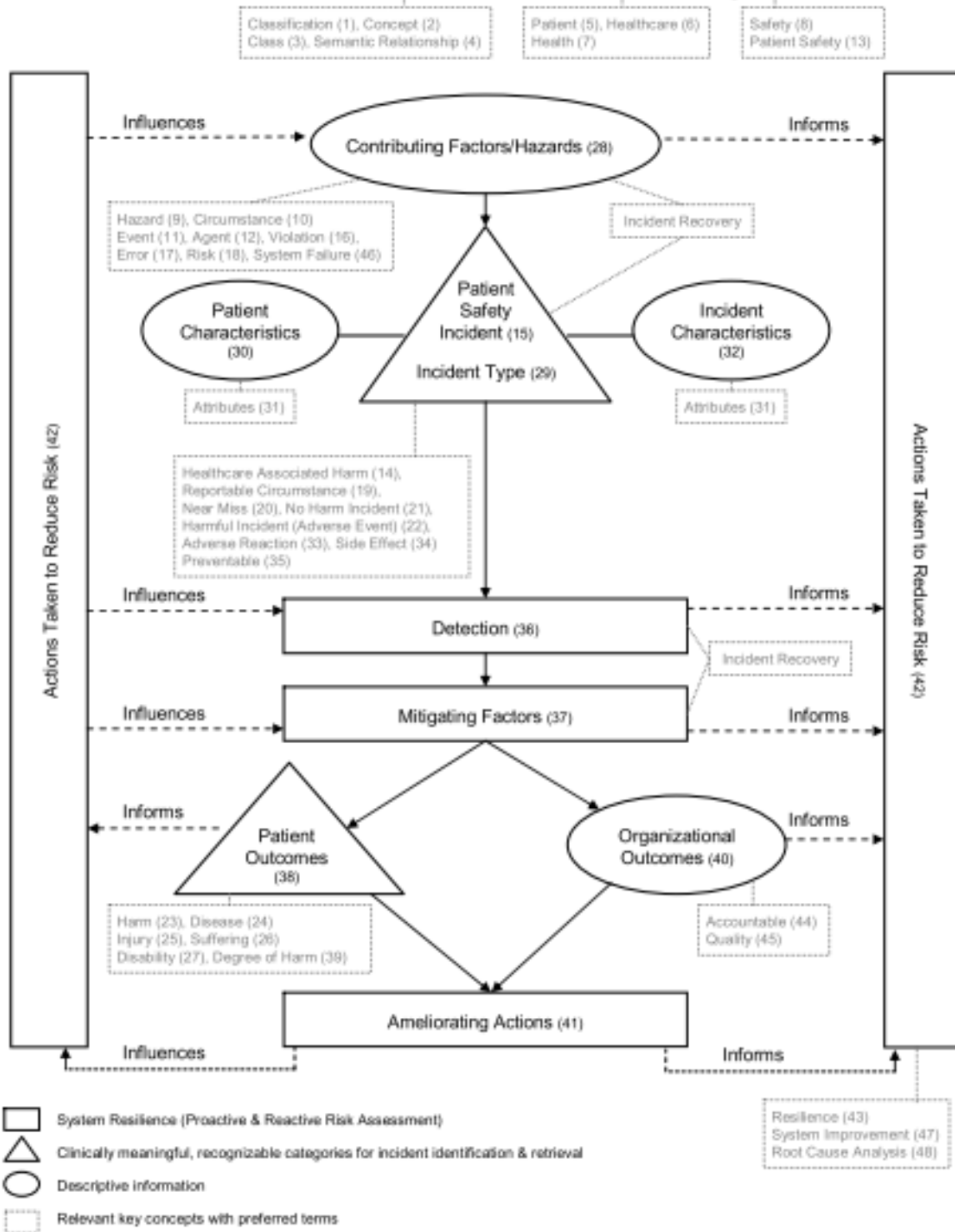
A number of terms are commonly used regarding organisational management. *Accountable* is being held responsible. *Quality* is the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge. *System failure* refers to a fault, breakdown or dysfunction within an organisation's operational methods, processes or infrastructure. Factors contributing to system failure can be latent (hidden or apt to elude notice) or apparent, and can be related to the system, the organisation, a staff member or a patient. A latent factor might be a breathing circuit disconnect alarm with no power failure warning or battery backup.

System improvement is the result or outcome of the culture, processes and structures that are directed towards the prevention of system failure and the improvement of safety and quality. Processes to counter the latent failure described would include modification of the equipment to alarm when the power supply is compromised, or use of an additional device, such as a capnograph, to alarm if carbon dioxide is not detected in expired air.

Finally, *root cause analysis*, a reactive form of risk assessment to inform the development of actions taken to reduce risk, is a systematic iterative process whereby the factors that contribute to an incident are identified by reconstructing the sequence of events and repeatedly asking "why" until the underlying root causes (contributing factors or hazards) have been elucidated.

Some concepts were excluded because their meanings vary across jurisdictions (e.g., negligence), they have discipline-specific meanings (e.g., accident – in aviation meaning the loss of an aircraft hull), are already being used with special meanings in a WHO classification (e.g., misadventure or sequela), or the conceptual definitions cannot be made universal. As a result, other concepts of relevance to patient safety and across all healthcare environments have been developed. For example, the concept healthcare-associated harm was included instead of iatrogenic and nosocomial harm. Iatrogenic and nosocomial harm are associated with physicians and hospitals, respectively. Healthcare-associated harm there acknowledges that healthcare is provided by many different individuals, including patients, in a variety of care settings (inpatient, ambulatory, mental health and community facilities, home, etc.). It should also be noted that this list of key concepts is dynamic. It will, and should, grow as knowledge in the field of patient safety grows.

Conceptual Framework for the International Classification for Patient Safety



The solid lines represent the semantic relationships between the classes. The black dotted lines represent the flow of information. The shaded dotted lines link the relevant concepts to the classes. The numbers next to the preferred terms represent the sequence in which they appear in the text and in glossary.

GLOSSARY OF KEY CONCEPTS AND PREFERRED TERMS

Preferred Terms:

Accountable (# 44)
Actions taken to reduce risk (# 42)
Adverse reaction (# 33)
Agent (# 12)
Ameliorating action (# 41)
Attributes (# 31)
Circumstance (# 10)
Class (# 3)
Classification (# 1)
Concept (# 2) Contributing
Factor (# 28) Degree of
harm (# 39) Detection (#
36)
Disability (# 27)
Disease (# 24)
Error (# 16)
Event (# 11)
Harm (# 23)
Harmful incident (adverse event) (# 22)
Hazard (# 9)
Health (# 7)
Healthcare (# 6)
Healthcare-associated harm (# 14) Incident
characteristics (# 32)

Incident type (# 29)
Injury (# 25)
Mitigating factor (# 37)
Near miss (# 20)
No harm incident (# 21)
Organizational outcome (# 40)
Patient (# 5)
Patient characteristics (# 30)
Patient outcome (# 38)
Patient Safety (# 13)
Patient safety incident (# 15)
Preventable (# 35)
Quality (# 45)
Reportable circumstance (# 19)
Resilience (# 43)
Risk (# 18)
Root cause analysis (# 48)
Safety (# 8)
Semantic relationship (# 4)
Side effect (# 34) Suffering
(# 26)
System failure (# 46) System
improvement (# 47)
Violation (# 17)

Definitions of Key Concepts:

1. **Classification:** an arrangement of **concepts** into **classes** and their subdivisions, linked to express the **semantic relationships** between them.
2. **Concept:** a bearer or embodiment of meaning.
3. **Class:** a group or set of like things.
4. **Semantic relationship:** the way in which things (such as **classes** or **concepts**) are associated with each other based on their meaning.
5. **Patient:** a person who is a recipient of healthcare.
6. **Healthcare:** services received by individuals or communities to promote, maintain, monitor or restore **health**.
7. **Health:** a state of complete physical, mental and social wellbeing and not merely the absence of **disease** or infirmity.
8. **Safety:** the reduction of risk of unnecessary **harm** to an acceptable minimum.
9. **Hazard:** a **circumstance, agent** or action with the potential to cause harm.
10. **Circumstance:** a situation or factor that may influence an **event, agent** or person(s).
11. **Event:** something that happens to or involves a **patient**.
12. **Agent:** a substance, object or system which acts to produce change.
13. **Patient Safety:** the reduction of risk of unnecessary **harm** associated with **healthcare** to an acceptable minimum.
14. **Healthcare-associated harm:** **harm** arising from or associated with plans or actions taken during the provision of healthcare, rather than an underlying **disease** or **injury**.
15. **Patient safety incident:** an **event** or **circumstance** which could have resulted, or did result, in unnecessary **harm** to a patient.
16. **Error:** failure to carry out a planned action as intended or application of an incorrect plan.
17. **Violation:** deliberate deviation from an operating procedure, standard or rule.
18. **Risk:** the probability that an **incident** will occur.
19. **Reportable circumstance:** a situation in which there was significant potential for harm, but no incident occurred.
20. **Near miss:** an **incident** which did not reach the patient.

21. **No harm incident:** an **incident** which reached a patient but no discernible harm resulted.
22. **Harmful incident (adverse event):** an **incident** which resulted in **harm** to a patient.
23. **Harm:** impairment of structure or function of the body and/or any deleterious effect arising there from. Harm includes **disease, injury, suffering, disability** and death.
24. **Disease:** a physiological or psychological dysfunction.
25. **Injury:** damage to tissues caused by an **agent** or **event**.
26. **Suffering:** the experience of anything subjectively unpleasant.
27. **Disability:** any type of impairment of body structure or function, activity limitation and/or restriction of participation in society, associated with past or present **harm**.
28. **Contributing Factor:** a **circumstance**, action or influence which is thought to have played a part in the origin or development of an **incident** or to increase the **risk** of an **incident**.
29. **Incident type:** a descriptive term for a category made up of incidents of a common nature, grouped because of shared, agreed features.
30. **Patient characteristics:** selected **attributes** of a **patient**.
31. **Attributes:** qualities, properties or features of someone or something.
32. **Incident characteristics:** selected **attributes** of an **incident**.
33. **Adverse reaction:** unexpected harm resulting from a justified action where the correct process was followed for the context in which the event occurred.
34. **Side effect:** a known effect, other than that primarily intended, related to the pharmacological properties of a medication.
35. **Preventable:** accepted by the community as avoidable in the particular set of circumstances.
36. **Detection:** an action or **circumstance** that results in the discovery of an **incident**.
37. **Mitigating factor:** an action or **circumstance** which prevents or moderates the progression of an **incident** towards harming a **patient**.
38. **Patient outcome:** the impact upon a patient which is wholly or partially attributable to an **incident**.
39. **Degree of harm:** the severity and duration of harm, and any treatment implications, that result from an **incident**.

40. **Organisational outcome:** the impact upon an organisation which is wholly or partially attributable to an **incident**.
41. **Ameliorating action:** an action taken or **circumstances** altered to make better or compensate any **harm** after an **incident**.
42. **Actions taken to reduce risk:** actions taken to reduce, manage or control any future harm, or probability of **harm**, associated with an **incident**.
43. **Resilience:** The degree to which a system continuously prevents, detects, mitigates or ameliorates **hazards** or **incidents**.
44. **Accountable:** being held responsible
45. **Quality:** the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge.
46. **System failure:** a fault, breakdown or dysfunction within an organisation's operational methods, processes or infrastructure.
47. **System improvement:** the result or outcome of the culture, processes, and structures that are directed toward the prevention of **system failure** and the improvement of **safety** and **quality**.
48. **Root cause analysis:** a systematic iterative process whereby the factors which contribute to an **incident** are identified by reconstructing the sequence of events and repeatedly asking