Groin Hernias and Unmet Need for Surgery in Uganda

Epidemiology, mosquito nets and cost-effectiveness

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To the future, for new challenges
Table of Contents

Table of Contents ........................................................................................................ i
Abstract........................................................................................................................ iii
Original papers.............................................................................................................. v
Abbreviations and acronyms....................................................................................... vi
Glossary and definitions ............................................................................................... vii
Enkel sammanfattning på svenska ........................................................................... xi
Prologue............................................................................................................................. 1

Background ..................................................................................................................... 3
Surgery and global health – where is the connection? ................................................. 3
Groin hernia – a common surgical condition ............................................................. 8
Health Economics............................................................................................................. 15
Conducting research in low- and middle income countries ........................................ 21
Uganda.............................................................................................................................. 23
Ethics................................................................................................................................. 24

Aims of the thesis............................................................................................................ 25

Materials and methods ............................................................................................... 26
Study 1. Groin hernia prevalence in adult males in the Iganga/Mayuge Health and Demographic Surveillance Site ....... 27
Study 2. Surgical volume, indications, interventions, outcomes and costs of surgery in Eastern Uganda ......................................................... 28
Study 3. Mosquito mesh versus commercial mesh in groin hernia surgery................................................................. 29
Ethical considerations.................................................................................................. 31

Key results ..................................................................................................................... 32
I. Prevalence of treated and untreated groin hernia in eastern Uganda ......................................................... 32
II. District level surgery in Uganda: Indications, interventions and perioperative mortality ................................................................. 33
   Perioperative mortality rate and cause of death ....................................................... 35
III. Cost of surgery in a low-income setting in eastern Uganda ... 36
IV. Low cost mesh in groin hernia repair - A double-blinded, randomised trial .............................................................................. 37
V. Cost effectiveness of groin hernia surgery using a low cost versus a commercial mesh.............................................................................. 39
Discussion .................................................................................................................. 40
Main findings ................................................................................................................ 40
Epidemiology of groin hernia ......................................................................................... 40
Health systems performance ......................................................................................... 41
Surgical methodology ................................................................................................... 49
Health economics ......................................................................................................... 50
Strengths and weaknesses of the thesis ....................................................................... 53
Conclusions and future perspectives ........................................................................... 55
  This thesis has documented that: ............................................................................. 55
  The way forward ....................................................................................................... 57
Acknowledgements ...................................................................................................... 60
References .................................................................................................................... 64
Abstract

Background Surgery has traditionally been considered more expensive than many other health care interventions and with little impact on the burden of disease in a global perspective. One of the reasons behind this misconception is that the effects of surgical conditions and their treatment have not been factored into the equation. Cost-effectiveness analyses of surgical interventions have largely been missing.

An estimated 20 million herniorrhaphies are carried out annually but over 200 million people suffer from groin hernias. Herniorrhapsy is one of the most commonly performed surgical procedures also in Low and Middle Income Countries (LMIC). However, the surgical repair method is not the same due to financial constraints. In high income countries a synthetic mesh is used and has reduced the risk of recurrence. This 125 USD mesh is too costly for the majority in LMIC. Mosquito mesh, which is cheaper but very similar to commercial meshes, is used in several settings but outcomes need to be investigated more extensively before this practice can be recommended in routine surgical service.

The Aims of this thesis were to define the prevalence of groin hernia, to relate it to the surgical capacity, outcomes and costs of surgery in eastern Uganda and to investigate the feasibility and difference in cost and cost-effectiveness of replacing a commercial mesh with a mosquito mesh in groin hernia surgery.

Methods Three studies (1-3) were carried out in eastern Uganda. 1: A cross sectional study investigating the prevalence of groin hernia in adult males in the Health and Demographic Surveillance Site (HDSS) in Iganga and Mayuge districts. 2: A facility based study with prospective data collection of all surgeries undertaken in the two hospitals providing surgery for the HDSS population. 3: A double blinded, randomised controlled trial comparing the outcomes of using a mosquito mesh relative using a commercial mesh in groin hernia surgery.

Results 1: the prevalence of untreated groin hernia among the study participants was 6.6%. 2: the rate of groin hernia surgery was 17 per 100 000 population. Thus, less than 1% of the estimated number of cases of groin hernia in the catchment area of the two hospitals are operated per year. A herniorrhapsy costs around 60 USD to perform. This corresponds to a third of the cost of TB treatment and a 15th of the cost of HIV/AIDS treatment per year in Uganda. 3: No significant differences in terms of recurrence rates, post operative and chronic complications and patient satisfaction were demonstrated between the patients operated using the mosquito mesh and
the commercial mesh. Cost-effectiveness was very high for both materials but total cost in the mosquito mesh group was 124 USD lower per surgery than in the commercial mesh group.

**Conclusion** There is a vast unmet need for groin hernia surgery. Cost of surgery compares favourably with other health care interventions prioritised by the international organisations and funders. A superior technique can be used in groin hernia surgery at low cost, with high cost-effectiveness in a Low Income Country.

*Keywords: Global surgery, groin hernia, groin hernia surgery, hernia epidemiology, low cost surgery, cost-effectiveness.*
Original papers


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### Abbreviations and acronyms

<table>
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>ASA</td>
<td>American Society of Anaesthesiologists Physical Status Classification (1-6)</td>
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<tr>
<td>CI</td>
<td>Confidence Interval</td>
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<tr>
<td>DALY</td>
<td>Disability Adjusted Life Years</td>
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<td>DW</td>
<td>Disability Weight</td>
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<tr>
<td>GDP</td>
<td>Gross Domestic Product</td>
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<tr>
<td>HDSS</td>
<td>Health and Demographic Surveillance Site</td>
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<td>HIC</td>
<td>High Income Countries</td>
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<td>HRQOL</td>
<td>Health Related Quality of Life</td>
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<tr>
<td>I/M HDSS</td>
<td>Iganga and Mayuge districts Health and Demographic Surveillance Site</td>
</tr>
<tr>
<td>INDEPTH</td>
<td>International Network for the Demographic Evaluation of Populations and their Health</td>
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<tr>
<td>LMIC</td>
<td>Low and Middle Income Countries</td>
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<tr>
<td>QALY</td>
<td>Quality Adjusted Life Years</td>
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<tr>
<td>SAO</td>
<td>Surgery, anaesthesia and obstetrics</td>
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<td>TTO</td>
<td>Time Trade Off</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>YLD</td>
<td>Years Lived with Disability</td>
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<tr>
<td>YLL</td>
<td>Years of Life Lost</td>
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# Glossary and definitions

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tr>
<td>ASA classification System</td>
<td>Scale for classification of the general health of patients. Scale ranges from 1 to 6. 1=normal healthy patient, 6=brain dead patient</td>
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<tr>
<td>Anaesthesia</td>
<td>Insensitivity to pain, induced by the administration of gases or injection of drugs, in this thesis used for the purpose of carrying out surgical procedures</td>
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<tr>
<td>Associated factor</td>
<td>An epidemiological term used for a factor which is associated with a specific outcome measure, without necessarily showing causality</td>
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<tr>
<td>Burden of disease</td>
<td>An aggregate measure of mortality and morbidity due to disease and disability</td>
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<tr>
<td>Capital cost</td>
<td>A cost incurred on the purchase of land, buildings, construction and equipment to be used in the production of goods or the rendering of services (1)</td>
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<tr>
<td>Clinical Officer</td>
<td>In Uganda, a midlevel health care provider with three years of training in medicine. The training can focus on specific areas such as orthopaedics or anaesthesia which the resulting title being orthopaedic officer and anaesthetic officer</td>
</tr>
<tr>
<td>Cost-effectiveness</td>
<td>A type of economic evaluation used to determine the best use of money available for medical care. It compares different kinds of interventions with similar, but not identical, effects on the basis of the cost per unit achieved</td>
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<tr>
<td>Chronic pain</td>
<td>Pain which persists longer than expected following surgery</td>
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<tr>
<td>Cross-sectional study</td>
<td>A study carried out at a specific point in time to assess prevalence of conditions or characteristics and exposure. It can show association between disease and exposure but not causality</td>
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<tr>
<td>DALY</td>
<td>The sum of years of potential life lost due to premature mortality and the years of productive life lost due to disability</td>
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<tr>
<td>Depreciation</td>
<td>Annuity or similar of a capital cost so that the one-time investment is distributed over time, often in relation to the useful life of the asset</td>
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<td>Term</td>
<td>Definition</td>
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<tr>
<td>Elective surgery</td>
<td>Planned surgical procedure for a condition that does not require immediate surgical intervention</td>
</tr>
<tr>
<td>Emergency surgery</td>
<td>Surgical procedure for a condition that requires immediate surgical intervention</td>
</tr>
<tr>
<td>Epidemiology</td>
<td>The study of the distribution and determinants of health-related states or events (including disease), and the application of this study to the control of diseases and other health problems</td>
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<tr>
<td>Global health</td>
<td>The area of study, research and practice that places a priority on improving and achieving equity in health globally</td>
</tr>
<tr>
<td>Global surgery</td>
<td>An area of study, research, practice, and advocacy that seeks to improve health outcomes and achieve health equity for all people who need surgical and anaesthesia care</td>
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<tr>
<td>Groin hernia</td>
<td>A collective term for inguinal and femoral hernia</td>
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<tr>
<td>Health system</td>
<td>All activities whose primary purpose is to promote, restore, and maintain health</td>
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<tr>
<td>HDSS</td>
<td>Research site where the population is monitored regularly with interviews in order to chart births, deaths, migration and health characteristics</td>
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<tr>
<td>Hernia</td>
<td>The projection of an organ or part through the lining of the cavity in which it is normally situated</td>
</tr>
<tr>
<td>Hernia repair</td>
<td>Surgical repair of a hernia</td>
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<tr>
<td>HRQOL</td>
<td>An individual’s or group’s perceived physical and mental health over time</td>
</tr>
<tr>
<td>INDEPTH</td>
<td>International Network for the Demographic Evaluation of Populations and their Health</td>
</tr>
<tr>
<td>Major surgery</td>
<td>Incision, excision, manipulation, or suturing of tissue that normally requires regional or general anaesthesia, or profound sedation to control pain</td>
</tr>
<tr>
<td>Medical officer</td>
<td>Medical doctor with five years training in medical school and a one year internship</td>
</tr>
<tr>
<td>Minor surgery</td>
<td>Surgical procedures that are not major surgery. Normally undertaken under nerve block or local anaesthesia.</td>
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</table>
Overhead cost
Cost for activities that are shares by different programmes different departments in a hospital. These activities can for instance be administration, laundry services, security and so on.

Perioperative mortality
Death that occurs during or following a surgical procedure within 30 days or before discharge from the hospital depending on which of the two that happens first.

Person Trade Off
Method to elicit disability weights, which are used to calculate disability adjusted life years (6).

Prevalence
The number of individuals in a defined population who have a particular condition or characteristic.

QALY
Health outcome measurement unit that combines duration and quality of life (7).

Qualified specialist
A medical officer with three years of formal post-graduate training in a specific speciality such as surgery, anaesthesia or obstetrics and gynaecology.

Recurrent cost
Ongoing expenditure of an organization, such as salaries and travelling expenses (1).

Risk factor
An epidemiological term of a characteristic or exposure which increases the risk of developing a disease or condition.

Surgery
Suture, incision, excision, manipulation, or other invasive procedure that usually, but not always, requires local, regional, or general anaesthesia (8).

Surgical disease
Any condition that requires suture, incision, excision, manipulation, or other invasive procedure that usually, but not always, requires local, regional, or general anaesthesia (8).

Time Trade Off
A method used for assessing preference of outcomes among respondents. Through this method, length of time is traded for quality of life (9).
Enkel sammanfattning på svenska

Bakgrund

Världens fattigaste två miljarder människor erhåller bara 3.5% av antalet operationer som utförs. Fem miljarder människor har inte tillgång till god kirurgisk vård till en överkomlig kostnad när de behöver den. Kirurgi har beskrivits som "det åsidosatta styvbornet inom global hälsa".

Tvärt emot vad man tidigare trott så bidrar kirurgiska åkommor till betydande sjuklighet på befolkningsnivå även i låg- och medelinkomstländer där 70% av världens alla dödsfall från kirurgiska sjukdomar inträffar. Den kirurgiska sjukdomsbördan är störst i Afrika där kirurgi skulle kunna rädda många liv.

Utvärdering av kostnadseffektivitet av kirurgi visar att många operationer är mycket kostnadseffektiva relativt andra interventioner inklusive vaccinationsprogram för barn, behandling av HIV/AIDS och tuberkulos. Kirurgiska insatser har pekats ut som en grupp förbisedda lågkostnadsmöjligheter för sjukvården i både Asien och Afrika.

Världsbanken har i sina planeringsunderlag identifierat just ljumskbråckoperationer som ett av de områden som bör prioriteras i utvecklingen av häls- och sjukvården i läginkomstländer. Ett ljumskbråck kan enklast beskrivas som en defekt (ett hål) i den nedre delen av bukväggen genom vilken bukfett, tarmar och andra inre organ kan passera. Detta märks oftast som en knöl i ljumsken som kan tryckas tillbaka eller som går tillbaka av sig självt när man lägger sig ned. Den enda effektiva behandlingen är kirurgisk och obehandelte kan ljumskbräck medföra betydande lidande och t.o.m. död. Över 200 miljoner människor är drabbade av denna mycket vanliga kirurgiska åkommor och med över 20 miljoner ljumskbråckoperationer per år är det ett av världens vanligaste kirurgiska ingrepp. De 180 miljoner som inte opereras representerar ett mycket stort, icke tillgodosett behov för kirurgi.


Ljumskbräck kan opereras på flera sätt. I höginkomstländer använder man idag oftast ett syntetiskt nät som förstärker bukväggen och minskar risken för att ljumskbräcket ska återkomma. Dessa nät kostar över 100 US dollar,
en mycket hög kostnad i läginkomstländer. Som en följd har många miljoner människor i dessa länder inte samma tillgång till bräckkirurgi av god kvalitet som de i rika länder. Lågkostnadslösningar som ej medför sämre kvalitet och utfall behöver identifieras.

Myggnät används som alternativ till de dyra kommersiella näten på flera håll i världen. Befintliga forskningsresultat är lovande men sakra belägg för myggnätens effektivitet vid ljumskbräcksreparation har saknats då genomförda studier har varit för små eller haft kort uppföljningstid. För att fylla denna kunskapslucka genomfördes avhandlingens tredje forskningsprojekt.

**Metoder**

Avhandlingens fem artiklar bygger på de tre delprojekten. Insamlade data har kunnat användas och analyseras på olika sätt för de fem resulterande artiklarna och har därför kunnat besvara avhandlingens olika frågeställningar.

Det första delprojektet var en tvärsnittsstudie som genom frågeformulär och klinisk undersökning undersökte prevalensen av både behandlade och obehandlade ljumskbråck i en väl definierad befolkning i östra Uganda.

Det andra delprojektet genomfördes samtidigt och samlade in data från de två sjukhus som tillhandahåller kirurgi för ovan nämnda befolkning. Alla större ingrepp registrerades under fyra månader medan de mindre ingreppen, som var fler, registrerades under tre månader. Data som samlades in var dels patientkaraktäristika, vilka ingrepp som utfördes, varför de utfördes och med vilket resultat. Även uppgifter om personal, tidsåtgång och materialförbrukning registrerades för senare beräkning kostnader.


**Resultat**

Prevalensen av obehandlade ljumskbråck hos vuxna män i studiepopulationen var 6,6% medan prevalensen av opererade bråck var 3,3%. Det vanligaste större allmänkirurgiska ingreppet på sjukhusen var ljumskbräcksoperation (n=84 av totalt 1051 patienter). Operationsfrekvensen av ljumskbräck på de två sjukhusen var därför 17 per 100.000
människor i befolkningen. En stor andel (44%) av bräcken opererades akut och andelen kvinnor bland bräckpatienterna var 24%. Ett dödsfall efter bräckoperation registrerades vilket motsvarar 1,2%. Två andra gynekologisk-kirurgiska ingrepp, kejsarsnitt (496 patienter) och skrapning efter missfall (244 patienter) var vanligare.

Högst dödlighet (8 dödsfall, 13,3%) sågs efter så kallad explorativ laparotomi. Mördadödligheten efter kejsarsnitt var 0,8% (4 dödsfall bland 496 patienter) medan 59 (11,6%) av barnen födda på detta sett antingen var dödfödda eller dog innan de lämnade sjukhuset. Kostnaden för att utföra samtliga av dessa större ingrepp var under 100 USD per operation.

I studien som jämförde myggnät med kommersiellt nät vid ljumskbräckskirurgi inkluderades 302 patienter. Av dessa följes 291 (97,3%) upp efter två veckor och 281 (95,3%) följes upp efter ett år. Inga betydande skillnader avseende risk för recidiv, komplikationer och patientnöjdhet identifierades. Kostnaden för operation med myggnät var 49,4 USD och kostnaden för operation med kommersiellt nät var 174,1 USD.

Kostnadseffektiviteten var mycket hög i båda grupperna. För myggnätsgruppen var kostnaden 16,8 USD per DALY och 7,3 USD per QALY medan kostnadseffektiviteten i den grupp som opererades med kommersiellt nät var 58,2 USD per DALY och 33,3 USD per QALY.

**Slutsatser**

Mindre än 1% av det förväntade antalet bräck i upptagningsområdet för de två sjukhusen opereras per år. Det icke tillgodosedda behovet för bräckkirurgi är omfattande trots att kostnaden är mindre än 100 USD per operation vilket är betydligt mindre än kostnaden att behandla till exempel HIV/AIDS och tuberkulos.

En oväntat stor andel av patienterna var kvinnor vilket gör att även prevalens av ljumskbräck hos kvinnor bör undersökas. En stor andel av patienterna opererades akut vilket är farligare än om de opereras planerat. En ökad tillgång på planerad kirurgi skulle kunna minska risken för död vid kirurgi. Framtida studier bör undersöka varför mortaliteten är så hög samt identifiera åtgärder för minska denna dödlighet.

Myggnät har visat sig vara ett säkert och effektivt alternativ till kommersiella nät. Ett år är dock kort tid för uppföljning och en framtida studie planeras genomföras för att även undersöka resultat på längre sikt. En operation med myggnät kostar inte mer än vad en bräckoperation utan nät kostar i dagsläget. Därför finns potential för att denna teknik kan införas på bred front och att det kommer vara hållbart över tid. Det är dock viktigt att betona att inte vilket nät som helst kan användas av vem som helst och hur som
helst. Införandet av denna teknik ska genomföras med hög kontroll, god uppföljning och tillräcklig träning för dem som ska utföra ingreppen.

Sammanfattningsvis har studierna visat att ljumskbräck är vanligt och att tillgången till kirurgi måste ökas betydligt samt att den kirurgiska teknik som används i höginkomstländer även kan användas i låginkomstländer utan några merkostnader. Detta medför mycket stor potentiell patientnytta för de miljontals bräckpatienter som lever i låg- och medelinkomstländer.
Prologue

A PhD can be done in as many ways as life can be lived. Combining the two – the better! My Ugandan life started in 2008, before I knew it myself. I first came to the small but crowded town of Iganga where I would be returning from time to time over the coming years. I wanted to see the "Real Africa".

That first time, I had come with a good friend to do a Minor Field Study on diarrhoea, a leading mass killer in children. Looking around me, I came to realise that there were many other questions left unanswered and that there was more to sub-Saharan Africa than infectious diseases.

My own prejudices were challenged when I understood that other aspects of health and health care could be equally important. I had found a solution to the seemingly unsolvable equation of wanting to pursue a career in surgery in parallel with an interest to explore the world beyond the boarders of my home country. This was my starting point for combining clinical training and academic achievements. By now, I have developed a lifestyle that is hard to beat and the way things are looking, it may never end.

After finishing university, seeing the world and a lot of Finland, I returned with a PhD plan that would challenge my ambitions. Not knowing what the day will bring and how things will turn out was such a relief. The is the beauty of leaving the known behind. The projects had their overall goals and aims but the exact way of getting there had to be figured out from day to day together with the research partners and our fantastic staff.

In the study team on site, we have spent enormous amounts of time driving around in peripheral parts of rural districts. The beauty of the land is as striking as the poverty but there are big differences between homes even there. If given a chance and some time, the patients and our study participants will teach you a lot about life. In the end, the similarities outweigh the differences.

Doctors like to bore each other, their friends and families with stories about their patients. So do I. One of our patients was a herbalist. He had herbs that could reduce an incarcerated hernia. However, he could not cure the disease. He decided to come for the screening session to participate in our study as he thought surgery was the last resort. Today, he still makes a living selling herbs to his fellow villagers but has promised to tell them at least seek medical attention if they get complications from their hernias. This gives an insight into how beliefs may affect health care seeking behaviour in our study setting.
Another time, a van was driving up and down the road, advertising herbs for hernia and other diseases. Follow up was unnecessary, it always works. The salesman had used it to treat his syphilis. In western countries, some cure cancer with homeopathy. Some surgical teams never have complications. Follow up is a good way to spoil a successful intervention. The similarities outweigh the differences.

Some patients with acute complications have also come for recruitment. Transportation is always a concern and a patient cannot go alone to the hospital. It is the responsibility of the family to take care of the patient while in the hospital. Once, we sent a very sick patient on a motorbike to hospital after his relative had gone home to pack a bag and after making sure that someone would be in the hospital to do the surgery and give the anaesthesia. That someone ended up struggling with gangrenous intestines for hours. Knowing that perioperative care is a challenge, and that stock outs are common, we felt obliged to make sure that our almost-patient got his medicines and care despite his lack of funds. He survived in the end but it was a close shot. This is a weak health care system experienced on grass root level, which is where the patients exist.

The PhD training has come to an end and that is about time. There are so many things remaining to be discovered and so many new challenges to face. So many partnerships to build and so many ideas to see through. Apart from the scientific training involved, the process has taught me not to pay so much attention to barriers and limitations. They are mainly a state of mind of myself and others. The time in Uganda has showed me that there is always a way to bypass an obstacle so that a goal can be achieved. The less the resources, the greater the inventiveness of the people, it seems. I will be the first to acknowledge, that the results are far beyond what I would have hoped for. When my Ugandan life begun, in 2008 before I knew it myself, I could never have guessed how things would turn out seven years later. And still, this is just the beginning!
Background

Surgery and global health – where is the connection?

Global health and the epidemiological transition

Global health has received much attention during the past decades. The field was defined in order to deal with conditions that were common or difficult to manage in resource scarce settings. Focus has to a large extent been on communicable diseases such as malaria, TB and HIV/AIDS. Also vaccination programmes have been prioritised and results have been significant. In 2000, the Millennium Development Goals (MDGs) were identified to improve the lives and health of people in Low- and Middle Income Countries (LMIC). Three MDGs are directly related to health; the reduction of child mortality (MDG4), the improvement of maternal health (MDG5) and the combat of HIV/AIDS, malaria and other diseases. Even though many countries have not achieved the MDGs in health, drastic improvements are seen in for instance the reduction of under 5 mortality that declined by over 50% between 1990 and 2015 (10).

Epidemiology is defined as "the study of the distribution and determinants of health-related states or events (including disease), and the application of this study to the control of diseases and other health problems" (11). Epidemiologic transition is a model for how disease and health patterns change over time and in relation to demographic, social, economic and other changes in society (12). In an early model originally published in 1971, three consecutive stages, were described. These were the age of pestilence and famine, the age of receding pandemics and the age of degenerative and man-made diseases. Recently, other stages have been added to the model (13). Whereas the disease transition in HIC may have been consecutive, it is now clear that this does not necessarily apply to LMIC where stages co-exist. Poor countries face a double, or even triple disease burden due to both communicable, non-communicable (NCDs) and socio-behavioural diseases (13).

As a consequence of the successes of the efforts invested in communicable diseases as well as a result from demographic and epidemiological transition, the burden of disease due to NCD, among those surgical conditions, is increasing. Susceptibility to most NCDs increase with age. Mortality rates depend much on the age distribution in a country and a dramatic increase of NCD deaths will be seen in Africa and other poor regions of the world due to population growth and ageing in a foreseeable future (14). The burden of NCDs has already surpassed the burden due to communicable diseases in the
world (15). Projections indicate that this trend will continue and that by 2020, 70% of all deaths will be due to NCDs (16). The age-standardized mortality rates from NCDs are highest in Africa and most of the deaths occur in LMIC where the affected individuals die from these diseases at younger ages than in HIC (17). For these reasons, research on and interventions towards NCDs in LMIC cannot wait until communicable diseases have been combatted (18).

**Surgical conditions and surgical interventions**

Surgical conditions are a broad variety of conditions that are included in the NCD family even though several of them are caused by or related to infections. They can be defined in several ways. One example is "any illness that requires surgical expertise" (19). However, such a definition leads you on to defining surgical expertise as many procedures can be and are carried out by both non-surgeons and non-physicians (20). The definition of surgical condition used in this thesis is therefore "any condition that requires suture, incision, excision, manipulation or other invasive procedure that usually, but not always, requires local, regional, or general anaesthesia" (8).

It includes interventions undertaken within all surgical specialities, such as general surgery, gynaecology and obstetrics, orthopaedics, and otorhinolaryngology among others. It excludes conditions that normally require surgical expertise but that are often not treated by surgical interventions.

**Global surgery**

Global surgery is a broad field defined as an "area for study, research, practice and advocacy, that places priority on achieving health outcomes and health equity for all people worldwide who are affected by surgical conditions or have a need for surgical care" (2).

This field is rapidly growing and the key focus is LMIC where the inequities in surgical provision are the largest (2). The burden of surgical illness is highest in Africa and surgical conditions have been estimated to cause around 30% of the global burden if disease (8, 21). Five billion people do not have access to safe surgery at an affordable price when they need it. In LMIC, nine out of ten people do not have access to basic surgical care (21). Two billion people, or nearly 35% of the world's population, live in low resource settings but receive only 3.5% of the surgeries performed (22). The situation represents a grave inequity with ethical implications that contradicts the universal right to the highest attainable standard of health (23, 24).
Surgery has not been prioritised by the international community and the funding for both surgical services and surgical research in relation to the estimated burden of disease is considerably lower than for other areas in health care (25, 26). Surgery has therefore been called the "neglected stepchild in global health" (27, 28).

One common misconception of surgery is that it is expensive and cost-ineffective and thus not relevant in low resource settings (25). On the contrary however, surgery shares the feature of many infectious diseases in that the treatment often is curative whereas a large proportion of other NCDs require long term treatment. Therefore, it should not come as a surprise that surgical services have been found to be highly cost-effective also in relation to other prioritised health care interventions in LMIC (29, 30). In fact, surgery has been identified as a missed low-cost opportunity in both South Asia and Africa (31).

Efforts are being made to address and emphasise surgery in a global perspective. This is crucial as the demographic and epidemiologic transition mentioned above is going to increase the need for surgery due to various NCDs in LMIC. However, not only NCDs drive the need for surgery. A significant proportion of communicable diseases are also treated with surgical interventions, both in HIC and LMIC (32).

In 2005, the WHO launched its Global Initiative of Emergency and Essential Surgical Care (GIEESC). The aim of this global forum is to convene stakeholders to reduce death and disability from a wide range of conditions within the surgical sphere. Still, the GIEESC with its around 1800 members is smaller, in number, than the Swedish Surgical Society (33)(34).

Year 2015 has been proclaimed as the year of surgery and the Lancet Commission of Global Surgery published their report on the situation and the way forward within this young but vast and rapidly growing field of health care (21). The 68th World Health Assembly passed the resolution of "Strengthening Emergency and Essential Surgical Care and anaesthesia as a Component of Universal Health Coverage". The agreed actions to take include aspects of awareness and political commitment; improved access and increased quality and safety of surgical services; strengthening the surgical workforce; improving data collection, monitoring and evaluation for policy and decision making as well as fostering global collaboration and partnerships within the field of surgery (35).

These initiatives are important and necessary steps in the right direction. However, the largest challenge remains with achieving the goals set and to convince the donor community and policy makers to prioritise the field of global surgery so that its enormous potential can be realised.
Figure 1 below illustrates how groin hernia relates to the broader fields of NCDs and global health and also shows which aspects of groin hernia and to a certain extent also global surgery that are highlighted in this thesis.

Figure 1. Overview of the connection between groin hernia, surgery and global health (red) and the aspects highlighted through this thesis (blue).

The health systems perspective of global surgery

Historically, joint efforts to address surgical issues from a clinical and scientific perspective have been scarce. Surgery has always been part of the health care systems in LMIC but this section of the health care systems has received little attention internationally.

Instead, individual surgeons, surgical teams and organisations from HIC have been operating in LMIC for decades. Such initiatives are still common and vary much in scope and productivity (36). In Uganda alone, there are several dozens simultaneous surgical initiatives (37). Whereas many
interventions assist those in need at that time and place it may have little long term effect and it has not been efficient in putting surgery on the agenda for either research or investments to increase and improve surgical capacity (38). Also, it has been reported that international groups may not focus on priority areas in the host country, with resulting ethical dilemmas (39). Hence, harmonization of the many actors on the surgical stage is a must (37).

The provision of safe and affordable surgery for all, when needed is not mainly a responsibility of individual, international and national surgical teams and the focus should lie on strengthening the health care systems overall. Key priority areas for achieving this goal have been highlighted in the report by the Lancet Commission of Global Surgery. These include health care delivery and management, national strategic plans for surgery, workforce training and education, economics and financing, information management, and research (21).

A number of indicators to monitor the progress towards reaching the goal of universal access to safe and timely surgery for all have been proposed. These consist of accessibility to surgical services, staffing levels and density of specialist surgery and anaesthesia providers, rates of surgical procedures, perioperative mortality rates and measures of catastrophic and impoverishing health expenditure among patients seeking surgical health care (21).

The global surgery research agenda

Agendas from system, intervention and disease specific perspectives have been suggested. The scarcity of, and need for further research from all these viewpoints have been pointed out repeatedly (40)(21)(19)(8). The body of evidence is growing but the knowledge gaps are still extensive. Therefore, research opportunities are close to endless.

The burden of surgical disease, or the epidemiology of surgical diseases, which is closely related to the surgical productivity, is insufficiently described (8)(41). Without measuring the burden of disease, estimating the need for surgery, and thus resources required to reduce this burden is very difficult (40).

The conditions with the largest burden of disease and which treatments are effective and feasible in resource constrained settings should be prioritised (42). Investigating financial aspects, such as cost and cost-effectiveness of surgical services is also key for the planning of future interventions and investments (43). Further research priorities concerning global surgery are quality and outcome of surgery, training and policy making (21).
From a procedure and disease specific perspective, the four areas of obstetric complications, injuries, acute abdominal conditions and elective surgery for common conditions such as club foot, cataract and hernia have been highlighted (8). Likewise, caesarean delivery, laparotomy and treatment of open fractures have been identified as key surgical procedures in any health care system (21).

The start off point in this thesis was groin hernia which has been studied in terms of epidemiology, volumes and outcomes of surgery, costs and cost-effectiveness of groin hernia repair as well as a possible solution to introduce a state of the art surgical technique in groin hernia repair at little additional cost. Groin hernia surgery exists in a context of multiple surgical conditions and interventions and therefore, some of these are also highlighted in this thesis.

**Groin hernia – a common surgical condition**

**Definition, symptoms and risks of groin hernia**

A hernia is a "protrusion of tissue, structure, or part of an organ through the bone, muscular tissue, or the membrane by which it is normally contained" (44). A groin hernia is collective term for inguinal and femoral hernia and is a protrusion of abdominal contents through a weakness in the abdominal wall in the groin. A groin hernia usually develops into a bulge in the groin which can often be reduced with pressure or by lying down.

Groin hernia commonly cause morbidity in terms of pain and discomfort. The degree of the symptoms can vary from mild to severe and may impact a persons ability to perform normal activities. Under certain circumstances, a groin hernia can incarcerate and become irreducible. If blood flow is impaired (strangulation), ischemia will occur and the contents of the hernia will swell, further reducing blood flow and aggravating the ischemia. This causes severe pain. Prolonged ischemia will lead to necrosis, i.e. death of tissue, a serious condition. Necrosis of the intestinal wall will hamper its function and lead to leakage of its bacteria-rich contents into the surrounding tissue. This can lead to septicemia which is a life-threatening condition.

**Epidemiology**

Groin hernia is a common surgical condition affecting over 200 million people, and over 40 000 people die due to its complications every year (45, 46). The estimated burden of disease due to groin hernia increased with 32.5% between 1990 and 2010 (47).
In western countries, the lifetime prevalence of groin hernia surgery is 27% in men and 3% in women (48). In low resource settings, access to surgery is very limited (50). Therefore, prevalence of groin hernia surgery is a poor proxy for lifetime groin hernia prevalence in such settings. Estimates of groin hernia prevalence in sub-Saharan Africa range from 3.15% to 25% (51-53). In a study from Jerusalem, the prevalence among adult men was 6.7% in the 1970s (54). Variations in these estimates largely depend on the different methodologies and definitions used.

Population-based studies with a defined denominator investigating groin hernia prevalence are scarce, the one from Jerusalem being the most reliable and most widely cited. Population based studies in SSA in general are rare and none of the above mentioned can be regarded to fulfil the criteria of a population based study.

Inguinal hernias are more commonly seen in males than in females whereas femoral hernias, which are much less common overall, are mainly seen in women (55-57). Groin hernias can be congenital or may develop later in life. Increasing age is associated with an increasing incidence and prevalence of groin hernia as well as groin hernia surgery (48, 54-56). Therefore, this is primarily a disease of very young boys and of ageing men. In settings where surgery is not readily available and paediatric hernias are not repaired, it becomes a condition that affects all ages.

Congenital inguinal hernias are almost always indirect and are a result of failure of obliteration of the processus vaginalis through which the testicles descend from the abdominal cavity to the scrotum in the male fetus. Undescended testicles and prematurity increase the risk of hernia formation as the processus vaginalis has not yet closed in these children (46).

A patent processus vaginalis does not always lead to hernia formation in childhood but will remain a risk factor for its development later in life (58). Risk factors for paediatric hernias are also genetic syndromes and connective tissue diseases such as Marfans and Ehler Danlos syndrome (59). Likewise, various collagen metabolism deficiencies appear to have a positive association with adult groin hernia formation (60). Other factors associated with an increased risk for developing groin hernia in adults are positive family history of groin hernia, low BMI and previous radical prostatectomy (55, 61, 62). Heavy physical labour and smoking are commonly stated risk factors but this is not clear (63).


**Groin hernia anatomy**

The groin, located between the lower region of the anterior abdominal wall and the thigh, is the gateway between the abdominal cavity and the lower limb and the genital area. Through its complex organization of abdominal wall muscles, their aponeuroses and fascia passes nerves, blood vessels, lymphatic vessels, the spermatic chord (in men) and the round ligament of the uterus (in women). Where these structures pass, there are natural weaknesses with potential for hernia formation. When the peritoneum, which seals the inside if the abdominal cavity pouches out through any of these weaknesses, it forms a hernia sack within which abdominal contents such as fat, omentum, intestines or other organs can herniate.

The anterior abdominal wall is built up of layers of muscles, their aponeuroses and fascia. Of importance for the groin, groin hernia formation and its repair are the three following muscles.

1. The external oblique muscle, whose aponeurosis also forms the inguinal ligament which runs between the anterior superior iliac spine to the pubic tubercle, and the external inguinal ring (see below).

2. The internal oblique muscle, which reinforces the anterior wall of the inguinal canal laterally (see below).

3. The transverse muscle with its adjacent transversalis fascia. Forms deep inguinal ring and the posterior wall of the inguinal canal (see below).

Key for the understanding of the inguinal hernia anatomy and inguinal hernia surgery is the inguinal canal. It begins after passing the internal ring which is an opening in the transversalis fascia located laterally to the epigastric vessels. This is the "exit" from the abdominal cavity. The inguinal canal then continues medially and is bordered posteriorly (transverse fascia), anteriorly (aponeurosis of external oblique muscle and internal oblique muscle), inferiorly (inguinal ligament) and superiorly (transversalis muscle and fascia and internal oblique muscle) before it ends in the external ring (formed by the aponeurosis of the external oblique muscle) medial to the inferior epigastric vessels. This is the "entrance" to the genital area (scrotum and labia majora, respectively).

Inguinal hernias arise above the inguinal ligament and are divided into direct (medial), and indirect (lateral) hernias (Figure 2). A direct hernia passes *directly* through a weakness in the abdominal wall, *medially* to the inferior epigastric vessels. An indirect hernia passes through the inguinal canal, and begins *laterally* to the inferior epigastric vessels.
Femoral hernias are located below the inguinal ligament and arise when a hernia sac develops and passes alongside with the femoral artery and vein within the femoral sheath from the abdominal cavity into the lower limb. Due to the very narrow anatomy in this space, and fibrosis formation of the hernia sac itself, femoral hernias have a much higher incidence of strangulation than inguinal hernias (46).

![Diagram of groin hernia anatomy](image)

**Figure 2. Groin hernia anatomy. Direct and indirect inguinal and femoral hernia.**

**Groin hernia surgery**

The only curative treatment of groin hernia is surgical repair. Around 20 million groin hernia patients are operated every year (64). It is also among the most commonly performed surgical procedures in LMIC (65-67). The purpose of groin hernia surgery is to restore normal anatomy so that tissues and organs are kept in place. In order to achieve this, the defect through which the hernia arises is repaired.

Attempts at groin hernia repair were made already during the times of the Egyptian Pharaohs over 1000 years BC (46). Results were probably not very encouraging. Several methods were developed over time, but most were unsuccessful and most hernias recurred. It was not until the late 19th century when the Italian surgeon Edoardo Bassini developed his technique
that surgical repair of groin hernias became successful. Contrary to many medical advancements then and today, his method was rapidly accepted and implemented by the surgical community of his time (68).

The method was further developed, or possibly rather corrupted, and today when a technique is referred to as Bassini or a modified Bassini it is hard to know what it means in reality.

In the 1950s the Shouldice repair was introduced and became the preferred repair method for the coming decades (46). These two techniques have many similarities and are both sutured techniques that put particular emphasis on repairing and strengthening the posterior wall and the internal ring of the inguinal canal in several layers (69).

Sutured techniques induce tension when opposing, often fragile, tissues. This carries a substantial risk of recurrence. Hence, a non-tension surgical repair method was called for. In 1984 Lichtenstein and his co-workers introduced a technique that uses a synthetic mesh to reinforce the abdominal wall and which opposes tissues without the strain incurred by the sutured techniques (46, 70, 71). The mesh induces inflammation and scar formation which further strengthens the abdominal wall. The risk of recurrence when using this technique in routine clinical practice is 50% to 75% lower compared to the sutured techniques (71, 72). Today, synthetic mesh is used in almost all groin hernia repairs on adults in HIC, but are rarely used in LMIC (63, 73). The mesh often costs over 100 USD and is thus unaffordable to the health care systems and most patients in LMIC.

**Hernia repair - an alternative use for mosquito nets?**

A superior surgical technique cannot be widely used in LMIC, where the majority of the world’s groin hernia patients live, due to the 100 USD cost of the mesh. Cheaper alternatives that do not compromise the safety or effectiveness of the mesh repair are needed. Mosquito mesh has been tried and is already used instead of commercial mesh in several locations (74).

Caution has to be taken when choosing a mosquito mesh for groin hernia surgery. Just as there are many alternatives when choosing commercial mesh, the number of available mosquito meshes is vast. All mosquito meshes cannot be assumed to be comparable in terms of material composition, durability, tensile strength, pore size, weight and whether they can be sterilised adequately.

Operation Hernia is a UK based organisation that provides groin hernia surgery using mosquito mesh in LMIC (74). The 100% polyethylene mosquito mesh used within this organisation, has been evaluated and compared to commonly used commercial meshes. It was found that the
mosquito mesh had similar characteristics to commercial low-weight meshes available on the market (75).

Commercial mesh is delivered ready to use. Mosquito mesh is available in large sheets and has to be prepared prior to use. It needs to be cleaned, cut to the right size and sterilised. Sterilisation affects different materials in different ways. Sensitivity to heat varies. Steam-autoclaving at 121°C for 20 minutes has been found to be an effective way for sterilisation but well functioning autoclaves with reliable temperature are required (76).

In support of the practice of using mosquito mesh in groin hernia surgery is a handful of publications. An animal study concluded that mosquito mesh is a feasible alternative to commercial mesh when the latter is unaffordable or unavailable (77). A randomised trial comparing mosquito mesh with commercial mesh in 40 patients from Burkina Faso found no differences in terms of short term outcomes at 30 days follow up (78). Hernia repair using mosquito mesh has been found to be highly cost-effective both in Ghana and in Ecuador (79, 80).

These results are promising and encouraging but do not clarify whether a mosquito mesh is comparable with commercial meshes. In order to respond to such research questions a large trial with long-term follow up is required. Further research to investigate effectiveness, recurrence and long term complications following repair using mosquito mesh is needed (81).

**Anaesthesia methods**

Anaesthesia options for groin hernia repair include general, regional and local anaesthesia. The choice of method depends on the facility, the patient, the surgeon and the availability and skills of the person administering the anaesthesia.

Lichtenstein and colleagues strongly recommended the use of local anaesthesia when performing the mesh technique (71). In groin hernia surgery, local anaesthesia has been shown to be well tolerated by patients and to be beneficial from a cost effectiveness perspective (82, 83). In the European Hernia Guidelines, local anaesthesia is the method of choice for elective groin hernia repair of primary, reducible groin hernias in adults (63). Still it is less commonly used than regional and general anaesthesia. In Sweden, for instance, only 12% of hernia repairs are performed under local anaesthesia (84).
Both surgical techniques and anaesthesia have developed over time. Before effective anaesthesia was introduced, the surgeon's physical strength was as important as his technical skills. The assistants were called "handlers" and their role was to keep the patient in place.
Health Economics

Health economics is an enormous field where health and health care is described according to economical principles. Its purpose is to form evidence upon which well informed decisions on resource allocation can be made. For such reasons, health economic analyses and projections are necessary and widely used in policy making. Below is a section that describes health economy and different ways to measure costs, health and cost effectiveness as well as how it can be interpreted. This section gives some background to the methods used in this thesis.

Costs of health care interventions

Seemingly straightforward, cost analysis of health care interventions is a complex task depending on a number of assumptions that have to be made. Firstly, one must decide which costs to include in a cost analysis. One may choose to look at an intervention from a societal, health care provider’s or patient’s perspective. An increased expenditure in one, may save costs in another.

One key feature in economics is that nothing is free of cost. If a service is provided free of charge, there is still an opportunity cost. The opportunity cost can be related to buildings and the potential income from these buildings if they had been leased to a tenant or another kind of service. The opportunity cost of staff working for free is the potential income that they could have gotten providing the same service elsewhere.

The time perspective is also important and there is a choice of looking at immediate or delayed costs of an intervention. In economics costs at different points in time are compared using a discount rate which assumes that peoples’ assessment of costs or benefits diminish with time.

The perspective of the society may include production losses due to an individual’s inability to work as a result of disease or disability. This can be measured as a loss of GDP. Costs to the patient can in addition to medical costs be associated with transportation and food as well as loss of income during the time spent in the hospital or recovering.

Costs to the health care provider are all costs incurred on the provider due to the care of the patient. This includes staff, equipment, materials, capital and overhead costs. The costs included in the studies of this thesis have been limited to immediate costs from the health care providers’ perspective.

Overhead costs are costs of services that are shared by different sections of the hospitals to different extents. If one is to investigate a particular service, such as groin hernia surgery, provided by the hospital, part of the overhead
cost has to be allocated to this service in a sensible way so that it reflects the proportional use of the particular service of the total overhead cost.

Capital costs due to buildings also have to be considered. This can be done in different ways and the method chosen has to be appropriate for the study setting. For instance, in the studies included in this thesis, the hospital buildings were so old that depreciation of the initial investments were no longer realistic. Rent was also not paid for the facilities. Therefore, opportunity costs were used instead.

Equipment are part of capital investments and capital costs have to be calculated. Equipment can be depreciated according to their expected life span. Often, depreciation rates according to given accounting principles in the country are used. In reality however, some equipment is used much longer than that.

Staff costs are also important in a cost analysis and can, as the above mentioned costs be allocated due to different principles. A rough estimate would be to divide all staff costs and assume all patients receive the same amount of attention by all the staff. A more accurate way is to undertake a time study so that the exact time consumption per patient receiving a particular service, such as groin hernia repair, can be measured. Thereafter the time consumption can be multiplied with the minute cost for the staff involved based on the salaries of these staff.

The assumptions of all these aspects in the cost analysis will have great impact on the result. When reading and comparing results from health economic analyses one has to be aware of this fact. A sensitivity analysis where assumptions are altered in different ways is a good way to assess the robustness of the results. Performing a sensitivity analysis will provide a range between minimum and maximum cost, rather than a specific cost.

**Outcome measurements**

Several outcomes may be useful in health economical analysis. Quantitative measures could be productivity such as number of consultations or operations in a particular clinic per day, years in remission, mortality rates and life expectancy. Extreme health indicators such as mortality and life expectancy are useful when health problems are dominated by deadly diseases. Overall mortality and life expectancy are also useful as aggregate measures as they reflect the general health in a population (85).

However, most diseases and illnesses cause morbidity, or impaired quality of life in addition to mortality. Some conditions predominantly cause morbidity and mortality may be a rare outcome. Groin hernia is a condition that fits this description and in order to measure the Health Related Quality of Life
(HRQOL) or level of morbidity, due to such conditions, requires more sophisticated measures. An example of a HRQOL measure is the Quality Adjusted Life Year (QALY). The QALY is commonly used when evaluating health care interventions (85).

An alternative measure to the QALY when the aim is to describe health or burden of disease on population level is the Disability Adjusted Life Year (DALY). The DALY was developed by the World Bank and the World Health Organization on order to assess disability due to specific diseases and conditions on population level on a global scale (7).

These two measures are similar in their structure as they are aggregate measures of duration of life and health. The QALY measures health in terms of quality of life whereas the DALY measures ill-health or disability (7). Therefore, an intervention with positive impact on health will lead to QALYs gained and DALYs averted.

**QALYs and DALYs are calculated according to the following formulas (7)(86):**

\[
\text{QALY} = \text{Number of years lived in a particular health state} \times \text{Health related quality of life weight}
\]

\[
\text{DALY} = \text{YLL} + \text{YLD}
\]

\[
\text{YLL} = \text{Years of Life Lost due to premature mortality} = \text{Number of deaths} \times \text{Standard life expectancy at age of death}
\]

\[
\text{YLD} = \text{Years Lost due to Disability} = \text{Prevalence} \times \text{Disability Weight} \times \text{Average duration of the condition until remission or death}
\]

The result will largely depend on how the health related quality of life weight and the disability weights are estimated as well as on the remaining life expectancy or the number of years lived with a particular condition. Issues related to these aspects of the QALY and the DALY are described below.

**Quality Adjusted Life Years**

As stated above, the HRQOL, measured in for instance QALY, takes into consideration the general health of a person or a group of people over time. According to the formula above, a health related quality of life weight, or an index value, is used. There are various multi attribute instruments available that will describe health states. Multi attribute means that several aspects of health are taken
into consideration. The instruments can be generic measuring overall health, or disease specific. The health states can in turn be converted into an index value that is preferably based on population based studies assessing how the general population value health and changes in health. This is investigated through different methods of assessing preference.

One example of a generic HRQOL instrument is the EuroQol-5D-3L (EQ-5D-3L) tool which was used for study 3 in this thesis. This tool has been developed and is provided by the EuroQol group. It describes health states in five dimensions; mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has three values (1-3, where one indicates no problem and three indicates extreme problem/disability). Including the states of “dead” and “unconscious” there is a total of 245 health states. Each respondent will get a health state defined in five numbers, such as 13221. The EQ-5D-3L also contains a VAS scale from 0-100. It should be noted that the zero value is anchored on worst imaginable health and not death as many other VAS scales. 100 indicates best imaginable health.

The five digit health state can be used in analysis when evaluating the impact of a health care intervention. One might for instance assess the change in each individual dimension before and after a particular intervention. Still, the health state itself cannot be directly used to calculate QALYs which is a convenient measure in cost-effectiveness analysis. As said before, the health state can instead be converted into an index value. The EuroQol group has carried out several regional and national surveys in different parts of the world. One such survey has been undertaken in sub-Saharan Africa (Zimbabwe). The study participants have been interviewed according to the Time Trade Off (TTO) method (87).

Very simply put, respondents interviewed according to the TTO method are trading time for health. They get to choose between a specific time in a particular health state followed by death and perfect health for a shorter duration of time followed by death. The time aspect is adjusted until the respondent is indifferent to the choice. The worse the health state, the more time a person will be willing to trade to live a shorter period of time in full health. For instance, a person suffering from severe pain is going to be willing to trade more time for perfect health than another person who only experiences mild pain. This method uses two certain, yet hypothetical, outcomes (88).
Figure 3. The Time Trade Off method of preference

By performing these interviews in a study population of sufficient size to give a representative result, each health state will be given an index value where 0 is equal to death and 1 equals full health. Also this measure can take a value less than 0 indicating that some health states are worse than death. Assuming that the study populations in such studies are representative of a general population, these index values can thereafter be used when translating health states from various studies into index values to be used for QALY calculations.

In addition to EuroQol 5D there are several generic HRQOL instruments. Examples are the Short Form 36, the Health Utilities Index and the Quality of Wellbeing. Describing them is beyond the scope of this thesis but I would like to highlight the fact that all take different aspects of health into consideration, have different numbers of possible health states and that their results are not directly comparable. Further on, there are different methods to investigate preference among people. The standard gamble is a well known method. It differs from the TTO method in the way that it includes uncertainty and therefore incorporates individuals’ different approach to risk. Yet another way to assess preference are the Willingness to Pay (WTP) and the Willingness to Accept (WTA) methods that directly links health to the willingness to pay money for improved health or the amount that would be acceptable to loose part of one’s health. These have nothing to do with how health care should be financed but are alternatives to assess preference of health outcomes in monetary terms.

Depending on the instrument used and the method for assessing preference that is used, the results expressed in QALYs can differ quite a lot (9). Therefore, one must be aware of the fact that not all QALYs are equal (88). If
the exact methodology used to calculate the QALYs and the underlying preferences are not clear in a publication, interpreting the results and comparing them to results from other studies is very hard.

**Disability Adjusted Life years**

As shown in the formula for DALY introduced above, disability weights (DW) are central to the DALY concept. They are specific to disease, condition or sequelae. Various methods for estimating the DW have been used. Similar to the index values for QALY calculations, the DW are estimated based on preference. In the first GBD study in the 90’s, experts were interviewed according to the Person Trade Off (PTO) method (89). It is similar to the Time Trade Off method but here respondents trade one group with a particular disability against another group with another disability. An example could be: "how many people with groin hernia should be returned to perfect health to produce the same value as returning 10 people who were about to die to full health?" This method is commonly used for policy making purposes and may be an option in resource allocation. Its usefulness when assessing the burden of disease has been disputed and therefore, another method was used in the most recent Global Burden of Disease Study.

A questionnaire based survey with over 30000 respondents from the general population in five countries and a web based survey was used instead. The method to yield DW was by pairwise comparison where the respondents were asked to state which of two individuals with particular conditions that were healthier overall. Due to change of methodology, the results are not comparable and the results in the new GBD study supersede all previous GBD results (15).

**Life expectancy**

Both the QALY and the DALY includes years of life lived in a particular health state or with a particular disability. As in Study 3 in this thesis, this may equal the remaining life expectancy. Mortality rates at different ages and life expectancy at birth varies greatly between countries and income groups in the world. The shortest country-based life expectancy at birth was in 2013 46 years (Sierra Leone), whereas the longest was 84 years (Japan). The absolute difference in life expectancy between low income countries and high income countries was 17 years (62 years versus 79 years, 90). The mean life expectancy in the world was 71 years (91). Therefore, there is more than one option when choosing which life expectancy to use. The Global Burden of Disease Study 2010 used the lowest death rates at each age across all countries (15). In essence this corresponds to a very high life expectancy only seen in a limited number of countries. This is suitable when the overall burden of disease in the world is to be measured. Using country
specific life expectancies would otherwise lead to that an early death in Japan would be valued much higher than an early death in Sierra Leone. The goal, as stated in the GBD 2010, is a life of maximum duration in full health.

In smaller scale studies, and where impact from different health care interventions is compared in a local or regional perspective, it may be more feasible to use country specific life expectancies. In study 3 in this thesis, we used the remaining life expectancy at each age in Uganda for the study participants.

**Cost-effectiveness of health care interventions**

Cost-effectiveness can simply be described as value for money. The cost and the health outcomes analyses can be combined to calculate the cost-effectiveness of a given health care intervention. A low cost does not necessarily mean that the investment is worth while and a high cost does not necessarily indicate the opposite. It is important to put the size of any given expenditure in relation to the effect of the intervention. As no health care system has an unlimited budget, cost-effectiveness analysis is important for resource allocation.

In addition to calculating the cost-effectiveness measure, one needs to decide a cut off point for when an intervention can be considered highly cost effective, cost effective and not cost effective. Cost-effectiveness thresholds recommended by the WHO is that an intervention is highly cost effective when the cost per DALY averted is lower than the per capita GDP in a particular country. It is cost effective when the cost per DALY is one to three times the per capita GDP in a country (92). These cut off points are relevant in resource allocation but cannot be used alone as the total resources available may not be enough to implement all cost-effective interventions. Again, it is how different interventions compare with each other that is important.

**Conducting research in low- and middle income countries**

**Population based research**

In many LMIC, there is no routine civil registration. This means that data on births, deaths, cause of death and other demographic and health indicators in the populations are unreliable (93). This has implications on policy making and planning of health care systems that rely on accurate information in order to meet the needs for health care services in the populations. Hence, the lack of civil registration in these countries makes population-based research hard, if not impossible, to carry out.
The International Network for the Demographic Evaluation of Populations and their Health (INDEPTH) consists of a network of 52 Health and Demographic Surveillance Sites (HDSS) in 20 LMIC in Africa, Asia and Oceania (4). It was founded in 1998 and aims to strengthen longitudinal, population based research capacity, enable multi-centre research and to facilitate research translation into practice and policy (94, 95).

A HDSS is a geographically defined area with its population. This population is followed over time with regular data collection on births, deaths and migration. The HDSS structure allows for population based research as the number of inhabitants, the denominator for incidence and prevalence calculations, is updated regularly. Even though civil registration is the golden standard, implementation of such a system requires time and resources. The INDEPTH organisation can be seen as an interim solution for the lack of reliable, population based data in many LMIC (96).

**Iganga and Mayuge districts Health and Demographic Surveillance Site**

The studies in this thesis, especially study I, utilised the Iganga and Mayuge districts Health and Demographic Surveillance Site (I/M HDSS) in eastern Uganda. This HDSS had a population of 70,244 people residing in 65 villages at the time of the study (2011). Of this population, 53% were below 18 years. Total fertility rate per woman was 4.5. The I/M HDSS households were followed with interviews twice per year.

**Prospective facility based studies and trials with long-term follow up**

Prospective facility based studies on surgical performance in LMIC are rare. Retrospective studies have been undertaken but an inherent issue to such study designs include bias, missing and inaccurate data and the lack of a population denominator (97). Commonly, also, information in records are rudimentary if records at all can be found due to variations in record keeping practices.

Prospective data collection is considered more reliable but requires more resources. It is better in terms of reliability of data, completeness of data and data is collected to respond to certain research question rather than the opposite. Staff can be trained so that inter-individuality in data collection is minimised.

Follow-up of patients after surgery may be challenging in LMIC (98). It has been stated that trials with long-term follow up in SSA are hard to carry out (76). Consequently the literature on surgical trials with long-term follow up in such settings is limited. Three large trials on the effect on risk of
contracting HIV/AIDS following male circumcision, however, have documented follow up rates of 90-92% up to two years after the intervention (99-101). A surgical intervention, male circumcision in these studies were undertaken for a medical indication and outcomes are not surgical. Still, it gives an indication that long-term follow up after other surgical interventions could also be possible.

Uganda

Country profile

Uganda is located on the equator in East Africa. In 2015, the population was 37.5 million and the annual population growth was 3.3 % (102). Today, life expectancy at birth is 59 years which is an increment of 11 years since 1990. Childhood mortality has decreased by 61% during the same period (103). There is an ongoing demographic transition but still more than 25% of the population is less than 15 years old (104).

Uganda is a low income country with a GNI per capita of 510 USD (World Bank definition, GNI per capita <1045 USD) much like its neighbours and many other countries in sub-Saharan Africa (105). 63% of the population live on less than 2 USD per day (106)

The health care system and the surgical work force

Uganda’s health care system consists of the public, the private not for profit and the private for profit sector which runs various types of health care facilities. Total health expenditure is 59 USD, or 9.8% of GDP (107)(108). Public health expenditure is 4.3% of GDP which is much less than the agreed 15% according to the Abuja Declaration in 2001 (109, 110). 38.4% of the total health expenditure is paid out-of-pocket (111). As a comparison, the total expenditure on health in Sweden and the United states is 5680 and 9146 USD, which corresponds to 9.7% and 17.1% of GDP in the respective countries (107, 108).

In Uganda, the public health care sector is divided into seven levels where the lowest level is the village health team and the highest level is the national referral hospital. District hospitals are level V and regional referral hospitals are level VI in Uganda. Specialist surgeons and gynaecologists/obstetricians should be available from level V and up but that has not been widely implemented. In 2012, there were around 200 surgeons, 125 obstetricians and 17 anaesthesiologists in Uganda (112). Of those registered, several may not be clinically active. Most major surgeries are undertaken by non-specialists (65).
Ethics

The base of the studies in this thesis is existing inequity in health and resource allocation. From an ethical point of view, resources should be allocated to where they are needed the most. Today, 90% of resources for research in the world are allocated to the diseases affecting only 10% of the world's population, mostly living in HIC (113). This is mirrored in the literature where a minority of high-impact publications arise from LMIC (114). For research in LMIC, there is a skew towards infectious diseases which disfavours attempts aiming at NCDs. In this respect, there is a mismatch of need in relation to the priorities of the donors (26).

Ethics is a pillar in all research and clinical activities. When these activities are undertaken in a foreign country, which culture and population may be different from your own, ethical considerations are even more important. This should be obvious but still it is reported that international teams may cause ethical dilemmas in clinical practice and that the research agenda of the visitor is not always within a priority area of the host (39).

Seven sins for humanitarian medicine have been suggested. Some of these have been of particular importance to the study design of the research documented in this thesis. Firstly, leaving a mess behind and failing to have a follow up plan, means that international teams may stay very short time in the host country and that complications occur after they have returned home (115).

Another important sin is the failure of matching technology with local needs and ability. Too advanced and technically demanding procedures are most often a bad buy in resource limited settings. Priority should lie on interventions that can be undertaken in a safe and cost-effective manner without high-tech machinery (115).

The best way of making sure that a particular research topic is relevant and how research can be conducted in a culturally and ethically acceptable way is to build a strong collaboration with local partners and to involve the local community (116). This has been the aim through the entire research process.
Aims of the thesis

The main aim of the thesis is to fill some of the knowledge gaps within the field of global surgery, primarily concerning groin hernia. This includes both epidemiology, health systems delivery in terms of quantity and some qualitative measures as well as cost and cost effectiveness and investigating the possibility of improving surgical methodology at little additional cost.

The specific objectives of the thesis are to:

- Define the prevalence and associated factors of groin hernia among adult men in a sub-Saharan population and to further estimate the met and the unmet need for groin hernia repair in the study population, (Paper I)

- Investigate the volumes and characteristics including surgical planning, staff and postoperative mortality following surgery undertaken in a rural and semi-urban setting in Uganda, (Paper II)

- Calculate the costs of common major and minor surgeries carried out in a rural and semi-urban setting in a low income country in sub-Saharan Africa, (Paper III)

- Investigate the possibility of introducing a superior surgical repair method for groin hernia by using a low cost material instead of a commercially available surgical mesh, (Paper IV)

- Calculate the cost effectiveness of groin hernia surgery using a low cost mesh compared to a commercially available mesh, (Paper V)
Materials and methods

The five papers in this thesis are the result of data from three different, but related research projects. Below, the methodologies used for each of these projects are described briefly (Table 1). For more detailed description of the methods used in the individual studies, see Papers I-V. Table 2 shows how the three studies were combined and used for the individual papers I-V.

Table 1. Methodologies used in studies 1-3

<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>Inclusion criteria</th>
<th>Outcome measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Surgical volume, characteristics and costs of surgery in Eastern Uganda</td>
<td>a. Prospective, questionnaire and facility-based, study. b. Cost analysis</td>
<td>All surgical interventions carried out in Iganga General Hospital and Buluba Mission Hospital</td>
<td>a. Volumes and characteristics of surgery. Perioperative mortality rate. b. Cost per surgery in USD.</td>
</tr>
<tr>
<td>3. Mosquito mesh versus commercial mesh in groin hernia surgery</td>
<td>a. Double blinded, randomised, controlled trial b. Cost effectiveness analysis</td>
<td>Adult (18 years and above), healthy, males with primary, unilateral, reducible groin hernia</td>
<td>a. Recurrence, postoperative complications, chronic pain and patient satisfaction b. Cost in USD per DALY averted and QALY gained</td>
</tr>
</tbody>
</table>
Study 1. Groin hernia prevalence in adult males in the Iganga/Mayuge Health and Demographic Surveillance Site

This was a cross sectional study with random selection of 900 adult (18 and above) males resident in the I/M HDSS at the time of the study. The 900 study participants were randomly selected from the HDSS database.

Field assistants carried out a questionnaire-based interview with information on basic individual characteristics, questions regarding symptoms of hernia and previous surgery. The assistants measured height and weight of the study participants for BMI calculations. Thereafter, the study participants were examined by a physician, focusing on the groins. It was recorded whether the study participant had a groin hernia, a scar following groin hernia repair or no groin hernia.

*Picture 2. A field assistant measuring height and weight of the study participants before the groin examination*
Study 2. Surgical volume, indications, interventions, outcomes and costs of surgery in Eastern Uganda

This prospective, questionnaire based study was carried out in Iganga General Hospital and Buluba Mission Hospital. Information on all surgical procedures was collected by hospital staff during three months (minor surgical procedures) and four months (major surgical procedures). Different parts of these data were thereafter used in Paper I-III.

Data that was used for Paper I was focused on the volumes of groin hernia repair as well as basic characteristics of these patients.

The bulk of the data was used for Paper II which describes the patients and the volumes of all surgical procedures undertaken and the indications for these operations. Other aspects included anaesthesia method, human resource in terms of which staff category that administered anaesthesia and who performed the operations. Finally, the in-hospital perioperative mortality rate and details surrounding the deaths were recorded.

Paper III was a cost analysis which included costs of materials, staff, overhead and capital costs for the three most commonly performed major and minor surgical procedures.

Material consumption in the theatre and in the ward was entered in the questionnaires and prices were retrieved from a price list from a large medical supplier in Uganda. Staff was costed according to their salary per minute which was multiplied by the average time consumption for each of the six procedures.

Overhead cost, based on the annual expenditure of the hospitals, and capital costs were allocated to surgical procedures based on space of the operation theatre and the wards. Capital costs for buildings were estimated based on the cost of leasing office space in the respective location.

Capital costs due to equipment were based on prices of these equipment if bought new at market price. Major equipment, such as autoclaves, operation tables and hospital beds were depreciated over five years. Intermediate equipment such as surgical instruments were depreciated over two years and minor equipment such as gowns and drappings were depreciated over one year.
Study 3. Mosquito mesh versus commercial mesh in groin hernia surgery

This was a double blinded, randomized controlled trial designed and carried out according to the CONSORT guidelines. The primary endpoints were hernia recurrence and postoperative complications. The secondary endpoints were chronic pain, quality of life and patient satisfaction. These endpoints were assessed through interviews and physical examination by two blinded physicians two weeks and one year postoperatively.

The power based sample size calculation was undertaken according to a superiority design. The following assumptions were made; power 80%, significance level 5%, expected success rate in the control group 100% and in the intervention group 95%. A 5% difference was the maximum tolerable difference from a clinical perspective. This yielded a total required sample size of 300. A per-protocol analysis of the data was performed.

The inclusion criteria were adult males (18 and above), without significant comorbidities (ASA 1 and 2), with primary, unilateral, reducible groin hernia. Exclusion criteria were inability to give informed consent, known or suspected coagulopathy and obvious substance abuse.

Data were collected at recruitment and inclusion into the study, as well as during the surgeries, before discharge from the hospital, two weeks and one year postoperatively. Questionnaires especially developed for the study were used. The first was the Inguinal Pain Questionnaire (IPQ), a scoring system where the study participants rate their groin hernia pain on a seven-degree scale ranging from one (no pain) to seven (severe pain, immediate medical attention sought, 117). The other was the EQ-5D-3L.

Recruitment and follow up was scheduled in the same location, often a health centre, close to the patients homes. Local chairmen and other authorities were included in the process and helped with recruitment and follow up. Before leaving the hospital, all patient received oral and written information about the surgical procedure including possible complications as well as contact details for the research team and an appointment with place, date and time for follow up.

Prior to the follow up date, patients were contacted by phone or through the Local Chairman. The rest of the follow up strategy, including making new appointment and finding individual solutions for patients who were unable to come to the meeting point is shown in the flow chart in Figure 4.
The outcomes in the cost-effectiveness analysis were expressed in QALYs and DALYs. QALYs were calculated using the information from the EQ5D-3L tools. DALYs were calculated using the results from the IPQ questionnaire. These results were translated into the DWs for mild, intermediate and severe abdominopelvic problem presented by the Global Burden of Disease Study 2010 (118). The exact details on how these calculations and the translation process were conducted are shown in Paper V.

Costs included were those of materials, staff, capital and overhead costs. Materials were costed according to the standard consumption per surgery. Staff, capital and overhead costs were calculated using the same methods as in the cost analysis of Study 2.

Figure 4. Follow up strategy in Study 3.
Ethical considerations

All studies were granted ethical approval by the Institutional Review Board at School of Biomedical Sciences, Makerere University, Uganda as well as the Uganda National Council of Science and Technology.

In study 1 and 3, patients were included after giving informed consent. In study 2, the Medical Superintendents of Iganga General Hospital and Buluba Mission Hospital approved data collection in their respective hospital.

Patients included were informed that they could withdraw from the study at any given time. Patients identified to have a hernia in need of surgery, were offered surgery free of charge.

Table 2. The studies (1-3) and their resulting papers (I-V)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study 1</th>
<th>Study 2</th>
<th>Study 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Prevalence of treated and untreated groin hernia in eastern Uganda</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>II. District-level surgery in Uganda: Indications, interventions and perioperative mortality</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>III. Cost of surgery in a low-income setting in eastern Uganda</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>IV. Low cost mesh in groin hernia repair - a double blinded, randomized, trial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V. Cost effectiveness of groin hernia surgery using low cost versus high cost commercial mesh</td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>
Key results

I. Prevalence of treated and untreated groin hernia in eastern Uganda

Of the 900 patients randomly selected from the I/M HDSS, 563 were located and agreed to participate in the study. The total groin hernia prevalence among the study participants was 9.4%; 6.6% untreated or with recurrence and 3.0% with scars. There was a positive correlation between hernia prevalence and age, and a negative correlation between hernia prevalence and BMI, as seen in Figure 5. Smoking and type employment or physical intensity of work were not related to the risk of having a hernia.

Figure 5. Probability of risk for hernia as a function of age and body mass index (BMI) among study participants in the hernia prevalence study (n=563)
II. District level surgery in Uganda: Indications, interventions and perioperative mortality

2701 patients underwent 2790 surgical procedures during the period of data collection. Of these, 1051 patients underwent major procedures. Most of these patients were women (n=914, 87%) and the mean age was 28.5 years. The procedures were mostly performed as emergencies (n=833, 79.3%) by a medical doctor (n=1037, 98.7%). The characteristics of the most commonly performed major surgeries, caesarean delivery, evacuation of uterus and hernia repair are shown in Table 3. The rate of major surgery was 225 per 100,000 persons and year and the rate of groin hernia repair was 17 per 100,000 persons and year in the catchment population of the two hospitals.

A total of 1666 minor surgical procedures were performed on 1650 patients. Most of these patients were male (n=1293, 78.3%), and the mean age was 18.4 years. These procedures were rarely performed by medical doctors (n=98, 5.9%). The characteristics of the three most commonly performed minor surgical procedures; circumcision for HIV prevention, repair of cuts and lacerations and incision and drainage of abscesses are shown in Table 4.

![Picture 3. Operation theatre in a district hospital (level V), Iganga.](image)
Table 3. Characteristics of the three most commonly performed major surgical procedures

<table>
<thead>
<tr>
<th>Indication, n (%)</th>
<th>Caesarean delivery, n=496</th>
<th>Uterine evacuation, n=244</th>
<th>Groin hernia repair, n=84</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Prolonged or obstructed labour, 196 (39.6)</td>
<td>1. Incomplete abortion, 210 (86.1)</td>
<td>1. Groin hernia, 84 (100, one bilateral)</td>
<td></td>
</tr>
<tr>
<td>2. Previous caesarean delivery, 156 (31.5)</td>
<td>2. Bleeding, 161 (66.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Cephalopelvic disproportion, 143 (28.8)</td>
<td>3. Retained placenta or membranes, 25 (10.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Malpresentation, 66 (13.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Fetal distress, 43 (8.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annual rate per 100 000 population</td>
<td>99.2</td>
<td>48.8</td>
<td>17.0</td>
</tr>
<tr>
<td>Proportion emergencies, %</td>
<td>91.7</td>
<td>99.6</td>
<td>44.0</td>
</tr>
<tr>
<td>Performed by</td>
<td>Medical officer</td>
<td>Medical officer</td>
<td>Medical officer</td>
</tr>
<tr>
<td>Anaesthesia method most commonly used</td>
<td>General</td>
<td>General</td>
<td>General</td>
</tr>
<tr>
<td>Average length of stay in hospital, days</td>
<td>6.3</td>
<td>1.5</td>
<td>5.5</td>
</tr>
</tbody>
</table>
Table 4. Characteristics of the three most commonly performed minor surgical procedures

<table>
<thead>
<tr>
<th></th>
<th>Circumcision, n=768</th>
<th>Repair of cuts and lacerations, n=293</th>
<th>Incision and drainage of abscess, n=238</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication</td>
<td>HIV prevention</td>
<td>Cuts and lacerations</td>
<td>Abscess</td>
</tr>
<tr>
<td>Proportion emergencies, %</td>
<td>0.1</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Performed by</td>
<td>Clinical officer</td>
<td>Theatre assistant*</td>
<td>Theatre assistant*</td>
</tr>
<tr>
<td>Anaesthesia method most commonly used</td>
<td>Nerve block</td>
<td>Local</td>
<td>Local</td>
</tr>
</tbody>
</table>

* A theatre assistant is trained on the job > 2 years

**Perioperative mortality rate and cause of death**

Fourteen patients died following major and two died following minor surgical procedures, resulting in an overall perioperative mortality rate of 0.6%. Two high-risk interventions were identified. These were exploratory laparotomy (8 deaths in 60 patients, 13.3%) and caesarean delivery (4 deaths in 496 patients, 0.8%). Of the 510 babies delivered through caesarean delivery, 59 (11.6%) were either stillborn or died before discharge from the hospital.

Most deaths occurred due to infection/sepsis or haemorrhage. Of the patients who died due to infection/sepsis following exploratory laparotomy all were prescribed fluids and all but one were prescribed antibiotics. One of the patients who died due to haemorrhage following caesarean delivery was given a 500 mL blood transfusion.
III. Cost of surgery in a low-income setting in eastern Uganda

Costing and productivity data from Study 2 were used for Paper III. The daily surgical productivity expressed as the average number of surgical procedures performed per day was 3.5 in BMH and in IGH it was 23.3.

The cost of the most commonly performed major procedures (caesarean delivery, uterine evacuation and groin hernia repair) range between 25.0 and 74.4 USD. The costs of performing the three most commonly performed minor surgeries (circumcision, repair of cuts and lacerations and incision and drainage of abscess) range from 10.1 to 24.6 USD. Table 5 shows the costs of these surgical procedures as well as costs of other common health care interventions in LMIC. The main cost driving components were the capital and the overhead costs. A very small proportion of the costs (0.5-5.6%) were due to salaries of the staff directly involved in the surgeries.

Table 5. Costs of surgery in Iganga General Hospital and Buluba Mission Hospital in relation to cost of other health care interventions

<table>
<thead>
<tr>
<th>Major surgical procedures</th>
<th>Caesarean delivery</th>
<th>Evacuation of uterus</th>
<th>Groin hernia repair</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of procedure (USD)</td>
<td>68.4 – 74.4</td>
<td>25.0 – 32.6</td>
<td>58.8 – 66.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Minor surgical procedures</th>
<th>Circumcision</th>
<th>Repair of cuts and lacerations</th>
<th>Incision and drainage of abscess</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of procedure (USD)</td>
<td>16.2 – 24.6</td>
<td>15.8 – 24.3</td>
<td>10.1 – 18.6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other prioritised health care interventions</th>
<th>Routine vaccination of children</th>
<th>HIV/AIDS management per year</th>
<th>Full course TB treatment in DOTS programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost (USD)</td>
<td>13-28</td>
<td>1086</td>
<td>186</td>
</tr>
</tbody>
</table>
IV. Low cost mesh in groin hernia repair - A double-blinded, randomised trial

Three hundred and two patients were included, randomised and operated in this trial. Three patients were excluded from further data analysis as they had been erroneously included and did not meet the inclusion criteria.

After two weeks, 291 (97.3%) of the patients were seen for the follow up interview and physical examination. One severe adverse event in form of a postoperative death occurred in the intervention group. It was investigated in detail and, according to the family and a clinic where he went for medical attention, all available information suggests that he died from a pre-existing condition unrelated to the operation.

At the one-year follow up, another four patients were excluded from data analysis as they had died due to other conditions. The follow up rate after one year was 95.2% (n=281).

One recurrence (0.7%) was identified in the intervention group. The most common postoperative complications were haematoma or swelling in the groin or scrotum (n=70, 24.1%, p=1), impaired wound healing (n=13, 4.5%, p=0.291) and superficial infection (n=10, 3.4%, p=0.377).

As shown in Table 6, there were no statistically significant differences between the intervention and the control groups in terms of either primary or secondary outcomes.

Picture 4. Preparation of the low-cost mesh.
Table 6. Outcomes two weeks and one year after surgery

<table>
<thead>
<tr>
<th>Intervention group, n (%) or mean (SD)</th>
<th>Control group, n (%) or mean (SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Two weeks after surgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>143</td>
<td>148</td>
</tr>
<tr>
<td>Patients with any postoperative complication*</td>
<td>44 (30.8)</td>
<td>44 (29.7)</td>
</tr>
<tr>
<td><strong>One year after surgery</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>140</td>
<td>141</td>
</tr>
<tr>
<td>Recurrence*</td>
<td>1 (0.7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Groin symptoms and pain</strong> **</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less groin symptoms compared to before the surgery</td>
<td>138 (98.6)</td>
<td>139 (99.3)</td>
</tr>
<tr>
<td>Maximum pain in the operated groin during the past week according to IPQ (1-7)</td>
<td>1.3 (0.7)</td>
<td>1.3 (0.7)</td>
</tr>
<tr>
<td><strong>Self stated health</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increment of self stated health (0-100) compared to before the surgery</td>
<td>25.1 (21.7)</td>
<td>26.8 (21.3)</td>
</tr>
<tr>
<td><strong>Patient satisfaction</strong> **</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Satisfied with the result of the operation</td>
<td>137 (97.9)</td>
<td>138 (98.6)</td>
</tr>
</tbody>
</table>

* Primary outcomes
** One response missing in the control group
V. Cost effectiveness of groin hernia surgery using a low cost versus a commercial mesh

The follow up rates of the study participants was the same as for Paper IV. The DALYs averted per surgery were 2.9 in the intervention group and 3.0 in the commercial mesh group (p=0.87). QALYs gained were 6.8 in the intervention group and 5.2 in the commercial mesh group (p=0.065). The total costs per surgery were 49.9 and 174.1 USD respectively in the intervention and the commercial mesh group. As seen in the sensitivity analysis presented in Table 7 below, costs largely depended on the geographical location of the hospital, productivity and duration of hospital stay. Also overseas participants, when fully costed, drove the total cost of surgery.

Table 7. Cost per DALY averted and QALY gained in USD

<table>
<thead>
<tr>
<th>Sensitivity analysis</th>
<th>Additional cost per surgery</th>
<th>Low-cost mesh</th>
<th>Commercial mesh</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DALY averted</td>
<td>QALY gained</td>
<td>DALY averted</td>
</tr>
<tr>
<td>Baseline</td>
<td>-</td>
<td>16.8</td>
<td>7.3</td>
</tr>
<tr>
<td>Sensitivity analysis</td>
<td>16.1</td>
<td>22.3</td>
<td>9.6</td>
</tr>
<tr>
<td>Tripled salary for directly involved local staff</td>
<td>208.5</td>
<td>87.7</td>
<td>38.0</td>
</tr>
<tr>
<td>Including all costs* for international team</td>
<td>269.5</td>
<td>108.5</td>
<td>46.9</td>
</tr>
<tr>
<td>Capital costs of buildings as in Kampala</td>
<td>17.0</td>
<td>22.6</td>
<td>9.8</td>
</tr>
<tr>
<td>Halved productivity</td>
<td>44.9</td>
<td>32.1</td>
<td>13.9</td>
</tr>
</tbody>
</table>

*Includes salaries (average salary including social security contribution for consultant in surgery and operation theatre nurse in Sweden), travel costs to Uganda from Sweden, and transportation and upkeep in Uganda
Discussion

Main findings

In the studies making up this thesis we have found that groin hernia is a common condition which is commonly operated in district hospitals in eastern Uganda but that surgical rates are far from meeting the needs for surgery in the study population. The high perioperative mortality rates seen following some surgical procedures indicate that quality improvements are needed. Costs of surgery are comparable to other prioritised health care interventions such as HIV/AIDS and TB treatment.

A mosquito mesh has similar outcomes in terms of recurrence rate, post-operative complications and patient satisfaction as a commercial mesh, but costs and cost-effectiveness favour the mosquito mesh.

Epidemiology of groin hernia

Groin hernia prevalence was investigated through the first population based study on groin hernia in adult males carried out in Africa. Previous estimations in Africa range from 3.15% to 25% and variations may be due to different non population-based methodologies employed (51-53). Factors associated with groin hernia were age and low BMI. This is in line with findings in previous studies (61). Smoking and type of work was not related to having a groin hernia.

The findings from only one study is not enough to determine the burden due to groin hernia on global scale, especially as the burden of disease ideally should include a qualitative measure such as morbidity, in addition to prevalence. For this reason, this study could be repeated in some of the other HDSSes. If the factors associated with groin hernia and a morbidity scale such as the inguinal pain questionnaire were also included, one could thereafter attempt to make population-based estimates of the global burden of disease due to groin hernia. Using the same methodology in several locations would give comparable results.

There are several other surgical conditions whose global burden of disease have not been sufficiently described. The HDSS system has proven to be useful for research on groin hernia and carrying out studies with focus on other surgical conditions should also be considered.
Health systems performance

Surgical capacity

Herniorrhaphy was, like in other settings, the most commonly performed procedure related to general surgery \(^{65, 67, 119}\). However, the annualised hernia repair rate was only around half the average of around 30/100 000 presented in other studies from sub-Saharan Africa and much lower than the rate of over 80/100 000 found in Sierra Leone \(^{45, 120, 121}\). Variability in surgical volumes in different regions and parts of countries may explain the low surgical rate in study 2. A new study is currently investigating the rates of surgery performed on a national level in Uganda.

The herniorrhaphy rates in HIC vary between 130 and 290/100 000 population, depending on, among other things, the indication used for surgery \(^{122, 123}\). If the HIC rates represent a baseline need for hernia surgery primarily catering for incident cases, all of the above rates from sub-Saharan Africa indicate that the quantitative need of surgery is far from met in this part of the world.

It has been estimated that a rate of 420/100 000 over 10 years would be sufficient to cater for incident cases and eliminate prevalent backlog of groin hernia cases in Ghana \(^{51}\). Thereafter, similar rates as seen in HIC, adjusted for the demographic structure in LMIC settings could be expected to suffice here too.

The overall annual rate of major surgery was 225/100 000 population. This is in accordance with previous estimations, but far less than the more than 11 000 surgeries per 100 000 population demonstrated in countries where annual health expenditure exceeds 1000 USD per capita \(^{22}\). As basic epidemiology of many of the conditions operated upon is not known, it is close to impossible to assess to what extent need for surgery is being met. However, if the rates of surgery in the high-expenditure countries is assumed to represent a largely met surgical need in such countries, the unmet need for surgery in the study setting must be considerable as the highest burden of surgical disease is seen in Africa \(^{8}\).

Caesarean deliveries and hernia repair have been suggested as proxy indicators for the total volumes of surgery performed \(^{67, 124}\). Perhaps the met and unmet need for groin hernia surgery could be used as a proxy indicator for met and unmet need for surgery in general. Such a proxy indicator could assist in health care planning. In order to do so, one must identify the associated and risk factors for surgical conditions that drive the need for surgical interventions.
Despite the vast unmet need for groin hernia surgery, a paradoxical under-utilisation of the surgical services in the hospitals was demonstrated in Paper III. Especially in the mission hospital, the overall rate of surgery indicates low productivity in the operation theatre. Theoretically, this could indicate that the need for surgery is met but that is not a plausible explanation.

Instead, the low productivity points to that there are other barriers than hospital capacity that hinders patients from accessing surgical care. Two important examples that keep patients from seeking surgical care are lack of money and fear of surgery (125). Availability of services will not necessarily lead to increased productivity if these and other barriers are very large. This leads us to the importance of surgical safety and health economy, resource allocation and health care financing in general. This is discussed below.

In addition to capacity and barriers to care, budget restrictions play a role for productivity levels. As described in Paper III, it is clear that the two hospitals will be unable to reach a productivity level under current circumstances where all hernia patients and those with other surgical conditions can have their surgical needs met. Drastic scaling up of services, both in terms of capacity and productivity, is needed. In Iganga General Hospital, two major operation theatres are currently under construction. This is a step in the right direction but also needs to be accompanied by human resource if productivity is going to increase.

**Human resource**

The specialist workforce within surgery, anaesthesiology and gynaecology/obstetrics (SAO) is unevenly distributed in the world and in several African countries, they are less than 1 per 100 000 population. This stands in stark contrast to the over 50 per 100 000 population in HIC (126). The Lancet Commission of Global Surgery recommends a level of 20 SAO providers per 100 000 population (21). This corresponds to an additional number of 1.27 million SAO providers worldwide (127).

Task shifting and task sharing are two concepts where surgical procedures are carried out by non-specialist SAO providers. Task shifting occurs when non-specialists perform these procedures independently and task sharing when specialists are available to assist and give guidance when needed. This is already common practice in our study setting. Major surgical procedures are mainly carried out by non-specialist SAO physicians and minor surgical procedures are carried out by clinical officers and nurses. Very few procedures were carried out by specialist surgeons and gynaecologists/obstetricians. Anaesthesia was always provided by anaesthetic officers. In the study setting, almost no procedures would have
been carried out if the non-specialist SAO providers had not been there. It may be possible to take this one step further and introducing non-phycisians into performing major surgeries too. This has proven to be a safe and cost-effective solution in obstetric surgery in Mozambique (28).

An estimated additional 143 million surgical procedures need to be undertaken every year in the world (21). To achieve this goal, both more specialist and non-specialist SAO providers will be needed. Who should be delivering which services has to be decided upon and may vary between countries. This will form the basis in the resulting need for increasing training opportunities.

Service delivery and training are related to costs. In Paper III and V it is clear that costs of staff directly involved in the surgical procedures contribute very little to the total cost of the service. Even tripled salaries of local staff represents a small additional cost in relation to the costs of the international participants.

A goal of cost-effectiveness analysis is to provide evidence on how resources are best utilised. When resources are extremely scarce, as in our study setting, deciding who should do what becomes even more important. International teams will continue to play a role in service delivery in resource scarce settings but these initiatives could be regulated in a way that best benefits the host country. Training the additional over one million SAO providers and also the non-specialist SAO providers needed will require large resources and capacity (127). Transfer of skills and knowledge within such a framework could be a focus of international teams. International collaboration for research is another area that should be prioritised (21, 39, 114).

In routine clinical practice, local staff should be the key providers. Only this way, sustainable service delivery over time can be achieved. Limited financial resources have been highlighted as barriers for the training, motivation and retention of surgeons in Uganda (128). Different options for remuneration linked to surgical provision and quality of care could be looked into.

**Perioperative mortality**

Perioperative mortality rate (POMR) is a metric which indicates both level of quality and accessibility of surgical services (98). It has been suggested as a key indicator for surgical and anaesthesia safety (21). Perioperative mortality has decreased steadily during the past half century but the decline has been faster in countries with a high Human Development Index (HDI) than in those with a low HDI (129). Capacity to perform safe surgery and facilities
where surgeries are undertaken are less than satisfactory in many LMIC (130).

Paper II shows that perioperative mortality rates (POMR) were significant. Two high-risk surgical procedures were identified. The first was exploratory laparotomy which resulted in postoperative death in 13.3%. Surgical conditions also cause significant mortality in other low resource settings and POMR following surgery for acute abdomen in Ghana and Sierra Leone was 9.9% and 10% respectively (131-133). In fact, mortality following explorative laparotomy is equally high in HIC even though the patients and their conditions may not be directly comparable. The patients in studies carried out in HIC are older and have more co-morbidities than those in our study setting (134-136). Therefore, the POMR in LMIC could possibly turn out to be lower than in HIC if sufficient efforts and resources were allocated to this group of high-risk surgical interventions.

The second high-risk procedure, caesarean delivery, with its 0.8% was much lower than that following exploratory laparotomy. In addition to that, over 11% of the babies delivered were either stillborn or died before discharge from the hospital. Both these rates are unacceptably high. The four women who died did so due to haemorrhage or sepsis. We cannot know if their lives could have been saved but improved perioperative monitoring, actions taken and adequate blood transfusions would probably have increased the chances of survival. The cause of death among the newborns was not established, but earlier research has shown that neonatal death is closely linked to maternal death and that risk factors for death and morbidity for mother and neonate overlap (137, 138).

The reduction of maternal death is expressed in MDG4 whereas the reduction of under five mortality, including neonatal death is part of MDG5. Surgery is one of the important interventions to reduce both maternal and neonatal death and morbidity. Of an estimated 56.6 million DALYs lost due to maternal haemorrhage, obstructed labour, obstetric fistula, abortion and neonatal encephalopathy, 37% are avertable with quality obstetric surgery in LMIC (139). Efforts should be invested to materialize these large potential health gains.

There are several ways to improve quality of health care delivery within the surgical framework. Not all are costly. Examples of low-cost and effective interventions are the use of pulse-oximetry, implementation of surgical checklists and treatment protocols (140, 141). Audit of deaths and severe complications would help pinpoint the exact areas of the surgical care that should be prioritised. The Lancet Commission of Global Surgery has identified ten needs for the provision of safe surgical and anaesthesia care
Meeting these needs should be an important step towards reducing the POMR.

As mentioned above, high mortality rates following surgery may impact health seeking behaviour negatively as a barrier to surgical care is fear of surgery (125). For this reason, reducing the POMR has two important purposes that both have potential to save lives.

**Surgical timing – elective versus emergency surgery**

Closely related to surgical outcome and perioperative mortality is timely management (21, 135). This involves undertaking emergency surgeries with minimal delay, planning of elective interventions and in the case of groin hernia, operating congenital hernias during childhood rather than postponing the intervention into adulthood.

In general, elective surgery is safer than emergency surgery. A high proportion of emergency surgery is common in resource scarce settings (73, 142). In Paper II, emergency rates varied depending on the procedure performed, but apart from male circumcision, elective procedures were uncommon.

Emergency surgery due to groin hernia carries a higher risk of mortality than elective surgery in both HIC and LMIC, and mortality rates following emergency hernia repair may be as high as 40% in some settings (73, 133, 143, 144). In Paper II, hernias were operated on as emergencies in 44% of the cases which is many times more than in HIC (48, 144).

There may be several reasons why surgery is so often carried out as emergencies. Part of the explanation could be the aforementioned barriers of seeking surgical attention, which is in line with the so called “Three Delays’ Framework”, defined by the Lancet Commission of Global Surgery (21, 125). For various reasons, patients may wait to seek formal care until the condition is advanced. This is the first delay. Accessing the right level of care is difficult where infrastructure and transportation is limited. This, the second delay, will contribute to the condition deteriorating even further. Once at the hospital, staff, materials and facilities may not be readily available for the treatment of the patient who may by now be in a grave condition needing an emergency intervention. This is the third delay. Considering the limitations of the facilities and human resource at hand in many LMIC, the capacity to care for unstable or very sick patients is inadequate and the risk of adverse outcome must be substantial (145-148).
If patients would appear at the facilities earlier, their interventions could be planned for. Groin hernia is a condition where elective intervention can be undertaken in most cases. It is suitable for day case surgery under local anaesthesia, which carries minimal risk for adverse outcome, as seen in Paper IV. In HIC watchful waiting in minimally symptomatic groin hernia patients is safe in healthy individuals as the risk of incarceration is low but still the majority of these patients end up having surgery within 7 years (149, 150). Even with a low risk of obstruction of groin hernia, external herniae are a leading cause of intestinal obstruction, for which surgery carries a considerable mortality in low resource settings (149-152).

The time frame between onset of incarceration and surgical attention in a hospital should be no longer than 12 hours, as the risk of needing a bowel resection increases after that time (153). Bowel resection in conjunction with hernia incarceration increases the risk for mortality 20-fold (144). Due to the three delays discussed above, few patients would receive surgical attention within 12 hours in our study setting and the risk of death would be high (142, 154).

Delayed presentation can also result in large hernias which may be more difficult to repair than smaller ones (155). Therefore, watchful waiting may not be either safe or practical in low resource settings and the best option is probably to plan for elective surgery as the diagnosis of groin hernia is made unless there are no apparent contraindications.

In Paper IV, day case surgery was shown to be safe and well tolerated by the generally healthy study participants. Similar to the recommendations in the European Hernia Guidelines, day case surgery could also be considered for all patients operated on electively in the study setting (63, 156). However, as accessibility to health care is often more limited in LMIC than in HIC, the importance of undertaking a clinical examination and to thoroughly consider the risk of possible severe complications before discharge must be stressed. Oral and written patient information for the post-operative period, including how, when and whom to contact if complications occur could further increase the safety of this practice.

Unfortunately, many other surgical and obstetric conditions and complications cannot be predicted. In these cases, other measures need to be taken to reduce delays to a minimum and to increase quality of care, thus reducing the risk of death and disability.
Gender perspectives in surgery

Major surgical procedures were most commonly performed on women as the most common interventions were due to conditions that are sex specific. In countries where fertility rates are high, it is possible that the need for surgical interventions is higher among women than among men. If that is the case, then the underfunding and under prioritisation of surgical services may in fact be a gender issue which affects women more negatively than men.

When looking at groin hernia surgery specifically, a surprisingly large proportion (24%) of the patients undergoing herniorrhaphy were women. This number is two to four times the rates reported in both HIC and LMIC (48, 142). It can be a result of a higher than expected prevalence among women in the study setting, but it can also be a result of gender differences in health seeking behaviour. The finding warrants further investigation as the burden of disease due to groin hernia among women is not yet known. A study to investigate groin hernia prevalence and associated factors in both women and children is planned.

Another important gender aspect of groin hernia is the fact that women are more likely than men to have femoral hernias. Femoral hernias have narrower necks, are more prone to incarceration and are more often operated on as emergencies (46). For this reason, mortality due to groin hernia is higher among women than among men (144).

As it may be hard to distinguish between an inguinal and a femoral hernia before surgery without access to imaging, it is important that femoral hernia is ruled out in female patients undergoing groin hernia surgery (63, 157). This is an effective way to avoid an "immediate recurrence", or a missed femoral hernia. As women have more femoral hernias than men, the surgical approach needs to be adjusted accordingly. In HIC laparoscopic repair is recommended in women (63, 158). Laparoscopic approach will be possible in LMIC with time but these are more expensive and are therefore not affordable in routine clinical practice today. Investigating which open surgical method that is effective, safe and affordable in women in LMIC settings is important.
Picture 5. Gender perspectives in groin hernia surgery. The rumour of an ongoing hernia surgery camp spreads quickly in the community. Women and children also need these services.
Surgical methodology

*Anterior mesh repair of groin hernia with mosquito mesh under*

In Paper IV, no significant differences in outcomes between the two study arms could be identified. Thus, the promising outcomes in previous studies have been corroborated (77, 78, 159). However, the following reservations must be stressed:

- A specific 100% polyethylene mosquito mesh produced by Amsa plastics India® was used in the trial. The study does not indicate that any mosquito mesh available on any market in LMIC is effective or safe to use in groin hernia surgery.

- The mosquito mesh was prepared and handled in a strict fashion. Absolute requirements for using this mesh in groin hernia surgery are an autoclave which controls the temperature reliably and staff who know how to use the machine and handle the mesh appropriately.

- The surgeries were carried out by qualified surgeons with thorough experience performing mesh repair of groin hernias. The study supports that when surgery is performed by qualified surgeons, the mosquito mesh repair could be recommended. Further research will need to evaluate the feasibility of non-surgeons using mosquito mesh in hernia repair.

- The surgeries were undertaken on adult males. The study does not support the use of (mosquito) mesh in children or that the Lichtenstein repair is the best method in groin hernia surgery in women as neither of these groups were part of the study population. Further research will need to explore this.

- Clinical follow up of one year is insufficient to predict long term outcomes. Therefore, follow up of included patients at a later stage is planned.

- Finally, the trial has also shown that high follow up rates after surgery for a surgical condition up to one year are achievable in this low-resource setting. This should be seen as an encouragement to carry out other relevant studies and trials with clinical follow up in the study setting.

Introducing the mesh technique in groin hernia surgery in Uganda and beyond should be a priority so that the millions of patients in low resource settings who cannot afford mesh repair with a commercial mesh can benefit from the same improved outcomes as patients in HIC (63, 72, 160).
Introducing the mesh technique will require thorough planning, monitoring and evaluation. Implanting a foreign material poses high demands on sterility and correct handling of the mesh in particular. Such a focus is likely to also improve sterility practices and for other surgeries.

**Local anaesthesia**

All patients were operated under local anaesthesia. It requires less monitoring than general and regional anaesthesia. In HIC, local anaesthesia is associated with reduced time spent in the operation theatre as well as the time to discharge from the hospital. It reduces post operative pain and the rate of post-operative micturition complications (82). Local anaesthesia is more cost-effective than regional and general anaesthesia in a high resource setting (83).

Reduced hospital stay is also cost saving in LMIC. As perioperative care and since facilities and health care infrastructure have severe shortages in LMIC, the use of local anaesthesia is probably safer than both general and regional anaesthesia in the study setting (147, 148).

Local anaesthesia in groin hernia repair in LMIC was recommended already in 1977 but according to previous studies, is not yet commonly practiced in sub-Saharan Africa (73, 161, 162). This indicates difficulties in putting research into practice and will have to be considered when designing an implementation strategy. However, preliminary results from an ongoing study in Uganda indicates that the use of local anaesthesia is much higher than in for instance Sweden where it is also recommended as first hand choice in elective hernia repair (unpublished data, 63, 84).

**Health economics**

**Costs and cost-effectiveness of surgery**

Paper III demonstrates that the most commonly performed major surgeries can be performed at a cost of less than 100 USD. Thus, costs of these major surgeries are less than for both management of HIV/AIDS and treatment of TB (163, 164). Costs of minor surgeries can be compared to costs of providing routine vaccination in children (165). In line with previous studies, costs of surgery compares favourably with other prioritized health care interventions in the study setting (79).

The cost of herniorrhaphy in routine clinical practice was 59 – 66 USD (Paper III). The cost per hernia repair in Paper V was 49 USD using the mosquito mesh and 174 USD using the commercial mesh. This difference was due to the different costs of the meshes. The difference between the
costs presented in Paper III, representing routine clinical practice, and Paper IV representing a study setting was mainly due to differences in duration of hospital stay and productivity.

In Paper III, the average duration of hospital stay following groin hernia surgery was 5.5 days and in Paper V it was 1 day. The associated cost saving was almost 50%. This a major gain of operating patients electively instead of as emergencies, when possible. Even though we did not investigate costs from the patients' perspective, a shortened duration of hospital stay is very likely to be financially preferable also for the patients and their families. Future studies could look into the possibility of reducing the duration of stay following other interventions too.

Capital and overhead costs were calculated so that a cost per day for the surgical services was generated. This cost was in turn divided by the total number of procedures per day. Therefore, the capital and overhead costs are negatively associated with productivity. If the productivity increases, the capital and overhead cost per surgery decrease. If productivity is maximised, the cost per surgery is minimised.

In Study 3, maximum productivity was in fact surpassed but it is unlikely that such productivity can be maintained in routine clinical practice. It leaves little flexibility to cater for unexpected events and emergencies and the staff available may not cope with such a work load. Also, the limited perioperative care during night, due to few staff on duty in crowded wards and sometimes with power cuts, is of concern when performing major surgeries late in the day. Patients needing much monitoring are best worked on in the morning but also patients who are planned for day case surgery should be operated on early in the day so that they can go home after a few hours observation. Patients cannot be sent home late in the afternoon as they ideally should return home before looked into.

Groin hernia repair using both mosquito mesh and commercial mesh were very cost effective using the threshold value set by the WHO (92). Irrespective of the alterations to costs made in the sensitivity analysis, groin hernia surgery remained very cost effective. As noted in the introduction however, it may not be possible to introduce all very cost effective interventions in a health care system. The resources available are fixed and these resources have to be distributed responsibly and due to different priorities. The cost-effectiveness of groin hernia repair under local anaesthesia as day case surgery compares favourably with interventions towards diarrheal diseases, HIV/AIDS and TB as well as management of childhood illnesses (165).
In addition to the use for cost-effectiveness analysis in resource allocation, absolute costs and possible cost savings are also important when resources are scant. The out-of-pocket expenditure for health care in low income countries, lower and upper middle income countries is 46.5%, 54.7% and 32.1% respectively and there is a significant risk of iatrogenic poverty (166, 167). Over 3 billion people are at risk of financial catastrophe should they need surgery and each year 81 million people face catastrophic health expenditure due to accessing surgical services (168). When patients carry a large proportion of the burden of the cost of health care there will be less scope to expand services that are relatively costly. Therefore, there is little room for patients to afford cost increments such as the cost of purchasing commercial mesh. However, Papers IV and V show that elective repair of groin hernia under local anaesthesia, as day case surgery, using a mosquito mesh can be performed at no additional cost compared to the routine clinical practice of today.

In order to provide high quality surgical services, training of health care providers is key. Training, monitoring and evaluation is resource demanding but is a duty within any health care system. In the particular case of groin hernia surgery with mesh, it has potential of being sustainable as it is not associated with any cost increment compared to the current practice.
Strengths and weaknesses of the thesis

Methodological considerations, internal, external validity and generalisability

Study 1. Prevalence of groin hernia was investigated in one out of several HDSSs. The location of the I/M HDSS was not chosen to be representative of either Uganda nor sub-Saharan Africa. However, this was the first population-based study on groin hernia prevalence carried out in a LMIC. Therefore, the results from this study is probably more generalizable than earlier studies that have estimated groin hernia prevalence using other methods. In order to more accurately define the prevalence on a global scale, the study could be repeated in one or more of the other HDSSs.

Study 2. Two hospitals in two districts in rural Uganda were investigated. The limited time period of data collection means that possible seasonal variations in surgical work load could not be detected. As all surgical interventions were recorded prospectively in both operation theatres and wards and as they were cross checked with hospital registries, internal validity for the time period of the study is high.

Surgical output will depend on both facilities and interest and skills of the staff available in a hospital. In higher level facilities, where specialist surgeons and obstetricians are more common, more specialised care is likely to be provided. However, several studies from district hospitals in sub-Saharan Africa have documented that caesarean delivery is the most commonly performed surgical procedure and that the most commonly performed general surgical operation is herniorrhaphy. If this distribution is a reflection on the relative need for different kinds of surgeries in the population, it is probable that a similar pattern would also be found in other hospitals in the region. As several studies report similar findings from hospitals of similar level, external validity is deemed to be reasonably good. To generalize for all of sub-Saharan Africa though, a multi-centre study using the same definitions and methodology for data collection would be necessary.

Study 3. The study had a superiority design with 80% power and 5% significance level to detect a difference of 5% between the two study arms. A 5% difference was regarded as the maximum tolerable difference from a clinical perspective. The study has not shown any significant differences but it does not suggest non-inferiority or equality as this was not the study design. A non-inferiority or an equality design would have been ideal from a statistical point of view but it requires a much larger sample size and was...
therefore not practical with the limited resources in terms of time and money at hand.

The study had strict inclusion criteria and the patients included were therefore a rather homogenous group of middle-aged, generally healthy adult males with unilateral, reducible groin hernia. All were managed in the same way apart from the meshes used. Follow up rates were high which reduces the risk for selection bias. Internal validity is therefore high. The strict selection of study participants has implications for the external validity. For instance, the study does not show that anterior mesh repair as case surgery under local anaesthesia is suitable in emergencies in the study setting.

Costs and cost-effectiveness depend much on a hospital’s total expenditure, location and productivity. Salary levels would have to increase by several hundred per cent in order to make a large difference to costs and cost-effectiveness of surgery. As stated in the section on health economics in the introduction, all cost-effectiveness analyses build on several assumptions. The assumptions and methods used for calculating costs used in Study 3 were adapted to best fit the study setting and the circumstances under which the study was conducted. The robustness of the assumptions and the results were tested through the sensitivity analysis.
Conclusions and future perspectives

This thesis has documented that:

• Groin hernia is a common condition among adult males in eastern Uganda. Its treatment can be performed at low cost and with very high cost-effectiveness but the need for surgery is far from met in the population studied;

• Women do most often undergo major surgery and many groin hernia patients are women in the study setting. Groin hernia prevalence among Ugandan women may be higher than in HIC;

• The majority of the surgical procedures are carried out as emergencies in the hospitals studied;

• High-risk interventions in the study hospitals are exploratory laparotomy and caesarean delivery. Most deaths were a result of sepsis or haemorrhage;

• The mosquito mesh used in Study 3 is an effective, safe and more cost-effective alternative to commercial mesh in the study setting;

• Local anaesthesia and day case surgery for elective groin hernia surgery in men is recommendable also in this low-income setting;

• The HDSS structure is useful for research on surgical conditions and interventions;

• It is possible to conduct population based studies, prospective facility based studies and double blinded, randomized, controlled trials with high follow up rates in this low-income setting.

These findings are important as they fill knowledge gaps about groin hernia and its treatment. In addition to this, the findings highlight some important aspects within the broader field of global surgery. The new knowledge will be disseminated and future studies and implementation strategies will build on these findings. During the research process, new knowledge gaps have been identified and these will be dealt with by carrying out further research.
Research is a core activity towards improving health and health care. The process can be described as a wheel where one moves from an identified knowledge gap, an idea or invention, through a research process that results in conclusions. Some conclusions will lead to new ideas and identify further knowledge gaps. Other conclusions can be disseminated and used as background for policy making and implementation.

Prior to implementation, governments, surgical societies, international organizations and funders need to be involved. Building partnerships and collaborations is key for the success of any implementation plan. One must also have goals in mind or progress will be hard to evaluate. The present state of the hernia surgery studies, the planned way forward and the goals are illustrated in Figure 6 and further described below.

**Figure 6. Present state and the way forward for the hernia surgery studies**
The way forward

Further research

Several proposed research agendas within the field of global surgery already exist. These are all highly relevant and should serve as important sources of inspiration for researchers worldwide. Below is a list of some topics that the research team has identified as important and are planning to investigate further.

We are currently planning to:

- Investigate the prevalence of groin hernia among children and women;
- Identify best surgical technique for groin hernia repair in women in resource scarce settings;
- Carry out longer term follow up of the participants in Study 3 as one year follow up is too short to evaluate long term results of groin hernia repair;
- Investigate health seeking behaviour and barriers to surgery in our study setting;
- Identify areas of improvement and cost-effective interventions to reduce the perioperative mortality rates following surgery;
- Investigate the option of using the met and unmet groin hernia repair as a proxy indicator for met and unmet need for surgery in general;
- Carry out an implementation study of low-cost mesh in groin hernia repair in routine clinical practice.

Information dissemination

Information dissemination is one of the duties of researchers. In addition to disseminating the results through conventional channels as publications, the research team has been active in attending and presenting findings at scientific conferences and meetings. These have included national and international meetings on surgery, global surgery and health economics. Further on, findings have been presented at hospitals and through media in Uganda.

These activities will continue and a special focus will lie on disseminating information in parts of the world where the research findings are most relevant and have potential to make a difference to health care practitioners and patients.
**Partnership and collaboration**

The core research team of Ugandan and Swedish participants who have carried out the studies making up this thesis have intentions of continuing the work together. One study is presently ongoing in Uganda and several others are planned, according to the above list. As the research scope expands, so does the number of participants.

Apart from planning new studies, there are also plans for implementation of research findings. For such activities, other types of partnerships are needed. We have made contact with key individuals at the ministry of health in Uganda, with the Ugandan Society of Surgeons as well as with the College of Surgeons of Eastern, Central and Southern Africa which is a large surgical association in sub-Saharan Africa. As soon as the last two studies are published, the work of strengthening these partnerships will move into a more active phase.

During the research process, the connection to the local community and their leaders has been central to the success of the individual studies. Any further activities will seek the continuous trust and collaboration on grass root level in the communities where research and implementation will take place.

**Implementation and policy making**

Making research findings useful for health care professionals and patients is a core goal of the research team. Implementation strategies and policy making is the next step following the dissemination of the results. It will be conducted through the above mentioned collaborations.

Some findings need to be translated into a practical format, such as clinical guidelines for the treatment of groin hernia. Other findings, can be used directly for implementation. This mainly concerns the use of low-cost mesh in groin hernia repair in men. An implementation study is in planning phase and the results from that study will give further guidance on how larger scale implementation and monitoring can be carried out at a later stage.

These are two activities that the research team can participate in and can add value to. Other activities are beyond the scope of individual researchers and will be the responsibility of governments, international organisations and surgical societies as well as donors. Their duty is to allocate resources to where they are most needed so that the effect in terms of health gain can be maximised. Groin hernia is one of many surgical conditions and should exist in an overall framework of improving surgical service delivery in large.
Key activities that need to take place with little delay are:

- Increased allocation of resources to improve capacity for surgical services;
- Training and retention of human resource to match the need for surgical services;
- Making surgical specialities appealing to health care professionals so that more staff can be recruited to this part of the health care system;
- Regulate the role of international teams so that their skills and knowledge can be passed on to clinicians according to where it is needed. The goal should be to develop a self sustainable system with national health care providers;
- Continuous quality control of surgical services;
- Introduce into routine clinical practice known low-cost interventions to improve the quality of surgical services;
- Provide a functional procurement system for equipment, medicines and low-cost mesh;
- Find a solution to minimise the risk of catastrophic health care expenditure and iatrogenous poverty among patients due to accessing surgical services

The goals

With the above stated planned research and implementation activities, the goals of the research team are to:

- Define the total burden of disease due to groin hernia and show how it can predict the total burden of surgical disease;
- Motivate and provide evidence on how and at what costs increased overall rates and quality of surgical procedures can be achieved;
- Show how quality of care in groin hernia surgery can be improved by introducing the low-cost mesh in routine clinical practice and to participate in its wide spread implementation;
- Customise care with the best possible hernia repair method for different patients;
- Finding solutions to how a shift from emergency to elective interventions can be achieved and how risks associated with surgical services can be reduced.
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72


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