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The Cost Of Saving A Child's Life: A Cost-Effectiveness Analysis Of A Pediatric Operating Room In Uganda

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– By –

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Abstract

THE COST OF SAVING A CHILD'S LIFE: A COST-EFFECTIVENESS ANALYSIS OF A PEDIATRIC OPERATING ROOM IN UGANDA. Ava C. L. Yap, Doruk E. Ozgediz, and Reza Yaesoubi (Sponsored by John Geibel). Department of Surgery, Yale University, School of Medicine, New Haven, CT.

This study examines the cost-effectiveness of constructing a dedicated pediatric operating room (OR) in Uganda, a country where access to surgical care is limited to 4 pediatric surgeons serving a population of over 20 million children under 15 years of age.

A decision tree model projected the cost and disability-adjusted life-years (DALY) averted by a Ugandan pediatric OR. OR cost data were collected by obtaining equipment price lists, anesthetic and operative reports, government salary scales. A patient family survey was administered over 6 months to collect out-of-pocket (OOP) costs. The OR case-log, pediatric surgical ward database and literature review informed patients' outcomes. A Monte Carlo simulation modelled the incremental cost-effectiveness ratio (ICER) of a pediatric OR. One-way and probabilistic sensitivity analysis was performed to assess parameter uncertainty. Net monetary benefit was calculated using the value of a statistical life approach.

Our model of a dedicated pediatric OR averted a total of 3004 DALYs in a year (95% uncertainty interval or UI 2,928 -3,080) and costed $240,526 (95% UI 236,264-244,789) to install and maintain for a year. The pediatric operating room had an ICER of $80.06 per DALY averted (95% UI 77.77-80.82), or $4,987.87 (95% UI 4,845.08-5,035.08) per life saved based on the country's average life expectancy in 2015. These values were well within the WHO guidelines of the cost-effectiveness threshold. The net economic benefit was $2,392,338 in a year, or $6,428 per patient. The model remained robust with one-way and probabilistic sensitivity analyses.

These findings support the construction and maintenance of a pediatric operating room in Uganda as a cost-effective, worthwhile investment, endorsing future decisions to enhance pediatric surgical capacity in the resource-limited settings of Sub-Saharan Africa.

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Introduction

Guided by the post-2015 Sustainable Development Goals (SDGs) issued by the UN, surgically treatable disease recently emerged into the global health spotlight.[1] The SDGs' vision to enhance access to essential healthcare services worldwide came with the responsibility to acknowledge surgery as "an indivisible, indispensable part of health care", as concluded by the recent Lancet Commission dedicated to global surgery.[2] Currently, approximately 5 billion people, or an astonishing two-thirds of the world do not have proper access to surgical and anesthesia services.[3] An estimated 32.9% of all lives lost in 2010 worldwide were due to surgically treatable disease, which was more than deaths caused by AIDS, tuberculosis, and malaria combined.[4] As a comparison, neglected tropical diseases account for 1.3% of the global burden of disease.[5] To face the growing need for surgical access, the Lancet Commission urges for global expansion of essential surgeries by 2030, while simultaneously calling for reliable metrics on the quality of surgical interventions to assess existing or potential service preparedness, delivery, and impact.[3]

Low-middle income countries (LMIC) shoulder a disproportionate burden of surgical disease, where 9 out of 10 individuals are unable to reach proper surgical services.[3] The surgeon-to-population ratio in LMICs ranges from 0.13-1.57 per 100,000, compared to 9 general surgeons per 100,000 in the United States.[6-8] The 2010 Global Burden of Disease study revealed that the onus of surgically correctable conditions is also growing[9], with traumatic injuries being the biggest offender, followed by obstetric conditions, malignancy, congenital anomalies and perinatal complications.[10] Yet there is still an enormous lag in a global effort to amass human resources to improve surgical access. Major challenges of surgical equity expansion include lack of established tools to measure the surgical burden of disease and the extent that interventions can alleviate this burden, as well as a scarcity of sustainable infrastructure to meet the surgical needs in these countries.[11]

The "appalling myth" that surgery is a complex, expensive luxury unworthy of public health investment is largely unfounded, but this prohibitive perception stalls efforts to improve surgical access worldwide.[12] The Lancet Commission on Surgery suggests that local surgical capacity expansion is affordable and could provide an reasonable return to the community in terms of health and productivity, citing a $10 gained for every $1 spent.[13] Just as building surgical capacity can promote economic growth, patients suffering from surgically correctable conditions can lead to huge costs of productivity loss to society. In 2010, surgical conditions were responsible for $4.0 trillion in total welfare costs spent on disability care on surgically treatable diseases in LMICs.[3] The Lancet Commission also warned that the detrimental economic effects would compound if no action was taken, reaching a 2% loss in annual GDP in LMICs by 2030 if surgical disease is not addressed sufficiently.[3]

Cost-effectiveness analysis (CEA) is an economic tool that was recently popularized by the Disease Control Priorities[14] and adopted by the global surgical community as a systematic way to inform the allocation of scarce resources towards surgical platform interventions.[15] By using standardized, universal metrics, CEA can assess the value of otherwise disparate interventions, allowing for the comparison of surgical and non-surgical treatment of different diseases. Past CEAs have suggested that surgery is a worthy public health investment that returns substantial health benefit. A systematic review of 26 CEA studies showed that many essential surgeries were cost-effective in resource-limiting settings, with cost-effectiveness ratios (CER) similar to that of vaccinations or malaria bed nets.[16] For example, the median CER for cleft lip or palate repair ($47.74 per DALY) was comparable to the BCG vaccine CER ($51.86-220.39 per DALY).[16] Surgeries offered by first-level hospitals are especially affordable, with costs ranging from US$10-220 per DALY averted for surgeries across numerous LMICs.[17-19] Recently, a surgical unit at a private hospital in India demonstrated an average of $165/DALY averted in total hospital operational costs with 9401 DALYs averted in a year.[20] In this way, CEA can help guide policy makers to channel limited resources towards the most efficient avenues, or "getting the best bang for the buck". Results from this type of analysis have helped change the landscape of global health to be more cognizant of surgical need. Notably, the latest edition of Disease Control Priority on Essential Surgery now devotes a full section on CEA as a tool to enable healthcare professionals to better evaluate surgical interventions.[14]

As multinational efforts are galvanized to expand essential surgical access, pediatric surgery has been a relatively neglected area. Congenital anomalies such as Hirschsprung's disease, anorectal malformation or bowel obstruction are now considered essential surgeries that should be offered in a fully functional healthcare system.[8] However, pediatric surgery has been named "unborn child" of a neglected disease,[21] and the disparity becomes amplified in countries like Uganda, where 48% of the population is under the age of 15. One study found as many as 85% of pediatric patients in Africa will have a surgically treatable disorder by the age of 15.[22] Uganda faces a huge unmet demand for pediatric surgical care, as there are currently only 4 qualified pediatric surgeons in the whole country to serve a pediatric population of over 20 million.[23] Neonatal surgery at Mulago Hospital in Kampala, the sole provider of neonatal surgical care in Uganda, averted an estimated 5072 DALYs, but could not address a potentially avertable 140,154 DALYs due to insufficient resources.[24] The effective coverage by the current surgical system in Uganda, or the ratio of met need to total need amounted to a mere 3.5%.[24] This drought of healthcare delivery is a result of a severe lack of resources, most remarkably in surgical infrastructure. Demonstrably, no dedicated pediatric operating facilities existed in the country until very recently.

In 2015, the ARCHIE Foundation, a non-governmental organization (NGO), partnered with local healthcare providers to fund the construction of the first dedicated pediatric surgical operating room (OR) in Naguru Hospital in Kampala, Uganda by donating surgical and anesthetic equipment.[25] However, the benefits of such a dedicated pediatric OR remain poorly described. While we know providers and children may benefit from these resources, no study has assessed return on such investment and compare this with competing healthcare needs, especially when expensive down payment is required. There is an urgent need for better metrics to justify the development of surgical interventions in the global setting. This study in particular seeks to quantify the disease burden averted by the Naguru OR to provide a better estimate of the cost and health consequences of furnishing a pediatric OR. Moreover, the study provides performance feedback to the charity, which will in turn be able to make financially sound decisions by directly drawing from our findings for future OR construction projects. The information can also serve to inform potential donor bases.

On a broader scale, we need better metrics to quantify the impact of current surgical intervention in the pediatric population, and only a few studies have utilized CEA for pediatric surgeries. 13.5% of surgeries in a Kenyan refugee camp needed for common congenital conditions were actually performed, and the cost-effectiveness of surgical intervention ranged from $40-88 per DALY averted.[26] Pediatric inguinal hernia repair in Uganda had a CER of $12.41 per DALY averted.[27] Ability to quantify the burden of pediatric surgical disease as well as cost-effectiveness of surgical procedures and facilities can help attract attention of policy makers to improve pediatric surgical interventions. However, studies on the cost-effectiveness of pediatric surgeries in LMIC are still scarce due to sparse data collection, overworked hospital personnel (who are usually spread thin from case overload), and inconsistent methodology.

A unique challenge arises from capturing costs from the patient's perspective. Out-of-pocket (OOP) expenditure are payments made directly by the patient receiving the health service. These personally accrued costs can lead to financial insecurity or even bankruptcy, and the burden usually rests most heavily on the poor, widening the economic inequity. In Kenya, the poorest quintile spent about a third of their household earnings on healthcare, compared to only an 8% in the richest quintile, and almost 1.5 million people are pulled into poverty because of health care payments.[28]

Studies suggest that 150 million people fall into financial catastrophe from healthcare spending each year.[29] Catastrophic healthcare expenditure (CHE) is usually defined by patient healthcare spending of more than 10% of their annual household expenditure,[30] or 40% of annual household expenditure after food expenses.[29] It is a problem that affects developing nations predominantly, with 90% occurring in low-income countries (LICs),[31] and occurs because of 3 main reasons: available healthcare services that require compensation, inadequate payer resources, and lack of health insurance.[32] The WHO states that a strong healthcare system must provide both quality healthcare delivery and financial protection, though policies tend to disregard addressing the latter objective.[33] The directive to provide financial risk protection in health is a now part of the SDGs, with key indicators made a priority by the United Nations.

Several out-of-pocket spending studies have recently been published for non-communicable diseases in Sub-Saharan Africa, where 8.7-20% of patients experience catastrophic expenditure.[34-36] To date, however, there are very few studies looking at the out-of-pocket spending for families of surgical patients in LICs, and even fewer focused on pediatric surgical patients.

A national surgical and anesthetic plan has not yet been developed in Uganda. More knowledge is needed to better understand the impact of and need for surgical care delivery, but the current sociopolitical atmosphere poses substantial challenges to amassing meaningful reform. In this setting, bringing attention to the unmet need of pediatric surgery is paramount, as surgically correctable conditions predominate in the pediatric population, and protecting child health has always been an important SDG even before the post-2015 reconstitution. However, the cost-effectiveness of pediatric surgical operating rooms and procedures in Uganda has yet to be fully characterized. An ideal place to start is the dedicated pediatric operating room at Naguru Hospital, where interpretation of pediatric surgical records has led to a deepened understanding of the met and unmet need. Policy makers such as the Ugandan Ministry of Health would need a reliable metric showing that local expenditure corresponds to favorable and economically efficient outcomes to consider investment in these underprivileged, underfunded areas.

In this context, CEA of a dedicated pediatric OR can a help guide otherwise difficult decisions to channel limited resources towards the most effective avenues. To date, there has been no cost-effectiveness study to quantify the cost proportional to health utility gained from an operating room. This study hopes to determine the cost-effectiveness of furnishing a pediatric OR from multiple cost perspectives.

Statement of Purpose, Hypothesis and Specific Aims

The overarching goal is to establish the cost-effectiveness of surgical interventions of pediatric surgical diseases treated in the Naguru Hospital pediatric operating room in Kampala, Uganda. **Hypothesis**: The construction of a pediatric operating room in Uganda is cost-effective (defined as the cost per DALY averted less than GDP per capita) after 1 year of operation, compared to other currently available healthcare interventions.

SPECIFIC AIMS

1. **Choose a model:** Construct a logical cost-effectiveness model that emulates all the pertinent possible scenarios of the patients undergoing surgical treatment in the pediatric OR.
2. **Develop a Cost Template Including Different Perspectives:**
    a. Charity perspective: Collaborate with ARCHIE Foundation and Medicaid International to obtain the budget sheets on the costs of donated large-scale pediatric surgical and anesthetic equipment.
    b. Patient perspective: Create a survey using previously validated cost questionnaires to capture out-of-pocket costs accrued by patient families, with categories including transportation, food and lodging, purchased pharmaceuticals and diagnostics, and opportunity costs/productivity loss. Pilot and administer questionnaire over a 6-month period to the families of post-operative inpatients staying in the pediatric surgical ward.
    c. Government perspective: Compile a cost list of variable and fixed goods purchased by the Ministry of Health, which include anesthetic drugs and

disposable equipment, and collect cost information from case operative reports, the Naguru Hospital central pharmacy and the Ugandan National Medical Store.

3. **Assess Disease Burden Averted:**
    a. Extract relevant data from the pediatric OR case-log to determine the types and frequency of pediatric surgical diseases that were treated over one year of operation. Organize diseases into 5 categories: congenital emergencies, non-emergent congenital disease, acquired emergencies, acquired electives, and neoplasia.
    b. Ascertain relevant disability weights and probabilities for each disease condition, and calculate the DALYs averted per surgery and total DALYs averted annually to determine the effectiveness of each procedure by using the pediatric operating room registry
4. **Cost-Effectiveness Analysis (CEA):** Calculate the OR incremental cost-effectiveness ratio (ICER) using cumulative DALYs and costs. Mathematically model the ICER to estimate the disease course and outcomes with and without the surgical intervention and compare it to the ICERs of other current healthcare interventions.
5. **Establish Confidence in CEA Model:**
    a. Deterministic method: Create scenario analyses to how sensitive the ICER is to changes in various input variables and plausible situations.
    b. Probabilistic method: Conduct a Monte Carlo simulation using randomized parameters of uncertainty to test the robustness of the model.
6. **Cost-Benefit Analysis:** Use willingness-to-pay threshold to calculate the net monetary benefit.

Methods

Aim 1: The Cost-Effectiveness Model

Attribution: Designed by myself, advised by Dr. Reza Yaesoubi PhD and Dr. Doruk Ozgediz MD.

Decision Model Framework: A decision tree base template was constructed to compare life trajectories that pediatric surgical patients take with or without surgical intervention, mirroring the model suggested by Shrime's CEA template.[15] To emulate realistic patient outcomes, the tree identified the plausible course of natural disease, as well as a range of post-treatment scenarios including immediate death and discharge, as well as long-term disability and successful cure. The incremental deltas between OR costs and disease burden averted by surgical treatment and those of the counterfactual were equivalent to the difference between the two branches at the decision (square) node (Figure 1-2). The annual disease burden averted was the sum of cumulative DALYs averted by procedures performed in the pediatric OR in a year, which were in turn informed by the pediatric surgical OR case-log and ward database. Model parameters included number of patients per year, number of procedures, OR equipment costs, variable costs including government purchased medications and equipment, out-of-pocket expenditure of patient families, and patient outcomes determined by severity of disease (in the form of disability weights) and probability of disease state.

The decision tree provided a suitable framework to compare the life trajectories of pediatric surgical patients with or without surgical intervention for the following reasons:

1) Surgery occurs at a singular time-point, and once postoperative morbidity is considered, the subsequent lifespan and quality of life of the patient remains relatively constant over time and seldom transitions between health states due to the surgical intervention or disease. The immediate nature of surgery is appropriate

for a decision tree model, which assumes that events unfold independent from the passage of time.

2) There is a limited number of possibilities at each branch point, since the patient outcomes for surgical disease tend to be binary, resulting in either a complete cure or residual disease burden. Therefore, the decision tree will have a manageable number of branch points, providing a straightforward visualization of all the main scenarios the patient may experience depending on whether surgery was provided, allowing the viewer to surmise outcomes easily.

3) The pediatric population is at a reduced risk of unaccounted co-morbidities compared to the adult population, because children will not have had the chance to acquire chronic diseases that may otherwise complicate or interrupt the patients' health states and life trajectories.

The decision tree exhibited one decision node: surgery or no surgery, and subsequent chance nodes to model all the possible outcomes of these patients. Each chance node branch harbored cost, disease burden, and event probability, values which were subjected to change based on the surgical disease modeled. The comparison between cumulative costs and outcomes of surgical treatment and that of the counterfactual was determined by calculating the difference between the two branches of the decision node. An archetypal decision tree diagram can be found in Shrime et al 2017's paper as a guiding example.

Setting and Time Horizon: The analysis characterized the cost-effectiveness of a pediatric operating unit in Naguru Hospital, Kampala, Uganda in the first year of service. We built our analysis around a single site because the Naguru OR was the first and only fully functional pediatric OR in the country. Our study scope included the annual number of cases performed in the Naguru OR, which catered to most of the pediatric surgical patients in Mulago

National Referral Hospital, the country's largest tertiary center in the public sector. Notably, the theatre opened for public use on 4/27/2015, and our study period spanned over a year exactly since its inauguration, with the last case included on 4/26/2016. One year was an appropriate study timespan, as the theater had been in service for approximately this long during our retrospective review of cases. Furthermore, wages and long-term investments such as surgical machine and equipment costs were best partitioned annually.

Counterfactual: The counterfactual scenario was defined as the natural course of disease in the absence of the pediatric OR, as prior to OR installation no dedicated pediatric operating facility existed to provide curative treatment for pediatric surgical diseases in this area. The new pediatric OR allowed surgery to proceed for all types of pediatric surgical conditions, especially for non-emergent and/or elective cases that still require treatment to avoid morbidity later in life. Additionally, pediatric surgical disease did not usually allow for non-surgical treatment alternatives, as the disease commonly involved an anatomical defect that requires manual repair, so it was reasonable to assume that the natural course of disease was most likely in the setting of no surgery.

Assumptions incorporated into the decision tree model are as follows:

1) Patients do not successfully seek curative measures besides surgery and therefore follow the natural course of disease, which is largely true in the setting of the Ugandan healthcare system as there are no alternatives to surgical treatment.
2) The counterfactual costs are therefore set to zero, and subsequently the only substantially costly intervention is surgical intervention.
3) The age of presentation is equivalent of the age of operation, as in, there is no delay of care that spans more than a year.
4) Death related to surgical treatment occurs within 1 year of surgery.

5) Permanent cure includes those who have complete post-operative non-surgical treatment where necessary (e.g. adjuvant chemotherapy in Wilms tumor).
6) Post-operative residual disability only has 2 routes - either death (accumulating YLL) or disability (accumulating YLD). Assumptions 4-6 are created to pare down the branch points of the decision tree to binary chance nodes, which streamlines outcome analysis and minimizes the number of unknown or unattainable variables (e.g. the age of premature death).

Aim 2: COSTS

Attribution: Costs collection structure created and executed by myself with the wonderful help of my collaborators. Charity costs were supplied by David Cunningham and Tim Beacon. Governmental costs were provided by Dr. John Sekabira MD, Dr. Mary Nabukenya MD, and Dr. Phyllis Kisa MD. OOP costs were collected by trained ward nurses, sisters Ann Nabirye RN and Scholastica Mukimba RN. Survey IRB for Mulago Hospital was written and submitted by Dr. Nasser Kakembo. Survey IRB for Yale University was submitted by Dr. Maija Cheung MD. Collection methodology were supported by advisors Dr. Reza Yaesoubi PhD and Dr. Doruk Ozgediz MD.

The overarching costs were taken from the perspective of the Ugandan healthcare system. Because the Naguru Hospital used resources pooled from several entities, both local and international, costs were sourced from 3 main sub-perspectives: charity or non-governmental organizational (NGO) costs, Ministry of Health or governmental costs, and out-of-pocket or family-centered costs, with the overall sum amounting to the cost to the healthcare system. Costs of baseline pediatric ward accommodation, land space, and ward staff were excluded, since these services are provided at steady-state without or without the intervention, and patients presenting with potentially surgical conditions were generally admitted into the hospital regardless of theater availability. All costs were reported in 2015 US dollars, with costs from other fiscal years and currencies (Great British Pound = GBP, Ugandan Shilling = UGX) converted to the common USD currency using purchasing power parity (PPP) rates reported by the World Bank, which was equivalent to 1,088.80 2015 UGX per 1 2015 USD.

Aim 2a: Costs - Charity Perspective (Largescale Equipment)

Core surgical OR furniture (OR table, anesthetic machines, cautery etc.) was procured from suppliers who offered subsidized prices. Participating NGOs (ARCHIE-Wood Foundation and Medical Aid International, a partner NGO that forged the purchases for vetted equipment) provided details of market and discounted prices, and number of units of specific equipment purchased. Composite replacement costs were reported, though individually marked items were not presented to preserve the agreement of pricing confidentiality between parties. Replacement costs for each piece of equipment was annualized by either its lifetime warranty drawn from a product catalog, or if unavailable, by an average of 9 years as reported by the US Government Office of Management and Budget.[37] Prices were converted from GBP currency to USD using PPP, and adjusted by an average inflation rate of **5.5%** in Uganda in 2015.[38]

Aim 2b: Cost – Government Perspective (Wages, Medication and Disposable Equipment)

Because both Naguru and Mulago Hospital are public hospitals, local workers' wages were designated by the Ministry of Public Service based on a predetermined salary scale, with income brackets (ranging from U1-8, with U8 as the lowest) spanning each level of employment. We obtained salaries in UGX currency of the applicable healthcare workers from the Ugandan salary schedule for the fiscal year of 2015-6, as published annually by the government of Uganda.[39] The job descriptions included were, in descending income order: consultant (attending) physician, principal medical officers (fellows), senior graduate medical officers (residents), senior nursing officer, nursing officer, entry medical officer (intern), scrub nurse, and theater attendant.

In terms of anesthetics and remaining hospital equipment, the bulk of in-hospital medications and disposable surgical equipment in the OR were provided free of charge to the patients by the Ugandan Ministry of Health and were supplied by government-controlled entities such as the Joint Medical Store and the National Medical Store (NMS). Price per unit provided by these institutions were obtained in the form of NMS order sheets and invoices, which were compiled by the central pharmacy department at Naguru Hospital. When unavailable, prices were obtained through the 2015 International Drug Price Indicator Guide (IDPIG).[40] Price sheets from the Naguru central pharmacy was also obtained for the majority of disposable and non-disposable items used in the OR and pediatric surgical ward. Because the Naguru OR also received services from other NGOs, a small fraction of medications and medical equipment utilized in the OR were donated by NGOs. These prices were not reported, as it was not possible to ascertain these prices.

Medication dose was weight-based, so costs of anesthetic and post-operative medication could be modeled as a function of the patients' weight, regardless of procedure. Because the Naguru OR had no access to a weighing scale, and local anesthetists inferred the weight using age calculations to accurately estimate dosage for patients. Thus, the anesthetic dosages and subsequent costs were modeled after an age-based algorithm obtained from the anesthetists. This age-to-weight conversion provided a reasonable estimate of the patients' utilization of peri-operative medications, because not only did the body habitus of these pediatric patients not vary widely within age groups, but also everyday practice in the OR relied on the algorithm, and so its utilization in our model reflected the actual pattern of drug administration.

To inform the age-weight medication method, a representative selection of anesthetic reports of the Naguru OR cases over the first year were collected to determine an archetypal list of the most commonly used peri-operative medications, and information on frequency and dosage of administered drugs were obtained to corroborate the age-based algorithm. This extra step helped validate the age-to-weight medication dose model by confirming that the age-based algorithm fitted well with the actual anesthetic and post-operative medications used in pediatric surgical operations performed in the Naguru OR over the year. Furthermore, the frequency of each medication's usage for each procedure served to inform the type and probability of medication charges in the decision-tree model.

Aim 2c: Costs - Patient's Perspective (Out-Of-Pocket Expenditure)

Despite the national infrastructure set up to distribute medical supplies through the public route, the JMS and NMS frequently experienced shortages and did not hold certain medications that were commonly prescribed in the pediatric surgical ward. As a result, the patients resorted to purchasing certain medications out of pocket (OOP) from privately-owned pharmacies, as there were no public means of access. Furthermore, while Mulago Hospital provided basic hematologic lab tests (e.g. complete blood count, electrolytes etc.), more expensive diagnostic tests such as ultrasonographic and radiologic imaging were usually also paid by the patient's family. Patients additionally had to pay for transportation and food and lodging costs. A prospective survey administered to the patients' families determined OOP expenditure, as these costs were not previously reported in the literature.

Institutional review board approval was granted by both Yale University and Mulago Hospital for this portion of the study. Survey respondents were selected from a convenience sample of family members taking care of patients admitted to the pediatric surgical inpatient ward for surgical procedures. Mulago Hospital was chosen as the study site as it is the national public referral hospital, and the main tertiary care center providing specialized treatment for pediatric surgical disease in the country.

From November 2016 to April 2017, ward nurses fluent in both Luganda and English administered electronic questionnaires to family members using Qualtrics software. Respondent inclusion criteria included the guardian(s) who accompanied the child to the hospital, with preference given to the parent of the patient. To capture the full extent of patient costs, questionnaires were administered post-operatively after the family had purchased post-operative medications and were a few days away from discharge, according to the physician's clinical judgement. Respondents who were transferred to another department for surgery or admitted in the ward for non-operative management were excluded from our study.

Query categories of family OOP spending on medical and non-medical expenses included (1) transportation, (2) diagnostic tests, (3) medications, (4) loans and pawned possessions, (5) food and lodging, and (6) cost of lost productivity for the current hospital stay. Survey questions were structured around previously validated tools including the Labor and Health Short Form Questionnaire and Household Consumer Expenditure Survey.[41-43] Demographic information gathered included the age, sex, home province, dates of admission, surgery and discharge, surgical diagnosis and intervention, and number of family members present to care for the child. Signed consent was waived as no identifying information was gathered. Participants were also asked to give an estimated total amount spent on the entire hospital admission. Monetary values were recorded in the local currency, UGX, and converted to

USD using PPP. Responses were recorded by the ward nurses trained to use an iPad or laptop computer in the pediatric surgical ward in Mulago Hospital. Surveys were then uploaded to the online Qualtrics platform and accessed remotely.

Round trip transportation costs were collected, as participants were asked to project their return trip back home after discharge. Mode of transportation and hours travelled were also collected to determine the lag time to accessing care. Spending on medicine and diagnostics were itemized and quantified and corroborated with the surgeon's recommendations on patient charts. When possible, consenting participants also produced receipts of purchased medications.

Participants missed work-days by staying in the hospital with the patients, and this productivity loss was captured by obtaining their employment status, daily income, and days of work per week. The opportunity cost was calculated by multiplying their daily income by the number of workdays missed. Some family members were also the patient's siblings and missed school days, which was recorded in a similar manner.

Responses were exported into an .csv file and descriptive statistical analysis was performed by Excel and R for each study parameter, with cost category stratification and subgroup analysis whenever possible. For mean values, 95% confidence intervals were calculated and presented along with ranges for each variable. Proportion of catastrophic expenditure was determined by comparing both total calculated expenditure and self-reported spending to the median household expenditure in Uganda in 2013, which was 3,113 USD, as reported by the Ugandan Bureau of Statistics.[44]

Aim 3: OUTCOMES

Attribution: Patient data was collected by myself and Harriet Nambooze, informed by Dr. Arlene Muzira MD, Dr. John Sekabira MD, Dr. Scott Corlew MD, Dr. Dan Poenaru MD, Dr. Maija Cheung MD, and Dr. Doruk Ozgediz MD. Collection methodology was vetted by Dr. Reza Yausoubi PhD.

Aim 3a: Outcomes - Primary Patient Data Sources

Outcome parameters were informed by previous literature and patient data retrospectively collected from the OR database in Uganda during the first year of service. Pediatric patients recorded in the Naguru OR case-log over the first year of operation were included. Information collected from the pediatric surgical ward database included age, gender, diagnosis, surgical intervention, healthcare personnel present at the surgery, duration of hospital stay, and most importantly patient outcomes (death or discharge). All entries were de-identified upon collection prior to analysis. Other surgical departments had also utilized this theater including orthopedics, otolaryngology, and ophthalmology. For the purposes of this study, we excluded these cases from the analysis to focus on the costs and outcomes solely from the pediatric surgical department. We had also excluded cases within the pediatric surgical service that were minor and idiosyncratic, as these cases lacked significant, predictable incidence rates making estimating disease-specific variables difficult. Moreover, the rare conditions would not contribute significantly to the overall aversion of disease burden.

Patient outcomes, namely death or hospital discharge, were verified by three other sources to ensure accuracy: the death certificate log, daily nursing reports, and patient files. We identified 48 unique surgical diseases along with their corresponding interventions that could be represented by the decision tree model template. Of note, obtaining data on immediate empirical surgical outcomes allowed for the realistic projection of disease burden averted for each surgical disease and corresponding intervention. Generally, individuals who were discharged should have been able to sustain their new health state and were unlikely to be readmitted. Complications usually occurred during the immediate post-operative hospital course while the patient was still inpatient, and so outcomes were largely determined on the immediate health condition of the patients during their inpatient stay post-operatively. This information and assumption was integral to informing our economic model. By establishing the proportion of patients that did not survive post-operatively, a relatively realistic estimate on the efficacy of each disease-specific procedure could be projected.

Aim 3b: Outcomes – Disability Adjusted Life Years and Disability Weights

We used the disability adjusted life year (DALY) as a metric to quantify the disease burden each possible patient outcome in the decision tree. DALYs were discounted at rate of 3% following Fox-Rushby's method and as recommended by Drummond et al.[45] The disease burden averted was also subject to a 4% age-weighting in scenario-based sensitivity analysis.[46] The DALY concept was first used by the World Bank and Disease Control Priorities Review to calculate global burden of disease in 1993. The method was further refined by Murray[47] and Fox-Rushby[46], and has since been used in to evaluate disease burden in a multitude of disease burden and cost-effectiveness studies. In this cost-effectiveness study, the DALY was used to quantify burden of disease averted and comprised of the total of years of life lost (YLL) and years lived in disability (YLD). Formulae used to derive DALYs are shown below and were incorporated into the cost-effectiveness model and analytical code in Aim 5 as VBA Excel arguments as the simulation model was constructed:

Disease Burden Formulae (Derived from Fox-Rushby)[46]

$$DALYs = YLLs + YLDs$$

Years of life lost (YLL) were calculated by the following formula:

$$YLLs(r,K) = \frac{KCe^{ra}}{(r+b)^2}\left\{e^{-(r+b)(L+a)}\left[-(r+b)(L+a)-1\right] - e^{-(r+b)a}\left[-(r+b)a-1\right]\right\} + \frac{1-K}{r}\left(1-e^{-rL}\right)$$

Where:

K – Modulates age weight inclusion (1 or 0)
C – Mathematical Constant (0.1658)
r – Discount rate (0%, 3%, or 6%)
a – Age at death
b - Parameter from age weighting function (0.04)
e – Natural logarithm root (2.72)
L – Life expectancy

When the discount rate is zero:

$$YLLs(0,K) = \frac{KCe^{-ba}}{b^2}\left[e^{-bL}\left(-b(L+a)-1\right) - (-ba-1)\right] + \left[(1-K)(L)\right]$$

YLDs were calculated using the following formula where D is the disability weight. In this equation ***a*** is age at onset of disease and ***L*** is number of years lived with the disability:

$$YLDs(r,K) = D\left\{\frac{KCe^{ra}}{(r+b)^2}\left\{e^{-(r+b)(L+a)}\left[-(r+b)(L+a)-1\right] - e^{-(r+b)a}\left[-(r+b)a-1\right]\right\} + \frac{1-K}{r}\left(1-e^{-rL}\right)\right\}$$

When the discount rate is equal to zero the formula simplifies to:

$$YLDs(0,K) = D\left\{\frac{KCe^{-\beta a}}{\beta^2}\left[e^{-\beta L}\left(-\beta(L+a)-1\right)-(-\beta a-1)\right]+\left[(1-K)(L)\right]\right\}$$

Adjustment of YLL to the year of disease onset was calculated using:

$$DALY\ at\ age\ x = DALY(y)e^{-rs}$$

YLD was further deconstructed into the number of years remaining alive multiplied by the disability weight (DW), which was a number between 0-1 assigned based the severity of a disease, with a higher value corresponding to greater disability. DWs for each condition were extracted from previous published literature, including the Global Burden of Disease Studies from 2010-5, which were aggregate numbers pooled from over 60,000 respondents globally.[48] Other sources included Badrinath 2015, Poenaru 2015 and 2017, which were studies that focused more on pediatric surgery specific congenital anomalies.[48-50] As we built our decision tree model, post-surgical DWs were curated using previously developed preference scales, as there were a number of conditions which were not completely curative. When there were no previous published DW for the surgical condition, validated severity score scales developed by McCord and McChowdhury (2003)[19] and the EuroQoL EQ-5D social tariff[51] were used, and numbers were agreed upon by a panel of pediatric surgeons. Country and gender specific life-expectancies in 2015 were used (60 years for males and 64 years for females) based on the most recent Global Burden of Disease study[52] since some conditions were more common in males than females (e.g. inguinal hernia is a male specific problem). Average age of presentation and remaining life-expectancy were implemented into the model separately for each disease state.

Probability of successful treatment (PST) and probability of post-operative death were estimated from previously published literature, and any disease with a greater than 95% cure rate had a PST of 1.[19] DWs and probabilities were estimated and agreed upon by a consensus from the co-authors.

Aim 4: Cost-Effectiveness Analysis and ICER

Attribution: Model was constructed by myself under the guidance of Dr. Reza Yaesoubi PhD.

The final metric was the incremental cost-effectiveness ratio (ICER), defined as ($\text{Cost}_{\text{OR intervention}}$ – $\text{Cost}_{\text{natural disease course}}$) / ($\text{DALYs}_{\text{OR Intervention}}$ – $\text{DALYs}_{\text{natural disease course}}$), and was presented as an absolute value in units of US dollars per DALY averted. According to the WHO guidelines, a cost-effective intervention should be under the threshold of three times the country's gross domestic product (GDP) per capita, which was $2,026 in Uganda in 2015.[53]

In the proposed decision tree model, there was one decision node where surgery was either performed or the disease is left untreated and the patient proceeds with the natural course of disease. Because of the variety of surgical diseases that were present in our case-log, a single decision tree would not adequately fit the range of different morbidity and mortality outcomes. Therefore, we grouped the diseases into main categories and devised variations off a base model. The disease categories were mainly dictated by the proportion of YLL and YLD accumulated; some diseases were inevitably fatal shortly after presentation if untreated (accruing YLL only e.g. intussusception), while others contributed to only patient morbidity, but no life-years are lost (YLD only e.g. inguinal hernia). These disease categories are presented in Table 9 in the Results section.

Aim 5: Establishing Model Confidence

Attribution: Statistics and associated coding were written by myself under the guidance of Dr. Reza Yaesoubi PhD.

Probabilistic Model: A multivariate Monte Carlo simulation was conducted to characterize the uncertainty of the ICER accumulated by the multitude of variables. Randomization of uncertain parameters occurred for both costs and outcomes. Outcome variables that were randomized included life expectancy, age of presentation, DWs, probability of successful treatment, and probability of death. For diseases and surgeries with at least 10 patients in the OR case log, continuous probability distributions (log-normal, Weibull, or gamma) were fitted with Java Math Package (JMP) statistical software, developed by Statistical Analysis

System (SAS) and was used to randomize age of presentation and life expectancy. For diseases with less than 10 patients to power a continuous function, uniform and triangle distributions were used. DWs and probabilities were fitted with a beta distribution using previously reported confidence intervals (CI), and when published data was unavailable, a CI range of +/-0.2 constrained between 0 and 1 was used, as proposed by previous cost-effectiveness studies.[54] Distribution curves for each uncertain parameter were entered as formulas and randomized using “=rand()” function as the probability.

Randomization of cost variables were included in each cost component. Drug and anesthetic doses were converted to costs and calculated based on the simulated patient’s weight, which was randomized by the corresponding age of presentation. Rescue drug costs (steroids, atropine, epinephrine) were included using probabilities derived by the actual frequencies used in the cohort of patients in the OR case log. For the most part, the amount of disposable equipment used was similar for each operation regardless of type of disease treated and was calculated as a constant incremental price per procedure. To better mirror a realistic operation, size and number of IV catheters per procedure was determined by age, with younger patients (i.e. under the age of 1) utilizing higher gauge needles in larger numbers as they tend to require more attempts at intravenous access. Foley catheter cost was included for a select cohort of simulation patients for procedures that lasted longer than an average of 2 hours, which included pull-throughs, nephrectomies, posterior sagittal anorectoplasties, cloacal and intestinal atresia repairs.

To emulate a facility-based study, simulated patients were batched in cohorts of 200-500 patients uniformly randomized, and disease empirically randomized to follow the distribution of cases of the Naguru OR case log. Cumulative DALYs were divided over the cumulative annual costs of running the OR to obtain the simulation ICER. 200 simulations were run on VBA script, and bootstrap uncertainty intervals were calculated for the ICER. Results of the Monte Carlo simulation were presented in a cost-effectiveness plane.

Scenario Analysis: One-way deterministic sensitivity analysis was also performed to model alternative scenarios in order capture plausible ranges of parameters that were subject to the most variation. Scenarios included changing time discounts and inflation rates, market value of equipment, age weighting, and number of patients treated without the OR intervention.

Aim 6: Cost-Benefit Analysis

Attribution: Cost-benefit calculations were conducted by myself with guidance from Dr. Reza Yaesoubi PhD and Dr. Doruk Ozgediz MD. The value of a statistical life was calculated using a customized algorithm built by Dr. James Healy MD.

The goal of a cost-benefit analysis (CBA) was to find out the monetary value of the DALYs averted in a healthcare intervention to better demonstrate the economic surplus. The underlying principle lay under the assumption that individuals who were treated and cured from their disease would go on to become productive citizens and contribute to the country's GDP. In this way, each DALY saved translated into a monetary amount that reflected the individual's projected economic productivity over a lifetime. This CBA was conducted using a value of statistical life (VSL) approach following the recommendation demonstrated in the 3rd edition of Disease Control Priorities[55] and a recent study on cleft-lip palate repair.[56] The economic benefit was calculated by converting the value of a statistical life in America to that of Uganda by using the ratio between the two countries' GDP per capita and an income elasticity of 1.5 that was consistent with LICs. Unless otherwise stated, costs were reported in 2015 USD. The following formula was used to diagram our CBA to determine the NMB:

Calculating Net Monetary Benefit (NMB)

$$NMB = (WTP) \times (E) - C$$

WTP = Willingness to Pay ($)

E = Effectiveness (DALYs Averted)

C = Cost of intervention

Results

Aim 1: Cost-Effectiveness Model

A decision tree model was designed to encapsulate all common possible patient scenarios for each disease and corresponding corrective procedure performed in the Naguru OR, with long term outcomes branching dichotomously from chance nodes (Figure 1). Immediate and chronic post-operative complications were included into the intervention branch of the model, as suggested by Shrime's CEA checklist and example.[15]

Figure 1: The skeleton of the decision tree to model pediatric surgical diseases treated in the OR. Square = Decision node between surgery and no surgery. Circle = chance nodes with probabilities. Triangle = end nodes with cost and outcomes of each branch.

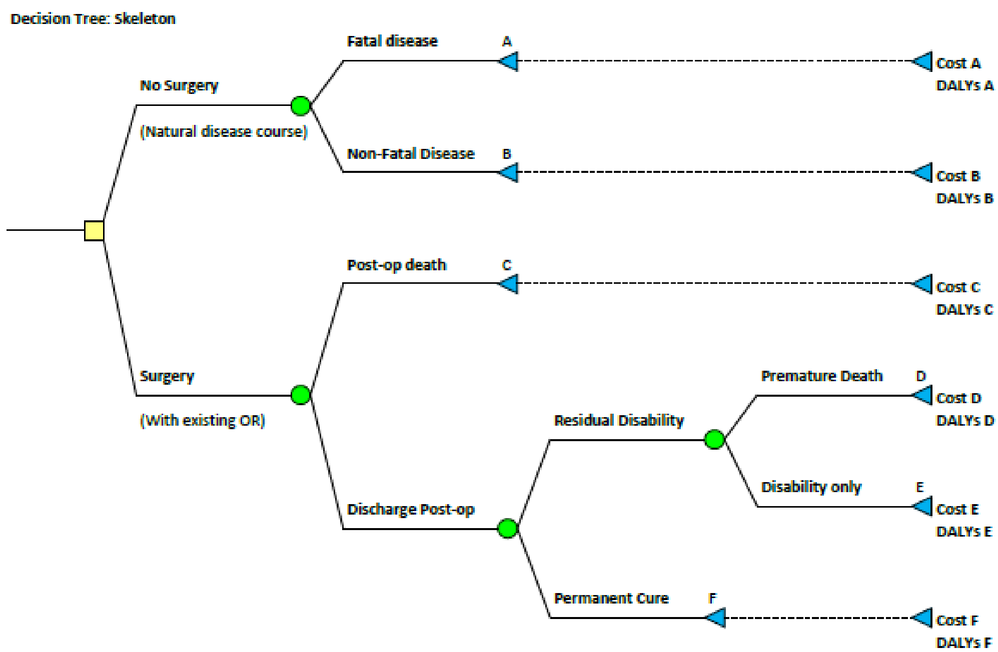
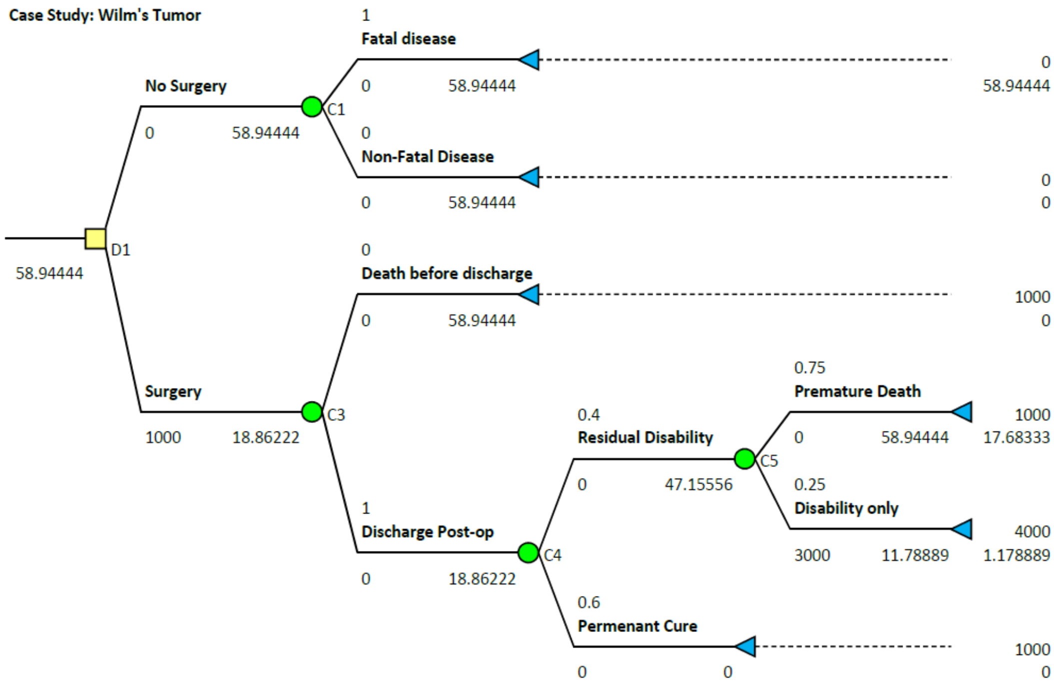


Figure 2: An example of modeling the possible scenarios of a specific disease, demonstrating the possible disease pathways for Wilms tumor.



Aim 2a: Charity Costs (Largescale OR Equipment)

The total cost of furnishing the pediatric OR purchased by the ARCHIE Foundation was $101,847.57 after adjusting for currency exchange and PPP, and encompassing items included the surgical and anesthetic equipment as well installation and delivery freight fees. This total value was reduced from the market value cost of $266,261.85, as ARCHIE purchased the equipment subsidized prices. Below is an itemized list of prices of the donated equipment with accompanying installation fares (Table 1). Annualized costs were calculated by dividing the total market price by the average lifetime of the equipment. The total annualized cost from the charity's perspective amounted to $41,316.53 after applying the 5.5% inflation rate. The annualized societal cost (at market price) was $64,330.16 with a 5.5% inflation rate.

Table 1: Equipment market values, lifetime, amount purchased, and annualized cost reported in 2015 USD

Equipment name (brand/model)	***Market Unit Price (2015 Pounds)*** [A]	***Lifetime (Years)***	*Source*	***No. bought***	***Total Market Price*** [B]	*Annualized cost with 5.5% discount*
Oxygen concentrator	£2,400.00	9	[37]	1	$3,464.66	($498.35)
Anesthetic machine: Mindray WATO EX35	£17,500.00	5	[57]	1	$25,263.13	($5,916.03)
Suction: MGE SAM EPS	£690.00	4	[58]	1	$996.09	($284.18)
Suction: MGE SAM 35	£1,246.00	4	[58]	1	$1,798.74	($513.17)
Suction: MGE SAM 12	£592.00	4	[58]	1	$854.62	($243.82)
Theatre table: Eschmann MR	£30,000.00	9	[37]	1	$43,308.23	($6,229.43)
Autoclave: ETC Big Bertha	£55,000.00	15	[59, 60]	1	$79,398.42	($7,910.12)
Theatre light: Brandon Medical Quasar	£13,500.00	5	[61]	1	$19,488.70	($4,834.55)
Electrosurgical Generator: Beilin DGD-300B-2	£7,500.00	4	[62]	1	$10,827.06	($3,088.90)
Surgical instruments set: Braun / Downs	£15,000.00	9	[37]	1	$21,654.11	($3,114.72)
Endoscopy Set	£3,200.00	9	[37]	1	$4,619.54	($664.47)
Patient Trolley: Anetic Aid QA3	£5,000.00	10	[63]	2	$14,436.08	($1,915.20)
Oximeter w/ finger probes	£750.00	9	[37]	Bundle	$1,082.71	($155.74)
Patient monitor: Mindray VS800	£1,770.00	2	[64]	3	$7,665.56	($4,151.80)
Theatre Furniture	£1,250.00	10	[37]	1	$1,804.51	($239.40)
Beds/Mattresses	£833.33	10	[37]	6	$7,218.01	($957.60)
Flights & Accommodation	£7,500.00	1	N/A		$10,827.06	($11,422.55)

Signage	£1,754.00	1	N/A	$2,532.09	($2,671.35)
Airfreight	£6,250.00	1	N/A	$9,022.55	($9,518.79)
Totals	£191,425.33			$266,261.8	($,64,330.16)

[A]ARCHIE Foundation's actual discounted prices were not reported to respect confidentiality in NGO pricing negotiations.

[B]Adjusted with Purchasing Power Parity based on World Bank values. 1 USD (2015) = 0.692709 GBP (2015)

Aim 2b: Government Costs (Wages, Medication and Disposable Equipment)

Government wages reported by the Ministry of Public Service in the form of salary scales for the fiscal year of 2015-2016 were recorded for healthcare staff who were associated with operating the pediatric OR (Table 2, Figure 3). To put the wages in perspective, the minimum wage in the US in 2016 was $1,256.67 per month (after factoring in purchasing power parity between Uganda and USA), and of all the involved OR staff only the attending and fellow had a higher salary than the US minimum wage. The resident level of pay was slightly less than US minimum wage. Of note, the Ugandan minimum wage was stagnated at 6,000 UGX or 1.68 USD per month since the law was enacted at 1984. The amount did not account for the country's inflation rate over time, as one would not be able to reasonably get by with $1 *per month* (the definition of 'extreme poverty' is earnings below $1.90 *per day* according to the World Bank in 2011 USD[65]). The median monthly wage in Uganda in 2013 was 110,000 UGX, or $115.82 in 2016 USD after adjusting for inflation.[44] Using this frame of reference, all the staff in the OR had a wage that was higher than that of the national average.

Table 2: The healthcare workforce involved with the functional pediatric operating room, their respective salary scales along with the actual salary reported by the workers, reported in 2015 USD.

DESIGNATION	SPECIFIC JOB TITLE	SALARY SCALE LOWER LIMIT (USD)	SALARY SCALE UPPER LIMIT (USD)	REPORTED MONTHLY WAGE (USD)
CONSULTANT	*Attending*	$ 2,165.13	$ 3,165.93	$ 2,413.74
PRINCIPAL MEDICAL OFFICERS	*Fellow*	$ 1,587.24	$ 1,890.41	$ 1,674.90
SENIOR MEDICAL OFFICER	*Resident*	$ 1,106.05	$ 1,284.33	$ 1,208.45
SENIOR GRADUATE OFFICERS	*Sr. Nurse*	$ 899.89	$ 1,038.95	$ 961.05
ENTRY POINT OF GRADUATES	*Nurse*	$ 552.30	$ 733.41	$ 664.83
ENTRY POINT FOR MEDICAL WORKERS	*Intern*	$ 692.38	$ 728.22	$ 710.06
TECHNICAL CADRE	*Scrub Nurse*	$ 433.58	$ 549.98	$ 493.58
PROMOTIONAL LEVEL FOR ANALOGOUS STAFF	*OR Attendant*	$ 382.64	$ 401.06	$ 391.50
ENTRY POINT FOR SUPPORT STAFF	*Ward Attendant*	$ 246.27	$ 265.76	$ 260.76

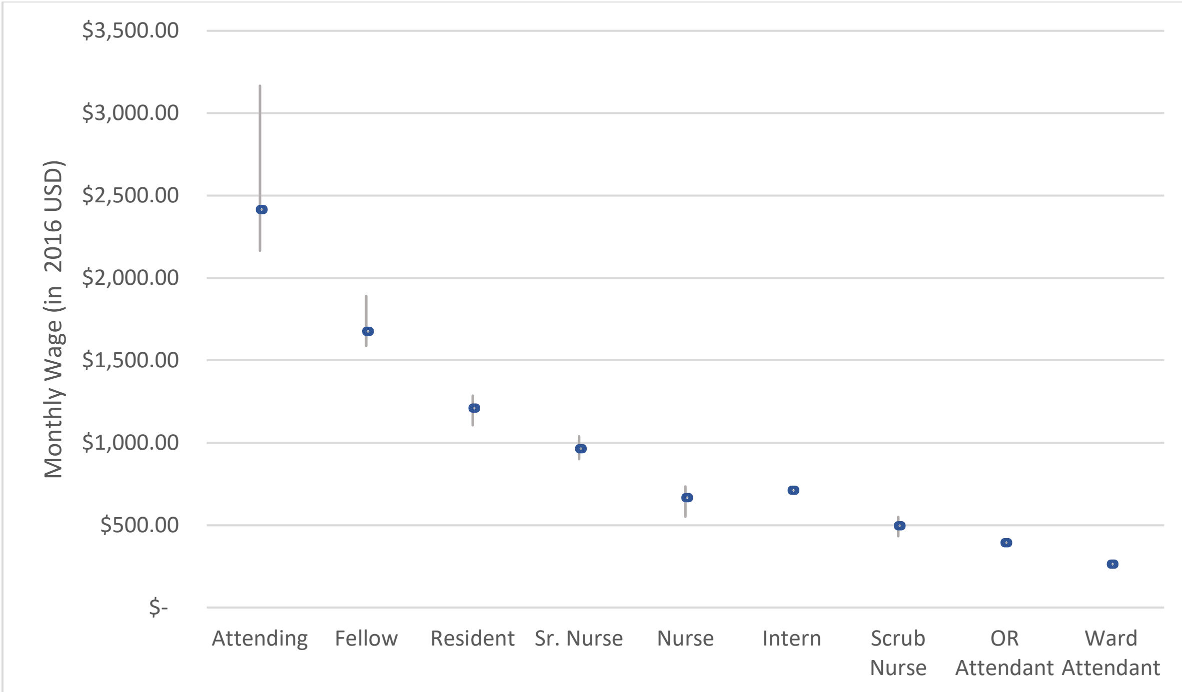


Figure 3: Graph depiction of the range of salary scales for each worker designation (gray line) and their actual wages (blue dot)

To ascertain government supplied medication costs, 117 anesthetic reports from the first year of Naguru OR cases were selected as a representation of the anesthetic and peri-operative medications used for the pediatric surgical procedures. Medications that were used intraoperatively and purchased by the government via the NMS were included, and their costs, reported below in 2015 UGX and USD, were obtained from the Naguru Hospital central pharmacy (Table 3). These prices were later incorporated in the sensitivity analysis to help determine the governmental cost aspect of the incremental cost-effectiveness ratio (See Results, Aim 4/5). The likelihood of each medication's inclusion was based on the proportion of operative reports documenting its utilization. Rescue medications (i.e. epinephrine, atropine, lidocaine, and hydrocortisone) were included into the analysis as a fixed variable cost per procedure, since intravenous injection solutions were prepared prior to each case regardless of whether they were utilized in the anticipation of the possible need for resuscitation.

Table 3: Government purchased medications used in the operating room, with respective prices drawn from the National Medical Store order lists in the 2015-2016 cycle

DRUG ITEM					
Maintenance Fluids	*Dosage*	*UGX per unit*	*mcg|mg|ml / unit*	*UGX per mcg|mg|ml*	*USD per mcg|mg|ml*
GLUCOSE 50% INJECTION 100ML BOTTLE	--	UGX 1,150.00	100	UGX 11.50	.0106¢
SODIUM CHLORIDE/ NORMAL SALINE 0.9% INFUSION 500ML BOTTLE	--	UGX 1,122.92	500	UGX 2.25	.0021¢
GLUCOSE (DEXTROSE) 5% INFUSION 500ML BOTTLE	--	UGX 1,041.67	500	UGX 2.08	.0019¢
Inhaled Anesthetics	*Dosage*	*UGX per unit*	*mcg|mg|ml / unit*	*UGX per mcg|mg|ml*	*USD per mcg|mg|ml*
HALOTHANE INHALATION 250ML (for induction only)	250ml/month	UGX 56,900.00	250	UGX 227.60	.2090¢
ISOFLURANE INHALATION 250ML	31.25ml/hr	UGX 166,150.00	250	UGX 664.60	.6104¢
Sedatives/Paralytics	*Dosage*	*UGX per unit*	*mcg|mg|ml / unit*	*UGX per mcg|mg|ml*	*USD per mcg|mg|ml*
THIOPENTAL SODIUM 500MG AMPOULE	4mg/kg	UGX 4,937.00	500	UGX 9.87	0.91¢
KETAMINE 500MG/10ML INJECTION IV/IM	2mg/kg	UGX 1,810.00	500	UGX 3.62	0.33¢
ATRACURIUM 10MG/ML 2.5ML INJECTION	0.4mg/kg	UGX 7,560.00	10	UGX 756.00	69.43¢
SUXAMETHONIUM CHLORIDE 100MG/2ML	2mg/kg	UGX 1,780.00	100	UGX 17.80	1.63¢

PROPOFOL 10 MG/ML, 50ML VIAL	4mg/kg	UGX 14,200.00	500	UGX 28.40	26.1¢
Analgesics	***Dosage***	***UGX per unit***	***mcg|mg|ml / unit***	***UGX per mcg|mg|ml***	***USD per mcg|mg|ml***
PARACETAMOL 125MG SUPPOSITORIES	30mg/kg	UGX 700.00	125	UGX 5.60	.51¢
DICLOFENAC SODIUM SUPPOSITORIES 50MG	0.5mg/kg	UGX 495.83	50	UGX 9.92	.91¢
PARACETAMOL 125MG/ML SUSPENSION	10mg/kg	UGX 1,150.00	125	UGX 9.20	.84¢
TRAMADOL INJECTION 100MG/2ML AMPOULE	2mg/kg	UGX 740.00	100	UGX 7.40	.68¢
BUPIVACAINE HCL 0.5% IN DEXTROSE 8.0% INJ, 4ML AMPOULE, SPINAL	2.5mg/kg	UGX 677.50	20	UGX 33.88	3.11¢
ORAL MORPHINE SOLUTION.50MG/5ML x 500ML A	0.1mg/kg	UGX -	50	UGX -	.00¢
FENTANYL CITRATE INJECTION 50MCG/ML 3ML AMPOULE	2mcg/kg	UGX 15,800.00	50	UGX 316.00	29.02¢
PETHIDINE 100MG/2ML INJ IV/IM/SC	1mg/kg	UGX 1,970.00	100	UGX 19.70	1.81¢
Rescue Drugs	***Dosage***	***UGX per unit***	***mcg|mg|ml / unit***	***UGX per mcg|mg|ml***	***USD per mcg|mg|ml***
EPINEPHRINE (ADRENALINE) 1MG/ML INJ IV/IM/SC	0.01mg/kg	UGX 669.00	1	UGX 669.00	61.44¢

ATROPINE 1MG/1ML INJ IV/IM	0.01mg/kg	UGX 113.00	1	UGX 113.00	10.38¢
LIDOCAINE HCL 2% INJECTION	2mg/kg	UGX 2,200.00	10	UGX 220.00	20.21¢
HYDROCORTISONE SODIUM PHOSPHATE 100MG INJECTION	10mg/kg	UGX 959.00	100	UGX 9.59	.88¢
Antibiotics	***Dosage***	***UGX per unit***	***mcg|mg|ml / unit***	***UGX per mcg|mg|ml***	***USD per mcg|mg|ml***
METRONIDAZOLE 500MG/100ML INFUSION	15mg/kg	UGX 700.00	500	UGX 1.40	.13¢
METRONIDAZOLE SUSPENSION 100MG/5ML 100ML BOTTLE	15mg/kg	UGX 1,050.00	100	UGX 10.50	.96¢
AMPICILLIN 500MG POWDER	100mg/kg	UGX 319.00	500	UGX 0.64	.06¢
CEFTRIAXONE SODIUM 1G POWDER FOR INJECTION	100mg/kg	UGX 1,450.00	1000	UGX 1.45	.13¢
CEFAZOLIN 500MG AMP IV B	40mg/kg	UGX 461.11	1000	UGX 4.15	.84¢
CLOXACILLIN 500MG INJ (PFR) IV/IM	25mg/kg	UGX 347.00	500	UGX 0.69	.06¢
GENTAMICIN 80MG/2ML INJ IV/IM	2.5mg/kg	UGX 147.50	80	UGX 1.84	.17¢

[A] Oral morphine is supplied to the store without a price attached

[B] Retrieved from the 2015 International Medical Products Guide pA-29[40]

Costs of disposable equipment were also obtained through the price sheets provided by the Naguru Hospital central pharmacy, which were drawn from the NMS in the 2015-2016 cycle. Items were split between those that were used once per case and then immediately disposed of (e.g. IV cannulas, syringes, Table 4), and those that could be used over multiple cases (e.g. surgical boots, oxygen tanks etc.) and had an intermediate lifespan (

Table 5). The size of the Foley catheter, endotracheal tube and nasogastric tube were selected based on the average age of 2.9 years old or the smallest available size on the catalog.

Table 4: Prices of government supplied surgical and anesthetic equipment that are used once per case and disposed of immediately after

Disposable Surgical Equipment	*UGX/Unit*		*USD/Unit*		*# used/case*
Basics					
CATHETER SUCTION FG 14 OD 4MM	UGX	550.00	$	0.51	1
NASAL OXYGEN CANNULA TWIN, 160CM PAEDIATRIC	UGX	1,600.00	$	1.47	1
TUBE ENDOTRACHEAL ORAL/NASAL CUFFED 6.5MM	UGX	3,250.00	$	2.98	1
GLOVES EXAMINATION LATEX, MEDIUM NON-STERILE	UGX	276.00	$	0.25	10
AD SYRINGES 10ML+ NEEDLE DISP. DETACHED	UGX	227.00	$	0.21	2
AD SYRINGES 2ML+ NEEDLE DISP. DETACHED	UGX	156.00	$	0.14	5
AD SYRINGES 5ML+ NEEDLE DISP. DETACHED	UGX	209.00	$	0.19	5
CANNULA I.V, WITH INJ. PORT & STOPPER 24G, 1.9MM [A]	UGX	327.00	$	0.30	10
CANNULA I.V, WITH INJ. PORT & STOPPER 22G, 0.7MM [A]	UGX	329.00	$	0.30	7
CANNULA I.V, WITH INJ. PORT & STOPPER 20G, 0.9MM [A]	UGX	341.50	$	0.31	5
Occasional Additional Items					
CATHETER FOLEY 3 WAYS CH 20, LATEX	UGX	34,500.00	$	31.69	1
COLOSTOMY BAG CLOSED 30MM, DIA 30MM 200X140	UGX	1,290.00	$	1.18	1
TUBE GASTRODUODENAL 12X80 CM OD 4MM	UGX	400.00	$	0.37	1
NASOGASTRIC TUBE - PAED - 6	UGX	300.00	$	0.28	1
BLOOD TRANSFER BAG 300ML	UGX	2,500.00	$	2.30	1

Surgical Instruments					
NYLON MONOFILAMENT G1, SL 100CM , 40MM	UGX	1,858.33	$	1.71	2
NYLON MONOFILAMENT G2/0, SL 45CM, 26MM	UGX	3,650.00	$	3.35	2
PGA G2 SL 90 CM,1/2 CIRCLE, TH, 40MM	UGX	6,175.00	$	5.67	3
PGA G2/0 SL 75CM,1/2 CIRCLE, TF, 30MM	UGX	2,208.33	$	2.03	3
BLADES SCALPEL SIZE 11	UGX	342.50	$	0.31	1
BLADES SCALPEL SIZE 12	UGX	971.00	$	0.89	1
BLADES SCALPEL SIZE 15	UGX	398.50	$	0.37	1
Protective Wear					
AUTOCLAVE MARKING TAPES, ROLL, 50M, 18MM WIDE	UGX	7,550.00	$	6.93	0.034
BIN LINERS (BLACK)	UGX	1,025.50	$	0.94	1
GLOVES SURGEON 7 1/2 STERILE	UGX	651.00	$	0.60	3

[A] Type of IV cannula utilization is determined by age of patient

Table 5: Prices (per annum) of government supplied equipment that are reusable in the intermediate period but have a lifespan of less than or equal to a year

Reusable Equipment							
Equipment	**UGX per unit**		**USD per unit**		**# / year**	**USD per year**	
SAFETY BOX FOR NEEDLE DISPOSAL	UGX	1,555.00	$	1.43	10	$	14.28
OXYGEN REGULATOR, CYLINDER MOUNTED	UGX	122,450.00	$	112.46	10	$	1,124.63
MATERIAL FOR THEATRE GOWN 40M ROLLS	UGX	380,200.00	$	349.19	3	$	1,047.58
BOOTS THEATRE WHITE, ANTISTATIC SIZE 7	UGX	26,700.00	$	24.52	5	$	122.61
GOGGLES/SAFETY GLASSES	UGX	21,100.00	$	19.38	10	$	193.79

Aim 2c: Patient Family Costs (Out-Of-Pocket Expenditure)

In the span of 6 months (between November 2016 – April 2017), 132 respondents participated in the out-of-pocket questionnaire. The average age of presentation was 2.17. All respondent families were from Uganda, distributed across 34 provinces throughout the country.

In the following section, “n” refers to the number of patient families, which could refer to one or more family members per unit. The most common home district was Wakiso (30.2%, n=35), followed by capital city Kampala (17.2%, n=20), where the Naguru OR is situated (Figure 4). Most respondents were mothers of the patient.

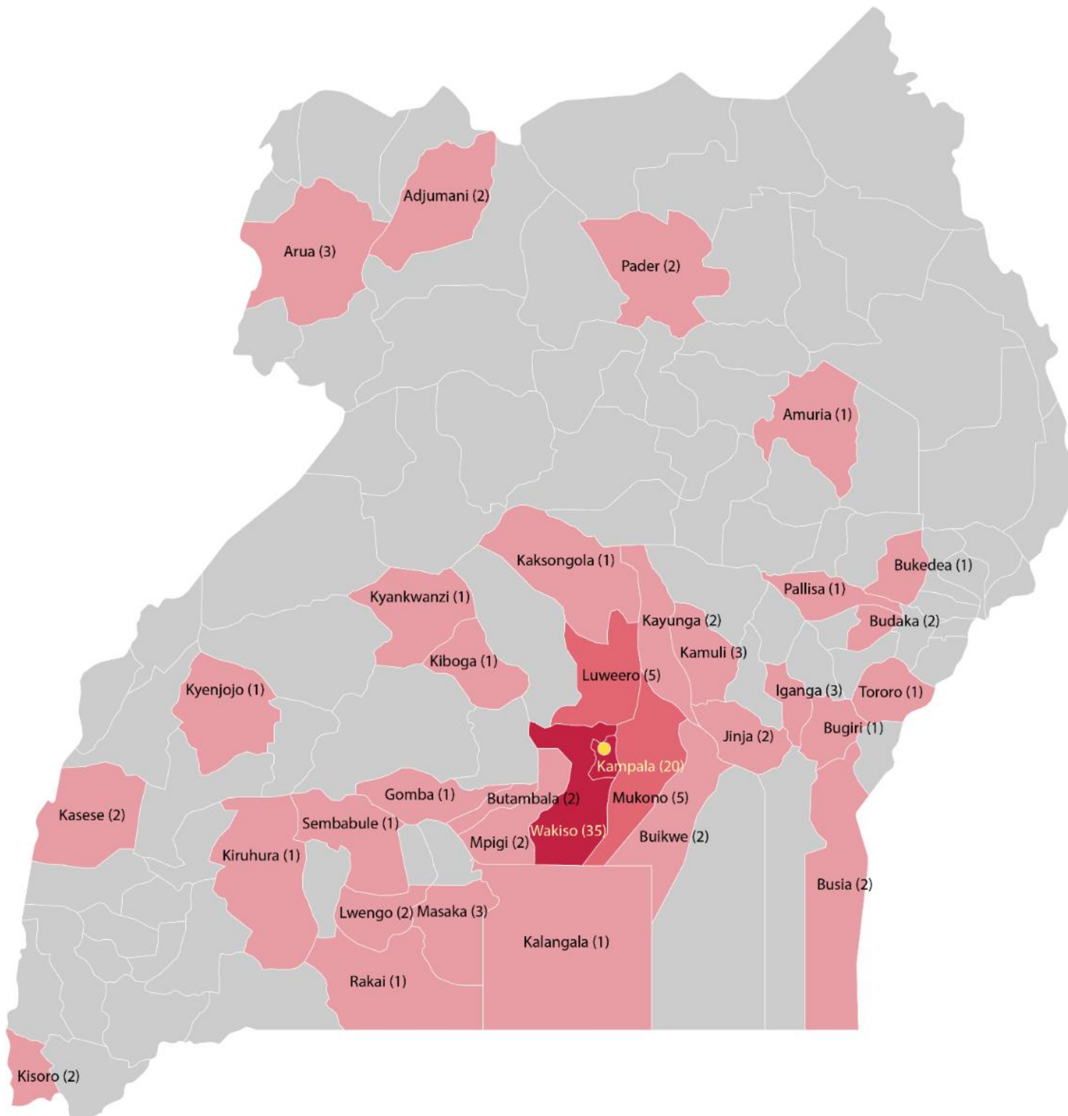
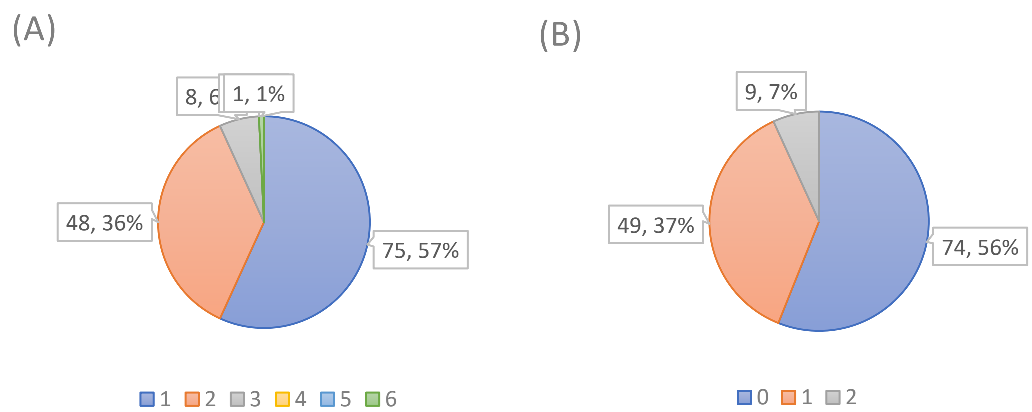


Figure 4: 34 districts of Uganda where the 132 out-of-pocket cost questionnaire respondents originate from. The yellow circle indicates the location of the Naguru OR, in the district of the capital city of Kampala.

The median inpatient waiting pre-operative period was 4 days, with the longest delay at 33 days. The median length of stay was 7 days, with the longest admission at 39 days. 14 patients underwent ambulatory hernia repairs that did not require overnight admission. All patients had family members present during the entire duration of the hospitalization, and most patients had 1 relative at bedside (57%, n=75).

Figure 5: (A) number of family members in the hospital per household (n=132); (B) number of working family members staying at the hospital per household (n=132)

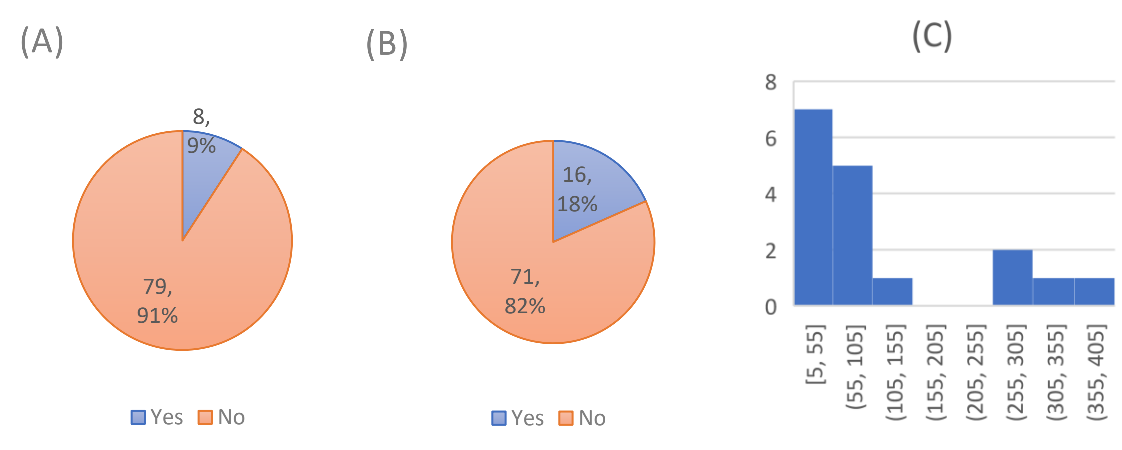


Majority of family members staying with patients were not employed (56%, n=74, Figure 5). Of the patients who were accompanied by working relatives (44%, n=58), 84% (n=49) had one working family member at bedside, while 7% (n=9) had two working relatives. Professions ranged from farmers and vendors with a daily wage of 3,000-10,000 UGX or less than 1 USD, to businesspersons who earned up to 100,000 UGX or 30 USD per day. Employees worked a median of 10 hours per day (range: 4-6 hours per day), and a median of 6 days a week (range: 1-7 days per week).

The missed days of work that these individuals accrued accounted for the economic productivity loss portion of the out-of-pocket costs. Of the 58 patients that had working members at bedside, the mean cost of productivity loss per household for patients with working family members at bedside was $235.18 (95% confidence interval or CI 148.73 – 321.63), and the median cost of productivity lost was $95.52. When including all the patients that did not have working family members (n =132), the productivity cost was reduced to a mean of $94.43 (95% CI 54.66 – 134.19). The median productivity loss dropped to zero, since more than half of the family members present at bedside were not employed.

Closely related to productivity losses were the proportion of families that needed to take out a loan or sell possessions to pay for hospitalization costs. 87 families agreed to respond to this portion of the survey. 18% of families borrowed money from their family or friends, at a mean amount of $105 (95% CI 81.7-129.53), and a median of $59.70 per household (IQR 33.29-126.28). 9% of families needed to sell household items, with possessions ranging from livestock (goat, pig) to furniture. Mean monetary value of sold items per household was $114.23 (95% CI 89.40-139.06), and median value was $64.29 (IQR 64.29-257.16).

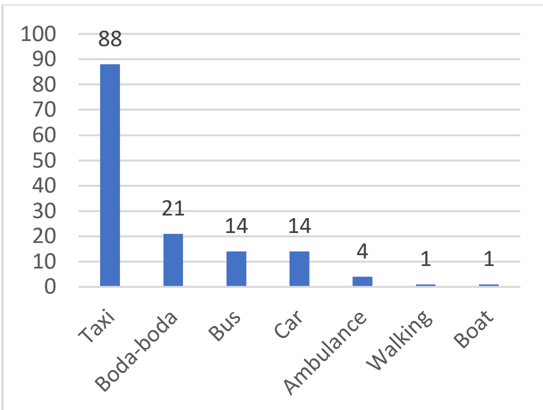
Figure 6: (A) proportion of households that sold items (n=87); (B) proportion of households that borrowed money (n=87) (C) Amount of money that households borrowed in USD (n=16)



Regarding transportation costs, private taxi was by far the most common form of transport, used by 61% (n=88) of patient families, distantly followed by boda-boda, which is a local motorcycle for hire (Figure 7). From Wakiso, transit time to and from the hospital was under an hour, and most patient families did not need to travel for more than a day.

Transportation costs ranged from a minimum of no money spent as one patient family walked to the hospital, to a maximum of 400,000 UGX or $367.38, spent by two patients: one who came by ambulance from the Kyankwanzi province, and another who travelled by private car from the province of Iganga (Figure 8). The mean cost of transportation was $42.59 per family (95% CI 32.58-52.60), and the median transportation cost was $26.63 per family (IQR 9.18 – 45.92).

Figure 7: Mode of patient transportation



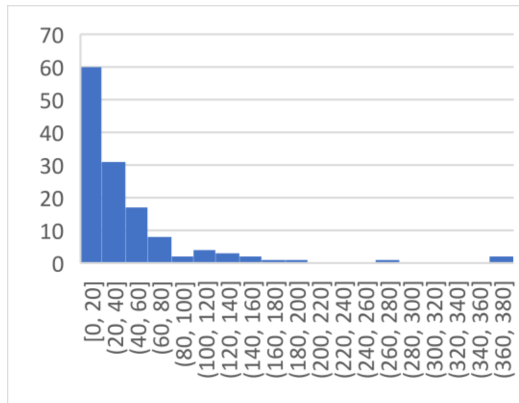


Figure 8: Transportation Cost in USD (round trip)

As the hospital does not support diagnostic imaging and more comprehensive laboratory tests, many patients were required to pay out of pocket for their own imaging and lab draws. A little more than half of the respondents had some diagnostic expense (51%, n=67). The average cost of each diagnostic test is shown, and the total mean cost spent on diagnostic testing per family was $120.41. Plain films and ultrasonography were the most common imaging tests purchased. The maximum amount spent on diagnostics per family was $688.83, which was the cost of the MRI study. The median cost of diagnostics per family was $27.55 (IQR 18.37 – 183.69).

Figure 9: (A) Distribution of diagnostic tests by type; (B) Total cost of diagnostic tests per family in USD (n=67)

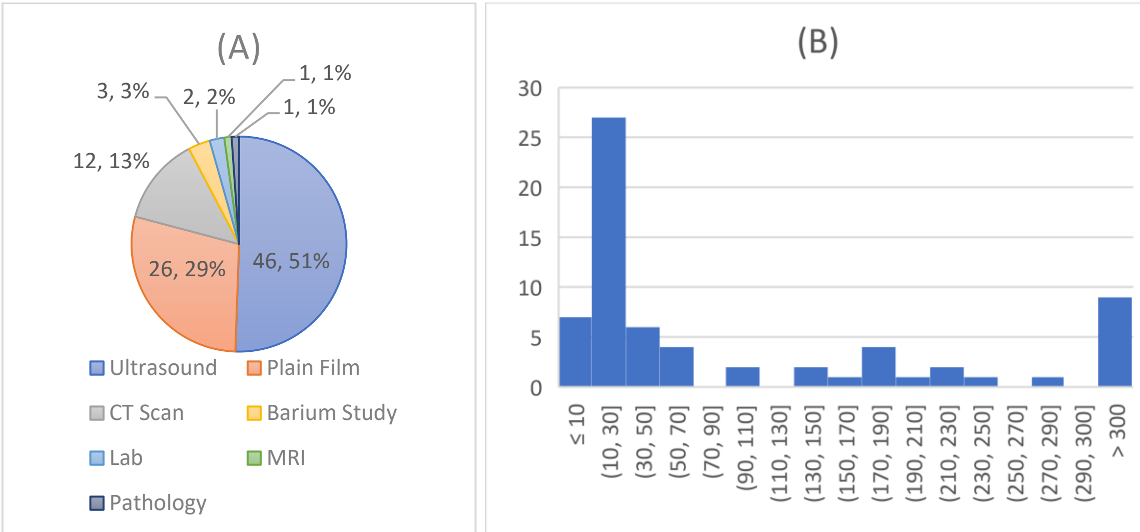


Table 6: Mean prices in Ugandan shillings and US dollars of diagnostic tests purchased out-of-pocket by patient families

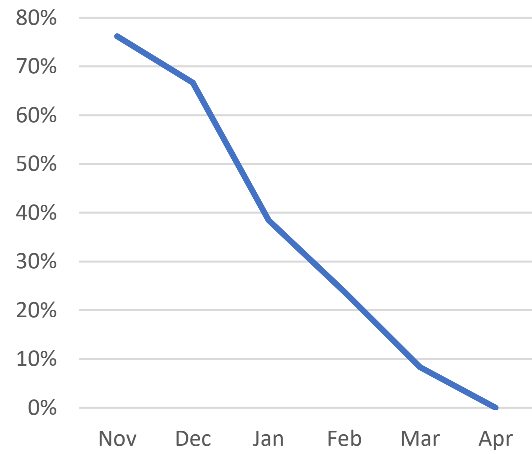
Diagnostic test	*#*	*Average Price in UGX*	*Average Price in USD*
Ultrasound	46	28,826.09	26.48
Plain Film	26	40,192.31	36.91
CT Scan	12	27.0833.3	248.74
Barium Study	3	136,666.7	125.52
Lab	2	57,500	52.81
MRI	1	750,000	688.83
Pathology	1	60,000	55.10

Costs of medications were obtained close to the end of the fiscal year, when the central pharmacy ran low in supplies. Therefore, patients had to frequently purchase their own medications from private pharmacies nearby for inpatient post-operative medications. Of note, frequency of medications purchased fell considerably starting January of next year, coinciding with the restocking of the NMS, with medication purchased by patients reaching 0% by April, although only 7 individuals were sampled that month.

Table 7: Percentage of patients purchasing OOP medications over time

MONTH	"YES"	#	%
NOV	16	21	76.19
DEC	14	21	66.67
JAN	10	26	38.46
FEB	5	21	23.81
MAR	3	36	83.33
APR	0	7	0

Figure 10: Trend of percentage of patient families purchasing medications out of pocket over time.



36% (n=48) of patient families in the 6-month period purchased medications from a private pharmacy, and most frequently bought from the closest located pharmacy next to the hospital. Rectal acetaminophen, intravenous dextrose and intravenous metronidazole were the 3 most common drugs purchased. The maximum amount a family spent on medications was $188.28 for a patient who required an extended duration of ceftriaxone and metronidazole. When averaging out the amount spent by families that paid for medications, the mean cost of medications per household was $30.83 (95% CI 21.00-40.66), and the median medication cost per household when factoring in all respondents was $18.36 (IQR 9.52 – 41.33).

Table 8: Prices and quantities of common medications purchased out of pocket by patient families.

REPRESENTATIVE MEDICATIONS	# OF FAMILIES PURCHASED	AVERAGE UNITS/ FAMILY	AVERAGE PRICE PER UNIT (IN UGX)	AVERAGE PRICE PER UNIT (IN USD)
ACETAMINOPHEN (5 X 125MG SUPPOSITORIES)	2	6.91	2,136.30	1.96
5% DEXTROSE IN WATER (500ML)	22	2.91	4,772.73	4.38
IV METRONIDAZOLE (500MG/100ML)	17	4.06	3,492.65	3.21
IV CEFTRIAXONE (1G INJECTION VIAL, POWDERED)	11	4.36	4,750.00	4.36
AMOXICILLIN SYRUP (250MG/5ML X 60ML)	1	1.00	3,000.00	2.76
SODIUM PHOSPHATE ENEMA (ENEMAX, 120ML)	2	1.50	18.500.00	16.99
IRON SUPPLEMENT SYRUP (HEMO-FORTE)	2	1.00	7,500.00	6.89
IV GENTAMICIN (80G/2ML INJECTION VIAL)	1	2.00	2,000.00	1.84

Figure 12: Distribution of OOP medication costs per household

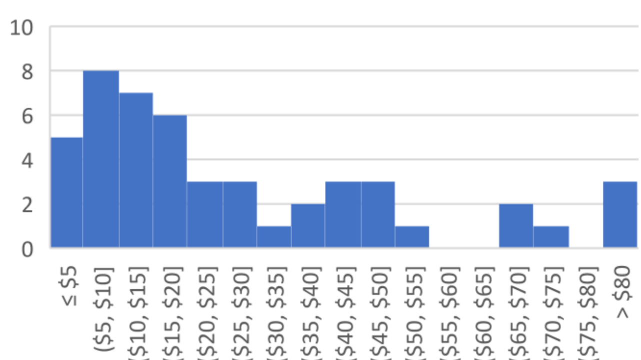
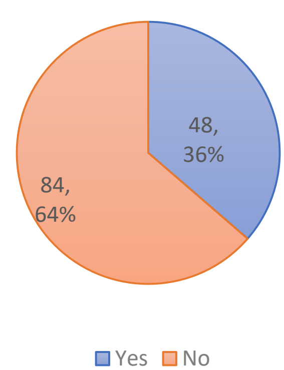


Figure 11: Proportion of households who paid OOP for medications

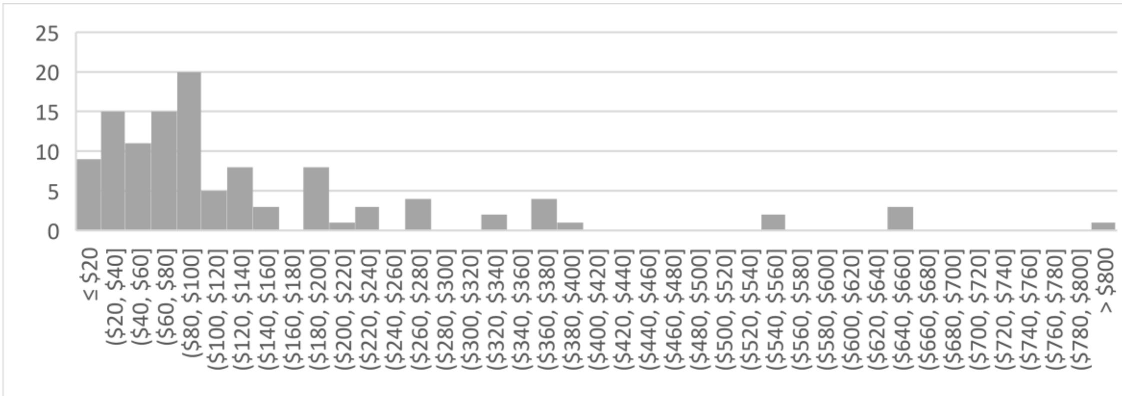


Food and lodging expenses were reported as a daily estimate from the respondents multiplied by the days of inpatient stay leading up to surgery, since discharge dates were not consistently recorded as surveys were usually administered inpatient. Mean daily lodging cost was \$10.12 per family (95% CI 8.95-11.28), and median daily lodging cost was \$9.18. Mean lodging cost per family during the total perioperative admission was \$59.80 (95% CI 44.90-74.70), and the median total lodging cost was \$32.60.

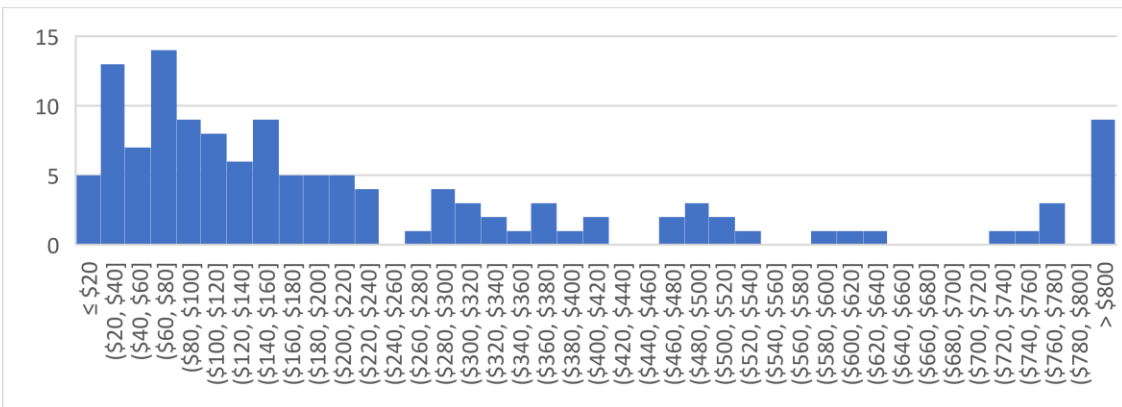
Estimated total cost per household reported by the family members for the duration of the hospital stay was a mean of \$139.81 (95% CI 111.49-168.14), and a median of \$91.85. Actual calculated OOP cost per patient family for the hospital stay was substantially higher at \$266.89 (95 CI 211.98-321.80), with a median total cost of \$150.62. The calculated mean cost was \$127.59 higher than the estimated mean cost, which was statistically significant ($p < 0.001$). Since the productivity loss cost was not traditionally counted towards direct costs and was more of an opportunity cost, the total OOP expenditure of direct costs excluding productivity loss had a mean of \$172.46, which was higher than the estimated reported OOP cost by \$33.16 ($p = 0.005$) (Figure 14).

Figure 13: Distribution bar plots of (A) estimated total amount spent OOP for the hospital visit (n=114); (B) calculated amount spent OOP for the hospital visit including cost from productivity loss from days of work missed (n=132); (C) calculated total amount spent OOP excluding productivity loss cost (n=132)

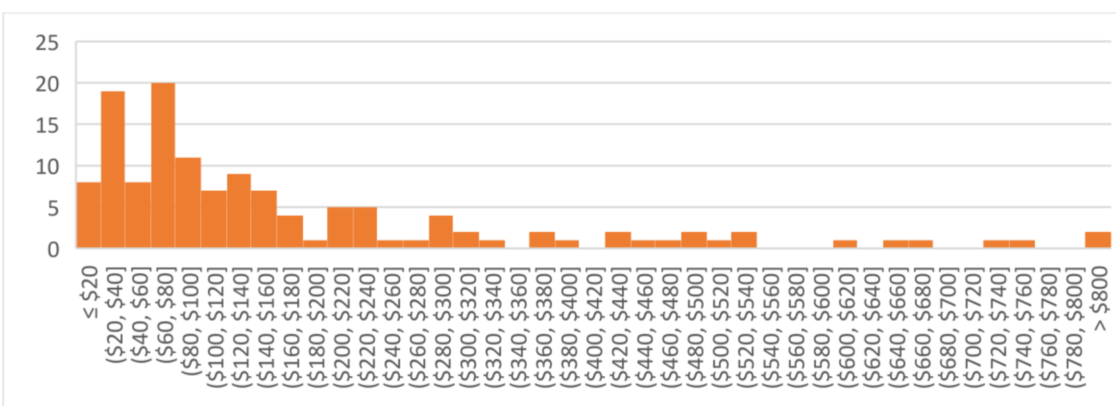
(A)



(B)



(C)



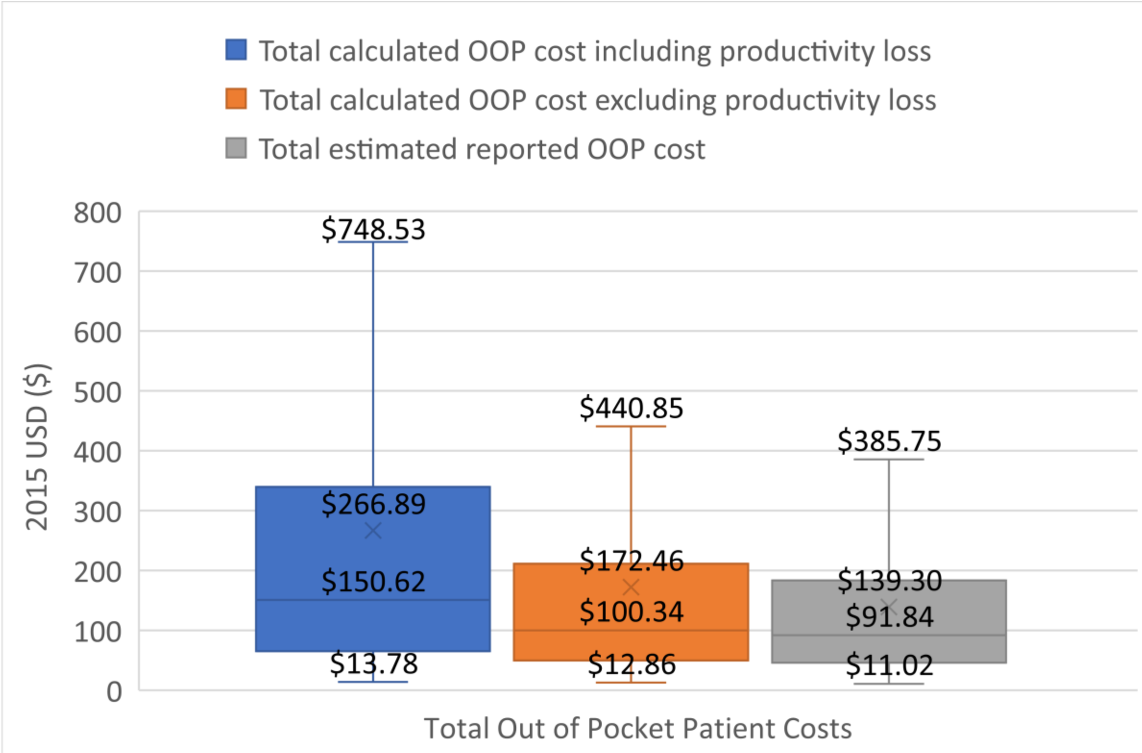


Figure 14: Box and whisker plot showing the comparison between reported estimated total OOP costs and actual caluclated total OOP costs, including and excluding costs due to productivity loss. Boxes depict interquartile ranges with the median shown as the dividing line, and the mean shown as the cross. Whiskers represent 1.5x interquartile range. Outliers are not presented. The percieved cost is significantly lower than actual total costs.

In Uganda, the average annual consumption expenditure per household in 2013 was $3,113 in 2015 US dollars, after adjusting for inflation rate and currency. Based on survey results, 36 out of 132 respondents, or 27% of households incurred CHE, defined as spending more than 10% of the average annual household expenditure (which meant spending more than $311.30 in Uganda). When productivity loss was excluded from the total calculated OOP cost for a hospital visit, 21 respondents, or 16% of households incurred CHE. In other words, 16-27% of households spent enough OOP to place them at risk of falling into poverty in the setting of inadequate financial protection, as stated by the World Health Organization. Figure 15 and 16 shows the breakdown of total expenditure of the sum of OOP costs for a hospital visit requiring an operation in the pediatric surgical ward. Notably, the opportunity cost from productivity loss comprised the largest proportion of all OOP spending.

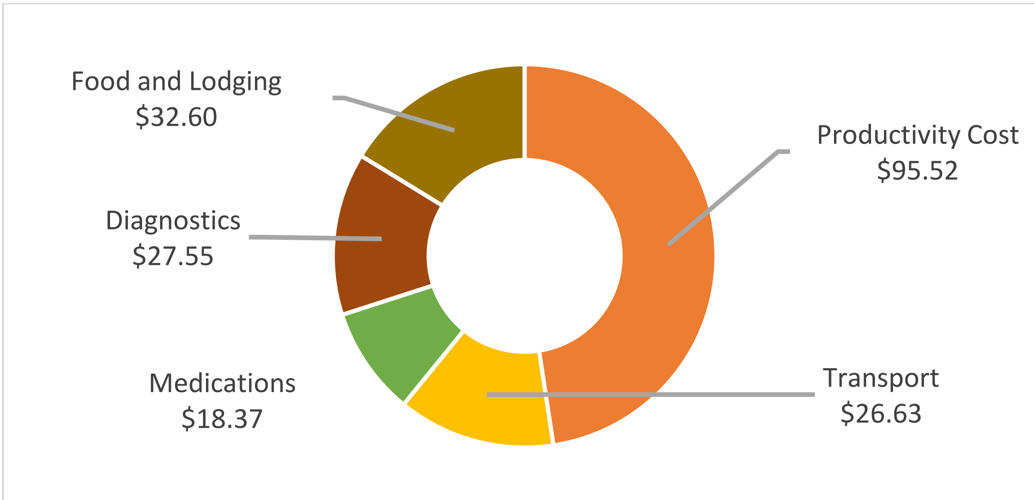


Figure 15: Breakdown of median Out-Of-Pocket Costs for an inpatient stay for pediatric surgery in Mulago Hospital. Note that these do not add up to the total average OOP costs for a hospital stay. See Figure 16 below.

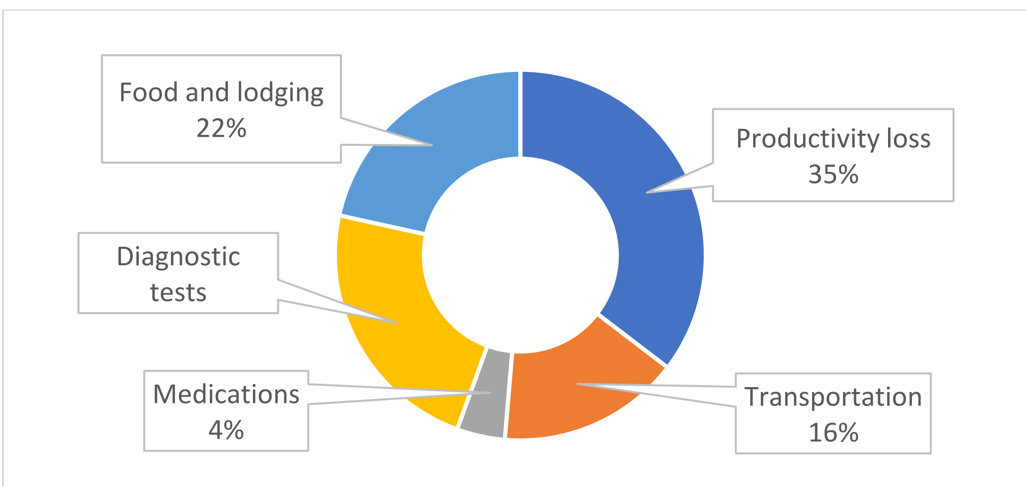


Figure 16: Proportion of the sum of out-of-pocket costs for an inpatient stay in each category.

Aim 3: Patient Outcomes in Disability Adjusted Life Years

Between April 2015 to April 2016, 326 patients with 48 unique pediatric surgical diseases underwent surgery in the Naguru OR, shown in Table 9 with corresponding frequency, DWs and corresponding 95% uncertainty interval (UI). Based on isolated analysis of the OR data using DWs previously reported by the Global Burden of Disease study and Poenaru et al.,[48, 50] a total of 3,973 discounted incremental DALYs were averted within the yearlong study period. Surgery for fatal congenital anomalies averted the most disease, and nonfatal congenital anomalies had the most cases (152 cases, 46.6%). (Figure 17)

Table 9: Disease Categories and corresponding interventions, case frequencies, age of presentation, disability weights with their 95% uncertainty intervals to inform distribution densities and source. ARM = anorectal malformation, PUV = posterior urethral valves, GBD = Global Burden of Disease Study 2013. Ex lap = Exploratory laparotomy.

Category 1: Elective Surgery		Surgical Intervention	N = 47	Age	Disability Weight (95% UI)	Disability Weight Source
1.	Rectal Prolapse	Mucosectomy	7	4.86	0.188 (0.125-0.267)	GBD (painful disfig. Lvl 2)
2.	Thyroglossal duct cyst	Excision	1	6.00	0.067 (0.044-0.096)	GBD (disfig. Lvl 2)
3.	Colostomy due to acquired disease	Colostomy reversal	16	3.08	0.106 (0.058-0.141)	GBD (stoma + disfig. Lvl 1)
4.	Ileostomy	Ileostomy reversal	12	5.51	0.209 (0.015-0.290)	GBD (stoma + AP problem Lvl 2)
5.	Lipoma	Excision	2	7.00	0.067 (0.005-0.021)	GBD (disfig. Lvl 2)
6.	Anorectal polyp	Polypectomy	2	2.79	0.067 (0.005-0.021)	GBD (disfig. Lvl 2)
Category 2: Emergent Cases		**Surgical Intervention**	**N = 28**	**Age**	**Disability Weight**	**DW Source**

7.	Esophageal strictures	Esophageal dilation	7	2.33	1	Fatal
8.	Intussusception (necrosis)	Ex lap, resection	2	0.21	1	Fatal
9.	Intussusception (reducible)	Ex lap, reduction	2	1.79	1	Fatal
10.	Appendicitis	Appendectomy	3	9.33	1	Fatal
11.	Primary peritonitis	Ex lap, drainage	6	5.25	1	Fatal
12.	Bowel perforation (necrotic)	Ex lap, stoma	1	7.00	1	Fatal
13.	Bowel perforation (salvageable)	Ex lap, resection, anastomosis	3	6.36	1	Fatal
14.	Wound dehiscence	Secondary closure	3	3.44	1	Fatal
15.	Intestinal Obstruction	Lysis of adhesions	4	5.79	1	Fatal
16.	Splenomegaly from lymphoma	Splenectomy	2	6.00	0.451 (0.307-0.600)	GBD (cancer, metastatic)
17.	Abscess/cellulitis	Incision and drainage	2	3.38	0.051 (0.032-0.074)	GBD (acute infection)
Category 3: Emergent Congenital		**Surgical Intervention**	**N = 65**	**Age**	**Disability Weight**	**DW Source**
18.	Intestinal atresia	Ex lap, primary anastomosis	19	0.13	0.758 (0.558-0.958)	Poenaru 2017 (Fatal)
19.	High ARM (1st presentation)	Colostomy placement	17	0.23	0.710 (0.510-0.910)	Poenaru 2017 (Fatal)
20.	Biliary atresia	Kasai's procedure	7	0.35	1	Fatal
21.	Gastroschisis	Reduction and closure	3	0.08	1	Fatal
22.	Pyloric stenosis	Pyloromyotomy	12	0.14	1	Fatal

23. Cloaca	Cloacal repair	3	1.50	1	Fatal
24. Cloacal exstrophy	Ostomy placement	3	0.58	1	Fatal
25. Choledochal cyst	Cystectomy	1	0.75	1	Fatal
26. PUV (temporary fix)	Vesicostomy	1	0.83	1	Fatal
27. PUV (permanent fix)	PUV ablation via cystoscopy	3	5.50	1	Fatal
Category 4: Non-emergent Congenital	**Surgical Intervention**	**N = 152**	**Age**	**Disability Weight**	**DW Source**
28. High ARM (post colostomy)	PSARP	24	2.08	0.451 (0.251-0.651)	Poenaru 2017
29. Hirschsprung's (1st presentation)	Colostomy placement	11	3.53	0.569 (0.369-0.769)	Poenaru 2017
30. Hirschsprung's (post colostomy)	Pull-through	8	3.21	0.351 (0.151-0.551)	Poenaru 2017
31. Vestibular anus (low ARM)	Primary repair	4	0.73	0.501 (0.339-0.657)	GBD (recto-vaginal fistula)
32. Other low ARMs	Primary repair	10	1.83	0.356 (0.156-0.556)	Poenaru 2017
33. Umbilical hernia	Herniotomy	13	4.37	0.080 (0.010-0.280)	Eeson 2015
34. Inguinal hernia	Herniotomy	23	1.76	0.096 (0.010-0.296)	Eeson 2015
35. Hydrocele	Hydrocelectomy	8	5.38	0.067 (0.044-0.096)	GBD (disfig. Lvl 2)
36. Undescended testes	Orchiopexy	14	5.36	0.317 (0.020-0.420)	Poenaru 2017
37. Hypospadias	Hypospadias repair	7	2.69	0.415 (0.214-0.614)	Poenaru 2017
38. Colostomy due to ARM	Colostomy reversal	17	2.46	0.209 (0.015-0.290)	GBD (stoma + AP problem Lvl 2)
39. Colostomy due to Hirschsprung's	Colostomy reversal	4	2.46	0.209 (0.015-0.290)	GBD (stoma + AP problem Lvl 2)

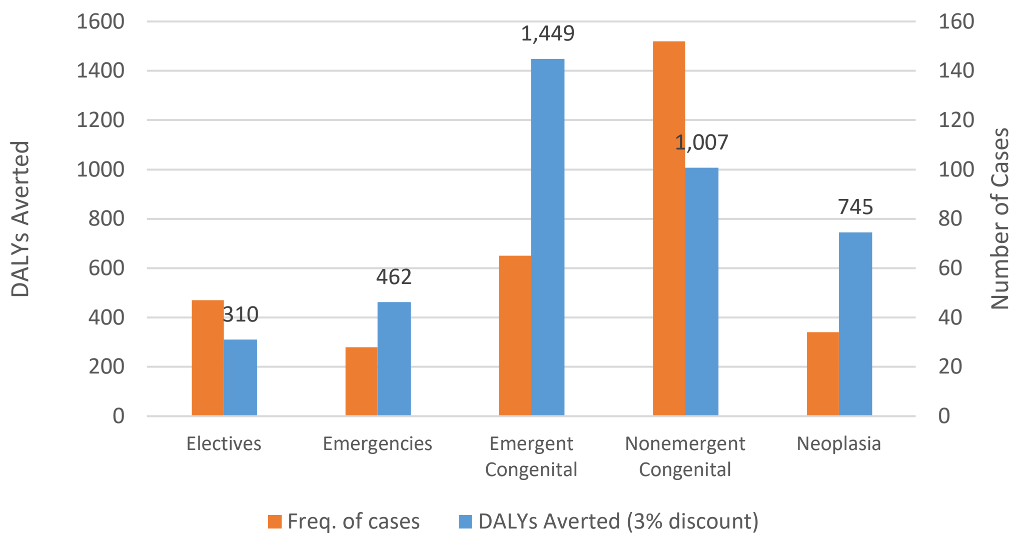
40.	Vesicostomy	Vesicostomy closure	2	2.50	0.106 (0.058-0.141)	GBD (stoma + disfig. Lvl 1)
41.	Phimosis	Circumcision	5	0.23	0.011 (0.005-0.021)	GBD (disfig. Lvl 1)
42.	Bladder exstrophy	Bladder Exstrophy closure	2	6.04	0.342 (0.227-0.478)	GBD (vesiculo-vaginal fistula)
Category 5: Neoplasia		**Surgical Intervention**	**N = 32**	**Age**	**Disability Weight**	**DW Source**
43.	Wilms tumor	Nephrectomy	18	3.72	1	Fatal
44.	Other lymphomas	Lymph node biopsy	1	7.00	0.451 (0.307-0.600)	GBD (Cancer, metastatic)
45.	Neuroblastoma	Ex lap, excision	3	10.00	1	Fatal
46.	Sacrococcygeal teratoma	Excision	6	1.33	1	Fatal
47.	Benign ovarian mass	Ex lap, excision	2	2.50	0.114 (0.078-0.159)	GBD (AP problem Lvl 2)
48.	Mass in limbs	Excision	4	6.00	0.067 (0.044-0.096)	GBD (disfig. Lvl 2)

Table 10: Basic patient demographics from the Naguru pediatric OR case-log.

NUMBER OF PATIENTS	**326**	
MEAN AGE (YEARS)	2.90	(3 days – 16 years)
FEMALE	117	(36%)
DISEASE GROUP		
- *ELECTIVE SURGERY*	47	(14.4%)
- *EMERGENCIES*	28	(8.6%)
- *EMERGENT CONGENITAL*	65	(19.9%)
- *NONEMERGENT CONGENITAL*	152	(46.6%)
- *NEOPLASIA*	34	(10.4%)

OUTCOME		
- DISCHARGED/TRANSFERRED	309	(94.8%)
- IMMEDIATE DEATH POST-OP	17	(5.2%)
- LIFESAVING PROCEDURES	123	(37.7%)
- DISABILITY AVERTING PROCEDURES	186	(57.1%)

Figure 17: Disease Burden Averted in 5 Disease Groups (in Discounted DALYs Averted).



Aim 4/5: Establishing Model Confidence with Sensitivity Analysis (Simulation ICER)

Randomization of Variables into the Simulation Model

A Monte Carlo simulation of the pediatric OR's annual costs and outcomes accounted for the variation of inputs that occurred from year to year. For example, the OR hosted the surgeries of 326 unique patients this year, but the caseload would almost certainly not remain at exactly 326 the following year, as the number of patients treated would fluctuate. Inputs that hold inherent variability and uncertainty were fitted with probabilistic distribution curves that were informed by empirical data available from the pediatric surgical database or existing price lists, or when unavailable, spread over a ±20% distribution of the reported value (Table 11). The distribution curves allowed randomization over continuous variables, which comprised most of the costs and all outcome variables.

Table 11: Input variables that contain inherent uncertainty, and their respective probability density functions to randomize and account for sources of uncertainty in the Monte Carlo probabilistic simulation model.

COSTS				
Input	***Category***	***Given Value***	***Density Function***	***Distribution Source***
Fixed large-scale equipment	Charity	$101,847.57	Gamma	±20%
Attending physician annual wage	Government - Wages	$ 2,413.74	Gamma	Table 2
Fellow physician annual wage	Government - Wages	$ 1,674.90	Gamma	Table 2
Resident physician annual wage	Government - Wages	$ 1,208.45	Gamma	Table 2
Senior Nurse annual wage	Government - Wages	$ 961.05	Gamma	Table 2
Registered nurse annual wage	Government - Wages	$ 664.83	Gamma	Table 2
Intern physician annual wage	Government - Wages	$ 710.06	Gamma	Table 2
OR attendant annual wage	Government - Wages	$ 493.58	Gamma	Table 2
Ward attendant annual wage	Government - Wages	$ 391.50	Gamma	Table 2
Perioperative medications	Government - Meds	Table 3	Single probabilities	Operative Reports [A]

Disposable equipment	Government - Equip	Table 4	Single probabilities	Operative Reports [A]
Reusable equipment	Government - Equip	Table 5	Single probabilities	Operative Reports [A]
Out of pocket family spending	Patient Family	$ 100.3	Gamma	OOP Surveys [B]
OUTCOMES				
Input	***Category***	***Given Value***	***Density Function***	***Distribution Source***
Disease disability weights	Patient Outcomes	Table 9	Beta	Table 9
Presentation Ages	Patient Outcomes	Table 9	Gamma, Weibull, Log-Normal, Triangle, Uniform	Table 9
Number of operations in a year	Patient Outcomes	326	Uniform	±20%
Probability of successful treatment	Patient Outcomes	Case-based	Beta	±20%
Probability of death after treatment	Patient Outcomes	Case-based	Beta	Pediatric Surgical Ward Database

[A] *Probabilities of the utilization of each drug were pulled from the OR anesthetic reports (n=114)*

[B] *Out-of-pocket surveys calculated total cost per family distribution (n=132)*

For medications and disposable equipment supplied by the NMS, costs were included per case based on a single probability of utilization drawn from the representative cohort of 114 anesthetic reports. For example, of the 4 anesthetic reports of vestibular anus repairs, 3/4 cases used succinylcholine, but none reported thiopental usage. Therefore, in the Monte Carlo Simulation, randomized cases of vestibular anus repair had a 0.75 probability of incurring a cost from using succinylcholine, but zero chance of incurring cost from using thiopental. There was no probability density function assigned to medication cost as a continuous distribution curve was not applicable to this type of parameter. In the model, variable costs of perioperative medications, reusable equipment, and out-of-pocket spending were accumulated and randomized per case. In contrast, fixed costs of large equipment, annual wages of OR staff, and reusable equipment were added on to the cost of each year and randomized as a lump-sum after the case-based variable costs were summated.

(18A) (18B)

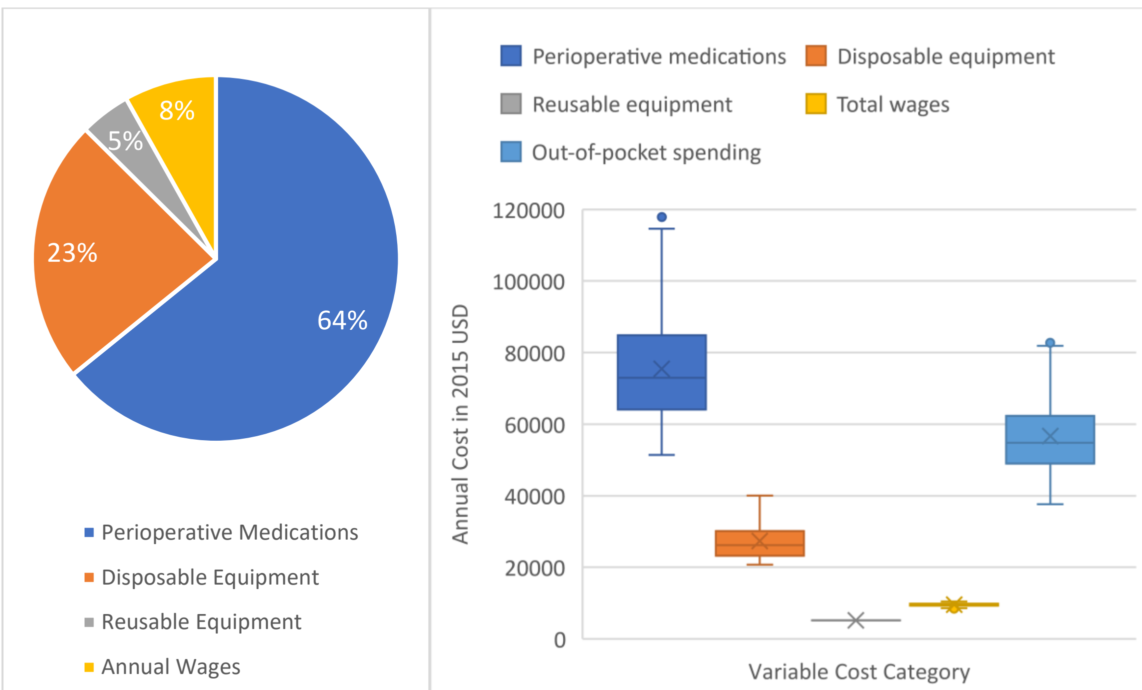


Figure 18: (A) Pie chart of the breakdown of medications and equipment purchased by the government in the Monte Carlo Simulation; (B) Box and whisker diagram depicting the spread of simulated values of government purchased medications, equipment, wages in the probabilistic model, with the out of pocket spending costs shown for comparison

Conducting the Monte Carlo Simulation to determine the ICER

A Monte Carlo simulation of 200 annual, facility-based iterations was performed for the pediatric OR model, which included all the above variables to produce cost and DALYs averted after one year of functioning OR. Accounting for annual inflation rate of 5.5% in 2015, mean cost of the OR was $240,526 (95% uncertainty interval (UI) 236,264-244,789). Mean simulation DALYs with 3%-time discount were 4,829 (95% UI 4,706-4,953) for the counterfactual with no OR available, and 1,825 (95% UI 1,774-1,876) for the pediatric OR intervention. According to the model, the incremental disease burden averted by the OR in one year amounted to 3,004 DALYs averted (95% UI 2,928-3,080). Mean simulation ICER was $80.06 per DALY averted (95% UI 77.77 -80.82), or $4,987.87 (95% UI 4,845.08-5,035.08) per life saved based on average life expectancy in Uganda in 2015 (62.3 years). The ICER was less than five percent and therefore well below the cost-effectiveness threshold of both one and three times Uganda's GDP per capita in 2015 ($2,026.71). In absolute terms, this meant that the intervention was likely cost-effective in the perspective of the Ugandan healthcare system. This ICER remained cost-effective when the highly conservative World Bank threshold of $240 per DALY averted was applied.

One-way deterministic sensitivity analysis was performed for plausible alternative case scenarios by changing parameters with significant variation. With all one-way scenario analyses, the ICER remained cost-effective and was relatively insensitive to scenarios for different time discounts of both costs and DALYs averted, DALYs age-weighting, market pricing for equipment, and a proportion of met need in the counterfactual (Table 12). The ICER was most sensitive to changes in the counterfactual scenario, with a scenario ICER of $100.08 after assuming 20% of the DALYs would be averted if there was no existing pediatric OR, or a change of 125% from the base case.

Table 12: One-way sensitivity analysis of different OR scenarios and cost perspectives.

Scenario (cost inflation, DALY discount)	***Incremental Cost***	***Incremental DALYs Averted***	***ICER***	***% of Base Case***
Base (cost 5.5%, DALYs 3%)	$240,526	3,004	80.06	100%

No discount (cost & DALYs 0)	$205,240	6,411	32.01	40%
DALYs Age Weight at 4%	$240,526	3,621	66.41	83%
Patient Perspective (OOP cost)	$56,647	3,004	18.86	26%
Government Perspective (wages & supplies)	$117,592	3,004	39.14	49%
Market Value of Costs (cost 5.5%, DALYs 3%)	$263,540	3,004	87.72	109%
No OR counterfactual meets 20% of need	$240,526	2,404	100.08	125%

The calculated and simulation incremental cost-effectiveness frontiers are shown in the cost-effectiveness plane. (Figure 19: Cost-Utility Analysis - Results of 200 Monte Carlo simulations with corresponding simulated ICERs.)

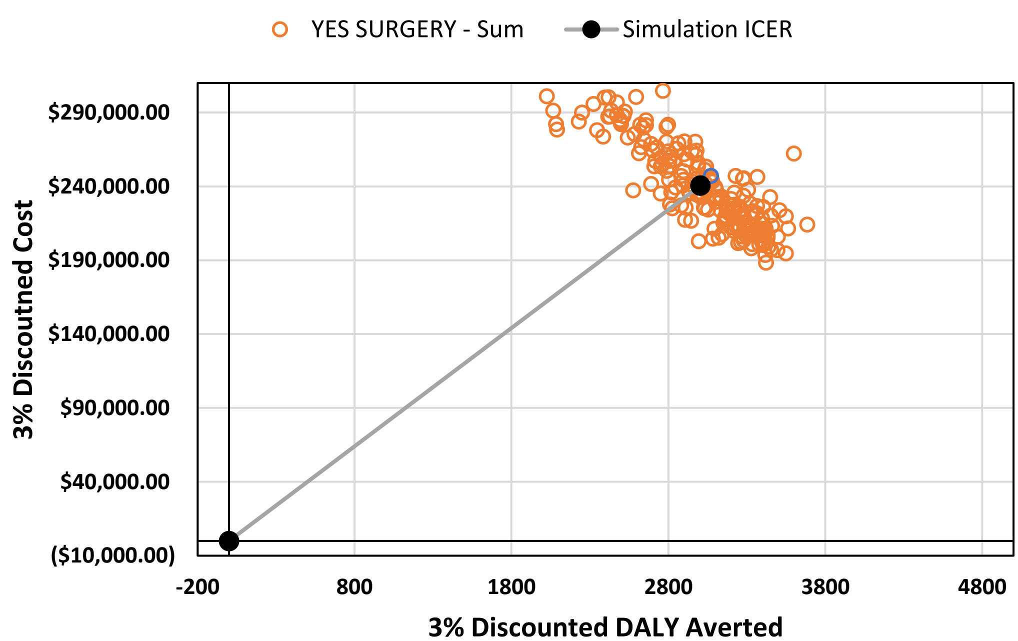


Figure 19: Cost-Utility Analysis - Results of 200 Monte Carlo simulations with corresponding simulated ICERs. Orange dots represent the incremental cost and DALYs as compared to the counterfactual.

Aim 6: Cost-Benefit Analysis

The economic benefit of the pediatric OR was derived from the DALYs averted multiplied by the value of a statistical life year in Uganda ($796.32 with a 3%-time discount). The net economic benefit (NMB) of the pediatric OR was $2,392,337.87 in a year, or $6,428.16 per patient. The NMB was divided by the annualized cost of the functioning OR to calculate the economic productivity earned, with a return of investment of $37.42 per every dollar spent on OR operation. The likelihood of the pediatric OR being cost-effective is represented in the NMB curve (Figure 20), spanning a range of stakeholder's willingness to pay (WTP) thresholds per incremental DALY averted. The pediatric OR became more cost-effective than no intervention at a WTP level of $81.06 (X-intercept in Figure 20). In other words, a stakeholder should decide to invest in the construction and upkeep of a pediatric OR rather than do nothing if they value averting a DALY at $81.06 or more.

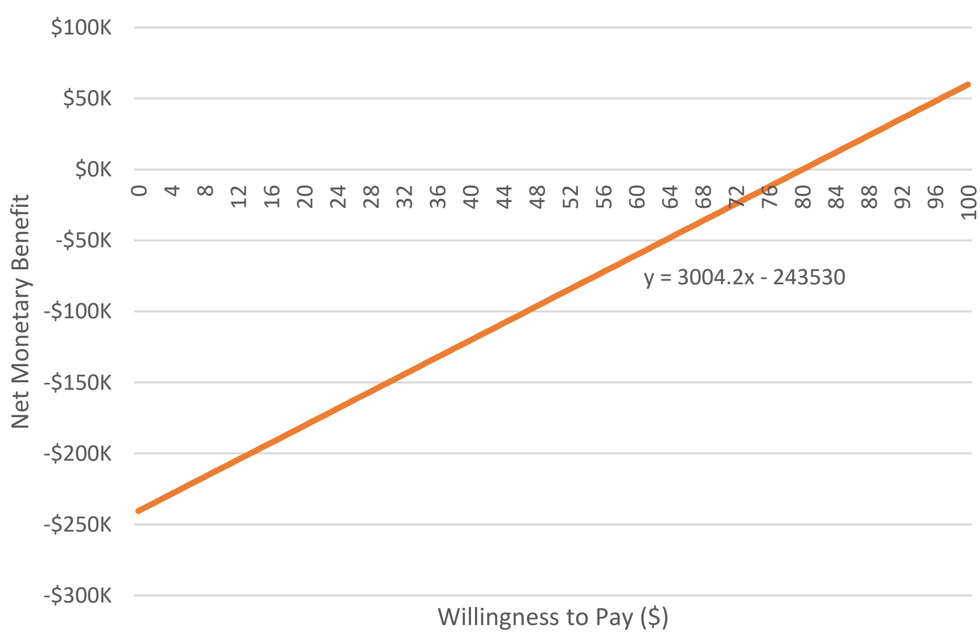


Figure 20: Net monetary benefit for a range of willingness to pay thresholds.

Discussion

To our knowledge, this is the first study to report the cost-effectiveness of a dedicated pediatric surgical facility in a low-income setting. We used a decision tree model and probabilistic Monte Carlo simulation to emulate one year of functioning pediatric OR time over multiple iterations. The decision tree allowed for a malleable skeleton with manifold input variables that could be adjusted to fit the characteristics of each disease and intervention scenario. The inclusion of multiple cost perspectives from the patient, government, and charity ensured a comprehensive estimate of the monetary investment, while the incorporation of the OR case log with over 300 cases adequately informed the patient outcomes to reflect realistic disease burden averted. The yearlong timespan also allowed for an extended period of observation to account for the background noise that may distort results over a shorter study duration.

Data Collection on Costs

Government Perspective: Wages were included as a conservative measure, since the hospital staff would still be employed on a flat rate salary regardless of whether the OR existed or not. Nevertheless, it was prudent to anticipate the possibility that these workers would find work elsewhere if the pediatric OR did not exist. Therefore, the cost differential for wages was factored into the OR intervention when compared to the counterfactual. The most significant finding was the relatively small range of $2,152.98 among worker salaries across the job hierarchy, which may demonstrate some amount of income equality within the public sector. However, absolute values of the incomes were consistently low across the entire salary scale, and only the fellow and attending physician earned marginally more than US minimum wage. When asked about the adequacy of their paychecks, attending physicians and interns divulged that they must find work outside their public service or ‘hustle’ to make a living, which usually entailed a privately paid position that offered more income, according to empirical accounts.

The combined load of working two jobs made it difficult for the attending and resident physicians to remain present at the public hospital to oversee patient care, hampering teaching and learning experiences and quality of clinical care. Attention must also be brought to the comparative wages between private and public sectors and across nations, as income disparity continues to spur a brain-drain towards more lucrative practices and higher-income countries, including the United States.[66, 67] As a result, local government hospitals could be left with a dearth of competent practicing specialists, especially in fields that require many several years of training which accrue considerable financial debt (a cost-analysis study in Mozambique reported that obstetric specialists spent a total of $74,130 and 11 years in training).[68]

In our model, perioperative medications (anesthetics, analgesics, and pre-operative antibiotics) took up the largest proportion of costs from the public perspective, accounting for more than two-thirds of government expenditure (Figure 18A). This could be related to the single use of anesthetics, the high unit prices for some of the less commonly available medications, and the specialized needs of the pediatric patient population, who might require tailored anesthetic regimens due to their increased sensitivity to medications and small body habitus (e.g. using ketamine instead of thiopental for induction to prevent hemodynamic instability). The most expensive medications that were frequently used were the inhaled anesthetics (halothane and isoflurane), atracurium or an equivalent muscle relaxant, and fentanyl. Rescue drugs such as epinephrine, atropine, and lidocaine also added significantly to the medication cost, as they were routinely freshly prepared as solutions prior to every operation, even though they were only sparingly administered for the rare instance of resuscitation. Simulated medication cost was somewhat sensitive to randomization and exhibited values over a range of $51,418-117,870, which was reasonable as medications were a function of patient number and presentation age. However, the variation was not sensitive enough to affect the pediatric OR ICER in the Monte Carlo simulation, which remained cost-effective.

Disposable and reusable equipment comprised a relatively small portion of government spending, which was likely due to the bulk purchase of these items in large quantities at the national level. The equipment costs were relatively insensitive to randomization, with a narrow range in the Monte Carlo simulation ($20,761-40,081 for disposable equipment, no variation in reusable equipment). This was expected as less variation occurred in equipment utilization between different procedures. For instance, each operation required the basic set of endotracheal tube, intravenous catheters, syringes, scalpels, and stitches. Longer cases (e.g. nephrectomies or bowel resection from atresias) had additional requirements for a urinary catheter, colostomy bag, and/or an nasojejunal feeding tube, and these procedure-specific items which were also incorporated into the simulation model.

Patient's family perspective: The overall median OOP cost for patient families was $150.62 per family per hospital stay, and consisted of the five categories: transportation, food and lodging, diagnostics, medications and productivity loss. At least 16% of households incurred CHE from direct medical and non-medical costs. When cost from productivity loss was included, the proportion of households incurring CHE rose to 27%. Both percentages were unexpectedly high considering that Mulago Hospital provides bed-space, operative facilities, and a daily meal, and healthcare should be free of charge to patients.

To date, this is the first report of OOP spending from the patient's perspective in a pediatric surgical setting in a LIC, though we could compare this study to related studies on OOP spending in the adult population in the same region of Sub-Saharan Africa. A study of Rwandan adult patients with peritonitis requiring surgery reported similar numbers, with 28% of patients at risk for catastrophic health expenditure when non-medical expenses were included.[69] The study did not however look at the cost of productivity loss from missed days of work. Our CHE percentage was also slightly lower than a previously reported 31% of Ugandan households incurring CHE in a rural regional referral hospital for all surgical and obstetric procedures[70].

Difference in hospital location may have accounted for the lower rate of CHE in our study, as Mulago Hospital is situated centrally in the capital city of Kampala and may attract families with higher income living in urban areas. Families that did not have the funds to transport their child to the national referral hospital from distant rural communities would not be able to take part in the survey, whereas a rural regional referral hospital may be more accessible to these patients. The indirect consequence was demonstrated in the Lancet Commission CHE simulation study, which showed that a higher proportion of patients in LMICs experienced CHE compared to that of LICs, presumably because a higher number of patients was able to access the hospital to have the need to pay for healthcare in the first place.[3, 31]

Pediatric patients might enjoy access to a larger resource pool compared to adult patients, as the combined family unit from parents who had potentially planned for a child could provide more social support compared to that of a single adult. Nevertheless, 16% of families subjected to catastrophic expenditure indicates a critical need for alleviate these OOP costs to sustainably provide surgical care indiscriminately to all wealth demographics.

To be sure, financial protection from CHE is key indicator in the Lancet Commission of Global Surgery, which sets the target to protect 100% of OOP surgical costs by 2030. Unfortunately, the gap in financial protection is still tremendous, as the Lancet model predicted

82.3 million cases of catastrophic spending due to surgical care annually, and 3.7 billion people (or approximately half of the world's population) were at risk of catastrophic expenditure should they need surgery, with the bulk of these individuals residing in sub-Saharan Africa and southeast Asia (Lancet Commission: key message 3).[3, 31, 71] Furthermore, a disproportionate burden of the cost fell on indigent patients. The world's poorest patients were 61 times more likely to suffer from CHE compared to the richest patients.[3]

Our patients' families OOP costs were derived mainly from productivity loss (33%) and to a lesser extent food and lodging, even when little less than half the family members were employed. The low employment rate could reflect the country's working demographics and the distinction between employment and work, as 43.2% of the working age population (16-64 years) were subsistence farmers and did not earn a solid for-profit income.[44] We could not to characterize this loss of farmed produce as we were only able to record the money that families earn. Therefore, the calculated loss was probably an underestimation of the actual productivity loss due to the missed opportunity to harvest crops. Nevertheless, the large proportion of OOP cost consisting of productivity loss was an important discovery, as other existing studies on surgical OOP spending did not account for the cost of missed days of work, although one study did report the proportion of jobs lost due to surgery.[70] It would be prudent to include the opportunity cost of forfeited wages in future OOP spending studies.

Five to six medications were purchased at a high frequency by families (acetaminophen, antibiotics and intravenous dextrose), which seemed to correlate with items that were in short supply in the NMS. A possible solution to this shortage would be to increase NMS stock of these medications, which might in turn reduce the need for families to purchase pharmaceuticals outside the hospital. However, the proportion of OOP cost attributable to purchasing medications was only 4%, so focusing on financial interventions may not prove as effective. A noticeable drop in family-purchased medications occurred in the latter portion of data collection – between January to March of 2018 (Figure 10). This substantial reduction in OOP medication costs could be explained by the NMS restocking at the end and beginning of the fiscal year, which is further evidence that patient purchased medications were responding to the lack of medications available in the hospital ward. In contrast, the costs and frequency of patient purchased diagnostics remained largely constant over the study period, as the supply of these tests were not replenished yearly.

A significant difference was also observed between perceived and calculated total costs, as patients consistently underestimated their OOP spending. This was especially apparent when productivity loss was taken to account, which was a large component of their total OOP cost. Nevertheless, the estimated cost was also significantly lower than the calculated OOP spending that only included direct costs. This underestimation could indicate unawareness of the financial burden that surgery posed for the patient's family, which could contribute to the caregiver's insufficient preparation to handle the child's healthcare expenses. A further exploration into the Ugandan family's ability to pay for its medical and surgical needs is warranted.

Relatedly, a significant proportion of families had to borrow money (18%) or sell household items (9%) to pay for their child's surgical care. This was also observed in a regional referral hospital of Uganda, albeit at a higher percentage of 53% and 21%, respectively, and the difference could again be accounted for the rural location of the hospital and the lower socioeconomic status of the surrounding patient population.[70] A OOP study of a district hospital in India showed that 47.2% of the poorest 20% of the population borrowed money to pay for surgical care, although the prevalence of catastrophic expenditure was much lower at 5.6%.[72]

Outcomes and the Cost-Effectiveness Analysis

Based on our economic model, the first dedicated pediatric OR in Uganda has an ICER of $80.06 per DALY averted, and a $4,987.87 per life saved compared to the prior practice where there was no consistently available curative treatment for pediatric surgical disease. Following the current WHO guidelines, the OR appears to be well below the cost-effective threshold of three times the country's GDP per capita, or $2,026.[53] However, the validity of the WHO-CHOICE method for establishing cost-effectiveness has been recently called into question for being too forgiving. To address this issue, we were also able to show that this intervention is also lower than more stringent willingness to pay thresholds, including one times the country's GDP per capita and the World Bank threshold of $240. We also showed that the OR intervention became cost-effective at a willingness to pay level of $81.06. Since the intervention stayed below multiple established cost-effectiveness thresholds, installing a pediatric OR in Uganda is likely a cost-effective healthcare strategy.

Perhaps the most significant interpretation of this study is the comparison of the OR ICER to existing (surgical and non-surgical) healthcare interventions, which demonstrates its strength as a cost-effective program. To our knowledge, this is the first study to examine the cost-effectiveness of a pediatric operating room in a LIC, as most studies focus on disease-specific interventions, and cost-effectiveness studies in pediatric surgical disease are still sparse in general. We can nevertheless compare this intervention to existing inventions within the area. As these comparisons are made, it is judicious to recognize that the methodology of the CEA varies among studies, as different costs and outcomes may be included or omitted depending on the scope of the analysis and data collection, which leads to varying degrees of study sophistication. Nevertheless, CEA and healthcare intervention ICERs usually encompass the major components of the intervention under scrutiny, so there is underlying value to cross-study comparisons.

A systematic review of 26 CEA studies showed that many essential surgeries had similar cost-effectiveness to that of non-surgical medical interventions such as vaccines or antiretroviral therapy in resource limited settings.[16] Our pediatric OR ICER was comparable to offering the BCG vaccine in low income countries ($51.86-220.39 per DALY averted).[16] Despite the general perception that surgical intervention would be unacceptably costly, the pediatric OR was approximately 10 times more cost-effective than anti-retroviral therapy treatment for HIV in Sub-Saharan Africa, with ICERs ranging from $350-$1,494 per DALY averted.[16]

In a Kenyan refugee camp, where a mere 13.5% of surgeries needed for common congenital conditions was met, the cost-effectiveness of congenital anomalies ranged from $40-88 per DALY averted.[26] Our ICER was higher than pediatric inguinal hernia repair in Uganda, which was another very cost-effective procedure at $12.41 per DALY averted. [27] This finding could be explained by our OR model's increased cost by treating more complex pediatric surgical conditions and the inclusion of an inpatient stay, both which an elective hernia repair would not require. Meanwhile, our ICER was similar to that of a cleft lip repair in the same region, a procedure with a mean averted 3.7 DALYs per patient, at a ICER of $81/DALY averted.[56]

We can also look at comparisons between facility-based CEAs. The OR ICER fared well when comparing to other studies that analyze OR related interventions or surgically oriented infrastructure. Even as a specialty service provided in a quaternary hospital center, the pediatric OR ICER sat squarely within the ICER range of surgical services provided at district hospitals worldwide ($42.78-121.86/DALY averted).[73] It was significantly lower than surgery offered at a trauma center in Nigeria ($183.42/DALY averted) and another in Haiti ($237.80/DALY averted).[18] Our ICER was also lower than that of the private hospital in India at $165/DALY averted[20], although it was higher than that of a small hospital in Sierra Leone (with ICER of $39.83/DALY averted).[74]

The pediatric OR's relative low ICER is likely due to the following reasons: (1) young patient demographics, (2) life-saving procedures, and (3) relative low cost of living in Uganda. The first two reasons both contribute to a large amount of DALYs averted. The young age of pediatric patients allows for substantial potential disease burden averted per patient. Furthermore, a large proportion of the surgical procedures are considered life-saving, and therefore the DALYs averted are whole life-years, not just years lived in disability. This is a significant distinction since previous cost-effectiveness studies on pediatric surgeries revolve mainly around disability averting procedures such as cleft lip/palate repair and inguinal hernia repair. The last reason is due to the low-income level of Uganda, allowing for purchases of relatively inexpensive capital and services, even when PPP is accounted for.

Of note, our empiric evidence on patient outcomes included discharge or death post-operatively, which means that our outcomes data were informed by actual patient prognosis. This type of real-time verification of patient outcomes is not usually available in cost-effectiveness studies. Other studies derive data mainly out of case logs that have little or no outcomes data and must rely purely on theoretical parameters. Thus, this added empirical data for patient outcomes is a strength in our study.

Casting implications of the study more broadly, the cost-effectiveness analysis methodology is not currently widely adopted to aid decision-making in LICs like Uganda, especially in the surgical sphere. Nevertheless, stakeholders express resounding enthusiasm to take advantage of this analytical tool. One recent study showed 78% of advanced healthcare personnel in Uganda had no exposure to CEA, even though 95% perceived this method to be important for clinical and policy decision-making.[75] In utilizing this analysis through the collaboration of local partners in the Ugandan healthcare system, studies like this could introduce key economic evaluation methods into the medical and public health education system as an important component of healthcare investigation. By demonstrating that the CEA can be valuable in informing healthcare policy changes in the resource limited settings of Uganda, this study could act as a knowledge broker in formulating a scholarly directive to further pursue economic analyses on complex healthcare decision-making.

Limitations

Costs: Accurate simulation to model medication utilization and cost was limited by small disease-specific sample sizes, as some diseases had only one accessible anesthetic report at our disposal. These conditions included splenomegaly, polycystic kidney disease, wound dehiscence, hypospadias, cloacal exstrophy, primary peritonitis, abscess/cellulitis, hydrocele, and lymphoma. Two main reasons limited the amount of anesthetic medication data that could be acquired. First, a large proportion of paper anesthetic reports could not be retrieved because patient charts were unable to be located after the pediatric ward relocated to a temporary site to adapt to the ongoing hospital renovation. Second, some of the pediatric surgical conditions were relatively rare and appeared in the OR case-log infrequently, which meant that the original sample size was small to begin with. Nevertheless, these limitations did not significantly hinder or deviate the calculation of medication costs, since the rare procedures did not contribute heavily to the total medication cost as the number of cases was so low.

The post-operative inpatient medication costs supplied by the government (and therefore not out of pocket) were also unattainable, since there was not a consistent record of the complete list of medications that was administered post-operatively to each patient in the operative reports or patient charts. However, a sizable proportion of these costs were captured in the out-of-pocket spending from families, as they frequently paid for post-operative medications when hospital supplies were running low.

Another limitation was the lack of empirical data to support the calculation of disposable equipment costs supplied by the NMS, as the model assumed that the inclusion of these items was constant regardless of operation type or duration. Some adjustments were made based on the complexity of surgery and patient age, but the equipment cost did not vary substantially between surgeries overall. Nevertheless, since these costs did not make up a large part of the overall costs from the government perspective, our assumptions did not interfere significantly with the final results in calculating the OR ICER.

In terms of large-scale equipment, maintenance staff wages and transport costs for personnel conducting check-ups were not included, although calculation of equipment costs based on the lifetime of the equipment accounts for gradual degradation over time, so upkeep costs were not necessary. Our model also used cost values derived from the charity's perspective, which were lower from the market value, though we included the market values of equipment in our one-way scenario sensitivity analysis.

Costs of ancillary services such as utility bills (electricity, water), administrative office space and staff, and OR space lease were also excluded from the study. This omission was made under the assumption that these resources were utilized and paid for regardless of the pediatric OR existence, as the charity's mission involves furnishing an OR in an available, previously existing space within the infrastructure of a fully functional hospital. For example, electricity and water were paid for by the government annually in a predetermined bundle at Naguru Hospital.

Collection of OOP spending costs was limited by survey setting, as questions had to be simple and non-sensitive so that families felt comfortable answering them in the busy pediatric surgical ward. As an anonymous survey, we relied on participants' memories of what they purchased, which may be subject to recall bias and we had no way of verifying the responses. This margin of error was minimized because the survey components were drawn from previously validated surveys, and the questions coincided with the inpatient stay so that the family's perception of their hospital expenditure should be up-to-date and accurate. We did not ask about monthly patient income, as a significant proportion of participants did not have a steady monthly wage or were unemployed. Moreover, as the survey was conducted in a public atmosphere, potentially sensitive topics such as socioeconomic status were waived. We also did not ask questions such as informal payments made to receive care, or the possibility of job loss due to hospital stay for similar reasons, though the opportunity cost based on the productivity loss from days of work missed served as a proxy. Furthermore, we could not calculate the respondents' household annual expenditure as we could not reliably ask participants for estimates on the families' spending in the last year. Instead, we used the average annual expenditure obtained from a national census, which provides a good approximation.

Outcomes and cost-effectiveness analysis: The biggest limitation of the sensitivity analysis and simulation model construction was the lack of supporting data surrounding the counterfactual. We assumed that in the absence of the OR, no surgeries occurred, and all patients lived out their natural diseases. Realistically, the pediatric surgical healthcare personnel pre-dated the OR and were trained to perform surgeries in adult ORs, so some surgeries would have been performed regardless of the presence or absence of the pediatric OR. However, since no pediatric OR existed in the country before this operating theater was constructed, pediatric surgical cases were performed exclusively in Mulago Hospital's adult surgical service. Fierce competition for the limited ORs amongst all surgical departments resulted in surgical treatment in only a fraction of life-threatening conditions. The construction of the Naguru OR allowed surgery for a variety of pediatric surgical disease to become much more feasible, especially for non-emergent and/or elective disease that still required treatment to avoid major disability later in life (e.g. Hirschsprung's).

The nature of pediatric surgical disease did not usually allow for significant non-surgical treatment alternatives, as the characteristics usually involve an anatomical defect that required manual repair. Since these patients will inevitably either live on handicapped by the disease or perish without life-saving surgery, it was reasonable to assume that the natural course of disease was likely in absence of surgery. This assumption did not account for the patient's family's search for alternatives either within or outside the formal health care system, as families tend to seek care through traditional African healers before consulting established medicine. Nevertheless, we did not include this alternative into the analysis because it would be impossible to quantify these costs, and their exclusion in fact rendered the OR cost calculations to be more conservative, as the counterfactual would have cost more.

To complicate matters, the hospital housing the pediatric surgical ward was under renovation at the time of this study, and the number of these hypothetical surgeries performed in previously existing ORs would be substantially lower than previous years. These unusual circumstances make the counterfactual difficult to quantify, because the proportion of surgeries that would have been completed if the main hospital was either fully or partially functional is unknown. Therefore, the study instead compared the best and worst-case scenarios, the best being a fully functional OR available for pediatric patients, versus no access to an OR at all. Generalizability is limited to a new pediatric OR introduced into a healthcare naive setting where no prior pediatric surgical service was available.

To partially address the uncertainty of the counterfactual, a scenario one-way analysis was performed where 20% of the disease burden was averted by existing hospital services without the pediatric OR. This scenario served to simulate this situation of partial met need, and its ICER remained robust.

In terms of calculating health utility saved, there were limitations to precisely gauge the actual disease prevented. It was known that the OR was not functioning at full capacity due to staff and resource constraints occurred throughout the year. Furthermore, the OR was also shared by three other surgical specialties that occupied about a third of the total operative time. Therefore, DALYs averted may have been underestimated as the fully functional potential of the surgical unit was not realized, and a substantial proportion of performed cases were omitted. Furthermore, since the OR allowed for elective cases to be treated that were previously backlogged, emergent cases may have been underrepresented since they were usually shuttled to the first available OR, which was likely an adult OR. The resulting selection bias might have lent itself to capturing less life-threatening cases, and therefore less disease burden averted.

The diverse disease pathology which ranged from simple hernias to complicated cloacal malformations posed substantial challenges to determining disease DWs and treatment probabilities. Some of the disease DWs, PSTs, and residual burden were estimated from expert opinion and may be subject to bias, as there has been little standardization on pediatric conditions in current literature, as shown by the exclusion of pediatric surgical DWs in the Global Burden of Disease studies. Therefore, the theoretical sources of several DW parameters must be considered when interpreting results. Nevertheless, the one-way and probabilistic sensitivity analyses had evaluated potential sources of uncertainty and the model ICER remained robust.

The Naguru OR also served as the only dedicated base for training pediatric surgical fellows in the country. Thus, the benefits of teaching in the OR extended beyond the number of lives saved and included long-term capacity building of the surgical workforce and the education of pediatric surgeons and anesthetists. Workforce expansion was one of the benchmarks that the 2015 Lancet Commission listed as goals on improving global surgery. However, this was not quantified in the traditional DALY averted approach of the CEA, so other methods could help assess the educational benefits of such a facility.

Ethical considerations: Although this cost-effectiveness analysis can inform healthcare decision makers about the economic efficiency of a surgical intervention, the methodology did not to take into consideration socio-cultural preferences of the specific patient population, placing the subjects at risk of subjective discrimination. The CEA premise rests on a utilitarian philosophy, where a health promoting intervention must return a certain value in terms of patient's life quantity and/or quality. In this sense, CEA assigns an explicit numerical and monetary amount to human life, and forces the approximation of the value of life to a price tag for human capital.[76]

This implication becomes apparent in DW assignments, where handicap is correlated to loss of function, which ignores more intangible aspects of disease such as suffering caused by psychological harm or social stigma. For example, the Global Burden of Disease study assigns a DW of 0.269 for acute back pain, but a 0.006-0.011 for infertility with the assumption that back pain is more disabling, but the numbers may undermine infertility's long-term consequences on the individual's perceived quality of life, especially if he/she plans on reproducing.

DWs are inherently subjective in nature as they are derived from a consensus of laypersons and expert opinion. This focus on economic productivity can also lead to discrimination against certain demographic groups in favor of others. The problem is best exhibited in the age weighting, which assumes that an individual's productivity is most robust in early adulthood and diminishes with advancing age, and thus discounts the disease burden of older individuals. Acknowledging these pitfalls as part of the analysis, this study strove to determine accurate DWs, proper modeling techniques, and a broad range of sensitivity analyses that minimized subjective bias and prejudice.

Conclusions

The pediatric OR is cost-effective. This study is the first to demonstrate the cost-effectiveness of furnishing and maintaining a pediatric OR in low-income setting from the perspective of the Ugandan healthcare system. The pediatric OR's low ICER at $80.06 per DALY averted supports OR installation and maintenance at an existing hospital as a viable intervention, provided that suitable healthcare personnel and infrastructure are present. This is the also the first study that explores the cost-effectiveness of treating life-threatening congenital anomalies such as anorectal malformations, Hirschsprung's disease, intestinal atresias and pediatric cancers; treating these diseases averted substantial disease burden per case and contributed to a dramatic ICER. The net monetary benefit is approximately 10 times the cost of investment, which implies that an OR intervention can be a very attractive option for healthcare capacity building in Uganda, and possibly other developing nations. Furthermore, this study demonstrates that economic analysis of surgical intervention in a LIC can inform sensible resource allocation.

Financial protection for patient families is needed. Our OOP cost analysis shows that financial protection for pediatric patients undergoing surgery in Uganda is not adequate, as at least 16% of these families are subjected to CHE. There is a critical need to alleviate these OOP costs to sustainably provide surgical care indiscriminately to all wealth demographics. Efforts could target cost categories that patients pay for the most, such as minimizing productivity loss by introducing more in-house staff, providing patients with more food, and gaining access to in-hospital diagnostic imaging. Social insurance or other means of risk pooling may also help, as has been described in other sectors. Increased surgical capacity (i.e. workforce and infrastructure) may also help and is a focus of the research groups' collaboration. These efforts would require liaisons with the Ugandan Ministry of Health and the public hospital system in Uganda.

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