Abstract

Background
Understanding the economic value of health interventions is essential for policy makers to make informed resource allocation decisions. The objective of this systematic review was to summarize available information on the economic impact of children’s surgical care in low- and middle-income countries (LMICs).

Methods
We searched MEDLINE (Pubmed), Embase, and Web of Science for relevant articles published between Jan. 1996 and Jan. 2015. We summarized reported cost information for individual interventions by country, including all costs, disability weights, health outcome measurements (most commonly disability-adjusted life years [DALYs] averted) and cost-effectiveness ratios (CERs). We calculated median CER as well as societal economic benefits (using a human capital approach) by procedure group across all studies. The methodological quality of each article was assessed using the Drummond checklist and the overall quality of evidence was summarized using a scale adapted from the Agency for Healthcare Research and Quality.

Findings
We identified 86 articles that met inclusion criteria, spanning 36 groups of surgical interventions. The procedure group with the lowest median CER was inguinal hernia repair ($15/DALY). The procedure group with the highest median societal economic benefit was neurosurgical procedures ($58,977). We found a wide range of study quality, with only 35% of studies having a Drummond score ≥ 7.
Interpretation

Our findings show that many areas of children’s surgical care are extremely cost-effective in LMICs, provide substantial societal benefits, and are an appropriate target for enhanced investment. Several areas, including inguinal hernia repair, trichiasis surgery, cleft lip and palate repair, circumcision, congenital heart surgery and orthopedic procedures, should be considered “Essential Pediatric Surgical Procedures” as they offer considerable economic value. However, there are major gaps in existing research quality and methodology which limit our current understanding of the economic value of surgical care.

Introduction

Surgically treatable conditions constitute a large portion of the global burden of disease.[1] The consequences of inadequate surgical care in low and middle-income countries (LMICs) are especially dire among children, where many conditions result in lifelong disabilities or premature deaths.[2, 3] In recent years there has been a growing interest in surgery as a global health priority and recognition of its role in a functioning health care system in the World Bank’s Disease Control Priorities in Developing Countries and the Lancet Commission on Global Surgery.[4, 5]

Understanding the economic value of health interventions is essential for policy makers to make resource allocation decisions. Common types of economic evaluation includes cost analysis, which reports the monetary costs per procedure; cost-effectiveness analysis, which relates costs to a standardized health outcome such as infections averted or a quantifiable health metric; cost-benefit analysis, which describes patients’ willingness to pay for a treatment; and societal economic benefit, which quantifies the economic losses that will be reduced for an individual and society as a result of successful treatment of a condition. Cost-effectiveness analyses necessitates the use of health outcome metrics such as the Disability-Adjusted Life Year (DALY), which is a composite measure of years of life lost due to premature mortality and years lived with disability. DALY estimates require several assumptions, most importantly a disability weight (DW), which reflects the severity of a health state and ranges from 0 (perfect health) to 1 (equivalent to death). DALY and DW estimates have been thoroughly summarized in the Global Burden of Disease (GBD) studies and other reports,[6–9] although estimates for surgical care remain problematic for many reasons, such as the large number of diagnoses and procedures, complexity of surgical interventions, and limited number of DWs for conditions requiring surgical intervention[10]

Several recent studies have demonstrated that many areas of surgical care are cost-effective compared with other common health interventions, although these studies do not focus on care of children.[11–13] In this report, we performed a systematic review to describe the economic impact of children’s surgical care in LMICs with three goals: 1) to summarize published research on cost and cost-effectiveness of children’s surgical procedures, 2) to construct a reference table of reported disability weights for conditions requiring surgical procedures, and 3) to describe the societal economic benefit of surgical care for children.

Methods

Selection Criteria

For our systematic review, we followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[14] (see S1 Checklist) and registered the study with
PROSPERO (registration number: CRD42015016059). Our search encompassed all English-language indexed articles published from January 1996-January 2015 that fulfilled each of the following criteria:

**Surgery**: studies analyzed surgical procedures, surgical facilities, or missions;

**Pediatric population**: recipients included children less than 18 years of age;

**Economic analysis**: studies reported care costs, DALYs averted, life years saved (LYS), quality-adjusted life years (QALYs) saved, health-adjusted life years (HALYs) gained, or societal economic benefit;

**LMIC**: care performed in a LMIC as defined by the World Bank as of February, 2015;[15]

**Data Sources**

We conducted a search for eligible studies in MEDLINE (PubMed), Embase, and Web of Science on February 1, 2015. Database-specific indexing terms were used, with the full search listed in S1 Table. We collected additional articles outside the search by consulting experts and reviewing bibliographies of identified studies. We excluded systematic reviews or other non-primary data sources.

**Article Selection and Data Extraction**

Two researchers (ATS and HER) screened abstracts of identified articles, and considered each full text for inclusion with disagreements settled by discussion. For each included report, we collected intervention type, population, cost, health outcomes, average cost-effectiveness ratio (CER), incremental cost-effectiveness ratio (ICER), and societal economic benefit. If a study did not report costs or health outcomes on a "per procedure" basis, we translated results to this format by dividing total amounts by reported procedure count. Interventions were organized into 36 procedure groups under 8 areas (cardiac surgery, otolaryngology/ear, nose, and throat surgery [ENT], general surgery, neurosurgery, ophthalmology, orthopedics, plastic and reconstructive surgery, and urology). We converted outcomes to 2015 United States dollars (USD) by using PPP conversion factors from the World Bank[16] and the Consumer Price Index Inflation calculator.[17] For studies spanning multiple years, we used the last year reported for conversion.

**Article Grading**

To assess the quality of each report, we used the 10-point checklist of Drummond.[18] Two observers independently graded each article with disagreements resolved by discussion. To translate individual Drummond scores into a metric that captures overall evidence quality for each of the 36 procedure groups, we adapted a grading scale from the Agency for Healthcare Research and Quality (AHRQ)[19] to reflect overall evidence quality, quantity, and consistency by the following criteria:

**High**: high level of assurance that research findings are valid; no important disagreement exists across studies; includes at least one study with a Drummond score of 9–10 per procedure type.

**Moderate**: moderate level of assurance that findings are valid; little disagreement exists across studies; includes at least two studies with a score of 7–8.5 or one study with a score of 9–10 per procedure type.
Low: low level of assurance that findings are valid; category includes studies with conflicting results; less than two studies have scores that exceed 6.5 per procedure type.

Disability Weight Reference Table
A reference table of disability weights for pediatric health conditions commonly requiring surgical procedures was created by compiling values from the GBD studies, with preference given to values reported by GBD 2013,[8] then GBD 2004,[7] and finally Poenaru et al.[20] There were no disability weights identified for cystic echinococcosis, inguinal hernia, or Ponseti clubfoot management in the aforementioned sources, so we reported disability weights published from articles in our review. For circumcision in Sub-Saharan Africa, we calculated a disability weight of 0.028 based on the assumption that a circumcision reduces HIV prevalence from 12% to 6%[21] with an average of 15.5 DALYs/case of HIV averted.[22]

Cost-Effectiveness Assessment
We followed WHO-CHOICE guidelines [23] to assign each intervention into a cost-effectiveness category. Interventions with a maximum CER of less than that country's gross domestic product (GDP) per capita as defined by the World Bank [24] were considered very cost-effective, interventions with a CER of less than three times the GDP per capita were cost-effective, and all others were not cost-effective. Using the upper and lower bounds of extracted CER (both average and incremental), we summarized the CER values reported from each article in the different procedure groups (using only those articles that used DALY as the health outcome). We also calculated median CERs for each procedure group using minimum and maximum values extracted from all articles that used DALYs as the base health metric. All statistical analyses were performed with STATA v14.1 (StataCorp LP).

Societal Economic Benefit
To determine the societal economic benefit gained from surgical care, we used a human capital approach. This method equates the value of a human life to the discounted market value of the economic output produced by an individual over an expected lifetime, and is frequently used by WHO for cost analyses.[25] For articles that reported economic benefits, we converted results to a "per procedure" basis and reported the minimum and maximum values. For articles without information on societal economic benefit, we calculated this benefit by multiplying reported minimum and maximum DALYs averted, QALYs gained, HALYs gained, or LYS by purchasing power parity (PPP) estimates of gross national income (GNI)/capita from the World Bank.[24] For articles that used DALYs as the health outcome, we summarized the societal economic benefit for each procedure group by presenting the values for each individual intervention within that group, and also reported median values of each procedure.

Results

Literature Search
We identified 4,125 articles through our initial search. Altogether, 86 studies met inclusion criteria (Fig 1),[26–111] with articles summarized into 36 different procedure groups.

Article Grading and Disability Weights
The studies had a wide range of quality, with 65% of studies (n = 56) with Drummond scores 0–6.5, 19% (n = 16) with scores 7–8.5, and 16% (n = 14) with scores 9–10 (Table 1, individual
scores in S2 Table). When summarized by procedure group, six had a high strength of evidence: inguinal hernia repair, trichiasis surgery, circumcision, cleft lip and palate repair, congenital heart defects, and orthopedic procedures. All other interventions had a moderate or low strength of evidence. Disability weights for pediatric surgical conditions identified from the GBD studies [7, 8] and others [20, 38, 72, 97] ranged from 0.005 for finger amputation, to 0.850 for posterior sagittal anorectoplasty (Table 2).

**Economic Outcomes**

Of the 86 studies in our search, 84 reported cost data (detailed in S3 Table), 24 reported CER, and 2 reported societal economic benefit. In total, 53 procedural CERs were extracted (Table 3). There were 45 of the 53 CERs that reported DALY as the basis of health outcome (of which 36 used average costs and 9 used incremental costs for ICER), 3 reported QALY (2 average, 1 incremental), 3 used life-years saved or gained (2 average, 1 incremental), and 2 reported HALY (1 average, 1 incremental). The procedure with the lowest minimum CER was $4-14/DALY for inguinal hernia repair in Uganda. [39] All interventions were very cost-effective at each country’s GDP level by WHO standards. When summarized by procedure group, there were 12 procedures with CER information using DALYs as the health outcome. Eight of these had a median CER below $100, and 11 had a median CER below $1,000 (Fig 2). Inguinal hernia repair had the lowest median CER ($15), followed by trichiasis surgery ($48). Not shown in Fig 2 was cystic echinococcosis treatment, which had only one observation with a CER of $1,628/DALY.

Many procedures were clinically effective as measured by averted DALYs, and most showed a substantial societal economic benefit (detailed in S4 Table). The intervention with the highest societal economic benefit was atrial septal defect repair in Brazil ($313,866). When summarized by procedure group, we were able to extract or calculate societal economic impact for 11 types of procedures based on articles that used DALYs as the health outcome. There were 9 out of those 11 procedure groups that had a median benefit greater than $10,000/procedure (Fig 3). Various neurosurgical procedures had the highest median economic benefit ($58,977), followed by inguinal hernia repair ($48,864).
Our review demonstrates that many areas of children’s surgical care in LMICs provide considerable economic value. These findings confirm the work of the *Lancet* Commission on Global
Surgery and others, and suggest that surgical care is a valuable investment and should be incorporated as an essential component of a functioning health care system. Although we have reviewed the largest set of existing reports of children’s surgical care in LMICs, the limited...
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Location</th>
<th>Cost-effectiveness ratio, as reported&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Unit of outcome</th>
<th>Cost-effectiveness ratio, 2015 USD&lt;sup&gt;b&lt;/sup&gt;</th>
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<tr>
<td><strong>Cardiac Surgery</strong></td>
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<td></td>
<td>percutaneous</td>
<td>R$230,641</td>
<td>QALY, incremental</td>
<td>$123,550</td>
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<td></td>
<td>Atrial septal defects:</td>
<td>R$631</td>
<td>QALY, average</td>
<td>$357</td>
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<td></td>
<td>surgical</td>
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<tr>
<td><strong>Ear, Nose &amp; Throat</strong></td>
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<tr>
<td>Wu et al (2013) [44]</td>
<td>Various ENT procedures</td>
<td>$42–95</td>
<td>DALY, average</td>
<td>$44–100</td>
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<tr>
<td><strong>General Surgery</strong></td>
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<td>Jha et al (1998) [29]</td>
<td>Appendectomy&lt;sup&gt;e&lt;/sup&gt;</td>
<td>$36</td>
<td>LYS, average</td>
<td>$58</td>
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<tr>
<td>Gosselin et al (2006)</td>
<td>Inguinal hernia repair&lt;sup&gt;e&lt;/sup&gt;</td>
<td>$74</td>
<td>LYS, average</td>
<td>$119</td>
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<td>Wang et al (2012) [97]</td>
<td>Cystic echinococcosis</td>
<td>$1,469</td>
<td>DALY, average</td>
<td>$1,628</td>
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<td><strong>Neurosurgery</strong></td>
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<td>Wu et al (2013) [44]</td>
<td>Various neurological operations</td>
<td>$26–65</td>
<td>DALY, average</td>
<td>$27–69</td>
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<tr>
<td>Davis et al (2014) [57]</td>
<td>Various neurological operations</td>
<td>$385</td>
<td>DALY, average</td>
<td>$387</td>
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<td><strong>Ophthalmology</strong></td>
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<tr>
<td>Baltussen et al (2005)</td>
<td>Trichiasis surgery</td>
<td>$10</td>
<td>HALY, incremental</td>
<td>$18</td>
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<td>Africa</td>
<td>$13–17</td>
<td>DALY, average</td>
<td>$18–23</td>
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<td></td>
<td>Americas</td>
<td>$49</td>
<td>DALY, average</td>
<td>$68</td>
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<td></td>
<td>Mediterranean</td>
<td>$36–78</td>
<td>DALY, average</td>
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<td>Southeast Asia</td>
<td>$24</td>
<td>DALY, average</td>
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<td>Western Pacific</td>
<td>$35</td>
<td>DALY, average</td>
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<td>Sub-Saharan Africa</td>
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<td></td>
<td>Cataract repair</td>
<td>$116–117</td>
<td>DALY, average</td>
<td>$86–110</td>
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range of economic analyses suggests that we have just examined the "tip of the iceberg" of pediatric surgical conditions.

As health care for children grows as a global health priority, this information should assist policy-makers for the development of funding priorities. However, as Baltussen et al. note, economic analyses should be used collectively with other criteria such as poverty reduction and

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<tr>
<th>Intervention</th>
<th>Location</th>
<th>Cost-effectiveness ratio, as reported(^a)</th>
<th>Unit of outcome</th>
<th>Cost-effectiveness ratio, 2015 USD(^b)</th>
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<tr>
<td>Cataract repair</td>
<td>$97</td>
<td>DALY, average</td>
<td>$118</td>
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</tbody>
</table>

**Orthopedics**

Grimes et al (2014)\([67]\) Various orthopedic procedures Malawi $92–139 DALY, average $95–144

Gosselin et al (2008)\([69]\) Various orthopedic procedures Cambodia $77 DALY, average $92

Gosselin et al (2011)\([72]\) Various orthopedic procedures Nicaragua $362DALY, average $395

Dominican Repub. $362 DALY, average $395

Haiti $343 DALY, average $374

Chen et al (2012)\([73]\) Various orthopedic procedures Nicaragua $270–719 DALY, average $295–787

Wu et al (2013)\([44]\) Various orthopedic procedures Kenya $34–72 DALY, average $36–76

**Plastic and Reconstructive Surgery**

Corlew (2010)\([60]\) Cleft lip & palate Nepal $29–73 DALY, average $35–89


Nicaragua $66–1,828 DALY, average $73–2,019

Kenya $96–1,193 DALY, average $106–1,318

Moon et al (2012)\([64]\) Cleft lip & palate Vietnam $43–97 DALY, average $47–106

Poenaru (2013)\([65]\) Cleft lip & palate Africa $72–134 DALY, average $79–146

Americas $35–85 DALY, average $38–93

Europe $35–89 DALY, average $38–97

Middle East $42–100 DALY, average $46–109

Southeast Asia $44–102 DALY, average $48–112

Western Pacific $35–87 DALY, average $38–95

Rattray et al (2013)\([43]\) Various reconstructive procedures Cambodia $99 DALY, average $103

Wu et al (2013)\([44]\) Various reconstructive procedures Kenya $35–79 DALY, average $37–84

**Urology**

Binagwaho et al (2010)\([45]\) Circumcision Rwanda $334 LYG, incremental $370

Wu et al (2013)\([44]\) Various urologic operations Kenya $56–119 DALY, average $59–126

Abbreviations include: DALY disability-adjusted life-year; LYS life-year saved; LYG life-years gained; HALY health-adjusted life-year; QALY quality-adjusted life-year; USD United States dollar; Int. $ International dollars (a hypothetical currency unit with the same purchasing power parity that the U.S. dollar has in the United States at a given time).

\(^a\) All values presented on a per-procedure basis.

\(^b\) Values converted to USD using purchasing power parity conversion factors from the World Bank\([16]\) and inflated to 2015 USD using the Consumer Price Index Inflation calculator.\([17]\)

do:10.1371/journal.pone.0165480.t003
severity of disease for a comprehensive approach to health care priority setting.[112] Use of a rights-based approach will ensure that a procedure that does not have a favorable cost-effectiveness or one that lacks adequate economic analysis is not excluded in provision of basic children’s health care services. Children’s surgical care should be thought of as an essential component of a “package of care,” as surgical care is an essential modality for the overall health care of children. Economic information should be taken into context by all local stakeholders, as local experts best understand the economic constraints within individual countries and the optimal methods to affect health care change.

Several particular areas of surgical care for children offer great economic value and are supported by high quality evidence. These should be considered as “Essential Children’s Surgical Procedures,” and include inguinal hernia repair, trichiasis surgery, cleft lip and palate repair, circumcision, congenital heart surgery, and orthopedic procedures. Our recommendations align with those of Mock et al.,[113] which prioritize surgical care based on health burden, success of a surgical intervention, and cost-effectiveness. We strongly advocate for increased investment in these “Essential Children's Surgical Procedures” to improve health for children and gain economic benefit for a society. Many other procedures may potentially be quite cost-effective, although the quality of economic analysis is not as well developed, such as for Hirschsprung’s disease, anorectal reconstruction, appendectomy, clubfoot, abscess,
meningoencephalocele, trauma, hydrocephalus, epilepsy, and cataracts. Although our study
strived to incorporate all available economic data on children’s surgical care, many areas still
lack adequate economic analysis to make clear recommendations. For instance, we did not
identify any economic studies for care of undescended testicles, typhoid perforation or intus-
susception. Although issues surrounding capacity and delivery of children’s surgical care are
not addressed in our review, some procedures may be more appropriate for care and offer max-
imal economic benefits within different levels of a health system (i.e. district hospital, tertiary
center).[114] Furthermore, innovative solutions such as task-sharing of surgical tasks to non-
physician healthcare workers may be vital to maximize the economic value of surgical care for
children.[115]

Moving forward, we encourage improvements in research methods to define the costs and
value of surgical care. First, we advocate for refinement of the use of the DALY, DWs, and
other output metrics for economic analysis of surgical treatments. Although a complete discus-
sion of the limitations of the DALY and DW metrics for surgical care is beyond the scope of
this review, they remains problematic for many reasons, such as the complexity of surgical care
and procedures, identification of surgical component of care for health states requiring multi-
disciplinary care, or impact of surgical complications on health state outcomes.[10] Second, we
support consistent use of WHO guidelines that define appropriate costs for economic analyses,
which should reflect all customary costs for care in a public hospital setting, including

Fig 3. Societal economic benefit of 11 pediatric surgical intervention categories, measured using a human capital approach. Individual
article references shown in brackets. Red diamonds represent median values, black bars represent the range of values from each article.
Abbreviations include: ENT ear, nose and throat; PRS plastic and reconstructive surgery; USD United States dollars.
doi:10.1371/journal.pone.0165480.g003
infrastructure (capital costs, maintenance and utility costs, management overhead) and staff salaries, as well as indirect costs such as for travel or lost wages.[23] Third, we encourage the use of national datasets as they become available for economic analyses, such that variation between hospitals or researchers is minimized.

Existing disability weights incorporated into DALY estimates have been widely criticized for producing seemingly unrealistic values and have garnered concern regarding universal valuation for people from different geographic, cultural, or socioeconomic backgrounds.[116] Alternative measures of characterizing health states and the burden of conditions amenable to surgery include the epidemiological modeling strategy of Higashi et al.[117] Their model utilized inputs from GBD data to characterize the DALYs from congenital anomalies that could be potentially addressable from surgical intervention in LMIC, thereby estimating the excessive morbidity and mortality associated with these conditions. Coupling novel modeling strategies to enhance DALY estimations with comprehensive cost data will markedly improve economic analyses and facilitate scale-up modeling to help guide policy to improve surgical infrastructure.

Our study has several limitations inherent to economic analyses, including dependence on a wide range of assumptions as well as limited granularity of input data. Many articles report evidence from surgical missions and non-governmental organizations, which tend to underestimate or omit critical costs such as use of the facility, equipment depreciation, and overhead.[13] Also, the cost-effectiveness of an operation will vary by location and type of facility.[13] For example, costs associated with a surgical mission may be very different from a second-level hospital. Although all costs and CERs were converted and inflated to 2015 USD for consistency, our review included a wide timeframe stretching back to 1998, and some of the procedures described here may be outdated and no longer considered standard of care. Furthermore, many of the studies use different methods for age-weighting and discounting, which can impact the cost-effectiveness of a procedure. Some have argued that these practices are not appropriate,[118] and they have been subsequently omitted from the GBD 2010 study. Finally, we recognize limitations in assessment of the quality of surgical studies using the Drummond checklist, which is increasingly used for comparison of economic analyses across different health settings. Several items of the Drummond checklist are difficult to apply towards surgical care as noted by Marseille and Morshed,[119] such as reliance on the equal weighting of all criteria elements. However, the final score does allow for general comparison between studies. By translating quality assessments into “high, medium, or low” categories using AHRQ guidelines, we sought to translate these findings into commonly used categories.

Many of the CERs presented here from LMICs were based on average cost-effectiveness, which is most appropriate for scenarios where performing the intervention and doing nothing are the only options. This metric does not reflect the availability of alternate options with intermediate cost and effectiveness, and are problematic when comparing different treatments.[120] Analyses using ICERs would be needed to compare interventions that are mutually exclusive. In our analyses, all but one study used standard of usual care as the comparator for ICER calculations. However, ICERs are often not generalizable across different settings, because the “next best alternative” might vary by location. Thus, the results presented here are not intended to be used as an absolute standard for comparison between procedures, but rather to define a pattern from existing data to describe the economic benefits of pediatric surgical interventions in LMICs.

In summary, we found that many areas of surgical care for children are quite cost-effective and result in substantial economic benefits for LMICs. However, there are major gaps in existing research methodology which limit our understanding of the actual value of pediatric surgical care. Despite these limitations, it is clear that improved investment in surgical care in many
setting is an extremely cost-effective approach to support health care for children, and should be considered as a key component of “packages of care” for children.

Supporting Information

S1 Checklist. PRISMA 2009 Checklist. (DOC)
S1 Table. Database Search Terms. (PDF)
S2 Table. Quality of Evidence using Drummon 10-Point Checklist. (PDF)
S3 Table. Costs of Pediatric Surgical Procedures. (PDF)
S4 Table. Health Outcomes and Societal Economic Benefit of Pediatric Surgical Procedures. (PDF)

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Conceptualization: AS DP DO DF HR.
Data curation: AS.
Formal analysis: AS HR.
Investigation: AS.
Methodology: AS DP DO DF ES HR.
Project administration: AS HR.
Resources: HR.
Software: AS.
Supervision: HR.
Validation: AS HR.
Visualization: AS.
Writing – original draft: AS HR.
Writing – review & editing: AS DP DO EA DF ES HR.

References


