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Outcomes and unmet need for neonatal surgery in a resource-limited environment: Estimates of global health disparities from Kampala, Uganda

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ABSTRACT

Purpose: Reported outcomes of neonatal surgery in low-income countries (LICs) are poor. We examined epidemiology, outcomes, and met and unmet need of neonatal surgical diseases in Uganda.
Methods: Pediatric general surgical admissions and consults from January 1, 2012, to December 31, 2012, at a national referral center in Uganda were analyzed using a prospective database. Outcomes were compared with high-income countries (HICs), and met and unmet need was estimated using burden of disease metrics (disability-adjusted life years or DALYs).
Results: 23% (167/724) of patients were neonates, and 68% of these survived. Median age of presentation was 5 days, and 53% underwent surgery. 88% survived postoperatively, while 55% died without surgery ($p < 0.001$). Gastroschisis carried the highest mortality (100%) and the greatest mortality disparity with HICs. An estimated 5072 DALYs were averted by neonatal surgery in Uganda (met need), with 140,154 potentially avertable (unmet need). Approximately 3.5% of the need for neonatal surgery is met by the health system.
Conclusions: More than two thirds of surgical neonates survived despite late presentation and lack of critical care. Epidemiology and outcomes differ greatly with HICs. A high burden of hidden mortality exists, and only a negligible fraction of the population need for neonatal surgery is met by health services.

Annually, 10.7 million children worldwide die before the age of five, 4 million of them in the first month of life [1]. 98% of these deaths are in lower and middle income countries (LMICs). Although advances in child health policies have led to a large decline in younger-than-five mortality, the rate of decline in neonatal mortality has lagged [2,3]. Therefore, a larger proportion of deaths younger than five occur in the neonatal period, primarily in LMICs. Sub-Saharan Africa had the largest increase in this proportion, from 26% to 34% — an increase of almost 31%, between 1990 and 2010 [2].

Although most of the neonatal mortality in these countries is attributed to perinatal infections, birth asphyxia and poor nutrition, surgical diseases such as congenital anomalies also contribute to this burden [4,5]. Congenital malformations disproportionately affect LMICs, where almost 94% of these anomalies occur [6]. Additionally, the proportional burden of these diseases on these countries may increase in the future, since combating surgical disease requires resources such as operating rooms and highly trained personnel that are not often the focus of healthcare development projects in LMICs.

In part, this reflects the neglect of surgical diseases by both governmental and nongovernmental child development programs in favor of other priority areas such as infectious disease and nutrition [7,8]. It has only been recently that studies have demonstrated the comparable cost-effectiveness of surgery to nonsurgical interventions in low-income countries [9,10]. Consequently, the already pervasive disparity in healthcare between resource-poor countries and the rest of the world is magnified with respect to surgical diseases in neonates.

Uganda, with 5 hospital beds, and 1.2 physicians per 10,000 people (compared to 30 and 24.2 respectively in the US), offers an excellent example of this disparity [6,11]. There are approximately 100 practicing surgeons in the country [12], with one clinically active specialist pediatric general surgeon. Neonatal surgery is only routinely performed at one center, the Mulago National Referral Hospital in the capital city, Kampala.

The first step for advocacy toward improved resource allocation to surgical diseases is a quantification of need. The Global Burden of Disease study records the disability adjusted life years (DALYs), a metric that combines mortality and morbidity, of various diseases. An initial rough estimate was that 11% of the total DALYs in LMIC are owing to surgical conditions [13]. While the study does list the burden attributable to congenital anomalies, there is no analysis by treatment modality, such as neonatal surgery [14]. A measure of the potentially avertable

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burden of neonatal surgical disease may support advocacy for resource allocation to this area. Additionally, knowledge of patterns of neonatal surgical cases would help identify appropriate intervention strategies to further decrease global neonatal mortality.

We reviewed all neonates presenting to the Department of Surgery at Mulago National Referral Hospital, Kampala, Uganda, in order to determine priority areas for intervention. Additionally, we attempted to quantify the burden of neonatal surgical disease in Uganda, using DALYs, to identify the proportion of this burden that is currently being addressed in this resource-limited setting, and the proportion that could potentially be averted if resources were improved.

1. Methods

Mulago Hospital is essentially the sole provider of neonatal surgery in Uganda. While there is no newborn intensive care unit, the hospital has a special care unit for sick newborns staffed by postgraduate physicians in pediatrics and several senior consultants in pediatrics with expertise in neonatology. There is no infant ventilator, although on occasion, anesthesia machines from the operating room have been used to ventilate neonates postoperatively. There is no long-term venous access or IV nutrition on any of the units. Surgical neonates are admitted to either the newborn special care unit or the general pediatric surgical unit.

Anesthesia is provided primarily by anesthesia consultants and postgraduate trainees, though there is no anesthetist with specialist qualification in pediatric anesthesia. During the year of the study (and currently), there was one clinically active trained pediatric surgeon (JS) at Mulago Hospital who performed the majority of these operations. While several private hospitals in Kampala have greater capacity for postoperative care of neonates, very few cases are performed in these facilities owing to access and human resource constraints.

After obtaining approval from the Mulago Hospital Institutional Review Board, all patients presenting to the pediatric surgery service at Mulago Hospital from January 1, 2012 to December 31, 2012 were included in a prospectively collected database. Information collected included demographic information (including age, gender, tribe, district, distance traveled), diagnosis, surgical intervention, complications and duration of hospital stay. Data were then analyzed using SPSS 19.0 (IBM Corporation, Armonk, NY). Statistical analysis was largely descriptive, looking at central tendencies and frequencies. Two-tailed chi-squared tests were used to identify relationships between categorical variables, with a $p < 0.05$ denoting significance.

Burden of disease was calculated for the six most common conditions encountered (conditions with at least 5 patients) using disability adjusted life years (DALYs) with methods outlined in the Global Burden of Disease report and associated studies [14]. Nine patients presented with necrotizing enterocolitis but were also excluded since it is related to prematurity, thereby making incidence and delayed care difficult to identify. Birth rate used was 47 per 1000 (1.6 million live births annually), and population used was 35 million [11]. Disease incidence was calculated with sub-Saharan Africa references where available. Incidences used for the conditions were: anorectal malformations (ARMs) – 1 in 2260, Hirschprung's disease (HD) – 1 in 4762, gastroschisis – 1 in 2222, omphalocele – 1 in 4000, GI atresias – 1 in 2860, teratomas – 1 in 35,000 [15–20].

As described in the Global Burden of Disease study, DALYs for any given health condition are the sum of years of life lost (YLLs) and years of life lived with disability (YLDs) [14]. For a neonatal condition where surgery provides a full cure and absence of surgery leads to death, the DALYs would simply equal the YLLs, which would be the country's life expectancy. For a condition where some patients may not necessarily die without surgery, or be "partially treated" by an operation, the DALYS averted include both YLLs as well as YLDs. The YLD calculation, as previously described, includes a disability weight for each condition from 0 to 1, with higher disability weights for greater disability.

Total need in DALYs was categorized into three categories: met need, unmet need, and unmeetable need for surgical care, as previously proposed [21]. Met need is a measure of the number of DALYs averted owing to surgery at Mulago, assuming that all patients that were discharged after surgery went on to complete full, disability-free lives, and would otherwise have died in the neonatal or infant period without surgery. Unmeetable need represents the number of DALYs in the Ugandan population that cannot be averted even with the injection of resources similar to a high-income country (HIC). This was calculated from estimates of mortality from HIC as the best possible outcome of neonatal surgical care. Specifically, the survival rates for each disease were as follows: ARMs – 97%, HD – 94%, gastroschisis – 92%, omphalocele – 78%, GI atresia – 96%, teratomas – 95% [22–27].

Unmet need (avertable burden) was a more complex calculation, especially for patients with ARMs and HD. With these diseases, it is possible to receive preliminary colostomy as definitive treatment, without permanent correction (i.e. pull through or anoplasty) and live with permanent disability. Alternatively, a subset of patients may live with the anomaly without surgery at all, but incur some degree of disability, but not death. The proportion of patients that fall into this category is hard to estimate, and again, for simplicity, we assume that of the patients born with these conditions who were not treated at Mulago, half undergo colostomies as definitive treatment or receive no surgical care and live with disability, and the other half receive no treatment and subsequently die. Therefore, the unmet need involves both the years of life lost (YLL) owing to early death for those who are completely untreated, and the years lost to disability (YLD) as a consequence of living with a colostomy or no treatment. For the other diseases, unmet need was assumed to come solely from YLL, since all neonates with these conditions would likely have died without surgical treatment.

As a final metric, "effective coverage" is the ratio of met/met + unmet need; it provides a measure of the success of the health system in providing a specific health service [28].

DALY calculations were performed assuming Mulago Hospital was the sole provider of neonatal surgeries in the country. While some smaller hospitals do provide some care, this assumption is largely true. However, as a consequence, values for met need are likely a slight underestimate, while unmet need is likely a slight overestimate.

A sample DALY calculation (using for Hirschprung's disease) is as follows:

$$\text{Met need} = \text{YLLs} = \text{Life expectancy} \times \text{number of patients discharged} = 58.3 \times 7 = 408.1$$

$$\begin{aligned}\text{Unmet need} &= \text{YLL} + \text{YLD} \\ &= (0.5 \times (\text{expected number of patients with disease–number of patients discharged}) \times \text{life expectancy} \times \text{disease survival}) + (0.5 \times (\text{expected number of patients with disease–number of patients discharged}) \times \text{life expectancy} \times \text{disease survival x DW}) \\ &= (0.5 \times (341–7) \times 58.3 \times 0.94) + (0.5 \times (341–7) \times 58.3 \times 0.94 \times 0.72 \\ &= 15723.1\end{aligned}$$

For unmet need for ARMs, a similar calculation was made. Again, for other conditions, YLD was assumed to be noncontributory, and all the unmet need was assumed to come from YLL owing to likely fatal outcome in the neonatal or infant period without surgical intervention.

2. Results

724 pediatric inpatients were evaluated by the pediatric surgery unit at Mulago Hospital, of whom 167 were neonates (23.0%). The median age at presentation was 5 days. 65.3% of neonates presented in the first week of life. Male to female ratio was 1.55:1. Anorectal malformations (21.7%) and omphalocele (16.3%) were the most commonly diagnosed conditions (see Table 1).

Mortality varied significantly with age group ($p < 0.01$), with a mortality rate of 43.5% in the first week of life, and steadily decreasing with

Table 1
Descriptive statistics for neonatal referrals to Mulago Referral Hospital, Kampala, Uganda.

	Freq	%		Freq	%
Total neonates	167	100			
Age			Conditions		
0–7 days	109	65.3	Anorectal malformation	36	21.7
8–14 days	20	12.0	Omphalocele	27	16.3
15–21 days	20	12.0	Intestinal atresia	21	12.7
>22 days	18	10.8	Gastroschisis	20	12.0
			Hirschsprung's	11	6.6
Gender			Necrotizing enterocolitis	9	5.4
Male	101	60.5	Sacrococcygeal teratoma	7	4.2
Female	66	39.5	Abcess/cellulitis	4	2.4
			Pyloric stenosis	4	2.4
Management			Inguinal hernia	2	1.2
Surgical	88	52.7	Hemangioma	2	1.2
Nonsurgical	75	44.9	Intussusception	2	1.2
			Cystic hygroma	2	1.2
Distance referred			Others	19	11.4
0–25 km	60	35.9			
26–100 km	43	25.7	Outcome		
101–200 km	29	17.4	Discharge	98	58.7
201–300 km	18	10.8	Death	54	32.3
>301 km	17	10.2	Transfer/other	12	7.2

subsequent age groups. However, only 40.2% of neonates in the first week of life had a surgical procedure, compared to more than 75% in each of the older age groups ($p < 0.001$, see Table 2).

Overall mortality in the neonatal period was 32.3%, and 52.7% of the patients underwent surgery. Outcome varied significantly based on whether or not a neonate underwent surgery ($p < 0.001$). Mortality dropped to 12.8% in neonates on whom surgery was performed, although there likely was selection bias present, as the sickest infants would not have been good candidates for surgery, especially in the absence of critical care resources.

Anorectal malformations, intestinal atresias and abdominal wall defects were the most common surgical conditions affecting neonates, together accounting for more than 60% of cases. Mortality rates varied significantly depending on diagnosis ($p < 0.001$). Among conditions that affected at least five patients, anorectal malformations had the lowest mortality rate of 11.4%. Gastroschisis, on the other hand had a mortality rate of 100%. These correlated with the rates of surgery for these conditions. 88.9% of neonates with anorectal malformations underwent surgery, compared to none of the patients with gastroschisis, as none were judged to be salvageable.

Despite extreme resource limitations, surgery was generally very successful, with a mortality rate of 12.8%. The highest postoperative mortality rates (among conditions afflicting at least five patients) were for intestinal atresias, with a postsurgical mortality rate of 30.8%. Surgery for anorectal malformations, on the other hand, had the lowest postsurgical mortality rate of 6.5%.

The most common presenting complaints were obviously visible signs such as the "protrusion of intestines" (26.5%) and "absence of an anus" (19.4%). Other common presenting complaints, although perhaps less obvious, were "excessive vomiting" (12.7%), "abdominal swelling" (11.1%) and "constipation" (8.3%).

Patients traveled anywhere from 3 km to 600 km to be seen at Mulago, with one patient even presenting from neighboring South Sudan. The average distance traveled was 120 km, with 39% of patients presenting from Kampala (the local district) and adjacent Wakiso district. Of note, of the patients who underwent surgery, duration of stay at the hospital was directly correlated with distance traveled ($p < 0.001$).

The six most common neonatal surgical conditions accounted for an estimated total of 157,736 DALYs annually. Using mortality rates in the Western literature as the best achievable outcome in the high-income setting, only 12,511 DALYs were deemed to be unmeetable by these standards. Assuming Mulago Hospital is the country's only provider of neonatal surgical services, it was determined that 5072 DALYs of the neonatal surgical need was met, amounting to 3.5% of the meetable need (see Table 3 and Fig. 1 for the disease-specific estimate of burden).

Table 3
Surgical neonates treated at Mulago and outcomes compared to the expected number of new cases for neonatal conditions.

Surgical condition	Number of new cases seen (discharged)	Number of new cases expected
Anorectal malformations	36 (33)	718
Hirschprung's disease	11 (7)	341
Gastroschisis	20 (0)	730
Omphalocele	27 (20)	405
Intestinal atresias	21 (12)	568
Sacrococcygeal teratomas	7 (6)	46
Total	132 (78)	2808

Note: Six most common neonatal surgical diseases included.

3. Discussion

The United Nations Millennium Development Goal 4 calls for the reduction in mortality in children younger than five years old by two-thirds between 1990 and 2015 [29]. Although there has been an impressive 35% reduction in younger than five mortality worldwide, the decline in neonatal mortality has lagged compared to younger than five mortality [2,3]. A small, but significant proportion of this mortality is from treatable surgical conditions, although this is poorly quantified. It is estimated that surgical disease in children account for 6–12% of all pediatric visits, while surgical disease in general accounts for around 11% of all DALYs in LMICs [13,30].

Surgical disease has generally been a neglected arena in the field of international development, even though basic surgical services have been shown to be as cost effective as other priority health interventions [9,10,13]. Neonatal surgery, in particular, has the potential to be a cost effective intervention since these conditions commonly have no non-surgical treatment, and do not exclude the possibility of a full, disability-free life expectancy upon surgical correction. Studies of

Table 2
Gender, choice of management and outcome organized by patient age groups for neonates presenting to Mulago Referral Hospital, Kampala, Uganda.

	Age groups				P value
	0–7 days	8–14 days	15–21 days	> 22 days	
Gender (% within age group)					0.01
Male	75 (68.8%)	12 (60.0%)	7 (35.0%)	7 (41.2%)	
Female	34 (31.2%)	8 (40.0%)	13 (65.0%)	10 (58.8%)	
Management (% within age group)					<0.001
Surgical	43 (40.2%)	16 (80.0%)	15 (75.0%)	14 (87.5%)	
Nonsurgical	64 (59.8%)	4 (20.0%)	5 (25.0%)	2 (12.5%)	
Outcome (% within age group)					<0.001
Death	47 (43.5%)	4 (21.1%)	3 (15.0%)	0 (0.0%)	
Other (discharged/transferred)	61 (56.5%)	15 (78.9%)	17 (85.0%)	17 (100.0%)	

P-value calculated using two-tailed chi-squared tests.

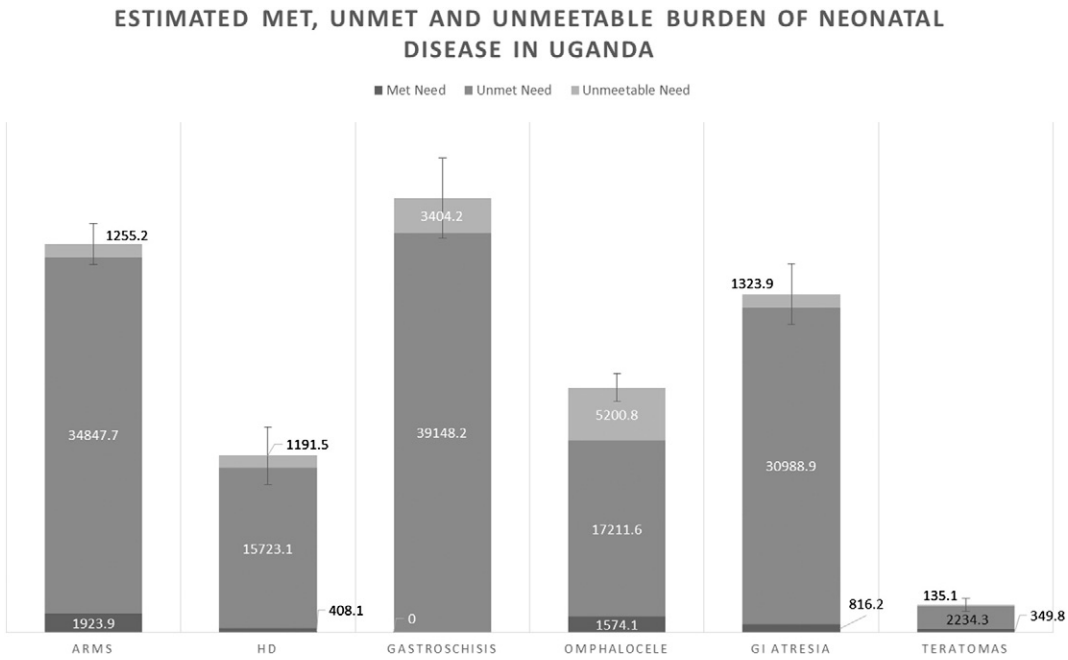

Fig. 1. Burden of the six most common neonatal diseases, categorized into met, unmet and unmeetable need.

congenital anomalies in LMICs have generally focused more on cleft lip, clubfoot, and hydrocephalus — conditions that generally require intervention on an elective basis, as compared with general surgical conditions that generally require more urgent and emergent intervention [31–33]. We estimated that more than 150,000 DALYs are attributable to common neonatal surgical conditions in Uganda annually. This amounts to 451 DALYs/100,000 people, comparable to tuberculosis (712 DALYs/100,000), protein-energy malnutrition (506 DALYs/100,000) and neglected tropical diseases (378 DALYs/100,000) [14].

Other studies have attempted to estimate the avertable burden if LMICs could scale up surgical care to achieve the outcomes of high-income countries. For example, it has been estimated that 2 million deaths in severely injured patients could be averted a year if this were possible [34]. Similar work has been done for selected congenital anomalies, with estimates that 60% of the burden of congenital heart anomalies, neural tube defects, and cleft lip/palate could be averted if surgical care was scaled up [35]. However, no estimates have been made for neonatal general surgical conditions. If our figures are extrapolated to other African countries with a similar GDP (PPP)/capita ($1000–$2000, 19 countries, population: 375 million, 14.53 million live births per year), we calculate that 1.47 million DALYs could be averted by programs aimed at surgical diseases in neonates in these countries. This would estimate only the impact of neonatal surgical diseases, which constitutes a small proportion of surgical diseases in children. The contribution of pediatric surgery as a whole is likely even more significant.

"Effective coverage" of health services by public health experts is a metric that has been instrumental for global policymakers [28,36]. Unsurprisingly, our data suggest that a very small fraction of the estimated neonatal surgical need in Uganda is met. By our calculations, it appears that only 3.5% of the meetable need is currently being fulfilled.

The low effective coverage in Uganda largely appears to be a problem of access. For the common neonatal surgical conditions, we estimated the affected population and found that only 3–7% of this group presented to Mulago Hospital (see Table 3). Additionally, parents traveled from more than a hundred kilometers on average, some coming in from neighboring South Sudan, reflecting the general lack of access to surgical care in the region. The correlation between length of stay and distance traveled may reflect the need for many patients to be observed for long periods postoperatively to ensure no complications arise before families board a long, and often relatively costly, bus ride home. Nonetheless, further work is required to determine specific barriers to access for children and families in the neonatal period [37].

This lack of access to care is accentuated by the lack of resources for pediatric surgery in Uganda, starting with human resources. One clinically active specialty-trained pediatric general surgeon (JS) serves the country. By American Pediatric Surgery Association (APSA) standards of 1 pediatric surgeon/100,000 children, 170 surgeons would be required in Uganda. It is likely that the need is even higher than this figure suggests, considering high fertility rates and poor prenatal care. This type of ratio is common in the region [38]. Similar extreme shortages of personnel also exist for specialist pediatric anesthesia personnel, as there is no Ugandan specialty trained pediatric anesthetist. The lack of adequate personnel and infrastructure results in delays in presentation, further increasing the morbidity and mortality of these diseases.

This was most striking for patients with gastroschisis, all of whom died. None of them received an operation, as most presented late with septic complications. Other conditions such as omphalocele (7.4% of patients operated on) and intestinal atresias (65% of patients operated on) also had much lower rates of surgery than might be expected. Even among patients with anorectal malformations, who had the best outcomes out of all neonatal surgical diseases treated, 1 out of every 10 was not able to receive an operation.

When surgery was performed, outcomes were generally successful, despite the extraordinary challenges posed by the lack of intraoperative and postoperative resources (advanced nursing, ventilation, TPN etc). Patients undergoing surgery had a 12.8% mortality rate, compared to a 57.3% mortality when surgery was not performed. Anorectal malformations, for example, had a 6.5% operative mortality rate, all with high ARMs. This is comparable to the 3% found in the Western literature [22]. Intestinal atresias had the worst postoperative prognosis in our population, with a 30.8% mortality rate. The equivalent mortality rate found in Western literature was between 0.8 and 4% [27]. This is perhaps reflective of increased complexity of these cases owing to a delay in presentation or treatment, as well as the lack of neonatal intensive care resources.

Other studies report similar outcomes following neonatal surgery in LMICs. In 223 neonates operated upon over 18 months in a tertiary center in Nigeria, the mortality rate was 8.7% [39]. Similar to our study, the highest mortality rate was owing to intestinal atresias, with a mortality rate of 50%. In another tertiary center in Nigeria, mortality

for neonatal surgical emergencies was 30.8% [40]. Similar to our study, the high mortality rate in these centers was thought to be associated with late presentation, shortage of specialized manpower, and inadequate facilities.

In Uganda, many interventions are being planned or underway to tackle these obstacles, and improve the disparity in care. For example, more surgeons are being recruited for training in pediatric surgery and anesthesia. For gastroschisis in particular, education of rural providers has been attempted to improve evaluation and early transport. Public health campaigns for club foot and cleft lip and palate that have increased early referrals have served as an example of what may be possible [41]. A program aiming to educate birth providers in identifying and referring babies with other visible anomalies has been piloted in neighboring Tanzania. It is essential for health planners to continue to target interventions at these obstacles, in order to improve the effective coverage for the almost 2 million avertable DALYs attributable to neonatal surgical diseases in sub-Saharan Africa.

Our study has numerous important limitations. As this was a pilot data study, a relatively narrow range of data was collected, not including specific surgical complications, delays in surgery, and case complexity, among other factors. Nonetheless, we felt that survival to discharge as an initial mortality estimate was a logical place to start. In addition, we had a relatively small sample size of 167 patients. However, this included all patients presenting to the hospital over one year, and represents the limited number of patients that accessed care. We also assumed in our calculations that Mulago is the only provider of neonatal surgery in the country. While there are several private hospitals where neonatal surgery may be performed, the surgical volume of these hospitals is small. It is also conceivable that neonates might have been treated by general surgeons in regional hospitals. However, we expect this volume was minimal. In fact, recent work in western Uganda has suggested that the volume of pediatric surgery performed, even in older children, is very low outside of services provided by elective plastic surgical mission groups [42].

For our calculations, we used accepted population-based estimates of incidence of congenital anomalies, though there has been suggestion that these may vary across populations [43]. Additionally, we assumed that some patients with anorectal malformations and Hirschprung's disease were partially treated, and that those who were discharged from Mulago went on to live disability-free lives. Finally, we made population based estimates using burden of disease methodology, which has been controversial, as alternative metrics may be more practical than the DALY [44]. Nonetheless, once again, we felt it was a reasonable starting point to demonstrate the current state of surgical care, and the significant burden of neonatal surgical diseases in the region.

4. Conclusion

This pilot study in Uganda estimates a significant burden owing to, and limited effective coverage for, neonatal surgical conditions. Some conditions such as gastroschisis, with nearly 100% survival in high-income countries, may have no survivors in LMICs. Hidden mortality for many conditions is likely very high as many children do not access the health care system. Surgical care in Uganda, as in other LMICs, has challenges of delayed presentation, a lack of trained personnel, and infrastructure. Nonetheless, the majority of postoperative patients survived, likely owing to careful care selection, adaptation of surgical techniques, and efficient use of very limited resources. More data about the met and unmet need for pediatric surgical diseases and their associated morbidity and mortality in LMICs, along with the development of better metrics, may aid advocacy for the role of pediatric surgery as a key component of global child health. The global pediatric surgery community, acting with local health planners, should work together for greater health equity for children and families born with correctable congenital anomalies in resource-limited settings.

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