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Determinants of morbidity and mortality following emergency abdominal surgery in children in low-income and middle-income countries

GlobalSurg Collaborative

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Paediatric Surgery Unit, Department of Surgery, College of Medicine, Lagos University Teaching Hospital, University of Lagos, Lagos, Nigeria

Correspondence to
Dr Adesoji O Ademuyiwa; adesojiademuyiwa@yahoo.co.uk

ABSTRACT

Background: Child health is a key priority on the global health agenda, yet the provision of essential and emergency surgery in children is patchy in resource-poor regions. This study was aimed to determine the mortality risk for emergency abdominal paediatric surgery in low-income countries globally.

Methods: Multicentre, international, prospective, cohort study. Self-selected surgical units performing emergency abdominal surgery submitted prespecified data for consecutive children aged <16 years during a 2-week period between July and December 2014. The United Nation's Human Development Index (HDI) was used to stratify countries. The main outcome measure was 30-day postoperative mortality, analysed by multilevel logistic regression.

Results: This study included 1409 patients from 253 centres in 43 countries; 282 children were under 2 years of age. Among them, 265 (18.8%) were from low-HDI, 450 (31.9%) from middle-HDI and 694 (49.3%) from high-HDI countries. The most common operations performed were appendectomy, small bowel resection, pyloromyotomy and correction of intussusception. After adjustment for patient and hospital risk factors, child mortality at 30 days was significantly higher in low-HDI (adjusted OR 7.14 (95% CI 2.52 to 20.23), p<0.001) and middle-HDI (4.42 (1.44 to 13.56), p=0.009) countries compared with high-HDI countries, translating to 40 excess deaths per 1000 procedures performed.

Conclusions: Adjusted mortality in children following emergency abdominal surgery may be as high as 7 times greater in low-HDI and middle-HDI countries compared with high-HDI countries. Effective provision of emergency essential surgery should be a key priority for global child health agendas.

Trial registration number: NCT02179112; Pre-results.

Key questions

What is already known about this topic?

- There are little prospective data describing the outcomes of paediatric surgery in low-resource settings.
- Emergency surgery is associated with more deaths and complications than elective surgery, but most studies carried out until now are in adults.

What are the new findings?

- After accounting for differences in case mix, the odds of death after emergency abdominal surgery could be as high as seven times greater in low-income countries compared with high-income countries.

Recommendations for policy

- The provision of effective essential surgery should be a key priority for global child health agendas and has significant potential to impact on the global burden of disease.

INTRODUCTION

Little data are available addressing the safety profile and risk factors affecting morbidity and mortality in children undergoing surgery globally. Most studies have been in adults and almost invariably were performed in high-resource countries.[1–3] Although it is estimated that about 234 million surgical procedures are performed annually worldwide, the percentage of these involving children remains unknown.[4]

Studies from low- and middle-income countries (LMICs) have shown that in the neonatal period, mortality is associated with sepsis, multiple exposures to anaesthesia (reoperation), postoperative bleeding and complex congenital anomalies.[5–8] Other risk factors include non-availability of trained personnel, delayed presentation, childbirth outside a hospital and financial constraints of the caregivers.[9–11]

Emergency surgery generally carries a higher morbidity and mortality compared with elective procedures.[12 13] An estimated 33 000 emergency laparotomies in all ages are performed annually in the UK with a 15–20%

mortality, which is 10-fold higher than that of elective cardiac surgery.[14] Reasons for this high mortality are multifactorial; as well as patient-related factors, these may include staffing issues, access to operating theatres or access to diagnostic investigations.[14] Unfortunately, most of these evidences have been derived from adult populations.

To date, no prospective, multicentre, international investigation has evaluated the determinants of morbidity or mortality after emergency abdominal surgery in children on a global scale. The aim of the current study was to evaluate the mortality and morbidity of emergency abdominal surgery in children across countries of different human development indices (HDIs).

METHODS

Study design

This was a cohort study of children under the age of 16 years recruited from multiple hospitals performing emergency abdominal surgery. Predefined data items were collected according to a previously published protocol (ClinicalTrials.gov identifier: NCT02179112)[15] using the Research Electronic Data Capture (REDCap) which is an online data capture system.[16] While the UK National Health Service Research Ethics review considered this study exempt from formal research registration (South East Scotland Research Ethics Service, reference: NR/1404AB12), individual centres obtained their own audit, ethical or institutional approval as appropriate.

The collaborative model used has previously been described elsewhere.[17] Investigators from self-selected surgical units identified consecutive patients within 2-week time intervals between 1 July 2014 and 31 December 2014. An open invitation for participation was disseminated through social media, personal contacts, email to authors of published emergency surgery studies and national/international surgical organisations. Short intensive data collection allowed surgical teams within these units to contribute meaningful numbers of patients without requiring additional resources. Multiple 2-week data collection periods within institutions was allowed.

Patients and procedures

Any hospital performing emergency abdominal surgery, which included paediatric patients, could choose to be included (self-selecting). Consecutive patients under age of 16 years undergoing emergency abdominal surgery during a chosen 2-week period between 1 July 2014 and 31 December 2014 were included. Emergency abdominal surgery was defined as any unplanned, non-elective operation, including reoperation after a previous procedure. Abdominal surgery was defined as any open, laparoscopic or laparoscopic-converted procedure that entered the peritoneal cavity. Elective (planned) or semielective procedures (where a patient initially admitted as an emergency was then discharged from hospital and readmitted at a later time for surgery) were excluded.

Data

Data were selected to be objective, standardised, easily transcribed and internationally relevant, in order to maximise record completion and accuracy. Recruited patients were followed up to day 30 after surgery or for the length of their inpatient stay where follow-up was not feasible. Records were uploaded by local investigators to the secure online REDCap website. The lead investigator at each site validated all cases prior to data submission. The submitted data were then checked centrally and where missing data were identified, the local lead investigator was contacted and requested to complete the record. Once vetted, the record was accepted into the data set for analysis.

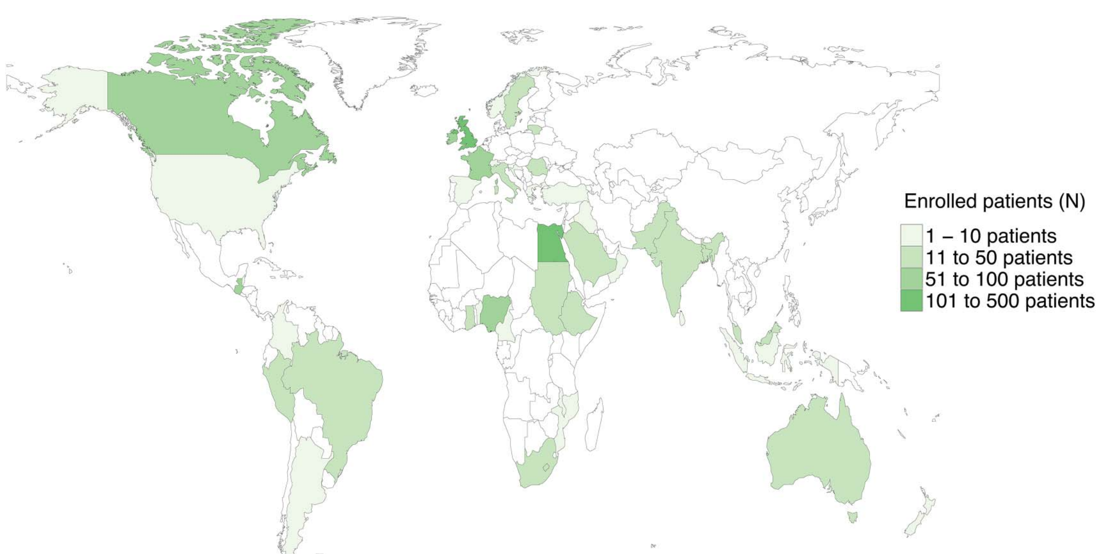

Figure 1 World map showing participating countries and number of enrolled patients.

Outcome measures

The primary outcome measure was 30-day postoperative mortality, defined as the number of patients in the cohort who died within 30 days of surgery.[18] In the event where 30-day follow-up was unavailable, outcome status at the point of discharge from hospital was recorded. A '30-day postoperative mortality/death during hospital stay', is shortened to '30-day mortality' to aid readability. The secondary outcome measures were 24-hour mortality, major and minor complication, and surgical site infection (SSI). Complications were defined on the Clavien-Dindo scale:[19] minor complications as grade I/II (any deviation from the normal postoperative course with or without a need for pharmacological treatment but without requirement for surgical, endoscopic and radiological interventions or critical care admission); reintervention as grade III (surgical, endoscopic or radiological reintervention, without requirement for critical care admission); and major complication as grade IV (complication requiring critical care admission).

Statistical analysis

The lack of pre-existing literature data in this subject meant that an a priori sample size determination was rendered difficult by unknown factors such as the effect of clustering and variation in mortality by diagnosis.

Table 1 Patient characteristics

	HDI tertile			
	High	**Middle**	**Low**	**p Value**
Age in completed years				
Mean (SD)	8.9 (5.1)	9.1 (5.0)	7.0 (5.6)	<0.001
Gender				
Male	388 (55.9)	275 (61.1)	152 (57.4)	0.216
Female	306 (44.1)	175 (38.9)	113 (42.6)	
Missing	0 (0.0)	0 (0.0)	0 (0.0)	
ASA grade				
1	507 (73.1)	354 (78.7)	154 (58.1)	<0.001
2	105 (15.1)	65 (14.4)	58 (21.9)	
3	51 (7.3)	12 (2.7)	37 (14.0)	
4	23 (3.3)	6 (1.3)	12 (4.5)	
5	8 (1.2)	13 (2.9)	4 (1.5)	
Missing	0 (0.0)	0 (0.0)	0 (0.0)	
Surgical safety checklist used				
No, not available in this hospital	35 (5.0)	192 (42.7)	95 (35.8)	<0.001
No, but available in this hospital	6 (0.9)	39 (8.7)	74 (27.9)	
Yes	653 (94.1)	217 (48.2)	96 (36.2)	
Missing	0 (0.0)	2 (0.4)	0 (0.0)	
Perforated viscus				
No	596 (85.9)	399 (88.7)	190 (71.7)	<0.001
Yes	97 (14.0)	49 (10.9)	68 (25.7)	
Missing	1 (0.1)	2 (0.4)	7 (2.6)	
Prophylactic antibiotics				
No, not available	6 (0.9)	16 (3.6)	0 (0.0)	0.404*
No, but available	90 (13.0)	55 (12.2)	36 (13.6)	
Yes	598 (86.2)	377 (83.8)	228 (86.0)	
Missing	0 (0.0)	2 (0.4)	1 (0.4)	
Whole blood/products				
No, but available in this hospital	661 (95.2)	385 (85.6)	201 (75.8)	<0.001*
No, not available in this hospital	8 (1.2)	7 (1.6)	1 (0.4)	
Yes, whole blood	2 (0.3)	30 (6.7)	54 (20.4)	
Yes, blood products	23 (3.3)	26 (5.8)	9 (3.4)	
Missing	0 (0.0)	2 (0.4)	0 (0.0)	

*χ^2 test is for yes versus no.
ASA, American Society of Anesthesiologists; HDI, Human Development Index.

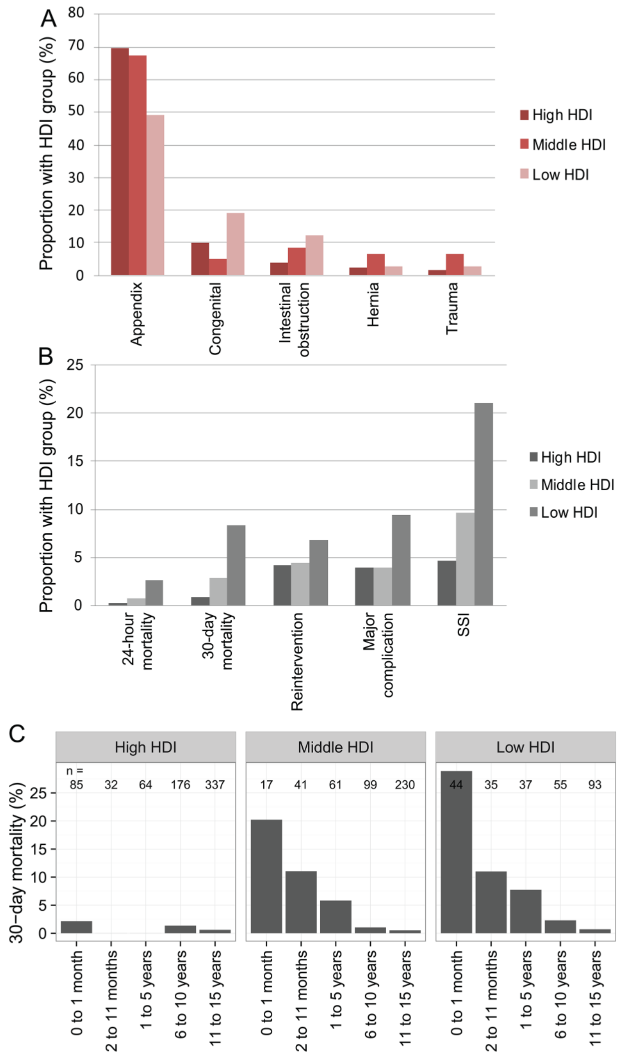

Figure 2 (A) Indications for emergency abdominal surgery in children across Human Developmental Index groups; (B) Surgical outcomes by Human Development Index group; (C) Adjusted 30-day mortality according to age groups. HDI, Human Developmental Index; SSI, surgical site infection.

Variation across different international health settings was assessed by stratifying participating centres by country into three tertiles according to the Human Development Index (HDI) rank. This is a composite statistic of life expectancy, education and income indices published by the United Nations (http://hdr.undp.org/en/statistics). Differences between HDI tertiles were tested with the Pearson χ^2 test and Kruskal-Wallis test for categorical and continuous variables, respectively.

Fixed effect binary logistic regression models were explored, and the variables determined to be statistically and clinically important were entered into full multivariable models. Final full model choice was guided by the Akaike information criterion (AIC). Hierarchical multivariable logistic regression models (random intercept) were constructed with country as the first level and patients as the second level. HDI tertile and other explanatory variables were included as fixed effects. Other than HDI tertile, all fixed effects were considered at the level of the patient. Coefficients are expressed as ORs with CIs and p values derived from percentiles of 10 000 bootstrap replications. Level 1 and 2 model residuals were checked and first-order interactions were tested. Goodness of model fit is reported with the Hosmer and Lemeshow test, and predictive ability described by area under the receiver operating characteristic (ROC) curve (c-statistic). All analyses were undertaken using the R Foundation Statistical Programme (R 3.1.1).

RESULTS

Patients

A total of 1409 patients aged under 16 years, from 253 centres in 43 countries, were included in this study (figure 1). At the time of operation, 282 (20.0%) were under the age of 2 years. Of all children, 694 (49.3%) were from high-HDI, 450 (31.9%) from middle-HDI and 265 (18.8%) from low-HDI groups. There were slightly more males than females in all HDI groups (table 1) (55.9% in high-HDI, 61.1% in middle-HDI and 58.1% in low-HDI groups). Missing data rates were low, with one missing outcome for 24-hour mortality and one missing outcome for 30-day mortality. In 1140/1409 patients, 30-day outcomes, which otherwise represent status at discharge, were confirmed by direct patient contact (80.9%; high 572/694, 82.4%; middle 358/450, 79.6%; low 210/265, 79.2%; χ^2 test, p=0.361).

Demographics

Children undergoing emergency abdominal surgery in low-HDI countries had higher American Society of Anaesthesiologists (ASA) grades than children in middle-HDI or high-HDI groups (table 1). Furthermore, the WHO surgical safety checklist was employed prior to surgery in less than half of children undergoing emergency abdominal surgery from the low-HDI and middle-HDI groups compared with over 90% in the high-HDI group. At operation, 214/1406 (15.2%) of the children were found to have a perforated viscus, and this varied with HDI group (high 97/694, 14.0%; middle 49/450, 10.9%; low 68/265, 25.7%). Use of laparoscopy was widespread in high-HDI nations (341/694, 49.1%), whereas in middle-HDI (30/450, 6.7%) and low-HDI (8/257, 3.0%) settings, rates were much lower (p<0.001).

Appendicitis was the most common indication for undergoing surgery across all groups, followed by congenital abnormalities, intussusception and hernia (figure 2A and online supplementary table S1). Emergency abdominal surgery for congenital abnormalities was significantly higher in low-HDI groups compared with middle-HDI and high-HDI groups (14.3% cf. 1.8% and 3.2%, respectively).

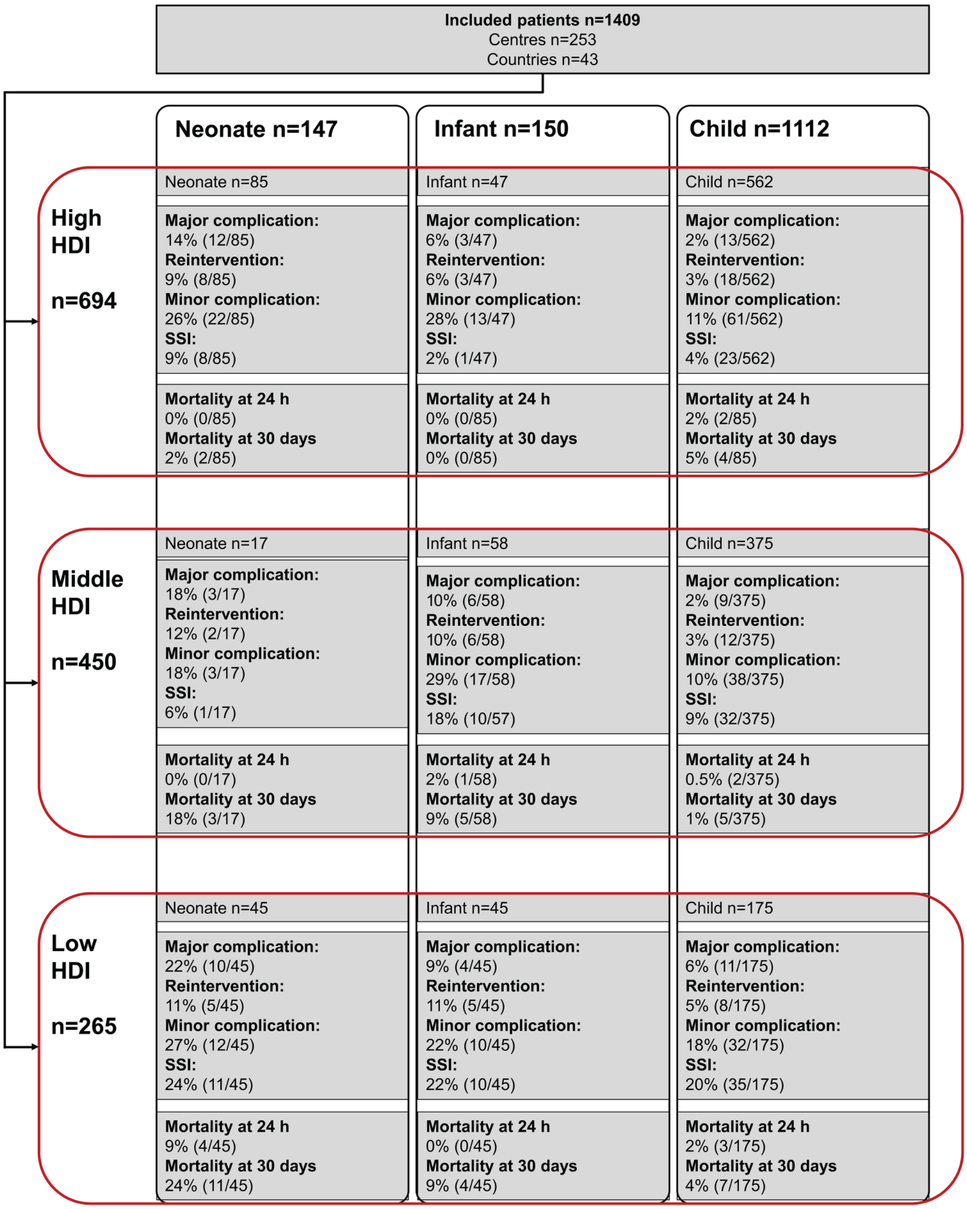

Figure 3 Patient complications and mortality profile according to Human Development Index. HDI, Human Developmental Index; SSI, surgical site infection.

Mortality

Overall, 30-day mortality following surgery was 2.9% (n=41/1409) (figure 3). Of these deaths, 29.3% (n=12/41) occurred within 24 hours and 70.7% (n=29/41) between 24 hours and 30 days. Mortality varied significantly with HDI, with significantly higher proportions in low-HDI countries at 24 hours (0.3% in high-HDI, 0.7% in middle-HDI and 2.6% in low-HDI groups, p=0.005) and 30 days (0.9% in high-HDI, 2.9% in middle-HDI and 8.3% in low-HDI groups, p<0.001). Other associations with 24-hour and 30-day mortality in univariable analyses included neonatal age, >1 ASA grade and non-appendicitis procedures. Perforated viscus was significantly associated with 30-day mortality. An inversely proportional relationship is seen between 30-day mortality and age in all HDI groups even after adjustment in models (figure 2C).

In multilevel models, the association between low-HDI country, and 24-hour (OR 7.08, 95% CI 1.39 to 36.10, p=0.018) (table 2) and 30-day mortality (OR 7.79, 95% CI 2.96 to 20.48, p<0.001) (table 3) persisted. Middle-HDI country was associated with a 30-day mortality (OR 5.57, 95% CI 1.90 to 16.39, p=0.002) but not 24-hour mortality. A perforated viscus was significantly associated with increased 30-day mortality, whereas appendicitis was associated with lower 24-hour and 30-day mortality compared with other indications.

An analysis of predicted excess deaths was performed using the final multilevel 30-day mortality model. Based on this model, if all children in low-HDI and middle-HDI

Table 2 Factors associated with 24-hour mortality

	Alive	Died	Univariate logistic regression OR (95% CI, p value)	Multilevel logistic regression OR (95% CI, p value)
HDI tertile				
High	692 (99.7)	2 (0.3)	–	–
Middle	446 (99.3)	3 (0.7)	2.33 (0.38 to 17.72, p=0.356)	3.71 (0.56 to 24.56, p=0.174)
Low	258 (97.4)	7 (2.6)	9.39 (2.25 to 63.28, p=0.005)	7.08 (1.39 to 36.10, p=0.018)
Age				
Child (>2 years <16 years)	1104 (99.4)	7 (0.6)	–	–
Infant (>1 month <2 years)	148 (99.3)	1 (0.7)	1.07 (0.06 to 6.05, p=0.953)	0.16 (0.02 to 1.45, p=0.102)
Neonate (≤1 month)	143 (97.3)	4 (2.7)	4.41 (1.14 to 14.79, p=0.019)	0.74 (0.16 to 3.33, p=0.694)
Gender				
Male	811 (99.5)	4 (0.5)	–	–
Female	585 (98.7)	8 (1.3)	2.77 (0.87 to 10.43, p=0.097)	3.47 (0.99 to 12.22, p=0.053)
ASA				
1	975 (99.8)	2 (0.2)	–	–
>1	421 (97.7)	10 (2.3)	11.58 (3.04 to 75.55, p=0.002)	5.22 (0.96 to 28.23, p=0.055)
Perforated viscus				
No	1177 (99.3)	8 (0.7)	–	–
Yes	209 (98.1)	4 (1.9)	2.82 (0.75 to 9.02, p=0.093)	1.57 (0.40 to 6.21, p=0.520)
Primary operation				
Non-appendicectomy	475 (97.7)	11 (2.3)	–	–
Appendicectomy	921 (99.9)	1 (0.1)	0.05 (0.00 to 0.24, p=0.003)	0.07 (0.01 to 0.59, p=0.015)

n=1398, AIC=120.2, c-statistic=0.922, H and L GOF=χ^2=3.438, df=8, p value=0.904.
AIC, Akaike information criterion; ASA, American Society of Anesthesiologists; df, degree of freedom; H and L GOF, Hosmer-Lemeshow Goodness of fit; HDI, Human Development Index.

countries were considered to have been in high-HDI countries but otherwise had the same characteristics, 29 lesser deaths are predicted (40 per 1000 procedures).

Major complications and reintervention

The overall rate of major complications following emergency abdominal surgery was 7.2% (n=102/1409) (figure 2B and online supplementary table S2). Major complications were significantly more common in low-HDI countries (11.3%, 30/265) compared with middle-HDI and high-HDI countries (6.4%, 29/450 and 6.2% 43/694, respectively, p=0.017). The rate of reintervention across the HDI groups mirrors these complications rates (low 6.8%, middle 4.4%, high 4.2%, p=0.222; online supplementary table S3).

Minor complications

Across all HDI groups, the minor complication rate (Clavien-Dindo I-II) was 14.8% (n=208). This varied across HDI groups, with higher rates in low-HDI countries (20.9%) compared with middle-HDI and high-HDI countries (13.1% and 13.8% respectively, p=0.010), but these differences did not persist in multivariable analysis (see online supplementary table S4).

Surgical site infection

The overall SSI rate was 9.3% (n=131). This varied significantly across HDI groups (low 21.1%, middle 9.6%, high 4.6%, p<0.001, online supplementary table S5).

DISCUSSION

The main findings of this study are sevenfold and fourfold higher 30-day mortalities in low-HDI and middle-HDI countries, respectively, compared with high-HDI countries. These rates are considerably greater than the threefold higher mortality previously reported among adult patients in low-HDI countries and account for an excess 40 deaths per thousand procedures in low-HDI and middle-HDI compared with high-HDI countries in this study alone.[20] The risk factors for this excess mortality are necessarily multifactorial, including a higher intestinal perforation rate, which may reflect delayed access to surgery and different patterns of disease.

The twofold higher rate of major and minor postoperative complications and the fivefold difference in SSIs are also noteworthy. Our study does not allow us to identify the main factors responsible for these differences, but other studies in the literature point out a variety of aetiological factors including sepsis, multiple exposure to anaesthesia in the neonatal period,

Table 3 Factors associated with 30-day mortality

	Alive	Died	Univariate logistic regression OR (95% CI, p value)	Multilevel logistic regression OR (95% CI, p value)
HDI tertile				
High	688 (99.1)	6 (0.9)	–	–
Middle	436 (97.1)	13 (2.9)	3.42 (1.34 to 9.79, p=0.013)	5.57 (1.90 to 16.39, p=0.002)
Low	243 (91.7)	22 (8.3)	10.38 (4.42 to 28.46, p<0.001)	7.79 (2.96 to 20.48, p<0.001)
Age				
Child (>2 years <16 years)	1095 (98.6)	16 (1.4)	–	–
Infant (>1 month<2 years)	140 (94.0)	9 (6.0)	4.40 (1.83 to 9.95, p=0.001)	0.91 (0.35 to 2.38, p=0.849)
Neonate (≤1 month)	131 (89.1)	16 (10.9)	8.36 (4.06 to 17.22, p<0.001)	2.27 (0.92 to 5.62, p=0.075)
Gender				
Male	794 (97.4)	21 (2.6)	–	–
Female	573 (96.6)	20 (3.4)	1.32 (0.70 to 2.47, p=0.382)	1.98 (1.00 to 3.94, p=0.051)
ASA				
1	964 (98.7)	13 (1.3)	–	–
>1	403 (93.5)	28 (6.5)	5.15 (2.69 to 10.37, p<0.001)	1.47 (0.67 to 3.25, p=0.337)
Perforated viscus				
No	1157 (97.6)	28 (2.4)	–	–
Yes	200 (93.9)	13 (6.1)	2.69 (1.33 to 5.17, p=0.004)	2.63 (1.21 to 5.73, p=0.015)
Primary operation				
Non-appendicectomy	447 (92.0)	39 (8.0)	–	–
Appendicectomy	920 (99.8)	2 (0.2)	0.02 (0.00 to 0.08, p<0.001)	0.04 (0.01 to 0.18, p<0.001)

n=1398, AIC=282.7, c-statistic=0.902, H&L GOF=χ^2=6.418, df=8, p value=0.601.
AIC, Akaike information criterion; ASA, American Society of Anesthesiologists; df, degree of freedom; H and L, Hosmer-Lemeshow Goodness of fit; HDI, Human Development Index.

postoperative bleeding, as well as complexity of congenital anomaly, delayed presentation, non-availability of trained personnel and financial constraints on the part of the caregivers.[5–11 21] While the overall commonest surgical procedure in children remains appendicectomy, other complex procedures for congenital anomalies and intestinal obstruction are commonly performed in children in resource-limited settings. The similarity in procedures performed across resource settings was not expected, but it does demonstrate the depth of training required by surgical personnel to be able to handle such complex cases. Minimal access surgery was infrequently used in low-HDI and middle-HDI countries, showing inequality in access to contemporary technology through lack of resources including training in use of such technology.[22]

The study was able to draw from a large and diverse patient population, spanning wide geographical and resource areas globally. Despite the convenience sampling employed, it offers a snapshot of essential paediatric surgery across the globe. The main body of data from the study highlights the differences in pathology, patient premorbid status, operative findings and outcomes based on HDI grouping. The higher ASA status of children requiring emergency abdominal surgery in low-HDI and middle-HDI countries settings is concerning, and it potentially reflects delayed access to care with the consequent negative impact on postoperative outcomes. Similarly, the percentage of perforated viscus encountered at surgery was also significantly higher in low-HDI and middle-HDI countries. The delay in access to care has been previously reported by studies from LMICs.[9–11] This may account for the poor survival of neonates with severe congenital anomalies in these settings, such as intestinal atresia, abdominal wall defects and oesophageal atresia.[11 23] A study from Nigeria indicated that delayed intervention time >72 hours, neonatal age and severe postoperative complications are associated with higher mortality in paediatric surgical emergencies.[21]

This study has some limitations. Being based on convenience sampling of hospitals, the data collected may not be truly representative of other sites which may be more poorly resourced. Collection bias, however, may result in the true outcomes being even worse in LMICs, as the lowest resource sites would be less likely to participate. In addition, other factors such as availability of personnel, availability of complex anaesthetic and intensive care support, and delay time before surgery were not analysed in this study but may significantly impact on postoperative mortality. The current study has documented differences in surgical outcomes in children based on HDI groups, but has not explored in depth the reasons for these differences. This will form the agenda for future studies, together with outcome studies, focusing on elective essential surgical procedures in children.

The main conclusion of this study is that emergency abdominal surgery in children is associated with significantly worse outcomes in LMICs. The documentation provided by this study is essential to the process of scaling up surgical services for children in low-resource settings. Good surgical outcomes require a multitude of factors, including trained personnel, good facilities and surgical supplies, as well as prompt access to surgical care. Thus, any single intervention in this multifaceted system has a high likelihood of failing to fully address these complex issues. This relates to many well-meaning efforts from high-income countries (HICs) to assist surgically in resource-limited settings. For instance, temporary platforms in the form of 'surgical safaris', the provision of surgical equipment alone, or short-term training courses outside one's normal work setting will likely have little long-term impact.[24 25] The likeliest context in which broad systematic change can occur is likely that of a long-lasting institutional partnership. In such a context of relationship with mutual understanding and trust, appropriate change can be implemented in whichever areas are most needed, and progress can be monitored and evaluated.[26]

The recent global recognition of surgery as an essential healthcare component has provided a unique impetus for provision of essential surgical services, especially in LMICs.[27 28] The task ahead is a huge one, in terms of access to and quality of care. The current study has documented relatively poor outcomes of emergency abdominal surgery in children in low-HDI and middle-HDI countries. Such data are essential in guiding efforts to improve the surgical care of children globally and prioritise it in the global health agenda.

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Patient enrolment and data collection

Argentina: Claudio Fermani, Ruben Balmaceda, Maria Marta Modolo (Hospital Luis Lagomaggiore);

Australia: Ewan Macdermid, Neel Gobin, Roxanne Chenn, Cheryl Ou Yong, Michael Edye (Blacktown Hospital), Martin Jarmin, Scott K D'amours, Dushyant Iyer (Liverpool Hospital, The University Of New South Wales), Daniel Youssef, Nicholas Phillips, Jason Brown (Royal Brisbane & Women's Hospital), Isaac Hanley (The Tweed Hospital), Marilla Dickfos (Toowoomba Hospital);

Bangladesh: Ashrarur Rahman Mitul, Khalid Mahmud (Dhaka Shishu (Children) Hospital), Antje Oosterkamp (Lamb Hospital);

Benin: Pamphile A Assouto, Ismail Lawani, Yacoubou Imorou Souaibou (Centre National Hospitalier Et Universitaire Hubert Koutoukou Maga);

Brunei: Giridhar H Devadasar, Chean Leung Chong, Muhammad Rashid Minhas Qadir, (Ssb Hospital), Kyaw Phyo Aung, Lee Shi Yeo, Chean Leung Chong (RIPAS Hospital);

Brazil: Vanessa Dina Palomino Castillo, Monique Moron Munhoz, Gisele Moreira (Conjunto Hospitalar De Sorocaba), Luiz Carlos Barros De Castro Segundo, Salim Anderson Khouri Ferreira, Maíra Cassa Careta (Hospital Da Santa Casa De Misericórdia De Vitória), Rafael Araujo, Juliana Menegussi, Marisa Leal, Caio Vinícius Barroso de Lima, Luiza Sarmento Tatagiba, Antônio Leal (Hospital Infantil Nossa Senhora Da Gloria);

Cameroon: Samuel Nigo, Juana Kabba, Tagang Ebogo Ngwa, James Brown (Mbingo Baptist Hospital);

Canada: Sebastian King, Augusto Zani, Georges Azzie, Mohammed Firdouse, Sameer Kushwaha, Arnav Agarwal (The Hospital For Sick Children, Toronto), Karen Bailey, Brian Cameron, Michael Livingston (McMaster Children's Hospital), Alexandre Horobjowsky, Dan L Deckelbaum, Tarek Razek (Centre for Global Surgery, McGill University Health Centre);

Colombia: Irene Montes, Sebastian Sierra, Manuela Mendez (Clinica CES), Maria Isabel Villegas, Maria Clara Mendoza Arango, Ivan Mendoza, (Clínica Las Vegas), Fred Alexander Naranjo Aristizã ¡bal, Jaime Andres Montoya Botero, Victor Manuel Quintero Riaza (El Hospital Pablo Tobón Uribe), Jakeline Restrepo, Carlos Morales, Maria Clara Mendoza Arango (Hospital Universitario San Vicente Fundación), Herman Cruz, Alejandro Munera, Maria Clara Mendoza Arango (Ips Universitaria Clínica León Xiii);

Croatia: Robert Karlo, Edgar Domini, Jakov Mihanovic (Zadar General Hospital), Mihael Radic, Kresimir Zamarin, Nikica Pezelj (General Hospital Sibenik);

Egypt: Ahmed Khyrallh, Ahamed Hassan, Gamal Shimy, Mohamed A Baky Fahmy (Al-Azher University Hospital); Ayman Nabawi, Muhammad Saad Ali Muhammad Gohar, Mohamed Elfil, Mohamed Ghoneem, Muhammad El-Saied Ahmad Muhammad Gohar, Mohamed Asal, Mostafa Abdelkader, Mahmoud Gomah, Hayssam Rashwan, Mohamed Karkeet, Ahmed Gomaa (Alexandria Main University Hospital); Amr Hasan, Ahmed Elgebaly, Omar Saleh, Ahmad Abdel Fattah, Abdullah Gouda, Abd Elrahman Elshafay, Abdalla Gharib, Mohammed Hanafy, Abdullah Al-Mallah, Mahmoud Abdulgawad, Mohamad Baheeg, Mohammed Alhendy, Ibrahim Abdel Fattah, Abdalla Kenibar, Omar Osman, Mostafa Gemeah, Ahmed Mohammed, Abdalrahman Adel, Ahmed Maher Menshawy Mesreb, Abdelrahman Mohammed, Abdelrahman Sayed, Mohamed Abozaid (Al-Hussein Hospital); Ahmed Hafez El-Badri Kotb, Ali Amin Ahmed Ata, Mohammed Nasr, Abdelrahman Alkammash, Mohammed Saeed, Nader Abd El Hamid, Attia Mohamed Attia, Ahmed Abd El Galeel, Eslam Elbanby, Khalid Salah El-Dien, Usama Hantour, Omar Alahmady, Billal Mansour, Amr Muhammad Elkorashy (Bab El-Sharia Hospital); Emad Mohamed Saeed Taha, Kholod Tarek

Lasheen, Salma Said Elkolaly, Nehal Yosri Elsayed Abdel-Wahab, Mahmoud Ahmed Fathi Abozyed, Ahmed Adel, Ahmed Moustafa Saeed, Gehad Samir El Sayed, Jehad Hassan Youssif (Banha University Hospital); Soliman Magdy Ahmed, Nermeen Soubhy El-Shahat, Abd El-Rahman Hegazy Khedr (Belbeis Central Hospital); Abdelrhman Osama Elsebaaye, Mohamed Elzayat, Mohamed Abdelraheim, Ibrahim Elzayat, Mahmoud Warda, Khaled Naser El Deen, Abdelrhman Essam, Omar Salah, Mohamed Abbas, Mona Rashad, Ibrahim Elzayyat, Dalia Hemeda, Gehad Tawfik, Mai Salama, Hazem Khaled, Mohamed Seisa, (El Dawly Hospital—Mansoura); Kareem Elshaer, Abdelfatah Hussein, Mahmoud Elkhadrawi (El Mahalla General Hospital); Ahmed Mohamed Afifi, Osama Saadeldeen Ebrahim, Mahmoud Mohamed Metwally (El Mataria Educational Hospital); Rowida Elmelegy, Diaa Moustafa Elbendary Elsawahly, Hisham Safa, Eman Nofal, Mohamed Elbermawy, Metwally Abo Raya, Ahmed Abdelmotaleb Ghazy, Hisham Samih, Asmaa Abdelgelil, Sarah Abdelghany, Ahmed El Kholy, Fatma Elkady, Mahmoud Salma, Sarah Samy, Reem Fakher, Aya Aboarab, Ahmed Samir, Ahmed Sakr, Abdelrahman Haroun, Asmaa Abdel-Rahman Al-Aarag, Ahmed Elkholy, Sally Elshanwany (El-Menshawy General Hospital); Esraa Ghanem (El-Shohadaa Central Hospital); Ahmed Tammam, Ali Mohamed Hammad, Yousra El Shoura, Gehad El Ashal, Hosni Khairy (Kasr Al-Ainy School Of Medicine); Sarah Antar, Sara Mehrez, Mahmoud Abdelshafy, Maha Gamal Mohamad Hamad, Mona Hosh, Emad Abdallah, Basma Magdy, Thuraya Alzayat, Elsayed Gamaly, Hossam Elfeki, Amany Abouzahra, Shereen Elsheikh, Fatimah I Elgendy (Mansoura University Hospitals); Fathia Abd El-Salam, Osama Seifelnasr, Mohamed Ammar, Athar Eysa, Aliaa Sadek, Aliaa Gamal Toeema, Aly Nasr, Mohamed Abuseif, Hagar Zidan, Sara Abd Elmageed Barakat, Nadin Elsayed, Yasmin Abd Elrasoul, Ahmed El-Kelany, Mohamed Sabry Ammar, Mennat-Allah Mustafa, Yasmin Makhlouf, Mohamed Etman, Samar Saad, Mahmoud Alrahawy, Ahmed Raslan, Mahmoud Morsi, Ahmed Sabry, Hager Elwakil, Heba Shaker, Hagar Zidan, Ahmed Elkelany (Menoufia University Hospitals); Hussein El-Kashef, Mohamed Shaalan, Areej Tarek (Minia University Hospital); Ayman Elwan, Ahmed Ragab Nayel, Mostafa Seif, Doaa Emadeldin Shafik, Mohamed Ali Ghoname, Ahmad Almallah, Ahmed Fouad, Ayman Elwan, Eman Adel Sayma (New Damietta University Hospital); Ahmad Elbatahgy, Angham Solaiman El-Ma'doul, Ahmed Mosad, Hager Tolba, Diaa Eldin Abdelazeem Amin Elsorogy, Hassan Ali Mostafa, Amira Atef Omar, Ola Sherief Abd El Hameed, Ahmed Lasheen (Quweisna Central Hospital, Quweisna); Yasser Abd El Salam, Ashraf Morsi, Mohammed Ismail (Ras El Tin General Hospital); Hager Ahmed, Mohamed A Amer, Ahmed Elkelany, Ahmed Sabry El-Hamouly, Noura Attallah, Omnia Mosalum, Ahmed Afandy, Ahmed Mokhtar, Alaa Abouelnasr, Sara Ayad, Ramdan Shaker, Rokia Sakr, Mahmoud Amreia, Soaad Elsobky, Mohamed Mustafa, Ahmed Abo El Magd, Abeer Marey, Amr Tarek, Mohamed Fadel (Shebin El Kom Teaching Hospital, Menoufia); Mohamed Moamen Mohamed, Amr Fadel, Emad Ali Ahmed (Sohag University Hospital); Ahmad Ali, Mohammad Ghassan Alwafai, Ehab Abdulkader Hemida Ghazy Alnawam, Abdullah Dwydar, Sara Kharsa, Ehab Mamdouh, Hatem El-Sheemy, Ibrahim Alyoussef, Abouelatta Khairy Aly, Ahmad Aldalaq, Ehab Alnawam, Dalia Alkhabbaz (Souad Kafafi University Hospital); Mahmoud Saad, Shady Hussein, Ahmed Abo Elazayem, Ahmed Meshref, Marwa Elashmawy, Mohammed Mousa, Ahmad Nashaat, Sara Ghanem, Zaynab M Elsayed, Aya Elwaey, Iman Elkadsh (Suez Canal University Hospitals); Mariam Darweesh, Ahmed Mohameden, Mennaallah Hafez (Suez General Hospital); Ahmed Badr, Assmaa Badwy, Mohamed Abd El Slam (Talla Q7 Central Hospital); Mohamed Elazoul, Safwat Al-Nahrawi, Lotfy Eldamaty, Fathee Nada, Mohamed Ameen, Aya Hagar, Mohamed Elsehimy, Mohammad Abo-ryia, Hossam Dawoud, Shorouk El Mesery, Abeer El Gendy, Ahmed Abdelkareem, Ahmed Safwan Marey, Mostafa Allam, Sherif Shehata, Khaled Abozeid, Marwa Elshobary, Ahmed Fahiem, Sameh Sarsik, Amel Hashish, Mohamed Zidan, Mohamed Hashish, Shaimaa Aql, Abdelaziz Osman Abdelaziz Elhendawy (Tanta University Hospital); Mohamed Husseini, Omar Khater, Esraa Abdalmageed Kasem, Ahmed Gheith, Yasmin Elfouly, Ahmed Ragab Soliman, Yasmein Hani, Nesma Elfouly, Ahmed Fawzy, Ahmed Hassan, Mohammad Rashid, Abdallah Salah Elsherbiny, Basem Sieda, Nermin Mohamed Badwi, Mohammed Mustafa Hassan Mohammed, Osama Mohamed, Mohammad Abdulkhalek Habeeb (Zagazig University Hospitals);

Ethiopia: Mengistu Worku, Nichole Starr (Dessie Referral Hospital), Semay Desta, Sahlu Wondimu, Nebyou Seyoum Abebe (Menelik IiHospital), Efeson Thomas, Frehun Ayele Asele, Daniel Dabessa (Myungsung Christian Medical Center), Nebiyou Seyoum Abebe, Abebe Bekele Zerihun (Tikur Anbessa Hospital);

France: Aurelien Scalabre, Fernanda Frade, Sabine Irtan (Trousseau Hospital, Sorbonnes Universités, UPMC Univ Paris), Valentine Parent, Amandine Martin, Alexis P Arnaud, Vivien Graffeille, Elodie Gaignard, Quentin Alimi (Rennes University Hospital), Olivier Abbo, Sofia Mouttalib, Ourdia Bouali (Hôpital des Enfants, Toulouse), Erik Hervieux, Yves Aigrain, Nathalie Botto (Hôpital Necker-Enfants Malades, Paris), Alice Faure, Lucile Fievet, Nicoleta Panait (Hôpital Nord, Marseille), Emilie Eyssartier, Francoise Schmitt, Guillaume Podevin (Pediatric Surgery Department, University Hospital, Angers), Cecile Muller, Arnaud Bonnard, Matthieu Peycelon (Robert Debré Children University Hospital);

Ghana: Francis Abantanga, Kwaku Boakye-Yiadom, Mohammed Bukari (Komfo Anokye Teaching Hospital), Frank Owusu (Offinso District Hospital), Joseph Awuku-Asabre, Stephen Tabiri, Lemuel Davies Bray (University For Development Studies, School Of Medicine And Health Sciences, General Surgery Department, Tamale Teaching Hospital);

Greece: Dimitrios Lytras, Kyriakos Psarianos, Anastasia Bamicha (Achillopoyleio General Hospital Of Volos), Christos Anthoulakis, Nikolaos Nikoloudis, Nikolaos Mitroudis (Serres General Hospital);

Guatemala: Gustavo Recinos, Sergio Estupinian, Walter Forno (Hospital De Accidentes Ceibal), Romeo Guevara, Maria Aguilera, Napoleon Mendez, Cesar Augusto Azmitia Mendizabal, Pablo Ramazzini, Mario Contreras Urquizu (Hospital General San Juan De Dios), Daniel Estuardo Marroquín Rodríguez, Carlos Iván Pérez Velásquez, Sara María Contreras Mérida (Hospital Regional de Retalhuleu), Francisco Regalado, Mario Lopez, Miguel Siguantay (Hospital Roosevelt, Guatemala);

India: SS Prasad, Anand Kirishnan, Nidhi Gyanchandani (KMC Hospital), Sriram Bhat, Anjana Sreedharan, S.V. Kinnera (Kasturba Medical College), Shravan Nadkarni, Harish Neelamraju Lakshmi, Puneet Malik (Sawai Man Singh Medical College & Hospitals, Jaipur, Rajasthan), Abid Bin Mahamood (Travancore Medical College Hospital), Monty Khajanchi, Savni Satoskar, Rajeev Satoskar (Seth Gordhandas Sunderdas Medical College And King Edward Memorial Hospital), Yella Reddy, Caranj Venugopal, Sunil Kumar (PES Institute Of Medical Sciences and Research); Indonesia: Eldaa Prisca Refianti Sutanto, Daniel Ardian Soeselo, Chintya Tedjaatmadja (Atmajaya Hospital), Fitriana Nur Rahmawati, Radhian Amandito, Maria Mayasari (Dr Cipto Mangunkusumo General Hospital, Jakarta);

Iraq: Ruqaya Kadhim Mohammed Jawad Al-Hasani, Hasan Ismael Ibraheem Al-Hameedi, Israa Abdullah Aziz Al-Azraqi (Al Sader Medical City), Lubna Sabeeh, Rahma Kamil, Marwan Shawki (Baghdad Medical City);

Ireland: Amoudtha Rasendran, Jacqueline Sheehan, Robert Kerley, Caoimhe Normile, Richard William Gilbert, Jiheon Song, Linnea Mauro, Mohammed Osman Dablouk, Michael Hanrahan, Paul Kielty, Eleanor Marks (Cork University Hospital), Simon Gosling, Michelle Mccarthy, Amoudtha Rasendran (Cork University Hospital and University College Cork), Diya Mirghani, Syed Altaf Naqvi, Chee Siong Wong (Limerick University Hospital), Simon George Gosling, Michelle Mccarthy, Amoudtha Rasendran, Ciara Fahy, Jiheon Song, Michael Hanrahan, Diana Duarte Cadogan, Anna Powell, Richard Gilbert, Caroline Clifford, Caoimhe Normile, Aoife Driscoll (Mercy University Hospital), Stassen Paul, Chris Lee, Ross Bowe (Midlands Regional Hospital Mullingar), William Hutch, Michael Hanrahan (University College Cork), Helen Mohan, Maeve O'Neill, Kenneth Mealy (Wexford General Hospital);

Italy: Piergiorgio Danelli, Andrea Bondurri, Anna Maffioli (Azienda Ospedaliera Luigi Sacco—Polo Universitario), Luigi Bonavina, Yuri Macchitella, Chiara Ceriani (University of Milan, IRCCS Policlinico San Donato), Ezio Veronese, Luca Bortolasi, Alireza Hasheminia (San Bonifacio Hospital), Francesco Pata, Angelo Benevento, Gaetano Tessera (Sant'Antonio Abate Hospital, Gallarate), Luca Turati, Giovanni Sgroi, Emanuele Rausa (Treviglio Hospital);

Lithuania: Donatas Venskutonis, Saulius Bradulskis, Linas Urbanavicius, Aiste Austraite, Romualdas Riauka, Justas Zilinskas, Zilvinas Dambrauskas (Lithuanian University Of Health Sciences);

Malawi: Ross Coomber, Kenneth Johnson, Jennifer Nowers (Queen Elizabeth Hospital);

Malaysia: Dineshwary Periasammy, Afizah Salleh, Andre Das (Hospital Kajang), Reuben Goh Ern Tze, Milaksh Nirumal Kumar, Nik Azim Nik Abdullah (Sarawak General Hospital), Hoong Yin Chong, April Camilla Roslani, Cheng Chun Goh (University Malaya Medical Centre);

Malta: Marija Agius, Elaine Borg, Maureen Bezzina, Roberta Bugeja, Martinique Vella-Baldacchino, Andrew Spina, Josephine Psaila (Mater Dei Hospital, Malta);

Martinique: Helene Francois-Coridon, Cecilia Tolg, Jean-Francois Colombani (Department of Pediatric Surgery, Mother and Children's Hospital, University Hospital Of Martinique);

Mozambique: Mário Jacobe, Domingos Mapasse, Elizabeth Snyder (Hospital Central Maputo);

New Zealand: Ramadan Oumer, Mohammed Osman (Whangarei Hospital, Northland District Health Board);

Nigeria: Aminu Mohammad, Lofty-John Anyanwu, Abdulrahman Sheshe (Aminu Kano Teaching Hospital), Alaba Adesina, Olubukola Faturoti, Ogechukwu Taiwo (Babcock University Teaching Hospital), Muhammad Habib Ibrahim, Abdulrasheed A Nasir, Siyaka Itopa Suleiman (Federal Medical Centre, Birnin Kebbi), Adewale Adeniyi, Opeoluwa Adesanya, Ademola Adebanjo (Federal Medical Centre), Roland Osuoji, Kazeem Atobatele, Ayokunle Ogunyemi, Omolara Wiliams, Mobolaji Oludara, Olabode Oshodi (Lagos State University Teaching Hospital), Adesoji O Ademuyiwa, Abdul Razzaq, Oluwagbemiga Lawal, Felix Alakaloko, Olumide Elebute, Adedapo Osinowo, Christopher Bode (Lagos University Teaching Hospital), Abidemi Adesuyi (National Hospital, Abuja), Adesoji Tade, Adeleke Adekoya, Collins Nwokoro (Olabisi Onabanjo University Teaching Hospital),Omobolaji O Ayandipo, Taiwo Akeem Lawal, Akinlabi E Ajao (University College Hospital),Samuel Sani Ali, Babatunde Odeyemi, Samson Olori (University of Abuja Teaching Hospital), Ademola Popoola, Ademola Adeyeye, James Adeniran (University of Ilorin Teaching Hospital);

Norway: William J. Lossius (Department Of Gastrointestinal Surgery, St. Olavs Hospital, Trondheim University Hospital), Ingemar Havemann (Søerlandet Hospital Kristiansand), Kenneth Thorsen, Jon Kristian Narvestad, Kjetil Soreide (Stavanger University Hospital), Trude Beate Wold, Linn Nymo (University Hospital Of North Norway, Troms);

Oman: Mohammed Elsiddig, Manzoor Dar (Sohar Hospital);

Pakistan: Kamran Faisal Bhopal, Zainab Iftikhar, Muhammad Mohsin Furqan (Bahawal Victoria Hospital), Bakhtiar Nighat, Masood Jawaid, Abdul Khalique (Dow University Hospital), Ahsan Zil-E-Ali, Anam Rashid (Fatima Memorial Hospital);

Peru: Wendy Leslie Messa Aguilar, Jose Antonio Cabala Chiong, Ana Cecilia, Manchego Bautista (Carlos Alberto Seguin Escobedo National Hospital, EsSalud), Eduardo Huaman, Sergio Zegarra, Rony Camacho (Hospital Nacional Guillermo Almenara), Jose María Vergara Celis, Diego Alonso Romani Pozo (Hospital De Emergencias Pediátricas), José Hamasaki, Edilberto Temoche, Jaime Herrera-Matta (Hospital De Policia), Carla Pierina García Torres, Luis Miguel Alvarez Barreda, Ronald Renato Barrionuevo Ojeda (Hospital Goyeneche), Octavio Garaycochea (Hospital Regional Ii-Ii Minsa Moyobamba), Melanie Castro Mollo, Mitchelle Solange De Fã Tima Linares Delgado, Francisco Fujii (Hospital Maria Auxiliadora), Ana Cecilia Manchego Bautista, Wendy Leslie Messa Aguilar, Jose Antonio Cabala Chiong (Hospital Nacional Carlos Alberto Seguin), Susana Yrma Aranzabal Durand, Carlos Alejandro Arroyo Basto, Nelson Manuel Urbina Rojas (Hospital Nacional Edgardo Rebagliati Martins-EsSalud), Sebastian Bernardo Shu Yip, Ana Lucia Contreras Vergara, Andrea Echevarria Rosas Moran, Giuliano Borda Luque, Manuel Rodriguez Castro, Ramon Alvarado Jaramillo (Hospital Nacional Cayetano Heredia), George Manrique Sila, Crislee Elizabeth Lopez, Mardelangel Zapata Ponze De Leon, Massiell Machaca, Ronald Coasaca Huaraya, Andy Arenas, Clara Milagros Herrera Puma, Wilfredo Pino, Christian Hinojosa, Melanie Zapata Ponze De Leon, Susan Limache, George Manrrique Sila, Layza-Alejandra Mercado Rodriguez (Hospital Regional Honorio Delgado Espinoza);

Réunion: Frederique Sauvat (Chu Réunion);

Romania: Lucian Corneliu Vida, Liviu Iuliu Muntean, Aurel Sandu Mironescu (Spitalul Clinic De Copii Brasov);

Saudi Arabia: Ibrahim N. Alomar, Saleh A. Alnuqaydan, Abdulrahman M. Altwigry (Buraydah Central Hospital), Moayad Othman, Nohad Osman (Imam Abdulrahman Al Faisal Hospital), Enas Alqahtani (King Abdulaziz Hospital Al Ahsa National Guard), Mohammed Alzahrani, Rifan Alyami, Emad Aljohani (King Abdulaziz Medical City), Ibrahim Alhabli, Zaher Mikwar, Sultan Almuallem (King Abdulaziz Medical City (King Khalid National Guard Hospital), Jeddah), Emad Aljohani, Rifan Alyami, Mohammed Alzahrani (King Abdulaziz Medical City, Riyadh), Abrar Nawawi, Mohamad Bakhaidar, Ashraf A. Maghrabi, Mohammed Alsaggaf, Murad Aljiffry, Abdulmalik Altaf, Ahmad Khoja, Alaa Habeebullah, Nouf Akeel (Department of Surgery, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia), Nashat Ghandora, Abdullah Almoflihi, Abdulmalik Huwait (King Fahad General Hospital), Abeer Al-shammari, Mashael Al-Mousa (King Fahad Hospital), Masood Alghamdi, Walid Adham, Bandar Albeladi, Muayad Ahmed Alfarsi, Atif Mahdi, Saad Al Awwad (King Fahd Hospital), Afnan Altamimi, Thamer Nouh, Mazen Hassanain (King Khalid University Hospital, King Saud University), Salman Aldhafeeri, Nawal Sadig, Osama Algohary (King Khalid General Hospital), Mohannad Aledrisy, Ahmad Gudal, Ahmad Alrifaie (King Khalid National Guard Hospital), Mohammed AlRowais, Amani Althwainy (Department of Surgery, King Saud University), Alaa Shabkah, Uthman Alamoudi, Mawaddah Alrajraji (National Guard Hospital), Basim Alghamdi, Saud Aljohani, Abdullah Daqeeq (RCYMC), Jubran J Al-Faifi (Security Forces Hospital);

South Africa: Vicky Jennings, Nyawira Ngayu, Rachel Moore (Chris Hani Baragwanath Academic Hospital), Victor Kong (Edendale Hospital), Colleen Sampson, Richard Spence, Eugenio Panieri (Groote Schuur), Myint Tun, Albert Mohale Mphatsoe, Jo-Anne Carreira (Leratong Hospital), Ella Teasdale, Mark Wagener (Ngwelezana Hospital), Stefan Botes, Danelo Du Plessis (Rob Ferreira Hospital);

Spain: Janet Pagnozzi, Jimy Harold Jara Quezada, Jose Luis Rodicio, German Minguez, Raquel Rodríguez-Uría, Paul Ugalde, Camilo Lopez-Arevalo, Luis Barneo, Jessica Patricia Gonzales Stuva (Hospital Universitario Central de Asturias), Jose Aguilar-Jimenez, Jose Andres Garcia-Marin (Hospital Morales Meseguer. SMS), Irene Ortega-Vazquez, Lorena Rodriguez, Norberto Herrera (Severo Ochoa University Hospital);

Sri Lanka: Prasad Pitigala Arachchi, Wanigasekara Senanayake Mudiyanselage Kithsiri Janakantha Senanayake, Lalith Asanka Jayasooriya Jayasooriya Arachchige (Department Of General Surgery, Teaching Hospital Kandy), Sivasuriya Sivaganesh, Dulan Irusha Samaraweera, Vimalakanthan Thanusan (The National Hospital Of Sri Lanka);

Sudan: Ahmed Elgaili Khalid Musa, Reem Mohammed Hassan Balila, Mohamed Awad Elkarim Hamad Mohamed (Ibrahim Malik Teaching Hospital), Hussein Ali, Hagir Zain Elabdin, Alaa Hassan (Jarash International Specialized Hospital), Sefeldin Mahdi, Hala Ahmed, Sahar Abdoun Ishag Idris (Khartoum Teaching Hospital), Makki Elsayed, Mohammed Elsayed, Mohamed Mahmoud (Omdurman Teaching Hospital);

Sweden: Hildur Thorarinsdottir, Maria Utter (Helsingborgs Lasarett), Sami Martin Sundstrom (Hudiksvall Sjukhus), Cecilia Wredberg, Ann Kjellin (Karolinska Universitetssjukhuset), Johanna Nyberg, Bjorn Frisk (Skaraborg Hospital Skovde), Yücel Cengiz, Sandra Ahlqvist, Ida Björklund (Sundsvall Hospital), Maria Hjertberg (Vrinnevi Hospital), Malin Sund, Linda Andersson, Ulf Gunnarsson (Department Of Surgical And Perioperative Sciences, Umeå University and Umea University Hospital), Hanna Royson, Per Weber (Vaxjo Central Hospital);

Switzerland: Roger Schmid, Debora Schivo, Vasileios Despotidis (Bürgerspital Solothurn), Stefan Breitenstein, Ralph F Staerkle, Erik Schadde (Kantonsspital Winterthur), Fabian Deichsel, Alexandra Gerosa, Antonio Nocito (Kantonsspital Baden), Dimitri Aristotle Raptis, Barbara Mijuskovic, Markus Zuber, Lukas Eisner (Kantonsspital Olten), Swantje Kruspi, Katharina Beate Reinisch, Christin Schoewe (Kreisspital für das Freiamt Muri AG), Allan Novak, Adrian F. Palma, Gerfried Teufelberger (Kreisspital Muri, Department Of Surgery);

Turkey: Ali Zeynel Abidin Balkan, Mehmet Gumar, Mehmet Ali Yavuz (Harran University Research and Treatment Hospital), Ufuk Karabacak, Gokhan Lap, Bahar Busra Ozkan (Ondokuz Mayis University, Medical Faculty);

UK: Ryan Adams, Robert Morton, Liam Henderson, Ruth Gratton, Keiran David Clement, Kate Yu-Ching Chang, David McNish, Ryan McIntosh, William Milligan (Aberdeen Royal Infirmary), Brendan Skelly, Hannah Anderson-Knight, Roger Lawther (Altnagelvin Area Hospital), Jemina Onimowo, Veereanna Shatkar, Shivanee Tharmalingam (Barking, Havering And Redbridge University Hospitals National Health Services (NHS) Trust, Romford), Evelina Woin, Tessa Fautz, Oliver Ziff (Barnet General Hospital), Shiva Dindyal, Sam Arman, Shagorika Talukder, Sam Arman, Vijay Gadhvi, Shagorika Talukder (Basildon and Thurrock University Foundation Trust), Luen Shaun Chew, Jonathan Heath (Blackpool Victoria Teaching Hospital), Gurdeep Singh Mannu, Dimitris-Christos Zachariades, Ailsa Claire Snaith (Buckinghamshire Healthcare NHS Trust), Thusitha Sampath Hettiarachchi, Arjun Nesaratnam, James Wheeler (Cambridge University Hospitals NHS Foundation Trust), Mark Sykes, Nebil Behar, Harriet Jordan (Chelsea And Westminster Hospital), Tan Arulampalam, Apar Shah, Damien Brown (Colchester Hospital University NHS Foundation Trust), Emma Blower, Paul Sutton, Konstantinos Gasteratos, Dale Vimalachandran (Countess Of Chester Hospital), Cathy Magee, Gareth Irwin, Andrew Mcguigan (Craigavon Area Hospital), Stephen Mcaleer, Clare Morgan (Daisy Hill Hospital), Sarah Braungart (Department of Paediatric Surgery, Leeds General Infirmary), Kirsten Lafferty, Peter Labib, Andrei Tanase, Clodagh Mangan, Lillian Reza (Derriford Hospital), Helen Woodward, Craig Gouldthorpe, Megan Turner (Diana, Princess Of Wales Hospital), Jonathan R L Wild, Tom AM Malik, Victoria K Proctor (Doncaster

Royal Infirmary NHS Foundation Trust), Kalon Hewage, James Davies (Dorset County Hospital), Andre Dubois, Sayed Sarwary, Ali Zardab, Alan Grant, Robert Mcintyre (Dr Gray's Hospital), Shirish Tewari, Gemma Humm, Eriberto Farinella, Sunil Parthiban (East And North Hertfordshire NHS Trust Lister Hospital) Nigel J Hall, Naomi J Wright, Christina P Major (Evelina London Children's Hospital), Thelma Xerri, Phoebe De Bono, Jasim Amin, Mustafa Farhad, John F. Camilleri-Brennan, Andrew G N Robertson, Joanna Swann, James Richards, Aijaz Jabbar, Myranda Attard, Hannah Burns, Euan Macdonald, Matthew Baldacchino, Jennifer Skehan, Julian Camilleri-Brennan (Forth Valley Royal Hospital), Tom Falconer Hall, Madelaine Gimzewska, Greta Mclachlan (Frimley Park Hospital), Jamie Shah, James Giles (George Eliot Hospital), Maleeha Hassan, William Beasley, Apostolos Vlachogiorgos, Stephen Dias, Geta Maharaj, Rosie McDonald (Glangwili General Hospital), Kate Cross, Clare M Rees, Bernard Van Duren (Great Ormond Street Hospital for Children NHS Foundation Trust), Emma Upchurch (Great Western Hospital), Sharad Karandikar, Doug Bowley, Ahmed Karim (Heart of England Foundation Trust), Witold Chachulski, Liam Richardson, Giles Dawnay, Ben Thompson, Ajayesh Mistry, Aneel Bhangu, Millika Ghetia, Sudipta Roy, Ossama Al-Obaedi, Millika Ghetia, Kaustuv Das (Hereford County Hospital), Ash Prabhudesai, DM Cocker, Jessica Juliana Tan (Hillingdon Hospital), Sayinthen Vivekanantham, Michael Gillespie, Katrin Gudlaugsdottir (Inverclyde Royal Hospital), Theodore Pezas, Chelise Currow, Matthew Young-Han Kim (Ipswich Hospital NHS Trust), Yahya Salama, Rohi Shah, Ahmad Aboelkassem Ibrahem, Hamdi Ebdewi, Gianpiero Gravante, Saleem El-Rabaa (Kettering General Hospital), Zoe Chan, Zaffar Hassan (King's College Hospital), Misty Makinde, David Hemingway, Ramzana Dean, Alexander Boddy, Ahmed Aber, Vijay Patel, Deevia Kotecha (Leicester Royal Infirmary), Harmony Kaur Ubhi, Simon-Peter Hosein (Luton and Dunstable Hospital), Simon Ward, Kamran Malik (Macclesfield District General Hospital), Leifa Jennings, Tom Newton, Mirna Alkhouri, Min Kyu Kang, Christopher Houlden, Jonathan Barry (Morriston Hospital), Michael S J Wilson, Yan Ning Neo, Ibrahim Ibrahim, Emily Chan, Fraser S Peck, Pei J Lim, Alexander S North, Rebecca Blundell, Adam Williamson (Ninewells Hospital, NHS Tayside), Dina Fouad, Ashish Minocha (Norfolk And Norwich University Hospital), Kathryn Mccarthy, Emma Court, Alice Chambers (North Bristol NHS Trust), Jenna Yee, Ji Chung Tham, Ceri Beaton (North Devon District Hospital), Una Walsh, Joseph Lockey, Salman Bokhari, Lara Howells, Megan Griffiths, Laura Yallop (Northwick Park Hospital), Shailinder Singh, Omar Nasher, Paul Jackson (Nottingham Children's Hospital, Queen's Medical Centre Campus), Saed Ramzi, Shady Zeidan, Jennifer Doughty (Plymouth Hospitals NHS Trust), Sidhartha Sinha, Ross Davenport, Jason Lewis (Princess Alexandra Hospital), Leo Duffy, Elizabeth Mcaleer, Eleanor Williams (Princess Of Wales Hospital), Rhalumi Daniel Obute, Thomas E Glover, David J Clark (Queen Elizabeth Hospital King's Lynn), Mohamed Boshnaq, Mansoor Akhtar, Pascale Capleton, Samer Doughan, Mohamed Rabie, Ismail Mohamed (Queen Elizabeth The Queen Mother Hospital), Duncan Samuel, Lauren Dickson, Matthew Kennedy, Eleanor Dempster, Emma Brown, Natalie Maple, Eimear Monaghan, Bernhard Wolf, Alicia Garland (Raigmore Hospital), Jonathan Lund, Catherine Boereboom, Jennifer Murphy, Gillian Tierney, Samson Tou (Royal Derby Hospital), Eleanor Franziska Zimmermann, Neil James Smart, Andrea Marie Warwick, Theodora Stasinou, Ian Daniels, Kim Findlay-Cooper (Royal Devon and Exeter NHS Foundation Trust), Stefan Mitrasinovic, Swayamjyoti Ray, Massimo Varcada, Rovan D'souza, Sharif Omara (Royal Free Hospital), Tamsin Boyce, Harriet Whewell, Elin Jones, Jennifer Ma, Emily Abington, Meera Ramcharn, Gethin Williams (Royal Gwent Hospital), Joseph Winstanley, Ewan D. Kennedy, Emily NW Yeung (Royal Hospital For Sick Children), Stuart J Fergusson, Catrin Jones, Stephen O'neill, Shujing Jane Lim, Ignatius Liew, Hari Nair, Cameron Fairfield, Julia Oh, Samantha Koh, Andrew Wilson, Catherine Fairfield, Francesca Th'ng, Nichola Robertson (Royal Infirmary of Edinburgh), Delran Anandkumar, Ashok Kirupagaran, Timothy F Jones, Hew D Torrance, Alexander J Fowler, Charmilie Chandrakumar, Priyank Patel, Syed Faaz Ashraf, Sonam M. Lakhani, Aaron Lawson Mclean, Sonia Basson (Royal London Hospital), Jeremy Batt, Catriona Bowman, Michael Stoddart, Natasha Benons (Royal United Hospital Bath), Tom Barker, Virginia Summerour, Edward Harper (Sandwell and West Birmingham Hospitals NHS Trust), Caroline Smith, Matthew Hampton (Sheffield Children's Hospital), Doug Mckechnie, Ayaan Farah, Anita Chun (Southend University Hospital), Bernadette Pereira, Kristof Nemeth, Emily Decker, Stefano Giuliani, Aly Shalaby (St.George's Healthcare NHS Trust and University), Aleksandra Szczap, Swathikan Chidambaram, Chee Yang Chen, Kavian Kulasabanathan, Srishti Chhabra, Elisabeth Kostov, Philippe Harbord, James Barnacle (St. Mary's Hospital), Madan Mohan Palliyil, Mina Zikry, Johnathan Porter, Charef Raslan, Mohammed Saeed, Shazia Hafiz, Niksa Soltani, Katie Baillie (Stockport NHS Foundation Trust), Ahmad Mirza, Haroon Saeed, Simon Galloway (The University Hospital of South Manchester), Gia Elena, Mohammad Afzal, Mohamed Zakir (United Lincolnshire Hospitals—Pilgrim Hospital), Peter Sodde, Charles Hand, Aiesha Sriram, Tamsyn Clark, Patrick Holton, Amy Livesey (University Hospital Coventry And Warwickshire), Yashashwi Sinha, Fahad Mujtaba Iqbal, Indervir Singh Bharj, Adriana Rotundo, Cara Jenvey, Robert Slade (University Hospital Of North Staffordshire NHS Trust), David Golding, Samuel Haines, Ali Adel Ne'ma Abdullah, Thomas W Tilston, Dafydd Loughran, Danielle Donoghue, Lorenzo Giacci, Mohamed Ashur Sherif, Peter Harrison, Alethea Tang (University Hospital Of Wales), Mohamed Elshaer, Tomas Urbonas, Amjid Riaz, Annie Chapman, Parisha Acharya, Joseph Shalhoub (Watford General Hospital), Cathleen Grossart, David McMorran (Western General Hospital), Makhosini Mlotshwa, William Hawkins, Sofronis Loizides (Western Sussex Hospitals NHS Trust), Peter Thomson, Shahab Khan, Fiona Taylor, Jalak Shukla, Emma Elizabeth Howie (Whipps Cross University Hospital), Linda Macdonald, Olusegun Komolafe, Neil Mcintyre (Wishaw General Hospital), James Cragg, Jody Parker, Duncan Stewart (Wrexham Maelor Hospital), Luke Lintin, Julia Tracy, Tahir Farooq (Yeovil District Hospital);

The USA: Melanie Sion, Michael S. Weinstein, Viren Punja (Thomas Jefferson University Hospital), Nikolay Bugaev, Monica Goodstein, Shadi Razmdjou (Tufts Medical Center).

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