Original article

Mortality of emergency abdominal surgery in high-, middle- and low-income countries

GlobalSurg Collaborative

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Background: **Surgical mortality data are collected routinely in high-income countries, yet virtually no low- or middle-income countries have outcome surveillance in place. The aim was prospectively to collect worldwide mortality data following emergency abdominal surgery, comparing findings across countries with a low, middle or high Human Development Index (HDI).**

Methods: **This was a prospective, multicentre, cohort study. Self-selected hospitals performing emergency surgery submitted prespecified data for consecutive patients from at least one 2-week interval during July to December 2014. Postoperative mortality was analysed by hierarchical multivariable logistic regression.**

Results: **Data were obtained for 10 745 patients from 357 centres in 58 countries; 6538 were from high-, 2889 from middle- and 1318 from low-HDI settings. The overall mortality rate was 1·6 per cent at 24 h (high 1·1 per cent, middle 1·9 per cent, low 3·4 per cent; $P < 0{\cdot}001$), increasing to 5·4 per cent by 30 days (high 4·5 per cent, middle 6·0 per cent, low 8·6 per cent; $P < 0{\cdot}001$). Of the 578 patients who died, 404 (69·9 per cent) did so between 24 h and 30 days following surgery (high 74·2 per cent, middle 68·8 per cent, low 60·5 per cent). After adjustment, 30-day mortality remained higher in middle-income (odds ratio (OR) 2·78, 95 per cent c.i. 1·84 to 4·20) and low-income (OR 2·97, 1·84 to 4·81) countries. Surgical safety checklist use was less frequent in low- and middle-income countries, but when used was associated with reduced mortality at 30 days.**

Conclusion: **Mortality is three times higher in low- compared with high-HDI countries even when adjusted for prognostic factors. Patient safety factors may have an important role. Registration number: NCT02179112 (http://www.clinicaltrials.gov).**

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Introduction

Global health priorities are typically assessed by measuring the burden of various diseases, including human immunodeficiency virus (HIV), tuberculosis, malaria and trauma. Surgery, however, contributes to the treatment of a very wide range of conditions and its significance may have been obscured by a disease-based approach to international health[1]. This is changing and the importance of surgery to human health and welfare has been highlighted by several recent studies[2–4]. For instance, 17 million of the 51 million people who died across the world in 2012 suffered from diseases needing surgical care[1,2]. Access to surgical care varies widely[3,4]. It has been estimated that less than one-third of the world's population has access to safe, timely and affordable surgery, and only 6 per cent of the 300 million surgical procedures performed each year take place in a low- or middle-income country (LMIC) despite one-third of the world's population living there[2]. There are firm moves, supported by the World Health Organization (WHO), to improve access to surgical care[3,5]. However, safe surgery requires considerable infrastructure, and improving coverage should go hand in hand with quality assurance[3]. Surgical mortality data are collected routinely in high-income health systems, but 70 per cent of countries lack routine surgical surveillance systems[4,6].

This study is the first step towards remedying the lack of outcome information by creating an international network of surgeons across all continents to measure mortality rates following emergency abdominal surgery. This is a common operation that is carried out with life-saving

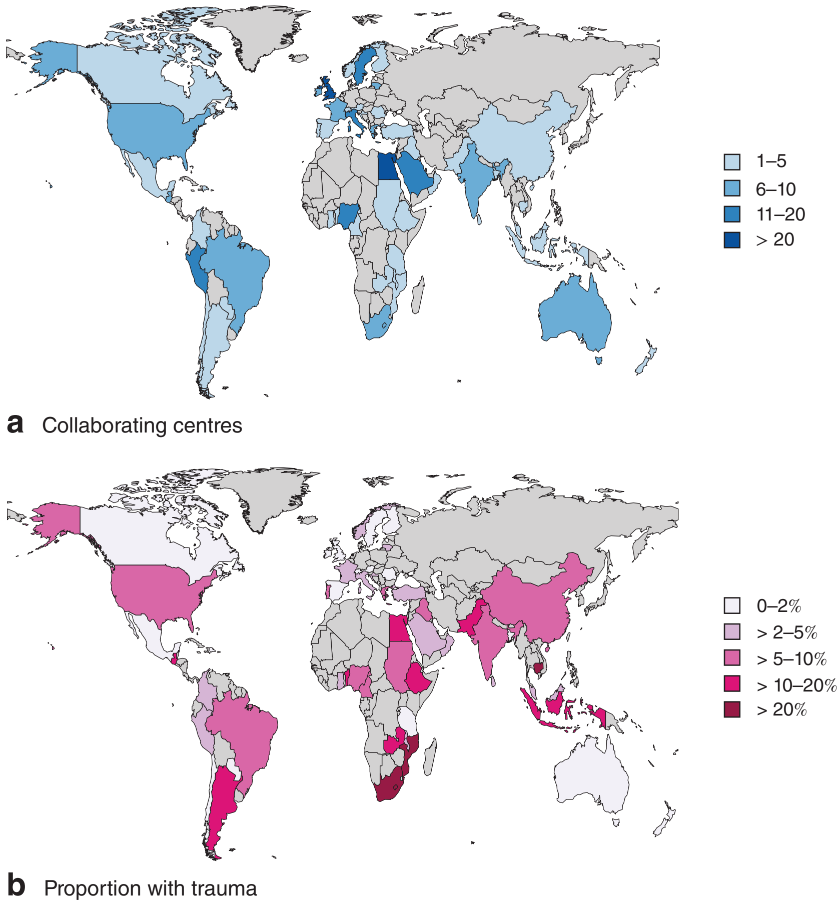

Fig. 1 **a** Collaborating centres and **b** proportion of enrolled patients with trauma diagnosis, by contributing country

intent, but which nevertheless carries substantial mortality. This makes it an important topic in its own right and a potential proxy for surgical care generally. The aim of this study was to collect postoperative mortality data and analyse variation in factors that might affect mortality. This first report describes the feasibility of collecting bedside patient-level data across low-, middle- and high-income settings using a new collaborative network. The study also compared the performance and practicality of using 24-h or 30-day postoperative mortality as the primary outcome measure in a wide variety of clinical settings. Variation in mortality was compared with markers of prognosis (including operation type) and service, marked by the availability and use of safety checklists.

Methods

An international, multicentre, prospective, observational cohort study was conducted according to a prespecified, registered and published protocol (ClinicalTrials.gov identifier NCT02179112)[7]. A 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. Results are reported according to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines[8].

Study interval

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 to participate was disseminated through social media, personal contacts, e-mail to authors of published emergency surgery studies, and national/international surgical organizations. Short intensive data collection allowed surgical teams within these units to contribute meaningful numbers of patients without requiring additional resources. The

Table 1 Demographic and preoperative data by Human Development Index tertile

	HDI tertile			
	High ($n = 6538$)	Middle ($n = 2889$)	Low ($n = 1318$)	P*
Mean(s.d.) age (completed years)	44·5(23·7)	33·4(19·6)	30·7(18·8)	< 0·001†
Sex				< 0·001
M	3162 (48·4)	1600 (55·4)	808 (61·3)	
F	3373 (51·6)	1289 (44·6)	510 (38·7)	
Missing	3 (0·0)	0 (0)	0 (0)	
ASA fitness grade				< 0·001
I	2701 (41·3)	1648 (57·0)	613 (46·5)	
II	2004 (30·7)	728 (25·2)	352 (26·7)	
III	1134 (17·3)	283 (9·8)	162 (12·3)	
IV	411 (6·3)	98 (3·4)	43 (3·3)	
V	102 (1·6)	65 (2·2)	69 (5·2)	
Unknown	183 (2·8)	66 (2·3)	76 (5·8)	
Missing	3 (0·0)	1 (0·0)	3 (0·2)	
Diabetes				0·622
No	6044 (92·4)	2686 (93·0)	1226 (93·0)	
Yes	491 (7·5)	203 (7·0)	92 (7·0)	
Missing	3 (0·0)	0 (0)	0 (0)	
Current smoker				< 0·001
No	4633 (70·9)	2247 (77·8)	1100 (83·5)	
Yes	1901 (29·1)	640 (22·2)	217 (16·5)	
Missing	4 (0·1)	2 (0·1)	1 (0·1)	
Diagnosis				< 0·001
Non-trauma/non-cancer	5522 (84·5)	2416 (83·6)	1049 (79·6)	
Neoplasm	407 (6·2)	80 (2·8)	57 (4·3)	
Trauma	143 (2·2)	290 (10·0)	159 (12·1)	
No disease identified	181 (2·8)	48 (1·7)	14 (1·1)	
Complication of previous procedure	285 (4·4)	55 (1·9)	39 (3·0)	
CT performed				< 0·001
No	3883 (59·4)	2354 (81·5)	1173 (89·0)	
Yes	2652 (40·6)	535 (18·5)	145 (11·0)	
Missing	3 (0·0)	0 (0)	0 (0)	

Values in parentheses are percentages by column unless indicated otherwise. HDI, Human Development Index; ASA, American Society of Anesthesiologists. *Pearson χ^2 test, except †Kruskal–Wallis test.

study covered an extended time interval to accommodate the availability of local investigators and variable holidays, while helping to smooth seasonal variation that can affect surgical pathology. An institution could collect over as many 2-week intervals as desired within the study time frame.

Patients and procedures

Consecutive patients undergoing emergency intraperitoneal surgery during the chosen 2-week interval were included. There were no age restrictions. Emergency surgery was defined as any unplanned, non-elective operation, including reoperation after a previous procedure. Intraperitoneal surgery was defined as any open, laparoscopic or converted laparoscopic procedure that entered the peritoneal cavity. Elective (planned) or semi-elective procedures (where a patient initially admitted as an emergency was then discharged from hospital and readmitted at later time for elective surgery) were excluded. Additionally, patients undergoing caesarean section were excluded as they represent a separate operative group with different management needs that have been studied elsewhere[9].

Data

Included patients were followed to day 30 after surgery or for the duration of their inpatient stay where follow-up was not feasible. Records were uploaded by local investigators to a secure online website, provided using the Research Electronic Data Capture (REDCap) system[10]. The lead investigator at each site checked the accuracy of all cases before data submission. The submitted data were then checked centrally and, where missing information was identified, the local lead investigator was contacted and asked to update and complete the record. Once vetted, the record was accepted into the data set for analysis.

Table 2 Operative data by Human Development Index tertile

	HDI tertile			
	High ($n = 6538$)	Middle ($n = 2889$)	Low ($n = 1318$)	P*
Procedure start time				< 0·001
08.00–18.00 hours (daytime)	3966 (60·7)	1230 (42·6)	586 (44·5)	
18.00–22.00 hours (evening)	1401 (21·4)	755 (26·1)	367 (27·8)	
22.00 to 08.00 hours (night-time)	1167 (17·8)	901 (31·2)	365 (27·7)	
Missing	4 (0·1)	3 (0·1)	0 (0)	
Admission to procedure time (h)				< 0·001
< 6	1382 (21·1)	1324 (45·8)	607 (46·1)	
6–11	1192 (18·2)	723 (25·0)	287 (21·8)	
12–23	1510 (23·1)	462 (16·0)	189 (14·3)	
24–47	1031 (15·8)	171 (5·9)	94 (7·1)	
≥ 48	1415 (21·6)	204 (7·1)	139 (10·5)	
Missing	8 (0·1)	5 (0·2)	2 (0·2)	
Surgical safety checklist used				< 0·001
No, not available in this hospital	422 (6·5)	1029 (35·6)	474 (36·0)	
No, but available in this hospital	146 (2·2)	248 (8·6)	421 (31·9)	
Yes	5967 (91·3)	1608 (55·7)	423 (32·1)	
Missing	3 (0·0)	4 (0·1)	0 (0)	
Senior surgeon > 5 years of training				< 0·001
No	182 (2·8)	1208 (41·8)	384 (29·1)	
Yes	6353 (97·2)	1676 (58·0)	934 (70·9)	
Missing	3 (0·0)	5 (0·2)	0 (0)	
Senior anaesthetist > 5 years of training				< 0·001
No	262 (4·0)	1395 (48·3)	524 (39·8)	
Yes	6273 (95·9)	1490 (51·6)	794 (60·2)	
Missing	3 (0·0)	4 (0·1)	0 (0)	
Anaesthetic type				< 0·001
General	6438 (98·5)	2213 (76·6)	1219 (92·5)	
Spinal or sedation	97 (1·5)	673 (23·3)	98 (7·4)	
Missing	3 (0·0)	3 (0·1)	1 (0·1)	
Laparoscopic approach				< 0·001
No	3369 (51·5)	2622 (90·8)	1238 (93·9)	
Yes	3169 (48·5)	267 (9·2)	80 (6·1)	
Bowel resection				< 0·001
No	5454 (83·4)	2608 (90·3)	1112 (84·4)	
Yes	1077 (16·5)	276 (9·6)	205 (15·6)	
Missing	7 (0·1)	5 (0·2)	1 (0·1)	
Stoma formed				< 0·001
No	5860 (89·6)	2732 (94·6)	1195 (90·7)	
Yes	674 (10·3)	152 (5·3)	123 (9·3)	
Missing	4 (0·1)	5 (0·2)	0 (0)	
Perforated viscus				< 0·001
No	5475 (83·7)	2406 (83·3)	913 (69·3)	
Yes	1059 (16·2)	476 (16·5)	377 (28·6)	
Missing	4 (0·1)	7 (0·2)	28 (2·1)	
Supplementary oxygen				< 0·001
No	239 (3·7)	515 (17·8)	101 (7·7)	
Yes	6296 (96·3)	2370 (82·0)	1187 (90·1)	
Missing	3 (0·0)	4 (0·1)	30 (2·3)	
Pulse oximetry				< 0·001
No	39 (0·6)	129 (4·5)	15 (1·1)	
Yes	6496 (99·4)	2756 (95·4)	1303 (98·9)	
Missing	3 (0·0)	4 (0·1)	0 (0)	
Prophylactic antibiotics				0·710
No	824 (12·6)	370 (12·8)	177 (13·4)	
Yes	5709 (87·3)	2514 (87·0)	1140 (86·5)	
Missing	5 (0·1)	5 (0·2)	1 (0·1)	

Values in parentheses are percentages by column. HDI, Human Development Index; ASA, American Society of Anesthesiologists. *Pearson χ^2 test.

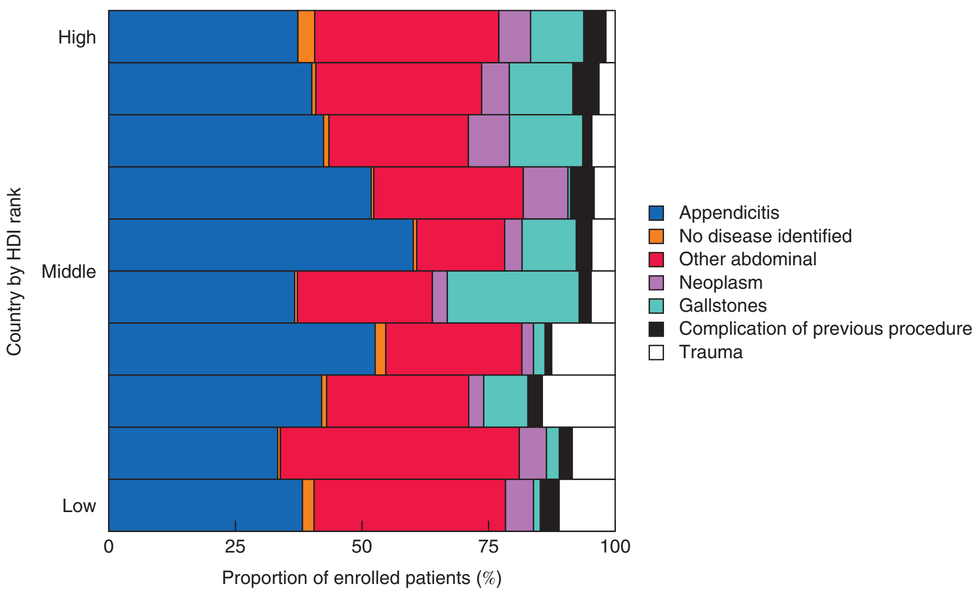

Fig. 2 Summary diagnostic groups according to Human Development Index (HDI) decile

Outcome measures

The primary outcome measure was the 24-h postoperative mortality rate. This was the number of deaths during the procedure, or within 24 h of the operation's conclusion, divided by the number of eligible operations performed[11]. The main secondary outcome measure was the 30-day postoperative mortality rate. Where 30-day follow-up was not available, survival status (alive or dead) at the point of discharge from hospital was recorded. Other secondary outcome measures included postoperative complication and reintervention rates. For the purposes of clarity, these will be described in subsequent reports where sufficient detail can be included.

Independent (exploratory) variables

The following patient-level factors were collected in order to adjust outcome. Patient factors were: age, sex, diabetes, smoking status and American Society of Anesthesiologists (ASA) fitness grade. Disease factors comprised seven major diagnostic groups, representing the spectrum of disease encountered; in addition, the presence of a perforated abdominal viscus found at operation was included. Hospital safety was also explored in terms of the availability and use of a surgical safety checklist for each patient.

Power considerations

The sample size was limited by practical factors, and estimation of power by uncertainty over critical quantities such as clustering and variation in mortality by diagnosis. An indicative power calculation is provided in the protocol.

Statistical analysis

Variation across different international health settings was assessed by stratifying participating centres by country into three tertiles according to 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). This aggregate measure of development keeps individual countries anonymous. Differences between HDI tertiles were tested with the Pearson χ^2 test and Kruskal–Wallis test for categorical and continuous variables respectively.

Hierarchical multivariable logistic regression models (random intercept) were constructed with three levels: patients nested within hospitals, nested within countries. 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 odds ratios with confidence intervals and P values derived from percentiles of 10 000 bootstrap replications. Model residuals were checked at all three levels and first-order interactions explored. 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).

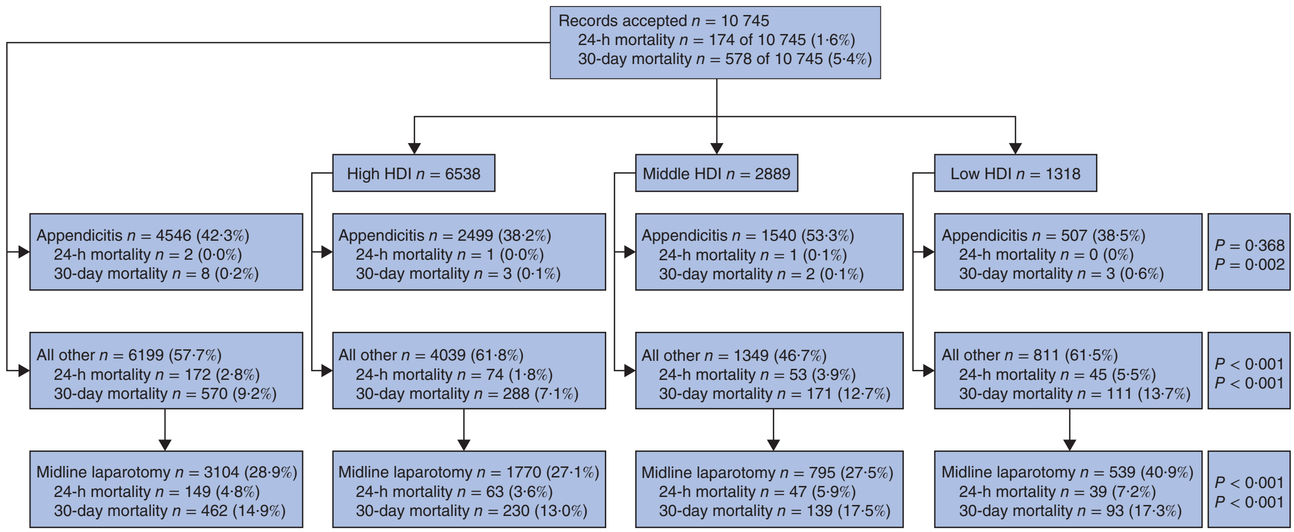

Fig. 3 Study process flow chart and key outcomes by Human Development Index (HDI) tertile. Pearson χ^2 test was used for statistical analysis

Table 3 Outcomes by Human Development Index tertile and American Society of Anesthesiologists fitness grade

ASA fitness grade	24-h mortality			30-day mortality		
	High	Middle	Low	High	Middle	Low
I	1 of 2701 (0·0)	8 of 1648 (0·5)	3 of 613 (0·5)	5 of 2701 (0·2)	25 of 1648 (1·5)	13 of 613 (2·1)
II	4 of 2004 (0·2)	8 of 728 (1·1)	11 of 352 (3·1)	23 of 2004 (1·1)	31 of 728 (4·3)	27 of 352 (7·7)
III	14 of 1134 (1·2)	15 of 283 (5·3)	9 of 162 (5·6)	82 of 1134 (7·2)	50 of 283 (17·7)	31 of 162 (19·1)
IV	18 of 411 (4·4)	12 of 98 (12)	6 of 43 (14)	110 of 411 (26·8)	43 of 98 (43·9)	15 of 43 (35)
V	31 of 102 (30·4)	9 of 65 (14)	11 of 69 (16)	57 of 102 (55·9)	18 of 65 (28)	17 of 69 (25)
Unknown	7 of 183 (3·8)	2 of 66 (3)	5 of 76 (7)	14 of 183 (7·7)	6 of 66 (9)	11 of 76 (14)
Missing	0 of 3 (0)	0 of 1 (0)	0 of 3 (0)	0 of 3 (0)	0 of 1 (0)	0 of 3 (0)

Values in parentheses are percentages. ASA, American Society of Anesthesiologists.

Table 4 Mortality between 24 h and 30 days after surgery

	All deaths ($n = 578$)	Deaths within 24 h ($n = 174$)	Deaths after 24 h within 30 days ($n = 404$)	P*
HDI tertile				0·024
High	291	75 of 291 (25·8)	216 of 291 (74·2)	
Middle	173	54 of 173 (31·3)	119 of 173 (68·8)	
Low	114	45 of 114 (39·5)	69 of 114 (60·5)	
Diagnosis				
Appendicitis	8	2 of 8 (25)	6 of 8 (75)	
No disease identified	17	3 of 17 (18)	14 of 17 (82)	
Other abdominal	339	90 of 339 (26·5)	249 of 339 (73·5)	
Neoplasm	78	16 of 78 (21)	62 of 78 (79)	
Gallstones	10	1 of 10 (10)	9 of 10 (90)	
Complication of previous procedure	44	12 of 44 (27)	32 of 44 (73)	
Trauma	82	50 of 82 (61)	32 of 82 (39)	

Values in parentheses are percentages by row, indicating distribution of deaths within 24 h *versus* after 24 h. HDI, Human Development Index. *Pearson χ^2 test.

Table 5 Factors associated with 30-day mortality

			Univariable analysis		Multilevel analysis	
	Alive	Died	Odds ratio†	*P*	Odds ratio†	*P*
HDI tertile						
High	6240 (61·5)	291 (50·3)	1·00 (reference)		1·00 (reference)	
Middle	2701 (26·6)	173 (29·9)	1·37 (1·13, 1·66)	0·001	2·78 (1·84, 4·20)	< 0·001
Low	1202 (11·9)	114 (19·7)	2·03 (1·62, 2·54)	< 0·001	2·97 (1·84, 4·81)	< 0·001
Standardized age (years)*	38·7(22·3)	58·5(24·3)	2·36 (2·16, 2·58)	< 0·001	1·68 (1·48, 1·91)	< 0·001
Sex						
M	5229 (51·6)	333 (57·6)	1·00 (reference)		1·00 (reference)	
F	4914 (48·4)	245 (42·4)	0·78 (0·66, 0·93)	0·005	1·14 (0·92, 1·41)	0·240
Diabetes						
No	9467 (93·3)	469 (81·1)	1·00 (reference)		1·00 (reference)	
Yes	676 (6·7)	109 (18·9)	3·25 (2·59, 4·05)	< 0·001	1·21 (0·92, 1·58)	0·174
Current smoker						
No	7569 (74·6)	395 (68·3)	1·00 (reference)		1·00 (reference)	
Yes	2571 (25·4)	183 (31·7)	1·36 (1·14, 1·63)	0·001	0·86 (0·69, 1·08)	0·195
ASA fitness grade						
I	4910 (48·4)	43 (7·4)	1·00 (reference)		1·00 (reference)	
II	2997 (29·6)	81 (14·0)	3·09 (2·14, 4·52)	< 0·001	1·64 (1·10, 2·45)	0·016
III	1415 (14·0)	163 (28·2)	13·15 (9·44, 18·72)	< 0·001	4·69 (3·15, 6·99)	< 0·001
IV	382 (3·8)	168 (29·1)	50·22 (35·70, 72·11)	< 0·001	18·21 (11·95, 27·74)	< 0·001
V	144 (1·4)	92 (15·9)	72·95 (49·31, 109·52)	< 0·001	30·23 (18·60, 49·14)	< 0·001
Unknown	292 (2·9)	31 (5·4)	12·12 (7·47, 19·46)	< 0·001	6·95 (3·90, 12·38)	< 0·001
Diagnosis						
Appendicitis	4532 (44·7)	8 (1·4)	1·00 (reference)		1·00 (reference)	
No disease identified	222 (2·2)	17 (2·9)	43·38 (19·08, 107·33)	< 0·001	32·52 (13·01, 81·32)	< 0·001
Other abdominal	3147 (31·0)	339 (58·7)	61·02 (32·40, 134·55)	< 0·001	20·09 (9·85, 40·99)	< 0·001
Neoplasm	464 (4·6)	78 (13·5)	95·23 (48·63, 215·20)	< 0·001	27·47 (12·88, 58·58)	< 0·001
Gallstones	937 (9·2)	10 (1·7)	6·05 (2·38, 15·88)	< 0·001	3·37 (1·31, 8·69)	0·012
Complication of previous procedure	331 (3·3)	44 (7·6)	75·30 (37·15, 173·90)	< 0·001	18·91 (8·58, 41·67)	< 0·001
Trauma	510 (5·0)	82 (14·2)	91·08 (46·64, 205·48)	< 0·001	23·04 (10·80, 49·12)	< 0·001
Perforated viscus						
No	8424 (83·3)	356 (61·9)	1·00 (reference)		1·00 (reference)	
Yes	1687 (16·7)	219 (38·1)	3·07 (2·57, 3·66)	< 0·001	1·82 (1·46, 2·27)	< 0·001
Surgical safety checklist used						
No, not available in this hospital	1793 (17·7)	128 (22·1)	1·00 (reference)		1·00 (reference)	
No, but available in this hospital	719 (7·1)	95 (16·4)	1·85 (1·40, 2·44)	< 0·001	1·28 (0·81, 2·03)	0·294
Yes	7628 (75·2)	355 (61·4)	0·65 (0·53, 0·81)	< 0·001	0·62 (0·42, 0·92)	0·016

Values in parentheses are percentages by column unless indicated otherwise; *values are mean(s.d.); †values in parentheses are 95 per cent confidence intervals. More detailed information on diagnoses is available in *Table S1* (supporting information). HDI, Human Development Index; ASA, American Society of Anesthesiologists. Confidence intervals and *P* values derived from percentiles of 10 000 bootstrap predictions. Total n =10 721. Akaike information criterion 2974; c-statistic 0·93; Hosmer–Lemeshow goodness-of-fit test: $\chi^2 = 13{\cdot}3$, 8 d.f., $P = 0{\cdot}102$.

To help visualize the relationship of outcomes with a continuous representation of the HDI (HDI rank), the final fixed-effect regression models were used with a restricted cubic spline for HDI rank (3 knots distributed equally across the range of HDI rank) to allow for potential non-linear relationships. Predictions were made for specified co-variable levels and bootstrapped confidence intervals generated.

A prespecified sensitivity analysis was performed. It was predicted that some patients would be discharged alive but not followed up at 30 days. For the main analysis, these patients were coded as alive. To test the validity of this approach, patients 'discharged alive and not followed up' were excluded and the 30-day mortality analysis rerun.

All analyses were undertaken using the R Foundation Statistical Program (R 3.1.1), with packages plyr, stringr, ggplot2, reshape2, jsonlite, RCurl, httr, Hmisc, rms, lme4 and knitr (R Project for Statistical Computing, Vienna, Austria).

Results

A total of 10 906 patient records were submitted and 10 745 records were accepted formally for analysis following the quality control algorithm described above. These patients came from 357 centres across 58 countries (*Fig. 1*), with 6538 (60·8 per cent) from high-, 2889 (26·9 per cent) from middle- and 1318 (12·3 per cent) from low-HDI

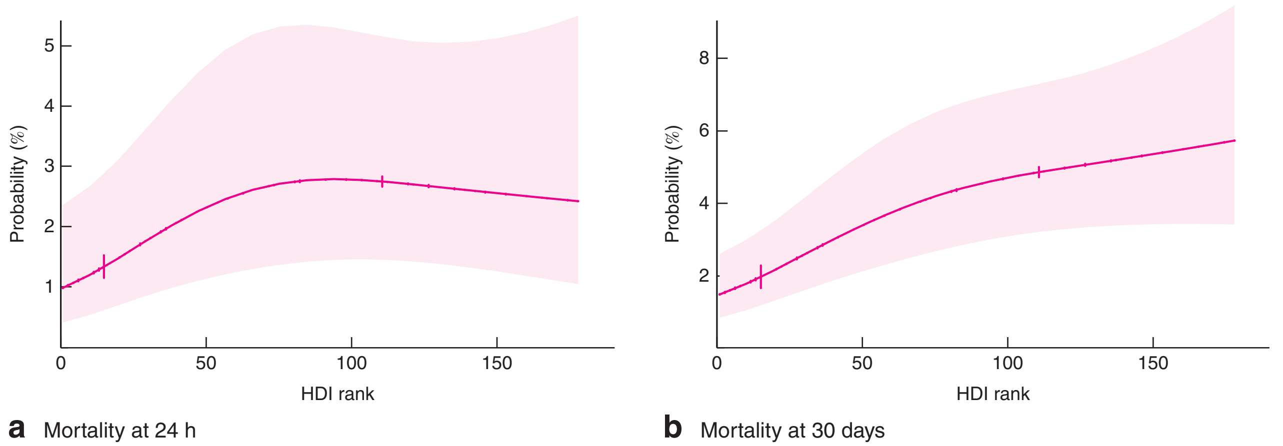

Fig. 4 Adjusted associations between Human Development Index (HDI) rank and mortality at **a** 24 h and **b** 30 days. Multivariable logistic regression models were repeated but using a continuous variable of HDI rank. A restricted cubic spline with three knots distributed equally across the range was applied to HDI rank. Predictions were made on the models and 95 per cent confidence intervals determined (shaded area). Vertical lines represent the relative proportion of patients for a given HDI rank. Co-variable levels: age, 35 years; diabetes, no; sex, male; smoker, no; American Society of Anesthesiologists fitness grade, I; diagnosis, trauma; checklist, no, not available. **a** P overall = 0·007, P non-linear = 0·112; **b** P overall < 0·001, P non-linear = 0·032

settings. A complete record with no missing data was achieved for 99·1 per cent of patients (10 644 of 10 745); 24-h outcome data were available for 99·9 per cent of patients (13 missing) and 30-day mortality for 99·8 per cent (24 missing).

Demographics

Differences in demographics and operative data across HDI groups are shown in *Tables 1* and *2*. Appendicectomy was the most commonly performed operation across all HDI settings (high 38·2 per cent, middle 53·3 per cent, low 38·5 per cent) (*Fig. 2*; *Table S1*, supporting information). Trauma was the indication for surgery in a higher proportion of patients in middle- and low-HDI countries (10·0 and 12·1 per cent respectively) compared with high-HDI countries (2·2 per cent). Use of a midline laparotomy for intraperitoneal access increased across the development index (high 27·1 per cent, middle 27·5 per cent, low 40·9 per cent). A surgical safety checklist was used in 74·4 per cent of procedures, varying significantly across HDI groups (91·3 per cent high, 55·7 per cent middle, 32·1 per cent low; $P < 0·001$).

Crude mortality across Human Development Index groups

The crude 24-h mortality rate was 1·6 per cent and the 30-day mortality rate was 5·4 per cent. The 24-h mortality rate increased threefold across HDI groups (high 1·1 per cent, middle 1·9 per cent, low 3·4 per cent; $P < 0·001$). Likewise, there was an inverse relationship between 30-day mortality and HDI (high 4·5 per cent, middle 6·0 per cent, low 8·6 per cent; $P < 0·001$).

Mortality varied across HDI group for some operations, but not others. Following appendicectomy, overall 24-h mortality (0·02 per cent) did not vary between groups, but there was a small absolute increase in 30-day mortality in low-income countries (high 0·1 per cent, middle 0·1 per cent, low 0·6 per cent). However, mortality following midline laparotomy was higher (4·8 per cent at 24 h and 14·9 per cent at 30 days) and varied across HDI groups (30-day mortality: high 13·0 per cent, middle 17·5 per cent, low 17·3 per cent; $P < 0·001$) (*Fig. 3*).

Trauma was the surgical indication with the highest 24-h mortality rate at 8·4 per cent (high 8·4 per cent, middle 6·6 per cent, low 11·9 per cent; $P = 0·144$), rising to 13·9 per cent at 30 days (high 13·3 per cent, middle 11·7 per cent, low 18·2 per cent; $P = 0·157$).

Mortality increased from high to low HDI at ASA fitness grades I–IV, but for patients with ASA grade V mortality reduced by half in the lower-income groups (30-day mortality: high 55·9 per cent, middle 28 per cent, low 25 per cent; $P < 0·001$) (*Table 3*).

Of the 578 patients who died, 404 (69·9 per cent) did so between 24 h and 30 days following surgery (high 74·2 per cent, middle 68·8 per cent, low 60·5 per cent). Most of the deaths in this interval related to non-traumatic indications for index surgery (92·1 per cent non-trauma, 7·9 per cent trauma) (*Table 4*).

Mortality adjusted for case mix

Models of mortality accounted for the clustering of patients within hospitals and patients/hospitals within countries. The effects of prognostic factors on 24-h death rates are shown in *Table S2* (supporting information), and on 30-day mortality in *Table 5*. After adjusting for case mix (including age, sex, history of diabetes, smoking history, ASA grade and diagnostic group, presence of a perforated viscus, checklist use), independent correlations between increased mortality in LMICs at 24 h and 30 days remained. Across the entire data set, use of a surgical safety checklist was associated with lower hospital mortality rates at 30 days. Having a checklist available, but not using it, was associated with increased mortality at 24 h but not at 30 days.

Mortality analyses were repeated using non-linear models (*Fig. 4*). These showed that 30-day mortality was a better discriminator of HDI than 24-h mortality.

Sensitivity analyses

Some 17·7 per cent of patients were discharged alive and assumed to be still alive at 30 days. Excluding these patients from analysis of main outcomes did not affect the size or direction of effects across HDI groups (*Table S3*, supporting information).

Discussion

This study measured mortality following emergency abdominal surgery systematically at a worldwide level, thereby enabling comparisons to be made across low-, middle- and high-HDI countries. It shows that a collaborative bedside network can collect mortality statistics following surgery on a large scale, even in low-HDI countries, and that follow-up to discharge or 30 days is achievable in the majority of survivors. The mortality rate after emergency abdominal surgery is two to three times higher in low- compared with high-HDI countries. More than half of the patients who died within 30 days did so after 24 h, strongly supporting 30-day perioperative mortality rate as an international benchmark. The present study supports inclusion of this standard in the 2014 WHO Global Reference List of 100 Core Health Indicators[5]. It also identifies appendicectomy as the most common emergency general surgical operation performed around the world and in all development tertiles.

The trend towards higher mortality (24 h and 30 days) in low-income countries remained after adjusting for observable prognostic factors. The association between increasing mortality and lower HDI may be explained by unobserved differences in prognosis in different HDI countries, differences in treatment, or both. Higher mortality was seen specifically after laparotomy for trauma, and in patients undergoing midline laparotomy. Death rates after appendicectomy were consistently low, although a slight increase was seen at 30 days in low-income countries. Mortality was also higher in LMIC countries for each ASA grade up to level V, where the trend reversed, perhaps because of reluctance to operate on those moribund patients in resource-poor settings.

Surgical safety checklists were included in this study as a marker of hospital safety. Use declined markedly across high- to low-HDI settings, and their use was associated with reduced mortality at 30 days, even after adjustment. Having a checklist available, but not used, was associated with higher mortality at 24 h but not 30 days, compared with hospitals systems without one at all. This may be a reflection of the urgency of surgery in these patients. However, this study cannot determine definitively whether the checklist itself is responsible for improved outcomes, or whether it is merely a marker of safer hospital systems[12,13]. The fact that risk adjustment for trauma did not affect the mortality gradient across HDI tertiles, and that checklist use was associated with reduced mortality, does suggest that some of the difference in outcome in LMICs was not the result of prognostic factors alone.

An important strategy in collaborator recruitment was to invert the traditional research model. Rather than department heads, junior clinicians were often the contact point for hospital involvement. Social media and technology played an important role in the recruitment and running of the study[14]. Collaborators, particularly in LMICs, were clear in their view that those providing the clinical care can generate high-quality data and lead international clinical research. By providing clear protocols, administrative support, secure web-based data collection, and continued direct access to collected data, the collaborative continues to be met with enthusiasm across a diverse range of settings. This collaboration has proved that large studies crossing cultures and levels of socioeconomic development are feasible without extensive resources when data collection is performed during a short but intensive interval[15]. This international surgical network includes strong LMIC partners, and has established the feasibility of a common data-sharing platform that is accessible on computers and mobile phones.

The strengths of this study lie in the scale of the network, range of countries included, duration of follow-up, low rates of missing data, and clinical and service detail obtained. Nevertheless, a study of this scale has some inevitable limitations.

It was not possible to audit entered cases independently against operative logbooks. However, case sheets were signed off by the head at each centre and the data set was not accepted centrally until remediable deficiencies had been corrected. The data are likely to be more accurate than local administrative data because they were collected by enthusiastic clinicians who understood the purpose. There was also more clinical detail than can be found in routinely collected data.

It was not possible to capture all risk factors. The risk adjustment strategy purposely used a limited number of variables to facilitate future comparisons, both locally and in other research studies. Access to surgery is poor in many LMICs with the consequence that patients may present late[2]. The effect of late presentation may not be captured fully in variables such as the ASA grade, which was collected[16,17]. The proportion of patients undergoing different types of operation varied by HDI tertile, but outcomes were compared by operation type and ASA grade, as well as overall. The short time frames for data capture by local collaborators are realistic, but do risk selection bias, such as seasonal variation in local presentations. Longer enrolment strategies will help quantify this potential bias.

Use of the HDI allowed a comparison between countries by an accepted classification, although other classifications exist, comprising different measures and cut-offs. By grouping countries, between-country variation will not be detected but is likely to be significant. There is likely to be a selection bias towards better resourced institutions taking part in this study, even in low-income settings. An indication that this was the case is provided by the observation that pulse oximetry was used in a very high proportion of procedures, despite known shortages in low-income settings[18]. Furthermore, a high proportion of procedures had a senior anaesthetist present, which may not be expected outside better funded centres. This selection bias may mean that data are not typical of some district or rural hospitals

Members of this network could now work together to develop quality improvement collaboratives of the sort that have driven improved standards in high-income countries[19]. A second cohort study allows increased participation (registration available at http://globalsurg.org/) with surgeons able to reaudit their practice. It will also enable testing of the impact of new risk factors, including HIV status and the influence of prehospital delays. The aim is to establish a consortium of representative centres to deliver large-scale trials with global reach[20]. A fundamental objective moving forward is the evidence-based identification of cost-effective interventions to reduce disparities in outcomes after surgery between countries.

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Supporting information

Additional supporting information may be found in the online version of this article:

Table S1 Diagnosis by Human Development Index tertile (Word document)

Table S2 Factors associated with mortality within 24 h of surgical procedure (Word document)

Table S3 Factors associated with 30-day mortality: sensitivity analysis including only patients confirmed to be alive at 30 days (Word document)

Editor's comments

All empires fall and even pyramids crumble. Especially the economic kind built on an isolated, immobile, low-income population with limited educational opportunity. Coalescent connectivity is the lesson to be learnt from this paper; the triumph that rendered international barriers and borders as virtual as the internet space where young surgeons breathed life into global health. There are no losers in a co-operative syncytium that illuminates healthcare inequality any more than there is magic to high-income countries' comparative performance. Outcome homogenization will follow the inevitable balancing of the discrepancies identified. Systematic attention to detail, adherence to safety protocols, and good perioperative care have made as much of an impact on surgical results as anaesthesia and prophylactic antibiotics. Technological advances undoubtedly unbalance the equation toward the resource-rich, but there is much more to learn from light shed on frugal healthcare excellence in low- and middle-income countries. This pyramidal inversion is the prism through which aggregated outcome data can be separated into packaged quanta to define global health standards. The GlobalSurg Collaborative have shown this to be a tangible concept worthy of further exploration.

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