Global burden of postoperative death

National Institute for Health Research Global Health Research Unit on Global Surgery

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Deaths within 30 days of surgery in low-, middle-, and high-income countries

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S1 Appendix: Methods and results

Approach to calculating postoperative deaths

The number of postoperative deaths occurring in high income countries (HICs) and low- and middle-income countries (LMICs) were separately calculated. These two figures were then summed to calculate a global total for deaths within 30 days of surgery.

The equation to calculate postoperative deaths in HICs was:

$$\sum_{1}^{14} c_{HIC} \times x_{HIC} \times y_{HIC}$$

Where:

c_{HIC} = total operations performed annually in HICs

x_{HIC} = proportion of HIC case-mix belonging to particular specialty

y_{HIC} = postoperative death rate in HIC settings for particular specialty

The equation to calculate postoperative deaths in LMICs was:

$$\sum_{1}^{14} c_{LMIC} \times x_{LMIC} \times y_{HIC} \times m$$

Where:

c_{LMIC} = total operations performed annually in LMICs

x_{LMIC} = proportion of LMIC case-mix belonging to particular specialty

y_{HIC} = postoperative death rate in HIC settings for particular specialty

m = postoperative death rate adjustment constant

Data sources

Surgical volume: The c constants are the estimated number of operations performed in HICs (c_{HIC}) and LMICs (c_{LMIC}). The total operations performed in HICs versus LMICs are not readily available, therefore health expenditure per capita was used as a proxy. Health expenditure per capita ≥$1000 per year was assumed to indicate HICs, and health expenditure <$1000 per year was assumed to represent LMICs. On this basis, 187,000,000 (95% confidence interval (CI) 155,800,000 to 224,500,000) operations are performed annually in HICs and 125,900,000 (95% CI 83,900,000 to 202,300,000) are performed in LMICs[1].

Case-mix: A key reason for differences in raw postoperative death rates between HICs and LMICs might be operative case-mix[2,3]. We therefore established separate estimates for case-mix in HICs (variable x_{HIC}) and LMICs (variable x_{LMIC}). Since there are no readily available LMIC national surgical registries, to estimate LMIC case-mix we have used data from the African Surgical Outcomes Study (ASOS)[2]. This prospective cohort study captured data on 11,422 patients across 247 hospital in 25 countries. ASOS reported case-mix split into 15 surgical specialties; we have merged 'thoracic (lung)' and 'thoracic (gut)' to produce a list of 14 specialties (S1 Table).

For HICs, case-mix was based on a single national registry of surgical activity from a universal health system: England's Hospital Episodes Statistics linked Office of National Statistics (HES-ONS) dataset. To produce HIC case-mix categories that would be directly comparable to the LMIC case-mix data, we first cleaned the 2010 HES-ONS to remove non-surgical (e.g. endoscopic and dental) procedures. This removed 28.8% (374/1,297) procedure codes. The remaining 923 codes were then categorised into the 14 specialties derived from ASOS to estimate case-mix (S1 Table).

HIC postoperative death rates: 30-day postoperative death rates were separately derived for each of the 14 specialties (variable y). For our main analysis we used the HES-ONS dataset. Postoperative death rates were defined as total deaths within 30 days of a procedure as a proportion of finished consultant episodes in that specialty. The overall postoperative death rate in the HES-ONS dataset was 1.09% (37,645/3,438,242).

Several studies over the past decade have reported national and international 30-day postoperative death rates, but their case-mix has varied. As a sensitivity analysis, we

further tested our base model to explore totals for postoperative death using other recently reported baseline postoperative death rates from high income settings:

- An analysis of 298,772 non-cardiac surgery cases from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database from 2005-2007 found the baseline postoperative death rate to be 1.34%[4]. Since per-specialty estimates were not available, we proportionately scaled the HES-ONS per-specialty rates by the ratio of the NSQIP (1.34%) to HES-ONS mortality (1.09%). However, since the NSQIP cohort excluded cardiac and obstetric surgery, the HES-ONS postoperative death rates were used for these specialties.

- The European Surgical Outcomes Study (EUSOS) captured data on patients undergoing non-obstetric, non-day case surgery across 498 hospitals in 28 European countries[3]. The overall postoperative death rate was 3.99% (1855/46539). Since the specialty categories reported in EUSOS did not match up with the categories established from ASOS and HES-ONS, we again proportionately scaled the HES-ONS per-specialty postoperative death rates based on the ratio of EUSOS (3.99%) to HES-ONS reported deaths (1.09%). Again, as the EUSOS cohort excluded obstetric surgery, the HES-ONS postoperative death rate for obstetrics was used.

Mortality adjustment: Although many studies have reported higher postoperative death rates in LMICs compared to HICs[5,6], most studies are difficult to interpret as most LMIC studies are single-centre or single-country and do not allow for a direct comparison with HIC data. The GlobalSurg Collaborative has published two prospective multicentre studies (GS1 and GS2) directly comparing postoperative death rates in LMICs versus HICs. In GS1, in 10,745 patients undergoing emergency abdominal surgery across 357 centres in 58 countries, the postoperative death rate was 6.8% (287/4,207) in LMICs versus 4.5% (291/6,538) in HICs[7]. GS2 included 12,539 patients who underwent either emergency or elective abdominal surgery across 343 hospitals in 66 countries, and showed that postoperative postoperative death rates were 2.5% (125/5,098) in LMICs versus 1.5% (110/7,130) in HICs[8]. However, since these GlobalSurg studies were limited to abdominal surgery, we wished to identify comparative data for this analysis that would be more broadly generalizable across all surgeries. A large systematic review by Bainbridge et al of global postoperative death across all surgical specialties found postoperative death rates to be 0.2% (589/309,245) in LMICs compared to 0.1% (5,981/6,738,683) in

HICs[9]. Therefore, the relative risk for postoperative death for LMICs versus HICs was 2.14 (95% CI 1.96 to 2.32).

At present, specialty-specific postoperative death rates have not been collected across a representative range of LMICs. Therefore, we applied Bainbridge et al's estimate for increased risk of postoperative death in LMICs to adjust our baseline HIC postoperative death rates (constant m).

All-cause deaths: The Global Burden of Disease (GBD) study estimated that in 2016 there were 54,698,600 deaths worldwide from all causes[10]. This figure was used as the denominator to calculate the proportion of total global deaths that occur within 30 days of surgery.

Main analysis

Our main analysis utilised HIC condition-specific postoperative death rates based on the HES-ONS dataset (S1 Table). We used the point estimates for surgical volume (c_{HIC}=187,000,000, c_{LMIC}= 125,900,000) and Bainbridge's relative risk of death in LMICs compared to HICs (m=2.14). Based on these parameters, we estimated that at least 4.2 million people die within 30 days of surgery each year (S2 Table).

To place 4.2 million annual postoperative deaths in context, we compared this figure to a ranked list of the ten leading global causes of death reported in GBD 2016 (Figure 1).

Sensitivity analysis

To determine the impact of using different baseline rates of postopoerative death to those provided by HES-ONS, we tested different scenarios based on the estimating HIC postoperative death rates from NSQIP and EUSOS (S2 Table).

Projection for expanded surgical capacity

At present, around 4.8 billion people worldwide lack timely access to safe and affordable surgery[11]. It is estimated that there is an annual unmet need for 143 million procedures in LMICs[12]. Increasing access to surgery is therefore a priority. In order to understand the implications of an increase in surgical volume, we estimated the number of additional postoperative deaths that might occur if 143 million additional procedures were performed in LMICs at the current rate of disparity in postoperative death rates.

S2 Appendix: Strengths and limitations

This analysis has necessarily required a series of assumptions to be made regarding global surgical volume, surgical case-mix, post-operative death rates in high income countries (HIC), adjustment for mortality from HICs to low- and middle-income countries (LMICs), the need for expansion of surgery in LMICs, and comparisons of postoperative death rates to the leading causes of death reported in the Global Burden of Disease (GBD) study. In this Appendix the strengths and weaknesses of each underlying assumption are discussed. Despite these limitations, we believe that this study represents the best estimate of total postoperative deaths possible using existing data. Moreover, our modelling is a baseline for future high-quality data to feed in to.

Surgical volume

Global surgical volume was most recently estimated in a modelling study by Weiser et al[1]. Surgical volume data were obtained for 66 countries. A model based on total health expenditure per capita and population was developed, to extrapolate surgical volume for other countries for which surgical volume data were not available. The authors provided a breakdown of total surgical volume by total health expenditure per capita: very low (≤$100), low ($101-400), middle ($401-1000), and high (>$1000).

A total of 136 of 139 LMICs (as designated in the DAC List of ODA Recipients) and 14 of 55 HICs were recorded by Weiser et al as having very low, low, or middle levels of total health expenditure per capita. Therefore, within the constraints of the data available, LMIC surgical volume was taken as the sum of operations performed in all countries with total health expenditure per capita ≤$1000. HIC surgical volume was based on total surgical volume in countries with expenditure >$1000 per capita.

The Weiser study was modelled to provide surgical volume for 2012. Given that global surgical volume expanded from an estimated 226 million cases per year in 2004 to 313 million cases per year in 2012, it is likely that surgical volume has continued to increase, with significantly more cases performed in 2018 than Weiser's 2012 estimate. This would lead to an under-estimation of total postoperative deaths.

Surgical case-mix

For HICs, case-mix was based on a national registry of surgical activity from a universal health system: England's Hospital Episodes Statistics (HES). Although

more recent operative volume statistics are available, case-mix estimates were based on the 2010 HES dataset to maintain consistency with use of the Hospital Episodes Statistics linked Office of National Statistics (HES-ONS) dataset for estimates of postoperative death rates. The HES dataset captures all procedures performed within National Health Service (NHS) hospitals, accounting for over 90% of total surgical volume in England. HES does not capture data for procedures performed in private hospitals. Since private hospitals in England typically focus on low to intermediate risk surgery, the HES dataset may overestimate volume in higher-risk surgical specialties. This would be likely to lead to an overestimation of total postoperative deaths.

The assumption that surgical case-mix in England is representative of case-mix across all other HICs represents a significant limitation since differing epidemiological profiles across HICs are likely to lead to differing surgical case-mix. The effect of this on the estimate of total postoperative deaths is uncertain.

There are no readily available LMIC national surgical registries. Therefore, the African Surgical Outcomes Study (ASOS) was used to estimate LMIC case-mix. This cohort was based on prospective data collection across 247 hospital in 25 African countries. Inevitably larger hospitals are more likely to participate in international studies and the ASOS data may not reflect the case-mix across all surgical units in Africa. Moreover, it is unknown how generalisable case-mix derived in Africa is to LMICs on other continents.

Postoperative mortality in high income countries

For the primary analysis, baseline HIC postoperative death rates were extracted from England's HES-ONS dataset, a national registry from a universal health system. The most recent publicly available HES-ONS linked dataset dates from 2010. Postoperative death rates in England have decreased since 2010[6], therefore using HES-ONS may either overestimate HIC postoperative death rates in 2018.

There are few robust national estimates of postoperative death rates encompassing the full scope of surgical activity. Amongst those postoperative death rates that are reported, the lowest is 0.54%, from the New Zealand the Perioperative Mortality Review Committee[13]. The highest rate is 3.99%, from the European Surgical Outcomes Study (EUSOS)[3]. The HES-ONS postoperative death rate (1.09%) is therefore amongst the lowest reported and is similar to the 1.34% rate reported by

the American College of Surgeons National Surgical Quality Improvement Program (NSQIP)[4]. Variation in reported postoperative death rates is partly a reflection of subtle differences in inclusion criteria, for example whether day-case procedures contribute to the reported postoperative death rate.

The main analysis utilised postoperative death rates based HES-ONS, as this dataset offered the greatest granularity, providing speciality-specific rates for the full scope of surgical activity, including day case surgery and Caesarean section. Specialty-specific postoperative death rates were important to obtain in order to account for differences in case-mix between HICs and LMICs.

In order to explore the effect of adopting higher baseline HIC postoperative death rates than that derived from HES-ONS, we performed a sensitivity analysis. We tested our base case model to estimate totals for postoperative death using the NSQIP and EUSOS data (S2 Table).

Postoperative death rate adjustment from high to low/middle income countries

Bainbridge et al study is the most extensive review of postoperative death rates across all surgical specialties. This systematic review included data from 87 studies on 21.4 million patients undergoing surgery with general anaesthetic. Although the baseline postoperative death rates identified by the Bainbridge study were low (0.2% in LMICs and 0.1% in HICs), the relative risk (2.14) for death following surgery in LMICs versus HICs was broadly consistent with the findings of the prospective, international GS1[7] (RR 1.53), GS2[8] (1.59), and ASOS/ISOS[2,14] (RR 2.20) studies. Since the GS1 and GS2 studies only included patients undergoing abdominal surgery, the Bainbridge study offers a more generalizable estimate for postoperative death rate adjustment, and is similar to the ASOS/ISOS comparison.

Using a single estimate for postoperative death rate adjustment for all surgery types may lead to underestimation of postoperative death rates for some specific procedures. For example, the postoperative death rate for caesarean section in the ASOS study was 0.53% (20/3,792) compared to 0.01% (16/158,229) in HES-ONS. Therefore, the estimate from the Bainbridge study that we have used to adjust HES-ONS mortality rates may be conservative, underestimating total postoperative deaths.

Need for expansion of surgery

Rose et al calculated the global unmet need for surgery by estimating the total required surgical volume and subtracting the current volume of surgery performed. Required surgical volume was derived by taking prevalence for 21 disease categories from the 2010 Global Burden of Disease (GBD) study and multiplying this by the rates of surgery for each disease category, based on New Zealand registry data. Whilst the study provides an estimate for the total need for surgery by surgery type, equivalent figures by surgery type for unmet need are not provided. Therefore it was not possible to determine the case-mix of the unmet need for surgery. Consequently, we assumed that in the event of all unmet surgical need being addressed, LMIC surgical case-mix would remain broadly similar to that recorded in the ASOS dataset. The effect of this on our estimate for total postoperative deaths that might occur if there were no unmet need for surgery is uncertain, as this depends on whether unmet need is predominantly for procedures with low or high postoperative death rates.

Global Burden of Disease study comparison

The main output from this study was an estimate for the absolute number of postoperative deaths. In order to put this figure in to context it was compared to the numbers of deaths associated with the top ten causes of death in GBD[10]. This comparison should be interpreted with caution. As postoperative death is not a recognised cause of death in GBD studies, each postoperative death has been double counted across one of the 249 causes of death reported by GBD, most likely the underlying condition for which the patient was operated. For example, the IHD category may include patients who died following complications of cardiac surgery, or as a result of a postoperative myocardial infarct. Similarly, the lung cancer category may include patients who die as a result of complications following surgery for lung cancer, and the stroke category is likely to include some patients who die as a result of postoperative stroke. However, this risk of overlap is common for many categories of global mortality, and represents a ubiquitous limitation of estimating global burden of condition-specific mortality more generally.

Importantly, we do not seek to imply causality between patients undergoing surgery and dying within 30 days. Some postoperative deaths may be entirely unrelated to the patient's surgery, for example, deaths resulting from trauma. For some patients postoperative death represents a failure of surgery as a treatment strategy; for

instance, a patient who succumbs despite attempted surgery for a ruptured abdominal aortic aneurysm. Many postoperative deaths however occur as a result of postoperative complications. Whilst on a global level we are unable to differentiate between these different categories of postoperative death, it is important to bring the overall scale of the postoperative death to policy makers' attention since many postoperative deaths could be prevented with improved perioperative care.

S1 Table: Baseline case-mix and postoperative death rates by specialty

Surgical specialty	Case-mix		Postoperative death rate
	HIC* (x_{HIC})	LMIC** (x_{LMIC})	HIC* (y_{HIC})
Breast	2.5%	2.1%	0.2%
Cardiac	1.0%	0.5%	2.9%
Gynaecological	6.0%	12.1%	0.1%
Head and neck	10.2%	4.2%	0.2%
Hepatobiliary	2.1%	1.6%	0.9%
Lower gastrointestinal	5.9%	8.7%	1.7%
Neurosurgery	4.2%	2.3%	1.2%
Obstetric	4.6%	35.2%	0.0%
Orthopaedic	21.0%	16.4%	1.0%
Thoracic	0.9%	1.4%	6.1%
Upper gastrointestinal	1.6%	2.8%	4.8%
Urology	6.5%	5.2%	0.4%
Vascular	3.7%	2.2%	5.4%
Other	29.7%	5.1%	1.0%

*High income country (HIC) baseline estimates based on the Hospital Episode Statistics linked Office of National Statistics (HES-ONS) dataset

**Low- and middle-income country (LMIC) baseline case-mix based on the African Surgical Outcomes Study (ASOS)

S2 Table: Estimates of total postoperative deaths

Source for baseline postoperatice death rate	Postoperative deaths			Proportion of global mortality attributable to postoperative death
	LMIC	HIC	Total	
HES-ONS	2,180,787	2,047,446	4,228,233	7.7%
Projection if surgical provision expanded	4,099,878	2,047,446	6,147,324	11.2%
NSQIP	2,580,824	2,421,633	5,002,457	9.1%
Projection if surgical provision expanded	4,851,948	2,421,633	7,273,581	13.3%
EUSOS	7,553,262	7,111,492	14,664,755	26.8%
Projection if surgical provision expanded	14,200,129	7,111,492	21,311,621	39.0%

EUSOS: European Surgical Outcomes Study; HES-ONS: Hospital Episode Statistics linked Office of National Statistics dataset; HIC: high income countries; LMIC: low- and middle-income countries; NSQIP: American College of Surgeons National Surgical Quality Improvement Program

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