Title: Surgically-avertable burden of digestive diseases at first-level hospitals in low and middle-income regions

Authors:

Hideki Higashi, PhD^{a,b}, Jan J. Barendregt, PhD^b, Nicholas J. Kassebaum, MD^{a,c}, Thomas G. Weiser, MD^d, Stephen W. Bickler, MD^e, Theo Vos, PhD^{a,b}

^aInstitute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA

^bSchool of Population Health, University of Queensland, Brisbane, QLD, Australia

^cDivision of Anesthesiology & Pain Medicine, Seattle Children's Hospital, Seattle, WA, USA

^dDepartment of Surgery, School of Medicine, Stanford University, Stanford, CA, USA

^eDepartment of Surgery, School of Medicine, University of California, San Diego, CA, USA

Correspondence to:

Hideki Higashi

Institute for Health Metrics and Evaluation, 2301 Fifth Ave, Suite 600, Seattle, WA 98121, USA

Tel: +1 206 897 2861 Fax: +1 206 897 2899

Email: h.higashi@uqconnect.edu.au

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ABSTRACT

Background: To quantify the burden of digestive diseases avertable by surgical care at first-level hospitals in low and middle-income countries (LMICs).

Methods: We examined four digestive diseases from the Global Burden of Disease (GBD) 2010 Study: appendicitis; intestinal obstruction; inguinal and femoral hernia; and gall bladder and bile duct disease. Using demographic and epidemiological data from GBD 2010 Study, we calculated the potential reduction in burden of digestive diseases if quality surgical services were universally available and accessible at first-level hospitals. The lowest case fatality rates for each age and sex grouping from all GBD regions were assumed to reflect the best possible state of full surgical coverage and treatment. These best scenario rates were applied to the GBD 2010 results from all LMIC regions to estimate surgically-avertable burden.

Results: Overall, 4.8 million disability-adjusted life years (DALYs), or 65% of burden related to the four digestive diseases, are potentially avertable with first-level surgical care in LMICs. Sub-Saharan Africa has the largest avertable burden in absolute DALYs (1.7 million) and in avertable proportion (83%). Intestinal obstruction accounted for the largest portion of avertable burden among the four digestive diseases (2.2 million DALYs; 64% avertable).

Conclusions: Improving the capacity of surgical services at first-level hospitals is essential for averting the burden of digestive diseases in LMICs. Practicable strategies for scaling up surgical capacities in rural districts are available, which must be given due attention.

Key words: digestive disease, burden of disease, surgery, appendicitis, intestinal obstruction, hernia, gall bladder

INTRODUCTION

Surgery has been a neglected component of the global health agenda.^{1, 2} It is being increasingly recognized as a crucial component of a functional health care system. Traumatic injuries, pregnancy-related complications, infectious diseases, disasters, congenital anomalies, and cancer are just a few broad categories where functional surgical systems may have the ability to prevent death, minimize or reverse disability, or potentially improve quality of life. Nonetheless, some common yet unwarranted beliefs about surgical care have diverted attentions from the global community. There are common notions that surgery is too costly to be implemented as a public health intervention, technically too complex to implement in resource-limited settings, and addresses only a minor segment of global burden of diseases and injuries.^{3, 4} Actual data as well as knowledge to support or challenge such beliefs, however, have been in severe shortage.

Recently, efforts have been emerging to address the lack of evidence in the surgical arena. An editorial in PLOS Medicine suggested surgery as an essential component to reach the Millennium Development Goals, referring to emerging knowledge concerning the following relevant topics: surgical conditions constitute a substantial global burden of disease, existence of wide-spread disparities in availability of global surgical care, surgery can be cost-effective and building surgical capacity will help strengthen health systems and primary care, and the feasibility to deliver surgical care even in the most resource-constrained settings.⁵ When the second edition of the Disease Control Priorities in Developing Countries was published in 2006,⁶ a chapter devoted to surgery suggested surgery to be an essential component of public health. The authors estimated that conditions amenable by surgery accounted for 11% of the global burden of diseases and injuries in 2001.⁷ While the study was clearly an innovative endeavor, the

approach was not data-driven, instead relying on pooled opinions of a limited number of experts in condition-specific proportions of the burden of disease amenable to surgery.

In this study, we have estimated the proportion of digestive disease burden amenable to surgery at first-level hospitals in LMICs. This work has been conducted as part of a systematic estimate of surgical burden for the updated Disease Control Priorities Project. We have incorporated data, methods, and resources of the Global Burden of Diseases, Injuries and Risk Factors (GBD) 2010 Study to arrive at the most comprehensive estimates of surgically-avertable burden of digestive diseases to date.⁸

According to the GBD 2010 Study, digestive diseases accounted for a point estimate of 29 million disability-adjusted life years (DALYs) in 2010 in LMICs, 1.3% of the total burden, or 2.6% of the non-communicable disease burden.⁸ While many surgical procedures related to non-communicable diseases require referral to advanced surgical care facilities (e.g. for most malignant neoplasms and cardiovascular diseases), many others can be managed with basic to intermediate levels of surgical skill appropriate for first-level hospitals.⁹ The World Health Organization (WHO) suggests that most abdominal conditions can be managed by first-level surgical practitioners,¹⁰ and, in some cases, should be managed at the first-level if conditions do not allow time for referral to tertiary care facilities. Given this concept, the WHO includes surgical procedures related to digestive diseases as essential elements of first-level surgical care.¹¹ Our aim was to quantify (estimate) the burden of digestive diseases in LMICs that could be averted should the delivery of first-level surgical care be scaled up to fully cover a population with access to quality care.

METHODS

Selection of conditions for analysis

We examined four digestive diseases from the cause list of the GBD 2010 Study considered amenable to first-level surgical care: appendicitis, intestinal obstruction without hernia, inguinal or femoral hernia, and gall bladder and bile duct disease. These conditions were included in our analysis on the bases of recommendations from literature and surgical guidelines,^{9, 11, 12} consultation with experts in global surgery, practicality in quantifying health outcomes (e.g. existence of clear health outcomes corresponding to specific surgical procedures), and the existence of a curative operative procedure.

Approach and analysis

Our analysis assumes a surgical package with various options that can be provided at first-level hospitals. We did not attempt to distinguish different options available for each procedure (e.g. laparoscopy vs. open surgery) because that type of approach is neither practical currently from a financial or training perspective and is beyond the aim of this study. We obtained data from the GBD 2010.⁸ Key parameters obtained from GBD 2010 for the analysis include population, standard life expectancy, cause-specific mortality, incidence, prevalence, and disability weights.^{2, 13, 14} The GBD 2010 employed a Bayesian-meta-regression program, DisMod-MR² to produce and extrapolate internally consistent set of an epidemiologic parameters for all regions that are specific to age, sex, and year. The GBD 2010 grouped the countries into 21 epidemiologic regions (of which 17 are LMICs) and seven super regions (of which six are LMICs). Our analysis was conducted at the super region level by aggregating regional level parameters.

Disability-adjusted life years (DALYs) are a summary measure of population health that sums up fatal burden and non-fatal burden into a single index: years of life lost (YLLs) and years lived with disability (YLDs). When considering digestive diseases, consideration of incidence rather than prevalence is most appropriate because of relatively short duration of disease, and the burden is predominantly due to fatal cases (see Table 1). The base population for the analysis was, therefore, all incident cases in 2010.

We split the reported DALYs of surgical conditions in 2010 into surgically ‘avertable burden’ and surgically ‘non-avertable burden’. The avertable burden was calculated as:

$$\text{Avertable burden} = \text{DALY} - \text{DALY}' \quad (1)$$

where *DALY* denotes the DALYs reported in GBD 2010, and *DALY'* the estimated DALYs if the delivery of surgical care had existed in a hypothetical state of full access to high quality surgical care such as what occurs in high resource environments. In order to estimate the epidemiologic parameters for a hypothetical state, information about the surgical coverage and access to quality of care available currently in each region was needed. Except for several individual countries in Africa and Asia where studies have been undertaken,¹⁵⁻¹⁷ there is a paucity of data, therefore, we assumed that the least fatality rates among the 21 epidemiologic regions for each age-group and sex reflect the hypothetical state (and hence the difference of those rates reflecting the service gap). Not surprisingly, the majority of least rates were from high-income regions (i.e. Asia Pacific High Income, Australasia, Europe Western, and North America High Income).

Based on this assumption, we first estimated the number of deaths for the hypothetical state in LMIC super regions with the following equation:

$$DEATH'_{i,j,k} = Incidence_{i,j,k} \times CFR'_{i,j,k} \quad (2)$$

where $DEATH'_{i,j,k}$ is the age (i) and sex (j) -specific number of deaths for the hypothetical state in each super region (k), $Incidence_{i,j,k}$ is the age and sex-specific number of incident cases in each super region estimated by DisMod-MR in the GBD 2010 Study, and $CFR'_{i,j,k}$ is the age and sex-specific case-fatality rates for the hypothetical state. We then multiplied the $DEATH'_{i,j,k}$ by the age-specific standard life expectancy used in GBD 2010 to estimate the fatal burden for the hypothetical state.^{13, 18}

Next, we estimated the non-fatal burden (YLD) for the hypothetical state of full surgical coverage. While scaling up surgical coverage would decrease the fatal burden (YLL), the averted deaths would still contribute to the non-fatal burden for a short-term: i.e. years lived with disability (YLDs). YLDs in GBD 2010 were calculated by multiplying the prevalent cases by disability weights that are unique to each disease condition (0.326 for appendicitis and intestinal obstruction without hernia, 0.012 for inguinal/femoral hernia, and 0.123 for gall bladder and bile duct disease).¹⁴ However, we did not know the direct impact of decreased case fatality rates on prevalence. Therefore, given the short nature of disease durations of the conditions being analysed (i.e. <1 year), we calculated the YLDs for the hypothetical state as:

$$YLD'_{i,j,k} = (Incidence_{i,j,k} - DEATH'_{i,j,k}) \times Duration \times DW \quad (3)$$

where $YLD'_{i,j,k}$ is the non-fatal burden in case of the hypothetical state, $Duration$ is the duration of disease calculated by dividing the prevalence by incidence (both obtained from the DisMod-MR

estimation), and *DW* is the disability weight attached to each condition. We assumed that cases that survive by scaling up surgical coverage would suffer from the same disability for the same duration as the average non-fatal cases. Finally, we summed up the fatal and non-fatal burden to derive the burden of disease for the hypothetical state.

Diseases-specific background information

In high-income countries, appendectomy for acute appendicitis is one of the most common surgical procedures.^{19, 20} The literature reports 7-9% lifetime risk of appendicitis and 19-35% perforation rates if untreated.^{19, 21-23} Both open surgery and laparoscopy are established approaches of appendectomy. The accurate diagnosis of appendicitis, however, remains a challenge, and historically up to 15-40% of operations were performed on misdiagnosed cases (negative appendectomy) due to the inevitable trade-off between diagnostic accuracy and early treatment given the greater mortality risk associated with perforated cases.²⁴⁻²⁶ Although Berry and Malt suggested many years ago (1984) a 23% negative appendectomy rate as being acceptable so as not to leave true cases untreated,²⁷ Blomqvist and colleagues identified a greater case fatality rate for appendectomy performed on negative cases compared to non-perforated appendicitis, and even greater standardized mortality ratio compared to perforated cases.²⁰ The associated excess mortality may have been caused by the surgical trauma itself or due to missed diagnosis of other critical conditions, thus leaving the acceptable rate of negative appendectomy controversial to date.

Intestinal obstruction, with and without hernia, comprise the largest global burden among the selected digestive diseases (see Table 1 for the burden of selected digestive diseases from GBD

2010). Although adhesions after abdominal operations are the most common causes of intestinal obstruction in high-income countries, incarceration and strangulation of bowel in a hernia are much more common in LMICs.²⁸ Strangulated hernia is a life-threatening emergency that requires urgent operation. Intestinal obstruction without hernia can be potentially treated by nasogastric tube, but failure of the obstruction to resolve is considered an indication for laparotomy.¹¹ While hernia contents may be reducible initially by manual reduction into the abdominal cavity, incarceration and strangulation require urgent operative interventions.¹¹

Gall bladder and bile duct diseases are caused most frequently by gallstones, often without symptoms.²⁹ Only 10-25% of patients develop symptoms in 20 years after incidental diagnosis,³⁰ and the annual risk of developing complications is 0.1-0.2%.³¹ In contrast, symptomatic patients have a 50% chance of recurrent pain in one year and the annual risk of complications is 1-2%, which is a 10-fold increase compared to asymptomatic cases.^{31, 32} Given these differences in natural history, there is controversy about when to provide cholecystectomy: should prophylactic surgery be offered for incidentally detected, asymptomatic cases or only for acute symptomatic cases. WHO recommendation for first-level surgery supports the latter.¹¹

RESULTS

Table 2 provides the surgically avertable deaths and burden for each condition and LMIC super region. Overall, 65% of the disease burden of these four digestive diseases in LMICs would be avertable by first-level surgical care. Over 80% of the digestive disease burden in Sub-Saharan Africa is surgically avertable at the first-level. This region constitutes the largest portion of

avertable DALYs among all LMIC regions. East Europe & Central Asia has the least proportion of avertable burden and second least portion of avertable DALYs.

In East Europe & Central Asia, 74% of the burden of inguinal/femoral hernia remains avertable, while only 22% remains for intestinal obstruction without hernia. Unlike East Europe & Central Asia, inguinal/femoral hernia has the least proportion of avertable burden in Sub-Saharan Africa, North Africa & Middle East, and East Asia Pacific (42%, 0%, and 15%, respectively). Conditions with the greatest proportion of avertable burden (i.e., least current surgical coverage) vary between super regions: appendicitis for Sub-Saharan Africa, North Africa & Middle East, and Latin America & Caribbean (95%, 66% and 78%, respectively); intestinal obstruction without hernia for Asia South (72%); inguinal/femoral hernia for East Europe & Central Asia (74%); and gall bladder and bile duct disease for East Asia Pacific (66%).

Figure 1 demonstrates the composition of avertable and non-avertable surgical burden for each condition and LMIC super region. Figure 1A suggests a uniformly high-proportion of surgically avertable burden of appendicitis in all LMIC regions. Among them, Sub-Saharan Africa dominates the surgically-avertable burden of appendicitis in absolute DALYs and in proportion. East Asia Pacific and Asia South have a relatively small proportion of avertable burden. The proportion of surgically-avertable burden of intestinal obstruction without hernia varies between regions (Figure 1B). East Asia Pacific and Eastern Europe & Central Asia have a relatively lessor proportion compared with other regions. Figure 1C indicates a relatively lessor proportion of burden of hernia avertable by surgery compared to other diseases for all regions, with an extreme case of North Africa & Middle East where no burden is surgically avertable (this is likely an

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4 artefact, see discussion below). Figure 1D shows a heterogeneous proportion of avertable burden
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6 of gall bladder and bile duct disease between regions. Asia South and Eastern Europe & Central
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8 Asia have relatively smaller proportion of surgically-avertable burden than others. Figures for
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10 deaths, YLLs and YLDs are provided in the online version only.
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17 **DISCUSSION**

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20 A large portion of the entire burden of digestive diseases could be averted potentially with the
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22 implementation of appropriate and safe first-level surgical care in LMICs. Our estimates have
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24 revealed that 145 thousand deaths and 4.8 million DALYs could be averted if first-level surgery
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26 were scaled up to cover the entire population with access to quality care in these countries. The
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28 largest potential in decreasing the burden of digestive diseases lies in Sub-Saharan Africa, while
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30 the least is in East Europe & Central Asia. This analysis in turn suggests that the proportion of
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32 overall burden that had already been averted as of 2010 was least in the former and greatest in
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34 the latter, reflecting surgical coverage at that time.
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42 Although a similar set of surgical skills and equipment is required to manage the four conditions,
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44 our estimates revealed a substantial heterogeneity of proportions of avertable burden between
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46 diseases within each super region as well as the patterns between regions for each condition.
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48 These differences reflect the areas of disparities in surgical coverage where rapid improvements
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50 might be feasible to attain. In East Europe & Central Asia, for example, the excess burden of
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52 hernias can likely be addressed with little additional resources; in contrast, the large burden
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54 imposed by appendicitis in Sub-Saharan Africa may be difficult to address without a
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56 comprehensive approach to the entire system of surgical delivery.
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7 While scaling up surgical capacities at first-level hospitals in LMICs can be challenging, there
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9 are a number of ways of improving surgical coverage, both in the short-run and in the long-run.
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11 A short-run solution may include surgical missions supported by foreign charities as has been the
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13 norm in addressing congenital conditions such as clefts or congenital heart anomalies.^{33, 34}
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15 Although such ‘parachute surgeons’ may not be able to serve for acute cases, elective surgeries
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17 such as for hernia could be provided. Alternatively, charities may establish permanent clinics
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19 such as the case with the fistula hospital in Ethiopia.³⁵ Along the line of foreign aid, it is worth
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21 noting of the Cuban health cooperation program that sends more than 35,000 clinicians,
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23 including surgeons, to fill in the gap of health workforce in over 70 LMICs, particularly those in
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25 Latin America, Africa, and more recently in the Pacific.^{36, 37}
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33 As a long-term solution, a number of countries have trained successfully physicians to perform
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35 surgical care,³⁸ and, in some cases, have even trained non-physicians to specialize in basic
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37 surgical care with high retention rates in rural hospitals. For example, since 1984, Mozambique
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39 has been deploying assistant medical officers ‘técnicos de cirugía’ (TC) to first-level hospitals.
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41 These TCs are recruited from mid-level practitioners or nurses and trained intensively for two
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43 years with an additional year of internship.^{39, 40} TCs have been conducting general, orthopedic,
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45 obstetric, and other surgical procedures successfully, including procedures included in our
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47 analysis.^{39, 41} Similar initiatives have been underway in other countries, including Burkina Faso,
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49 Tanzania, Ghana, Ethiopia, Malawi, etc.^{42, 43} Trainings have been provided by local governments,
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51 of which process may be accelerated with support from foreign charities engaged in training.⁴⁴
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Given these advancements in Sub-Saharan Africa, scaling up of surgical coverage in LMICs is a viable endeavor.

Our study may be the most rigorous, data-driven estimation of the surgically-avertable burden of digestive diseases to date. As with any modelling and estimation exercise, some assumptions were required. First, we assumed that the least fatality estimates from the 21 epidemiologic regions reflect the ideal case of full surgical coverage. While most of the estimates were from high-income regions, it is not clear if those figures are applicable to other settings. Even if barriers to access surgical care are removed both physically and financially, health seeking behavior may vary substantially between regions and cultures. The non-trivial variations of fatality rates among high-income countries may imply that none of the health systems truly reflects a state of comprehensive, high quality surgical coverage, although differences in coding practices may have a role in the variations. In addition to full population coverage, quality of surgery and anesthesia is a critical precondition of this analysis that, if compromised, could add to excess mortality itself.

The parameters for our analysis are primarily from GBD 2010, and as such our analysis is subject to the limitations of GBD 2010. The number of deaths from appendicitis in Sub-Saharan Africa is dominated by the West Africa region that contributes close to half the global deaths. The mortality from appendicitis in GBD 2010 was extrapolated using information from other regions, given the complete absence of reliable data from West Africa. If the total burden in West Africa had been over-estimated, so was the avertable burden in our analysis. Nevertheless, the

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4 impact on the proportion of avertable burden is not a concern as both the denominator and the
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6 numerator are affected simultaneously and thus would be largely cancelled out.
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11 The relatively small proportion of avertable burden of hernia in some regions warrants due
12 attention (particularly Sub-Saharan Africa). Unlike other digestive diseases, the burden of hernia
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14 is dominated by years lived with disability (YLDs) rather than years of life lost (YLLs) in GBD
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16 2010 (see Table 1). Data used for modelling the non-fatal burden of hernia in GBD 2010 have all
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18 come from high-income countries that were applied to rest of world. This assumption may have
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20 caused an over-estimation of cases that result in YLDs than in YLLs, leading to a composition of
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22 burden that seems counter-intuitive for LMICs. While surgery for hernia, particularly in the
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24 setting of acute incarceration, is primarily life-saving with a high proportion of avertable deaths
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26 (see Table 2), the dominating non-fatal burden remains unchanged resulting in a small proportion
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28 of avertable burden overall. Hernia in North Africa & Middle East reinforces this argument
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30 because a 0% avertable burden does not seem plausible. This ostensible small proportion of
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32 avertable burden is possibly caused by differences in coding practice of deaths, leading to an
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34 under-estimation of surgically-avertable fatal burden of hernia that is coded elsewhere; however,
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36 its impact on the overall findings is minimal given the small burden of hernia compared to other
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38 digestive diseases.
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50 Finally, we did not attempt to perform an uncertainty analysis around our estimates, although
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52 GBD 2010 provided uncertainty intervals for the epidemiologic parameters. Much of the
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54 uncertainty in our analysis was due to the number of assumptions we had to make. Using the
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4 uncertainty intervals from GBD 2010 estimates provides a false sense of precision because they
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6 do not include this main source of uncertainty.
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10 11 12 **CONCLUSIONS** 13 14

15 Improving the capacity of surgical services at first-level hospitals is essential for averting the
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17 burden of digestive diseases in LMICs. There are practicable strategies for scaling up surgical
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19 capacities in rural districts as has been demonstrated by a number of countries in Sub-Saharan
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21 Africa. While considering universal coverage of health care as part of the global health agenda
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23 beyond 2015, surgical care must be given due attention if disparities are to be decreased and
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25 improvements in care realized.
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Figure legends

Figure 1. Surgical burden of digestive disease in six LMIC super regions. A) Appendicitis, B) intestinal obstruction without hernia, C) inguinal/femoral hernia, and D) gall bladder and bile duct disease

Table 1. Burden of selected digestive diseases in low and middle-income regions, 2010

	Appendicitis	Intestinal obstruction without hernia	Inguinal or femoral hernia	Gall bladder and bile duct disease
Death	31	115	15	65
YLL	1,257	3,379	325	1,544
YLD	162	11	379	362
DALY	1,419	3,390	703	1,906

YLL: years of life lost; YLD: years lived with disability; DALY: disability-adjusted life year

NB: Units are in thousands (uncertainty bounds are not reported here)

Table 2. Surgically-avertable burden of digestive diseases in low and middle-income regions

	East Europe & Central Asia	Sub-Saharan Africa	North Africa & Middle East	Asia South	East Asia Pacific	Latin America & Caribbean	Total
Appendicitis							
Death	1,773 (75%)	14,248 (97%)	1,035 (76%)	1,712 (63%)	3,905 (66%)	3,614 (85%)	26,287 (84%)
YLL	52,535 (84%)	715,658 (99%)	43,117 (87%)	92,009 (82%)	140,301 (79%)	110,511 (90%)	1,154,131 (92%)
YLD*	-22 (0%)	-171 (0%)	-13 (0%)	-20 (0%)	-48 (0%)	-43 (0%)	-317 (0%)
DALY	52,513 (73%)	715,487 (95%)	43,104 (66%)	91,989 (60%)	140,253 (61%)	110,468 (78%)	1,153,814 (81%)
Intestinal obstruction without hernia							
Death	938 (10%)	17,637 (69%)	4,622 (52%)	23,360 (57%)	4,525 (23%)	5,945 (57%)	57,027 (50%)
YLL	50,732 (22%)	663,567 (79%)	164,908 (65%)	976,086 (72%)	175,455 (37%)	146,495 (65%)	2,177,243 (64%)
YLD*	-6 (0%)	-81 (0%)	-20 (0%)	-110 (0%)	-24 (0%)	-27 (0%)	-268 (0%)
DALY	50,726 (22%)	663,486 (79%)	164,888 (65%)	975,976 (72%)	175,431 (37%)	146,468 (65%)	2,176,975 (64%)
Inguinal/femoral hernia							
Death	3,810 (99%)	816 (95%)	0 (0%)	4,459 (97%)	1,279 (84%)	3,700 (98%)	14,064 (96%)
YLL	68,840 (99%)	37,018 (98%)	0 (0%)	119,949 (98%)	24,266 (85%)	75,298 (99%)	325,371 (97%)
YLD*	-18 (0%)	-3 (0%)	0 (0%)	-20 (0%)	-6 (0%)	-17 (0%)	-64 (0%)
DALY	68,822 (74%)	37,015 (42%)	0 (0%)	119,929 (54%)	24,260 (15%)	75,281 (67%)	325,307 (46%)
Gall bladder and bile duct disease							
Death	3,672 (59%)	9,123 (84%)	1,950 (66%)	2,087 (35%)	21,605 (79%)	9,477 (79%)	47,914 (74%)
YLL	74,848 (64%)	327,739 (90%)	48,694 (70%)	104,666 (57%)	447,726 (80%)	188,760 (81%)	1,192,433 (78%)
YLD*	-35 (0%)	-84 (0%)	-19 (0%)	-18 (0%)	-207 (0%)	-90 (0%)	-453 (0%)
DALY	74,813 (47%)	327,655 (79%)	48,675 (51%)	104,648 (38%)	447,519 (66%)	188,670 (66%)	1,191,980 (63%)
Total of four digestive diseases							
Death	10,193 (47%)	41,824 (80%)	7,607 (58%)	31,618 (59%)	31,314 (58%)	22,736 (75%)	145,292 (64%)
YLL	246,955 (52%)	1,743,982 (89%)	256,719 (69%)	1,292,710 (73%)	787,748 (64%)	521,064 (79%)	4,849,178 (75%)
YLD*	-81 (0%)	-339 (0%)	-52 (0%)	-168 (0%)	-285 (0%)	-177 (0%)	-1,102 (0%)
DALY	246,874 (45%)	1,743,643 (83%)	256,667 (58%)	1,292,542 (64%)	787,463 (51%)	520,887 (68%)	4,848,076 (65%)

NB: Percentages in parentheses are the avertable proportion

*Negative values of YLDs reflect the short-term non-fatal burden that is experienced by the averted death cases

Figure1A

Figure1B

Figure1C

Figure1D