



The global burden of unsafe medical care: analytic modelling of observational studies

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ABSTRACT

Objective To contextualise the degree of harm that comes from unsafe medical care compared with individual health conditions using the global burden of disease (GBD), a metric to determine how much suffering is caused by individual diseases.

Design Analytic modelling of observational studies investigating unsafe medical care in countries' inpatient care settings, stratified by national income, to identify incidence of seven adverse events for GBD modelling. Observational studies were generated through a comprehensive search of over 16 000 articles written in English after 1976, of which over 4000 were appropriate for full text review.

Results The incidence, clinical outcomes, demographics and costs for each of the seven adverse events were collected from each publication when available. We used disability-adjusted life years (DALYs) lost as a standardised metric to measure morbidity and mortality due to specific adverse events. We estimate that there are 421 million hospitalisations in the world annually, and approximately 42.7 million adverse events. These adverse events result in 23 million DALYs lost per year. Approximately two-thirds of all adverse events, and the DALYs lost from them, occurred in low-income and middle-income countries.

Conclusions This study provides early evidence that adverse events due to medical care represent a major source of morbidity and mortality globally. Though suffering related to the lack of access to care in many countries remains, these findings suggest the importance of critically evaluating the quality and safety of the care provided once a person accesses health services. While further refinements of the estimates are needed, these data should be a call to global health policymakers to make patient safety an international priority.

INTRODUCTION

Most efforts to improve healthcare globally have focused on improving care for diseases

that cause substantial morbidity and mortality, hoping to increase access to lifesaving therapies for the world's population. These efforts have begun to pay off, with increasing access to antimalarial drugs and anti-retroviral therapies for patients with HIV.¹ However, institutionalising these gains will require focus on healthcare systems and their ability to deliver safe, effective care. This will be especially important in low-income and middle-income countries that are growing economically, and are looking to improve their health systems to care for a growing population.²

One lens through which to examine the functioning of healthcare systems is that of patient safety. Unsafe medical care—where patients are harmed by the medical care designed to help them—can have wide-ranging consequences.³ Adverse events, or injuries as a result of medical care, lead to direct harm and waste, and have spillover effects on patient confidence in the healthcare system.⁴ Many policymakers have primarily considered patient safety as an issue for high-income countries, where most of the population has access to basic healthcare. Indeed, estimates suggest that tens of thousands of citizens are injured, or die, due to medical errors in these countries.⁵ While the lack of access to basic healthcare services in many countries remains a clear policy challenge in the context of health systems strengthening, the extent to which people face suffering due to unsafe care once accessing medical services is less obvious. In other words, the extent to which unsafe medical care—or adverse events resulting from medical care—is a problem for developing and transitional countries, once a person accesses these health services, is not well known.

WHO undertook the challenge of estimating the global burden of unsafe care as an essential step to guide global actions in strengthening health systems. The global burden of disease (GBD) is a standard metric used by policymakers throughout the globe to determine how much suffering is caused by individual diseases. Its application has been more recently expanded to examine events like road accidents and other public health dangers.⁶ The GBD uses disability-adjusted life-years (DALYs) lost to quantify the morbidity and mortality associated with individual conditions and injuries.⁶ Understanding the GBD of unsafe medical care would be helpful to quantify the degree to which the world's population encounters harm from unsafe healthcare interventions, allowing policymakers to better compare the DALYs lost from unsafe medical care to other causes of human suffering. Such data would allow policymakers to better prioritise the interventions likely to improve care and health for the world's citizens.

Therefore, in this study, we sought to answer three questions: first, what is the global burden of unsafe medical care? Second, to what extent does the issue of unsafe medical care affect low-income and middle-income countries (LMICs) compared with high-income countries (HICs)? And third, are there certain types of adverse events resulting from unsafe medical care that are particularly harmful that policymakers can target in order to eliminate unnecessary suffering?

METHODS

Definition of terms

For the purposes of this analysis, we consider *adverse events* as unsafe experiences in an inpatient hospital setting and are thereby contingent on people having access to these medical services. We then explore the 'clinical outcomes' (eg, the proportion of patients who die, the proportion who have an injury and the duration of an injury) of these adverse events in order to quantify the burden of these adverse events or unsafe medical practices on human suffering.

Identifying types of adverse events

In July 2007, WHO's Patient Safety programme convened a panel of international experts to discuss priorities for research on patient safety. The committee identified 20 topics that were of importance to patient safety, including structural factors, process of care and outcomes of unsafe care.⁷ Of these twenty, twelve adverse events were candidates for estimating the GBD of unsafe medical care. After consultation with the WHO committee, and an exhaustive literature review, we excluded five of the 12 outcomes due to severe data limitations (eg, substandard or counterfeit drugs, unsafe blood products, unsafe injections, medical devices and surgical errors, although we captured some of the injuries from surgical care in

venous thromboembolism or nosocomial pneumonia). Due to the inadequacy of these data on adverse events in the ambulatory care setting, we elected to focus only on inpatient adverse events. As such, the final set of seven outcomes or types of adverse events used for the analyses were: (1) adverse drug events (ADEs), (2) catheter-related urinary tract infections (CR-UTIs), (3) catheter-related blood stream infections (BSIs), (4) nosocomial pneumonia, (5) venous thromboembolisms (VTEs), (6) falls and (7) decubitus (pressure) ulcers. Hospitalisations resulting from these adverse events occurring to outpatients were excluded. Additionally, we excluded hospitalisations due to childbirth, as we had little information about adverse events among these hospitalisations.

Data sources

We used two primary sources of data: a literature review and findings from recent WHO-commissioned epidemiologic studies. First, the literature review strategy, as detailed in the online supplementary methodological appendix, was designed to be a comprehensive examination of both peer-reviewed and non-peer-reviewed studies that focused on the seven aforementioned adverse events of interest, the clinical features of the patients who were injured (eg, age), and their outcomes. For this analysis, we relied upon two separate literature reviews; the first was conducted in late 2007 through early 2008, and it was then repeated in 2011.⁷ We supplemented the literature review with discussions with international experts in each topic area to ensure that key studies had been identified. The outcome of our literature review, including the specific studies that contributed incidence data for our models, is reported in the online supplementary methodological appendix.

The second data source for this study came from epidemiologic studies that were commissioned by WHO, which aimed to estimate the scale to which inpatient adverse events harmed patients. These studies have previously been described.^{8,9} In brief, they consisted of the identification of adverse events by a two-stage medical record review: initial screening by nurses or junior physicians using 18 explicit screening criteria followed by a review by a senior physician for determination of the adverse event, its preventability and the resulting disability. The studies were conducted in 26 hospitals across eight low-income and middle-income countries in the Eastern Mediterranean and North African regions, and 35 hospitals across five countries in Latin America.^{8,9} These studies also provided incidence data for our models.

Global burden of disease model

The GBD, run by WHO, uses disability-adjusted life years (DALYs) to measure morbidity and mortality due to a specific condition. The GBD DALYs model requires several key inputs: the number of people

affected, the age at which they are affected, and the clinical consequence of the adverse events, including the type of disability encountered (ie, clinical outcomes). Due to the paucity of data, we used a single average age per event, as opposed to standard GBD calculations done by age group and sex. The details of the model, including the formulae used, are detailed in the online supplementary methodological appendix.¹⁰ For all our modelling approaches, we estimated each input separately for high-income versus low-income or middle-income (LMIC) countries (as defined by the World Bank).¹¹

Identifying inputs for the GBD model

Incidence of adverse events: We estimated the incidence of each of our seven adverse events in a hospitalised population based on reported data from the literature review and epidemiologic studies described earlier. Given that there was a range of estimates for both HICs as well as for LMICs, we generally took the median incidence for each category as our 'best estimate' but allowed the entire range of incidence estimates in the Monte Carlo models (see analysis below).

Number of adverse events: In order to calculate the number of patients harmed due to adverse events after accessing medical services, we needed to estimate the number of hospitalisations that occur globally. To our knowledge, there is no single source where such data are available. Consequently, we used data from WHO, the World Bank, the Organisation for Economic Co-operation and Development (OECD), and others, including the Centers for Disease Control and Prevention in the USA to create these estimates. We used the median as our 'best estimate' for the number of hospitalisations, but allowed the modelling to take into account the entire range of data identified. For each of our seven outcomes or adverse events of interest, we multiplied the number of hospitalisations by the incidence to estimate the number of adverse events that occurred.

Demographics and outcomes of adverse events: We used data from the literature review to estimate demographics (eg, age and gender) of patients injured from an adverse event as well as their clinical outcomes (eg, the proportion of patients who typically die, the proportion that would suffer a long-term and a short-

term injury, the duration of that injury, and the proportion that would suffer only minor injuries but no sustained disability). The distribution of age at the time of acquiring the condition and the outcomes for these injuries are shown in the online supplementary methodological appendix.

Calculating DALYs: To calculate DALYs, this required that we apply disability weights for the injuries or harms that are attributable to the seven adverse events explored in this analysis. We used WHO's GBD reports to identify disability weights for injuries when available; when not available, we identified the closest analogue or clinical condition for which there were disability weights available (see online supplementary methodological appendix). As is standard in these models, we assumed that the life expectancy was 81.3 years based on model life-table West Level 26, which has a life expectancy at birth of 82.5 for females and 80.1 for males.¹²

Analysis

Our primary analytic approach was to build a Monte Carlo simulation model with 1000 simulations for each of the seven adverse events within LMICs, and then separately for HICs. In these models, the best estimate was assumed to be the midpoint of the range with a triangular distribution. Therefore, we had 14 sets of Monte Carlo models (one for each of the seven adverse events for HICs and for LMICs). These models yielded the best overall aggregate estimate of the global burden of harm resultant from these adverse events. Moreover, the models produced distributions for each of the input variables, as well as each of the output variables (see online supplementary methodological appendix). Analyses were performed using SAS V.9.2.

RESULTS

We estimated that there were 117.8 million hospitalisations among the approximately 1.1 billion citizens in HICs in 2009, while there were 203.1 million hospitalisations among the 5.5 billion citizens of the LMICs. Hospitalisation rates for HICs were higher (mean 10.8 per 100 citizens per year) compared with those for LMICs (mean 3.7 per 100 citizens per year; see table 1).

Table 1 Hospitalisation rates in high, middle and low income countries

	High-income countries	Low-income and middle-income countries	Total
Hospitalisation rates*			N/A
Mean (95% CI)	10.8 (8.6 to 13.2)	3.7 (2.0 to 6.1)	
Total population	1 056 300 000	5 554 000 000	6 610 300 000
Total number of hospitalisations (estimated range)	117.8 M (94.3 M—143.4 M)	203.1 M (121.9 M—312.2 M)	421 M (225.5 M—616.3 M)

*Rates are per 100 citizens per year; M, million

Table 2 Incidence rates of adverse events among high versus low and middle-income countries

	High-income countries (%)	Low-income and middle-income countries (%)
Catheter-related UTI	1.1 (0.8 to 1.5)	2.0 (0.5 to 3.5)
Adverse drug events	5.0 (2.7 to 7.2)	2.9 (0.6 to 5.2)
Falls in the hospital	1.1 (0.3 to 2.0)	1.6 (1.3 to 2.0)
Catheter-related blood stream infection	0.4 (0.2 to 0.6)	0.4 (0.3 to 0.6)
Nosocomial pneumonia	0.8 (0.7 to 1.1)	0.4 (0.2 to 0.6)
Decubitus ulcers	2.4 (0.8 to 4.7)	2.4 (0.8 to 4.7)
Venous thromboembolisms	3.3 (1.9 to 4.8)	3.0 (1.0 to 4.8)
Overall incidence rate of adverse events	14.2	12.7

*Rates are means (95% CIs) per 100 hospitalisations per year.

We found large variations in the reported incidence of adverse events both within HICs and LMICs (see table 2). Of the seven adverse events analysed in the inpatient hospital setting, the most common type in HICs was adverse drug events with an incidence rate of 5.0% (CI 2.7% to 7.2%) while the most common in LMICs was venous thromboembolism (incidence rate of 3.0%, CI 1.0% to 4.8%). We found comparable incidence between HICs and LMICs of three types of adverse events: catheter-related blood stream infections, venous thromboembolism, and decubitus ulcers. We found lower rates of adverse drug events in LMICs compared with HICs (2.9% vs 5.0%) and nosocomial pneumonia (0.4% vs 0.8%), while rates of two types of adverse events (catheter-related urinary tract infection (CR-UTI) and falls) were higher in LMICs compared with HICs (see table 2). Based on these incidence data, we estimated that of every 100 hospitalisations, there were approximately 14.2 of these adverse events in HICs and 12.7 in LMICs. The age at which these adverse events occurred was generally 8 to 19 years higher in HIC (see online supplementary methodological appendix).

We estimate that there are approximately 16.8 million injuries annually due to these adverse events

among hospitalised patients in HICs. LMICs, which have five times the population of HICs, experienced approximately 50% more adverse events (25.9 million, see table 3). The number of adverse events varied substantially depending on the type of event examined, and the estimates for each type of adverse event corresponded with wide confidence intervals. For instance, we estimated that there were approximately 1.4 million (95% CI 0.8 million to 2.0 million) catheter-related urinary tract infections among HICs, while there was a substantially higher number and rate in LMICs (4.1 million, 95% CI 0.5 million to 9.2 million).

Based on these findings, we estimate that there were 22.6 million DALYs lost due to these adverse events in 2009 (table 4). The number of DALYs lost were more than twice as high in LMICs (15.5 million) as they were in HICs (7.2 million). The biggest source of lost DALYs appeared to be venous thromboembolism (5.4 million DALYs in LMICs, 95% CI 1.1 million to 11.7 million) and 2.3 million in HICs (95% CI 1.1 million to 3.9 million). Although the underlying numbers of several of the infections were much smaller, they caused a comparable number of DALYs lost, often because the clinical outcomes were poor when these infections occurred (table 4).

For most of the adverse events explored in this study, the primary source of DALYs lost was premature death: 78.6% of all adverse events in HICs and 80.7% in LMICs. The proportion of DALYs lost due to short-term or long-term disability (as opposed to premature death) ranged from as little as 0.8% (catheter-related UTI) to a high of 32.9% (falls in the hospital) in all countries (table 4). While premature death constituted the primary source of DALYs lost, disability (both short and long term) were generally more common than death itself (see data presented in online supplementary methodological appendix).

DISCUSSION

Injuries secondary to adverse events from unsafe care present significant challenges to health systems across the globe.¹³ We projected a collective 22.6 million

Table 3 Annual number of cases for selected adverse events

	High-income countries	Low-income and middle-income countries
Catheter-related UTI	1.4 M (0.8 M to 2.0 M)	4.1 M (0.5 M to 9.2 M)
Adverse drug events	5.8 M (2.7 M to 9.5 M)	6.0 M (0.6 M to 13.9 M)
Falls in the hospital	1.3 M (0.3 M to 2.5 M)	3.3 M (1.7 M to 5.7 M)
Catheter-related blood stream infection	0.5 M (0.1 M to 0.8 M)	0.9 M (0.4 M to 1.6 M)
Nosocomial pneumonia	1.0 M (0.7 M to 1.4 M)	0.9 M (0.3 M to 1.7 M)
Decubitus ulcers	2.9 M (0.7 M to 6.2 M)	4.9 M (1.1 M to 12.1 M)
Venous thromboembolisms	3.9 M (1.9 M to 6.3 M)	6.0 M (1.2 M to 12.8 M)
Total	16.8 M	25.9 M

M, Million

Table 4 Disability-adjusted life-years (DALYs) lost and source of the DALYs, in 2009

	DALYs*	Short-term disability (%)	Long-term disability (%)	Premature death (%)
High-income countries				
Catheter-related UTI	402 (214–620)	2.2	0.1	97.7
Adverse drug events	779 (350–1332)	5.7	0.3	94.0
Falls in the hospital	27 (6–51)	27.5	6.0	66.5
CR blood stream infections	1126 (328–2088)	3.0	0.2	96.8
Nosocomial pneumonia	2545 (1673–3703)	1.4	0.0	98.5
Decubitus ulcers	134 (58–268)	5.9	4.4	89.8
Venous thromboembolisms	2282 (1054–3855)	28.2	7.4	64.4
Total	7208 (5371–9271)	15.7	5.7	78.6
Low-income and middle-income countries				
Catheter-related UTI	3420 (450–8012)	0.7	0.0	99.4
Adverse drug events	1435 (126–3453)	2.3	0.1	97.6
Falls in the hospital	76 (6–169)	26.9	5.9	67.2
CR blood stream infections	2150 (958–4065)	3.0	0.2	96.8
Nosocomial pneumonia	2674 (996–5403)	1.4	0.0	98.5
Decubitus ulcers	291 (104–652)	30.0	5.6	64.4
Venous thromboembolisms	5399 (1126–11 730)	26.8	7.0	66.1
Total	15 454 (9009–23 607)	14.1	5.2	80.7
Total (combined)				
Catheter-related UTI	3822 (844–8412)	0.8	0.0	99.4
Adverse drug events	2214 (807–4274)	3.4	0.2	96.7
Falls in the hospital	103 (29–199)	27.0	5.9	68.1
CR blood stream infections	3276 (1752–5379)	3.0	0.2	98.2
Nosocomial pneumonia	5219 (3226–8120)	1.4	0.0	99.1
Decubitus ulcers	426 (209–804)	13.8	4.8	82.7
Venous thromboembolisms	7681 (3115–14 034)	27.3	7.1	70.7
Total	22 644 (15 899–30 979)	14.4	5.3	80.2

*All DALY numbers are in thousands.
DALYs, disability-adjusted life years.

DALYs lost due to adverse events experienced by the world's hospitalised population. Compared with other conditions, the combination of these seven adverse events alone estimated in this study rank as the 20th leading cause of morbidity and mortality for the world's population. It is unlikely that these are 'new' previously undiscovered DALYs, but rather that they are captured within the injuries and deaths attributed to other conditions such as cardiovascular disease. We suspect that these DALYs resulting from unsafe medical care may be one of the reasons why patients are disabled or die from these other conditions.

While lack of access to healthcare, especially hospital care, is clearly a major source of ill health and poor outcomes, especially in low-income countries, our work focuses on the safety of care once a person has accessed the medical resources available to them. We are unaware of any prior effort to examine the global burden of unsafe care across multiple types of adverse events. WHO estimates that the global burden of unsafe injection practices was over 9.2 million DALYs lost per year in the year 2000 alone.¹⁴ If we had included those estimates, the resultant GBD from unsafe care would have been over 33 million DALYs,

placing it as the 14th leading cause of morbidity and mortality in the world, comparable to the burden from tuberculosis or malaria. Including adverse events that were not possible to include in this study due to data limitations, such as unsafe surgery, harm due to counterfeit drugs, unsafe childbirth and unsafe blood use, as well as safety issues with ambulatory care, would further raise these estimates substantially. A recent systematic review¹⁵ found that healthcare-associated infections are ubiquitous and occur at much higher rates in low-income countries than in HICs. Although these investigators did not calculate the GBD of these infections, their data underscore and support our findings that adverse events once reaching a hospital setting are common and likely cause unnecessary suffering across the globe.

These findings should prompt policymakers across the globe to invest further into systematic data collection, as well as programmes to measure and improve the safety of the healthcare systems. While the lack of access to care presents substantial harm, it is important to maintain high standards for safety and quality within the healthcare systems that we subject patients to across the globe. Unsafe medical care may even

lead patients, especially in low-income countries, to opt out of using the formal healthcare system, thereby making unsafe care a potentially significant barrier to access for many of the world's poor. Such a phenomenon would suggest that the distinction between access and quality (or in this case, safety) may not be so clear. Finally, other costs of unsafe care, such as increased consumption of resources due to prolonged stay and extra care—and loss of wages and productivity—are important, and would benefit from further investigation.

Limitations

This work has important limitations. The primary one is the lack of availability of high-quality data. Although there are nearly five times as many people living in LMICs, the number of adverse events we calculated was only 50% higher, primarily due to the lower hospitalisation rates and the poor quality of data sources in LMICs (including medical records). These poor quality data sources lead to undercounting of adverse events that are often not recorded. Nevertheless, the number of DALYs per event was substantially higher, likely due to a combination of a younger age at which these events occur, and the worse outcomes that often result. While this limitation may raise concerns about the validity of our findings, we used data from a large number of sources, and reassuringly found a consistent rate of adverse events.

The paucity of data also limited our ability to run calculations per age group and sex, leading us to calculate average estimates. Additionally, the data limited our analysis to reporting the aggregate harm resulting from total adverse events as opposed to preventable adverse events. While estimating preventable harm would be valuable, there is even greater uncertainty about how much harm is preventable at any given time, and as technology and clinical care changes, the proportion of adverse events that are preventable, likely will, as well. While our estimates are imprecise, we believe that as more data on adverse events become available, WHO will be able to refine these estimates and track them over time.

Second, while there are several high-quality studies, few use standardised definitions or approaches to identifying adverse events. Therefore, the data we relied on all used slightly different approaches and likely lead to some degree of imprecision.

Third, we elected to use the same life expectancy value for all individuals, and although this has been controversial, it is the standard approach used by WHO. Had we chosen different life expectancies for different countries, we likely would have estimated a lower number of DALYs lost, especially for low-income and middle-income countries.

Fourth, we excluded publications not written in English, which may have affected the precision of our estimates. Nearly all major epidemiologic studies of

adverse events from HICs over the past decade have found that they occur in 8–15% of hospitalised patients. Data from LMICs suggest that the rates are even higher. Further, we excluded studies that were clearly of low quality, including those that used non-standard methods (such as convenience samples), or had unclear denominators, or extremely small sample sizes. Whether and to what degree these exclusions biased our findings is unclear.

Fifth, as described above, key inpatient adverse events that the WHO Committee on Patient Safety viewed as important were excluded due to data limitations (eg, unsafe childbirth), leading us to underestimate the true burden of harm from unsafe medical care. Also, we excluded adverse events in the ambulatory setting, which recent data suggest are a major source of harm.

Finally, we lacked disability weights specifically designed for the injuries we examined attributable to our seven adverse events. However, most of the injuries did have clinically analogous events for which there were disability weights. In other words, we identified 'proxy' conditions for each adverse event, usually choosing diseases that affected the same organ system with a generally similar level of severity. We attempted to use the most conservative disability weight in the model, though we recognise that our efforts at matching are imperfect. For example, for catheter-related infections, we used the proxy condition of endocarditis which has a disability weight range from 0.17 to 0.32. This is more fully described in the online supplementary methodological appendix. WHO has a well designed and rigorous process for creating disability weights, and the potential impact of these results will likely spur them to create specific disability weights for these injuries.

Although our estimates are quite conservative, they still represent a relatively wide range of possible outcomes because of inadequate data. Poor quality data on health systems, especially on adverse events, hampered our ability to effectively calculate the number of DALYs lost due to unsafe care, especially within LMICs. Even in HICs, these data are not routinely measured and made publicly available,¹⁶ hampering not only our ability to calculate their consequences, but also limiting the ability of clinical leaders and policymakers to track the potential impact of policies designed to increase the safety of healthcare. As LMICs prosper economically, it is hopeful that citizens will have greater access to medical services, and more encounters with the healthcare system. Without concomitant improvements in the safety of health systems, the number of injuries will likely grow.

CONCLUSION

Using a conservative approach, we estimated that there are at least 43 million injuries each year due to medical care, and that nearly 23 million DALYs are

lost as a consequence. A large majority of these injuries and harm occur in developing and transitional countries—and these numbers will likely grow. Given the magnitude of these effects, our findings suggest that to improve the health of the world's citizens, we will need to improve access to care and also to invest substantial focus on improving the safety of the healthcare systems that people access worldwide. When patients are sick, they should not be further harmed by unsafe care. This should be a major policy emphasis for all nations.

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