Appendix:

The Global Burden of Unsafe Medical Care: An Observational Study

The World Alliance for Patient Safety commissioned a comprehensive review of the literature on patient safety in 2007. This review, conducted with the input of the committee on research for patient safety, identified 23 topics of patient safety. These included adverse events, which were postulated to cause substantial morbidity and mortality. From this review, we identified ten different types of adverse events on which to base our models (See Table 1 below). We further narrowed our search to exclude 5 of the 10 domains of adverse events, usually because adequate data on these topics were not widely available or were significantly outdated. Additionally, it became evident that the best data available were based on potential causes of harm due to medical care received within the hospital. Therefore, we excluded adverse events in the outpatient setting. We based our approach on the remaining seven types of adverse events. The case definitions are primarily based on how each of these adverse events are defined in the literature, accounting for modest variations among these definitions. When the studies had no case definition or were defined in ways that appeared to be very different than the cases as defined below, we generally excluded those studies.

Table 1. Domains of adverse events

1	Injuries due to counterfeit and/or substandard drugs*
2	Injuries due to medical devices*
3	Injuries due to medications
4	Injuries due to surgical errors*
5	Injury due to health-care associated infections a. Hospital-Acquired Infections : Nosocomial Pneumonia

	b. Hospital-Acquired Infections: Catheter-related Blood Stream Infections c. Hospital-Acquired Infections: Catheter-related Urinary Tract Infections
6	Injury due to unsafe injections / blood products*
7	Injuries at the time of childbirth for mother and child*
8	Injuries due to thrombo-embolism from medical care
9	Injuries from falls in the hospital
10	Injury due to pressure sores and decubitus ulcers

*These adverse events were excluded because of inadequate data available.

Summary of the Data from our Literature Review and Case Definitions

An iterative systematic literature review was performed at the Harvard School of Public Health (HSPH) between March 2008 and April 2011. Co-Investigators at HSPH, Brigham and Women's Hospital (BWH), and the Johns Hopkins Bloomberg School of Public Health first reviewed the data and then commented on and requested additional data. Countries were classified as either "low- or middle-income" (LMIC) or "high-income" (HIC) based on categorization by the World Bank. Country demographic and health statistics data were obtained from the World Health Organization, OECD, IMF, and World Bank "World Development Indicators."

Study staff consulted with trained librarians at Harvard University to develop an appropriate and comprehensive search strategy. Primary Medical Subject Headings (MeSH) terms were identified in collaboration with librarians, Co-Investigators, and study staff. Articles not written in English and before 1976 were excluded and the rest were screened for merit. Although we did not use a formal screening criteria, 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. The *Global Burden of Disease: 2004 Update*, sponsored by the World Health Organization, was consulted to ensure the search strategy captured all pertinent publications.

The search examined the global burden of disease in five domains, for a total of seven (7) adverse events:

1. Adverse Drug Events
2. Hospital-Acquired Infections : Nosocomial Pneumonia
3. Hospital-Acquired Infections: Catheter-related Blood Stream Infections
4. Hospital-Acquired Infections: Catheter-related Urinary Tract Infections
5. Venous Thrombo-embolisms
6. Falls in the Hospital
7. Decubitus Ulcers

For each of the seven adverse events noted above, up to five types of data were collected from each publication: incidence, clinical outcomes, demographics, costs, and study design/setting. These data were used to project the number of people affected (both short-term and long-term), clinical outcomes (e.g., proportion of affected population who fully recover, have short-term disability, have long-term disability, or die due to unsafe care), life expectancy, and the disability-adjusted life years (DALYs). The details of the search and the yields are described below in the section on case definitions and search results. Moreover, we provide in the table below a summary of the primary data sources used for inputting incidence rates into our model for each of the aforementioned seven adverse events.

Our search highlighted the paucity of systematic global data available for our chosen adverse events. Particularly in LMICs, the variability in data was extensive and presented substantial challenges to our work. For example, rates of hospitalizations among these nations varied more than 10-fold. To be a truly robust indicator, the global burden of disease model requires more specific data on patient demographics, the number of people who are hospitalized, the severity of disability that results from adverse events, and the duration of injury, many of which were not directly available. We focused on data where they were available and made best estimates using existing data. For instance, given that the clinical outcomes of adverse events were generally not available for LMICs, we often assumed that these patients' outcomes would be no better than those for patients suffering identical injuries in HICs. Whenever we had to make estimates based on existing data, we sought to make the most conservative assumptions possible.

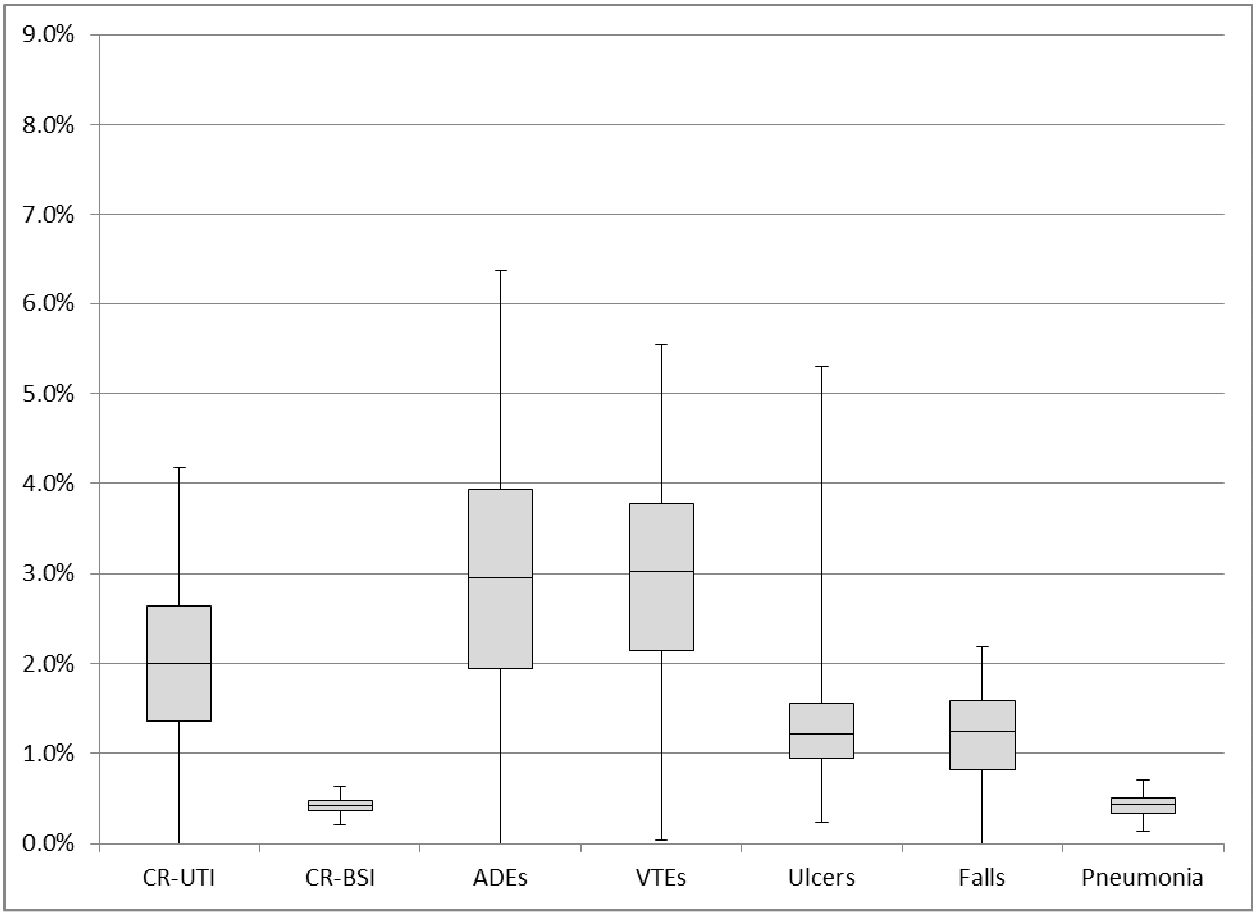
Incidence Rates

To begin our calculation of incidence and/or prevalence rates for each adverse event, we gathered information regarding total number of hospitalizations for both HICs and LMICs. We calculated the range of total hospitalizations for HICs to be between 94.3 million (M) and 143.4 M. The total number of hospitalizations for LMICs was estimated between 121.9 M and 312.2 M.

The first major challenge was to estimate the number of people who were affected by these adverse events. The incidence rate was defined as the number of new cases per population in a given time period. The prevalence rate was defined as the number of cases of a given disease in a specified population at a designated time.[1] In cases in which only incidence or only prevalence

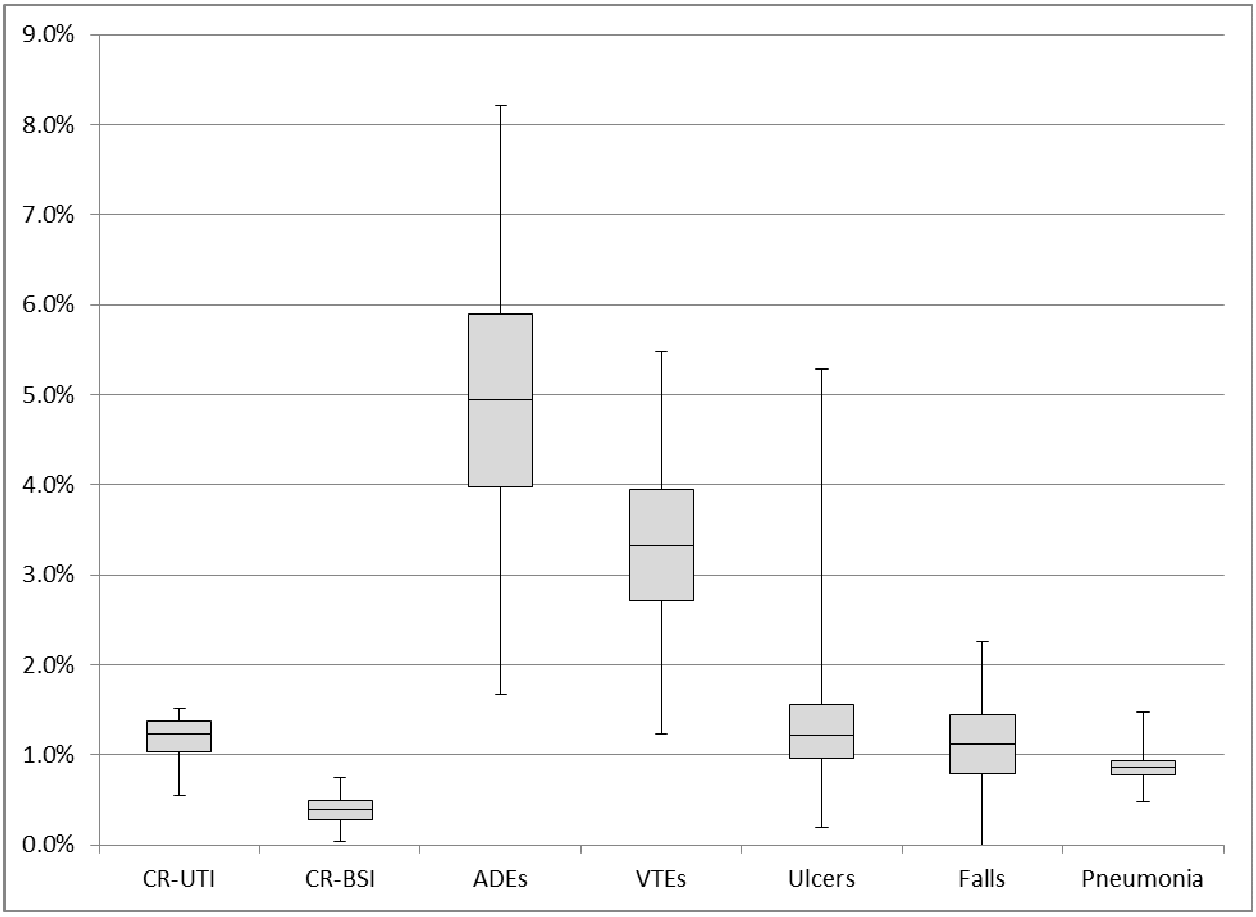
was available, we estimated the missing parameter using the relationship: prevalence = incidence x duration. Since no population-level estimates were available, we created them by multiplying the rates of adverse events for hospitalized patients by the number of hospitalizations. That is, if the rate of adverse drug events was 5.0 per 100 hospitalizations, and we estimated that there were 117.8 million hospitalizations in HICs, then we would estimate that there were 5.8 million adverse drug events in HICs (these numbers are approximate because the number of ADEs presented in Table 3 actually come from the Monte Carlo model which presumes a range of hospitalizations and a range of incidence). Our most reliable data stemmed from incidence rates reported by HICs.

Figure 1a. Range of incidences used in modelling for low and middle income countries.



CR-UTI is catheter-related urinary tract infections; CR-BSI is catheter-related blood stream infections; ADE is adverse drug events; VTEs is venous thrombo-embolism; Ulcers is decubitous ulcers; Falls is hospital-acquired falls; and Pneumonia is hospital-acquired pneumonia.

Figure 1b. Range of incidences used in modeling for high income countries.



CR-UTI is catheter-related urinary tract infections; CR-BSI is catheter-related blood stream infections; ADE is adverse drug events; VTEs is venous thrombo-embolism; Ulcers is decubitous ulcers; Falls is hospital-acquired falls; and Pneumonia is hospital-acquired pneumonia.

Below is a case definition and a detailed description of the search and results for each of the seven adverse events of interest in this study:

1. Adverse Drug Events

Adverse drug events (ADEs) are noxious, unintended, and undesired events that occur as a result of an error at any point in the process of administrating a medication, including ordering, transcribing, dispensing, and administering medications.[2] Patients who experience these events may suffer from injury or death as a result of the error,[3] and the costs to treat these patients are substantial due to longer lengths of stays and increased treatment.[4] To calculate the health and financial burden of ADEs, our literature review excluded studies in which ADEs were either the primary diagnosis for hospitalization, occurred in the outpatient setting, focused only on rates of drug-specific ADEs, or occurred due to patient noncompliance.

The primary search resulted in 508 publications from years 1980-2010. Thirty of the 508 publications were from low-income countries. To ensure all publications for low-income countries were captured, new searches specific to these countries were then carried out. These searches resulted in an additional 193 articles. The articles from which we drew incidence rates are reported in Table 7.

2. Hospital-Acquired Infections (HAIs)

a. Nosocomial Pneumonia

Nosocomial pneumonia (NP) or hospital-acquired pneumonia is defined as pneumonia occurring more than 48 hours after hospital admission and excluding any infection that is incubating at the

time of hospital admission.[5] Most patients with nosocomial pneumonia are those with severe underlying disease, immune suppression, depressed sensorium, and cardiopulmonary disease, and those who have had thoraco-abdominal surgery.[6] The major causative organism for the disease is aerobic Gram-negative bacilli, particularly Pseudomonas Aeruginosa.[7]

The primary literature search produced 1,318 articles, of which 133 were from low-income countries. Supplemental searches were carried out, which produced approximately 2,000 additional articles. We hand-sifted through these abstracts and included any that provided relevant inputs for the modeling (e.g. incidence rates) that we employed for this project..

b. Catheter-related Blood Steam Infections

A catheter-related blood stream infection (CR-BSI) is defined as bacteremia or fungemia in a patient who has an intravascular device and one or more positive blood culture samples obtained from a peripheral vein, has clinical manifestations of infection (such as fever, chills, and/or hypotension), and has no apparent source for bloodstream infection (other than the central venous catheter). In addition, one of the following should be present: (1) a positive result of semi-quantitative (15 colony forming units [CFU] per catheter segment) or quantitative (10^2 CFU per catheter segment) CVC culture, whereby the same organism is isolated from a CVC segment and a peripheral blood sample; (2) simultaneous quantitative cultures of blood samples with a ratio of not less than 5:1 (CVC versus peripheral); and (3) differential time to positivity (positive blood culture occurs at least 2 hours earlier in the sample from the CVC than in the peripheral blood).[8]

The literature search located 280 articles. Of these, 19 were from low-income countries and 254 were after the year 1995.

c. Catheter-related Urinary Tract Infections

A catheter-related urinary tract infection (CR-UTI) in patients with indwelling urethral catheters, indwelling suprapubic catheters, or undergoing intermittent catheterization is defined by the presence of symptoms or signs compatible with UTI with no other identified source of infection along with greater than or equal to 10^3 colony-forming units per milliliter of greater than or equal to 1 bacterial species in a single catheter urine specimen or in a midstream voided urine specimen from a patient whose urethral, suprapubic, or condom catheter has been removed within the previous 48 hours.[9]

The primary search for Urinary Tract Infections resulted in 212 articles. Of these, 108 were published after 1995 and 22 were from LMICs. Supplemental searches found an additional 275 articles.

3. Venous Thrombo-embolisms

Venous thrombo-embolism (VTE) is a disease that includes both deep vein thrombosis (DVT) and pulmonary embolism (PE). It results in long-term complications including chronic thrombo-embolic pulmonary hypertension (CTPH) and the post-thrombotic syndrome (PTS). Venous thrombo-embolism results from a combination of hereditary and acquired risk factors, also known as thrombophilia or hyper-coagulable states. Vessel wall damage, venous stasis, and increased activation of clotting factors are the fundamental basis for thrombosis. Deep vein

thrombosis commonly presents with pain, erythema, tenderness, and swelling of the affected limb.[10]

The primary literature search produced 8,383 articles. Additional searches were carried out to identify additional sources, and produced over 2,000 additional publications. The majority of these secondary searches focused on low-income countries. We hand-sifted through the abstracts of these publications, yielding a total of 442 studies that appeared to provide relevant data to consider for this project To calculate the health and financial burden of VTEs, our literature review excluded studies in which VTEs were the primary diagnosis for hospitalization

4. Falls in the Hospital

An inpatient fall is defined as an unintentional descent to the floor or ground in a conscious patient.[11] Our literature review specifically focuses on falls that occur in the hospital while a patient is hospitalized for a medical or surgical condition.

Many articles examined falls in general, and were not exclusive to the inpatient setting. The primary search found 188 articles, of which only 1 article was from a low-income country. Further searches were carried out to expand the breadth of articles. However, due to the dearth of publications in this area, we were able to locate less than 200 additional articles, many lacking merit or published solely in foreign languages.

5. Decubitus Ulcers

A decubitus ulcer is a defect in the skin that may extend through the subcutaneous layer into the underlying fascia. It results from necrosis of tissue caused by vascular occlusion, which occurs when the skin is pressed against a firm surface and has a bony prominence, or when vessels are deformed and collapse.[12] Susceptibility to pressure ulcers comes from a combination of external factors (pressure, friction, shear force, and moisture), and internal factors (e.g. fever, malnutrition, anaemia, and endothelial dysfunction).[13] Patients undergoing surgery are prone to develop pressure ulcers during the surgical procedure.[14]

The primary literature search produced 206 articles. Secondary searches produced over 500 more articles but few of these contributed additional information after we hand-sifted through the abstracts.

The Global Burden of Disease Model

The key inputs for the GBD model are discussed in this section. These data were used to project the number of people affected (both short-term and long-term), the clinical outcomes (e.g. proportion of affected population who fully recover, have short-term disability, long-term disability, or die due to unsafe care), life expectancy, and Disability-Adjusted Life Years (DALYs).

Disability–Adjusted Life Years (DALYs)

For each condition, we established a methodology for calculating the Disability-Adjusted Life Years (DALYs) lost due to each of the seven adverse events identified above. We established these estimates separately for HICs and LMICs. This model follows standard calculation for

DALYs. For each condition, the data collection included the following outcomes, following standard Global Burden definitions when possible:[1]

- Hospitalization Rates: Hospitalization rates are defined as the number of age-standardized acute-care admissions per 100,000 citizens per year.
- Incidence Rates: Incidence rates are defined as the number of new cases per population per year.
- Age of Occurrence: The age of occurrence is defined as the mean age at which a disease or condition is first diagnosed.
- Duration of Disease or Condition: The duration of disease or condition is defined as the mean number of years following diagnosis during which the disease or condition (i.e. sequela of the injury) is present.
- Disability Weight: The disability weight places a value on the extent of the disability associated with the years of life with the disability (ranges from zero – perfect health – to one – death).
- Clinical Outcomes:
    - Injuries leading to full recovery: Injuries where there is no residual disability by the time of hospital discharge.
    - Injuries leading to short-term disability: Injuries for which there is residual disability following hospital discharge, but no residual disability at one year.
    - Injuries leading to long-term disability: Injuries for which there is residual disability at one year, which may range from mild to severe

- Injuries leading to mortality: Injuries leading to mortality were defined as injuries resulting directly or indirectly in a case fatality during or after the initial hospitalization.

Calculated Parameters

Another key parameter is life expectancy, which is necessary to calculate L_{death} (see model below). Following convention in the calculation of DALYs, we used 81.3 as the value for life expectancy, 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.[15] After estimating the numbers of hospitalizations that occur, we multiplied these data with our incidence (or prevalence) data on the number of patients injured within each adverse event, giving us population-level estimates for number of adverse events in HICs and LMICs.

We also used these data to estimate the age at which the adverse event occurred, again making these estimates separately for HICs versus LMICs whenever possible. Here, the individual studies varied in terms of the age at which the adverse event occurred and the specific type of adverse event. We identified a range of ages for each type of adverse event and input those ranges into the Monte Carlo model (see below) to calculate a best estimate for age for each type of adverse event, separately for HICs versus LMICs.

We estimated, based on the literature, the proportion of patients who had an adverse event who fell into each category of clinical outcomes (e.g., no substantial disability, short-term disability, long-term disability, and death, see Table 4). In many, though not all, of the studies, the clinical sequelae (the proportion that died or had long-term injury, for instance) was reported. We used

those reports to make estimates of how often patients are injured or killed due to adverse events. When data were not available from LMICs, we used data on the clinical sequelae from HICs.

Next, we used the literature to define the duration of the injury. Again, the duration varied across studies and across adverse events. We generally found good data on duration of injury from studies in high income countries but poor data on duration of injury from low income countries. We used a range of duration for short-term disability. When ranges were not available, we assumed that the range was 20% higher or 20% lower than the estimates from the literature. We also assumed (due to a lack of data) that the duration of short-term injuries was the same in the LMICs as that for HICs (see Table 5). These data were used in the Monte Carlo model.

We used the WHO GBD reports to identify disability weights for each type of adverse event.[1] There were very few adverse events for which we had a direct disability weight available, although for nearly every type of adverse event, we were able to find a clinically analogous condition for which WHO had created a disability weight (see Table 6). We defined a condition as "clinically analogous" if it generally affected the same organ system and cause a similar level of disability or death. We recognize, however, that the lack of an exact match between our adverse events of interest and the current disability weight classification scheme is a limitation. The models included the number of people at risk, rate of hospitalization, average age at the time of acquiring the condition, four clinical outcomes (1) death, 2) short-term disability followed by long-term disability, 3) short-term disability then full recovery, and 4) no or minimal disability), duration of the condition, average direct costs related to care of condition per episode, and disability weights. For each condition, it is necessary to have a disability weight to place a value

on the extent of the disability associated with the years of life with disability. By definition, the disability weight will range from zero (perfect health) to one (death).[16]

The distribution of the incidence rates are outlined above and the distributions of other key input variables are shown in tables below.

Disability-adjusted life years model

DALYs are a measure of health gaps – the difference between actual life years lived and those that would have been lived in a state of full health. As such, DALYs are a negative measure – an indicator of the gap between actual health and potential health that results from disability and premature death. Calculating DALYs due to a specific condition therefore involves aggregating the Years of Life Lost (YLL) due to premature death and the Years of Life with Disability (YLD).

The formula for YLL is:

$$N * \left\{ \frac{KCe^{ra}}{(r+\beta)^2} * \left\{ e^{-(r+\beta)(L+a)}[-(r+\beta)(L+a)-1] - e^{-(r+\beta)a}[-(r+\beta)a-1] \right\} + \frac{1-K}{r} * (1-e^{-rL}) \right\}$$

Where:

K = age weighting modulation factor (set at 1)

C = constant (0.1658)

r = the discount rate (0.03)

a = the age of death

β = parameter from age weighting function (0.04)

L = life expectancy at age a

N = the number of people living affected by the condition

And the formula for YLD is similar, with the addition of the disability weight for the specific condition (D): [16]

$$N * D\left\{\frac{KCe^{ra}}{(r+\beta)^2} * \left\{e^{-(r+\beta)(L+a)}[-(r+\beta)(L+a)-1] - e^{-(r+\beta)a}[-(r+\beta)a-1]\right\} + \frac{1-K}{r} * (1-e^{-rL})\right\}$$

Where the variables are as above, except:

L = duration of disability

a = the age at which the disability begins

D = the disability weight for that particular condition.

Table 2. Mean age at acquiring condition, by level of income

	Low- and Middle-Income			High-Income		
	Best Estimate	Low Estimate	High Estimate	Best Estimate	Low Estimate	High Estimate
Catheter-related UTI	65	59	72	75	68	81
Adverse drug event	49	44	54	65	59	72
Falls	54	49	60	70	63	77
Catheter-related blood stream infections	55	50	61	55	50	61
Nosocomial pneumonia	53	48	58	60	54	66
Decubitus ulcers	54	49	60	62	56	68
Venous thrombo-embolism	41	37	45	60	54	66

Table 3. Disability weights associated with adverse events

	Short-term Disability			Long-term Disability		
	Disability	High	Low	Disability	High	Low

	Weight	end	end	Weight	end	end
Catheter-related UTI	0.05	0.06	0.04	0.1	0.12	0.08
Adverse drug event	0.05	0.06	0.04	0.05	0.06	0.04
Falls	0.05	0.06	0.04	0.27	0.324	0.216
Catheter-related blood stream infections	0.2	0.24	0.16	0.2	0.24	0.16
Nosocomial pneumonia	0.28	0.336	0.224	0.1	0.12	0.08
Decubitus ulcers	0.07	0.084	0.056	0.1	0.12	0.08
Venous thrombo-embolism	0.1	0.12	0.08	0.1	0.12	0.08

Table 4. Clinical outcomes of adverse events (%)

	Low- and Middle-Income				**High-Income**			
	No injury	Long-term disability	Mortality	Short-term disability	No injury	Long-term disability	Mortality	Short-term disability
Catheter-related UTI	0.0%	0.0%	6.0%	94.0%	0.0%	2.0%	2.0%	96.0%
Adverse drug event	0.0%	2.9%	1.3%	95.8%	0.0%	6.0%	1.1%	92.9%
Falls	65.0%	1.4%	0.15%	33.5%	65.0%	1.4%	0.15%	33.5%
Catheter-related blood stream infections	0.0%	5.0%	18.0%	77.0%	0.0%	5.0%	18.0%	77.0%
Nosocomial pneumonia	0.0%	5.0%	20.0%	75.0%	0.0%	5.0%	20.0%	75.0%
Decubitus ulcers	0.0%	6.0%	0.5%	93.5%	0.0%	6.0%	0.5%	93.5%
Venous thrombo-embolism	0.0%	20.0%	3.0%	77.0%	0.0%	20.0%	3.0%	77.0%

Table 5. Duration of disability (best estimate, range), in years

	All Countries
	Duration of injury in years
Catheter-related UTI	0.1 (0.08, 0.12)
Adverse drug event	0.2 (0.16, 0.28)
Falls	0.5 (0.4, 0.6)
Catheter-related blood stream infections	0.4 (0.32, 0.48)
Nosocomial pneumonia	0.2 (0.16, 0.24)
Decubitus ulcers	0.5 (0.4, 0.6)
Venous thrombo-embolism	0.8 (0.64, 0.96)

Table 6. Clinically Analogous Conditions (Proxies) Used To Estimate Disability Weights

	Short-term Disability	Long-term Disability
	Disability Weight	Disability Weight
Catheter-related UTI	0.05	0.1
PROXY: Nephritis (Acute)	**0.107**	**0.107**
Adverse Drug Event	0.05	0.05
PROXY: Multiple potential complications including renal failure, liver failure, etc.)	**Range from 0.05 to 0.2**	**Range from 0.05 to 0.2**
Falls	0.05	0.27
PROXY: Sprains (Short-term), Femur fracture (long-term)	**0.067 (sprains)**	**0.272**
Catheter-related blood stream infections	0.2	0.2
PROXY: Endocarditis	**0.17 to 0.32**	**0.17 to 0.32**
Pneumonia	0.28	0.1
PROXY: Lower Respiratory Infections	**0.28**	**0.099**
Decubitus Ulcers	0.07	0.1
PROXY: Open Wound	**0.108**	**0.108**
Venous Thrombo-embolism including pulmonary embolism	0.1	0.1
PROXY: COPD symptomatic cases	**0.19 to 0.42**	**0.19 to 0.42**

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Table 7. Primary Data Sources for Estimating Incidence Inputs for Adverse Events, low-income (LMICs) and high-income (HICs) countries.

HOSPITAL ACQUIRED INFECTIONS (HAIs) **Cather-Related Blood Stream Infections (BSI)**	
AUTHOR LAST NAME (YEAR)	**REPORTED INCIDENCE RATE OF ADVERSE EVENT**
High-income	
US CDC 2009[1]	**0.12%** (ICU and inpatient)
EU 2008 Report[2]	**0.43%**
Klevens 2007[3]	**0.67%**
National Quality Report, AHRQ 2009[4]	**4%** (Medicare beneficiaries FFS with CVC placement)
Pronovost 2006 [5]	**0.62%** (in ICU)
Shorr 2003 [6]	**3.3%** (weighted overall rate of CLBSI based on 61 prospective trials)
Siempos 2009[7]	**1.57%(** in ICU, combination of studies from Mexico, USA, Belgium, Argentina, France, Spain)
The RAISIN Working Group 2009[8]	**0.794%** (French ICU)
Rosenthal 2010[9]	**2.0% (1.9-2.2)**
Vonberg 2006[10]	**0.43%**
Low-income	
Rosenthal 2009[11]	**7.4%** in 18 INICC countries **13.9%** (NICU) **4.4%** (ICU)
Leblebicioglu 2007 [12]	**12.2%** (ICU, Turkey)
Rosenthal 2009[11]	**0.16%-2.31%** (ICU) ; **0.24%-0.60%** (neonatal ICU)
Starling 1997[13]	**0.58%**
Lahsaeizadeh 2008[14]	**1.3%**
Cetin 2005[15]	**0.02%**
Klavs 2003[16]	**0.3%**
Duerink 2006[17]	**0.26%**

Moreno 2006[18]	**5.8%** (ICU)
Jaballah 2007[19]	**5.9%**
Madani 2009[20]	**13.5%**
Inan 2006[21]	**0.969%**
The RAISIN Working Group 2009[8]	**0.327%** (ICU)
Urinary Tract Infections (UTI)	
High-income	
Edwards 2007[22]	**0.31%-0.75%**
Gastmeier 2001[23]	**1.2%**
Bouza 2001[24 25]	**0.7%**
Stamm 1991[26]	**2-4%**
Doyle 2001[27]	**3%**
Vonberg 2006[10]	**0.68%**
Saint 2006[28]	**13.1%** (indwelling catheter) **7.0%** (condom catheter)
Klevens 2007[3]	**424,060 UTIs** in adults and children (not including ICU)
Vonberg 2006[10]	**0.68%**
Low-income	
Rosenthal 2010[9]	**6.3%** (adult ICU) **4.0%** (PICU)
Leblebicioglu 2007 [12]	**8.9%** (ICU)
Starling 1997[13]	**0.9%**
Lahsaeizadeh 2008[14]	**3.7%**
Cetin 2005[15]	**0.25%**
Danchaivijitr 2005[29]	**1.4%**
Klavs 2003[16]	**1.2%**
Leblebicioglu 2003[30]	**1.7%**
Durmaz 2000[31]	**0.41%**

Sujijantararat 2005[32]	**31.68%**
Moreno 2006[18]	**2.5%** (ICU)
Inan 2006[21]	**1.363%**
Pneumonia	
High-income	
Horan 1986[33]	**0.42-0.77%**
Klevens 2007[3]	**0.67%**
Jokinen 1993 [34]	**1.11%**
Almirall 2000 [35]	**0.162%**
American Thoracic Society 1996[36]	**0.5-1.0%**
Low-income	
Klavs 2003[16]	**0.3%**
Starling 1997[13]	**0.65%**
Ellidokuz 2003[37]	**0.25%**
Durmaz 2000[31]	**0.2%**
Alp 2004[38]	**6.8% (ICU patients)**
Mandani 2009[20]	**54.6% of all HAIs were VAP**
Moreno 2006[18]	**4.0% ICU patients (VAP)**
Inan 2006[21]	**20.76 infections/1000 ventilator-days (VAP)**
ADVERSE DRUG EVENTS (ADEs)	
Low-income	
Arulmani 2008[39]	**3.74%**
Baniasadi 2008 [40]	**1.3%**
Benkirane 2009 [41]	**4.24%**
Bhatt 1999[42]	**2.4% – 6.7%** (India)
Jha 2007 [43]	**0.86%**
Jose 2006[44]	**0.15%**

Khan 2005[45]	**0.36%**
Major 1998 [46]	**6.72%**
Mehta 2008[47]	**5.64%**
Pourseyed 2009[48]	**11.75%**
Ramesh 2003[49]	**3.7%**
Uppal 2000[50]	**0.3%**
High-income	
National Quality Report 2009[4]	**3.4%-8.9%**
Classen 1997[51]	**2.43%**
Classen 1991[52]	**1.67%**
Bates 1995[53]	**6.5%**
Bates 1999[54]	**0.147%** ADEs (before CPOE) **0.096%-0.149%** (after CPOE)
Bates 2003[55]	**0.66%** (Brigham and Women's Hospital) **3.33%** (Wishard Memorial Hospital)
Gurwitz 2003[56]	**5.01%**
Hallas 1992[57]	**11.4%** (prevalence)
Hanlon 2006[58]	**0.192%**
Holdsworth 2007[59]	**6.3%** (before CPOE) **3.1%** (after CPOE)
Jha 1998[60]	**14.2%**
Lazarou 1998[61]	**6.7%**
Miller 2006 [62]	**10.4%** (reported ADE to GP in past 6 months)
Pirmohamed 2004[63]	6.5% (1225 out of 18,820) of admissions related to ADR
Schmader 2004[64]	**0.20%** (geriatric inpatient unit) **0.19%** (general inpatient unit) **0.20%** (geriatric outpatient clinic) **0.20%** (general outpatient clinic)
Runciman 2003[65]	**26%** of hospital related incidents were medication related

Thomas 2000[66]	**2.9%**
Thomsen 2007[67]	**14.9%** (4.0%-91.3%)
Van de Hooft 2008[68]	**3.5%** (122 of 3515 of all admissions were classified as ADR related)
Bates 1995[69]	**1.47%**
Baker 2004[70]	**7.5%**
FALLS IN HOSPITAL	
Low income	
An 2009[71]	**1.2%** of patients had fallen in hospital
Peden 2002[72]	WHO estimates that in 2000, 283,000 people died as the result of falls, globally
High-income	
Bates 1995[73]	**0.66%**
Fischer ID 2005[74]	**0.31%**
Halfron 2001[75]	**0.24%**
Hitcho 2004[76]	**0.38%**
Izumi 2002[77]	**12.5%**
Krueger 2001[78]	**52.8%**
Morgan 1985 [79]	**2.0%**
Nakai 2006[80]	**1.3%**
Healey 2008[81]	**0.3%-1.4%**
Mahoney 1998[82]	**2%**
Oliver 2006[83]	**0.4%–1.4%**
Halfon 2001 [75]	**0.22%**
Morgan 1985[79]	**1.87%**
Hitcho 2004[76]	**0.338%**
Nakai 2006 [80]	**1.3%**
Schwendimann 2006 [84]	**7.2%**
Schwendimann 2006[85]	**12.2%**

Tan 2005[86]	**0.132%**
Vassallo 2005[87]	**18.2%**
Webster 2010[88]	**9.2%** (prevalence)
VENOUS THROMBO-EMBOLISMS (VTE)	
Low-income	
Agarwal 2009 [89]	**34%**
Atichartakarn 1988[90]	**4%**
Baeshko 1999[91]	**33.6%**
Bagaria 2006 [92]	**6.12%**
Darze 2005[93]	**9.1%**
Dhillon 1996[94]	**62.5%**
Diogo-Filho 2009[95]	**1.7%**
Jain 2004[96]	**4.4%**
Leizorovicz 2005 [97]	**0.2% to 1.2%**
Osime 1978[98]	**30%** (men, post-surgery) **70%** (women, post-surgery)
Pandley 2009[99]	**0.01746%**
Piovella 2005 [100]	**41.0%**
Phornphibulaya 1984[101]	**12.2%**
Prasannan 2005[102]	**57%** of surgeons reported VTE-related morbidity
High-income	
Caprini 2003 [103]	**5% -20%** (with adequate thromboprophylaxis after THRS) **50%** (in the absence of thromboprophylaxis after THRS)
Cushman 2004[104]	**0.192%**
Geerts 2003[105]	**13-31%** (critical care patients without prophylaxis)
Geerts 2001 [106]	**25%** (after general surgery without prophylaxis)
Geerts 2004[107]	**10%-40%** (medical or general surgical patients) **40 to 60%** (following major orthopedic surgery)

Hansson 1997[108]	**0.138%**
Meyer 1995[109]	**6%-9%**
Oger 2000[110]	**0.183%**
Prandoni 1996[111]	**4.9%** after 3months **8.6%** after 6 months **17.5%** after 2 years **24.6%** after 5 years **30.0%** after 8years
Robinson 1997[112]	**2.5% (**asymptomatic prox DVT)
Rosencher 2005[113]	**1.34%** (symptomatic VTE at 3mos)
Samama 1999[114]	**15%** (medical patients without prophylaxis)
White 2003[115]	**0.8%**
DECUBITUS ULCERS	
Low-income	
Bork 2007[116]	1% of all hospital discharges (25% of which were present upon admission)
Chauhan 2005 [117]	**4.94 %**
Fu 1998[118]	**1.63 %**
Karadag 2006[119]	**54.8%**
Leblebici 2007[120]	**1.6%**
Manley 1978[121]	**4.5%** (prevalence)
Sayar 2009[122]	**14.3%**
Sae-Sia 2005 [123]	**47%**
Suriadi 2008 [124]	**7-29%** (international)
Kwong 2005[125]	**2.1%-31.3%**
Srisupan 2005 [126]	**5.76 – 10.8%**
Uzun 2007 [127]	**9.9%**
High-income	
Allman 1995[128]	**12.9%**

Bennett 1989[129]	412,000 patients in UK annually (7.95 million inpatients at risk annually)
Kaltenthaler 2001[130 131]	**4.7%-32.1%**
Frantz 2004[132]	**7%-38% (**based on studies from the late 1990s)
Graves 2005[133]	Mean number of cases per region = 95,910 (8 regions)
Hengstermann 2007[134]	**16.7%** (prevalence, geriatric patients)
Muurinen 2009[135]	**15.1%** (prevalence, nursing home residents) **22.1%** (prevalence, long-term care hospitals)
Lahmann 2012[136]	**10.1%**
Lahmann 2005[137]	**16.8 %**
Lindgren 2004 [138]	**11.7%**
Lindholm 2008[139]	**16%**
Takahashi 2008[140]	**14.8%** (prevalence)
Tannen 2008 [141]	**18.1 – 28.8 %** (German hospital patient) **28.1 – 41.1 %** (Dutch hospital patients)
Thomas 1996[142]	**12.9%** (prevalence of Stage 2 or greater pressure ulcers)
Thomas 2001[143]	**0.017%**
Vanderwee 2007[144]	**18.1%** (prevalence in hospital convenience samples)
Wann-Hansson 2008[145]	**13.2 %**
Whittington 2004[146]	**7%-9%**
Lahmann 2005[147]	**11.7%** (prevalence)
Bours 2002[148]	**23.1%** (prevalence)
Wilborn D 2006[149]	**8.3-15.3%** (prevalence in hospitals and nursing homes)

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