__Penn Center for Evidence-based Practice Advisory__

MORTALITY FROM REASONABLY-PREVENTABLE HOSPITAL-ACQUIRED INFECTIONS

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Summary

- Survey data from the National Nosocomial Infections Surveillance (NNIS) system, National Hospital Discharge Summary, and American Hospital Association report the incidence of hospital-acquired infections (HAIs) and the mortality resulting from them.
    - In 2002, there were 1.74 million HAIs and 99 thousand attributable deaths.
    - Two-thirds of those deaths are the result of bloodstream infections and ventilator-associated pneumonia.
    - There was a decreasing trend in HAI incidence from 1975 to 2002.
- An Agency for Healthcare Research and Quality (AHRQ) report published in 2007 surveyed the evidence on various interventions to reduce HAIs.
    - The AHRQ reviewers found that the quality of evidence was low, and that there was little consistency in patient populations and interventions examined. Therefore, they did not combine the results of the studies into a single numeric result estimating the ability of interventions to reduce HAIs.
- We used the 2002 estimate of HAIs and resulting deaths from the NNIS survey and the range of HAI reductions observed in the AHRQ report to calculate the number of preventable HAIs and HAI deaths per year:
    - Bloodstream infections: 18%–82% of infections preventable, 5,520–25,145 preventable deaths per year
    - Ventilator-associated pneumonia: 46%–55% of infections preventable, 13,667–25,537 preventable deaths per year
    - Urinary tract infections: 17%–69% of infections preventable, 2,225–9,031 preventable deaths per year
    - Surgical site infections: 26%–54% of infections preventable, 2,133–4,431 preventable deaths per year
- There is considerable uncertainty in these figures because of the numerous assumptions going into them. One should not base policy decisions on these figures without understanding the sources of uncertainty.

Background

To inform policy discussions regarding the reduction of infections in hospitals, the Center for Evidence-based Practice at the University of Pennsylvania Health System was asked to estimate the number of annual deaths in U.S. hospitals from reasonably-preventable cases of hospital-associated infections (HAIs), particularly bloodstream infections (BSI) and ventilator-associated pneumonia (VAP).

Methods

An accurate estimation of this figure requires accurate estimates of two underlying figures: the current total of annual deaths from HAIs and the proportion of these deaths that are "reasonably preventable." Uncertainty in either of these components will necessarily lead to uncertainty in the final estimate.

A best-evidence approach was used to obtain the source data for this calculation. To estimate the number of HAIs and resulting mortality, we used estimates from the National Nosocomial Infections Surveillance (NNIS) system, National Hospital Discharge Summary, and American Hospital Association as reported by Klevens and colleagues.(1) To estimate the proportion of HAIs that could be prevented, we used the estimates of HAI risk reductions resulting from quality improvement strategies as reported in an Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center (EPC) report.(2) Given the limited quality of the studies reviewed by the AHRQ report, we only used HAI risk reductions reported from US studies that were graded as good quality by AHRQ, and that examined risk reductions in BSI, VAP, urinary tract infections (UTI) and surgical site infections (SSI). When there were fewer than three studies that met these criteria, we also included studies graded as moderate quality.

Because the patient populations and interventions tested in the published studies of HAI prevention varied from study to study, it was not appropriate to combine the risk reductions into a single summary estimate. Thus, to calculate a range of possible risk reductions for each HAI, we simply used the highest and lowest infection reductions for each HAI as listed in the AHRQ report. We then multiplied this range of risk reduction for each HAI by the frequency of that HAI as reported by the NNIS survey to calculate a range for the number of preventable infections for each HAI. To estimate a range for the number of preventable deaths for each HAI, we multiplied the risk reduction for each HAI by the reported frequency of deaths for that HAI.

Number of Annual Deaths

A comprehensive estimate of annual incidence of and mortality from hospital-acquired infections was reported by Klevens and colleagues of the Centers for Disease Control and Prevention (CDC) in 2007.(1) (Table 1) This estimate was based on broad surveys of U.S. hospitals so the risk of uncertainty from measuring an unrepresentative sample is low. However, the survey data is from 2002, so changes in infection rates and mortality resulting from improved care practices implemented between 2002 and today are not captured in these figures. If care has improved since that time, the current number of infections and deaths will be lower than observed in 2002. That would continue the trend observed since 1975-76, when the total number of hospital-associated infections estimated by the CDC's SENIC project was 2.15 million. (3) Infection-related deaths were not estimated in that project.

The survey data show that BSI and VAP cause more than two-thirds of the deaths resulting from HAIs, and that they are five times more deadly than the other infections. Thus it may make sense to target these two types of infections first for reduction measures.

Table 1. Hospital-acquired infections in 2002

Type of infection	Number of infections (2002)	Deaths from infections (2002)	% Fatal infections
BSI	248,678	30,665	12.3%
VAP	250,205	35,967	14.4%
UTI	561,667	13,088	2.3%
SSI	290,485	8,205	2.8%
Other	386,090	11,062	2.9%
Total	1,737,125	98,987	5.7%

Data from Klevens (1)

Proportion of Deaths that are Preventable

We based our estimates of the preventability of infection-related deaths on the evidence tables of the AHRQ EPC report. (2) An earlier review by Harbarth and colleagues (4), done in much less detail, has similar findings.

Description of Studies Included in the AHRQ Report

The quality of the evidence base reviewed in the AHRQ report was poor. For example, half of the BSI studies met none or one of the reviewers' three internal validity standards. The AHRQ report divided the before-after studies into "good", "moderate", and "poor" quality categories (Table 2) but did not explain how the categories were defined. They did not grade the quality of controlled and interrupted time series trials.

The AHRQ investigators reported that there was little consistency among patient groups studied or among interventions tested. Therefore they could not perform any quantitative synthesis of the data, and they did not attempt to make a summary estimate of the proportion of infections or deaths that could be considered preventable.

The highest quality studies in the AHRQ report examined interventions to reduce BSI, VAP, UTI and SSI. For prevention of other HAIs, the evidence bases were even weaker and any numeric conclusions are even more speculative.

Table 2. Description of infection prevention studies examined in AHRQ report

Infection type	N	Controlled trials	Time series	Simple before-after studies		
				Good	Moderate	Poor
BSI	19	2	1	6	2	8
VAP	12	0	0	3	4	5
UTI	10	3	0	0	6	1
SSI	28	4	2	1	6	15

Not all studies in this table were used to calculate results, since they did not all report infection results.

Data from AHRQ EPC report (2)

Estimates of Preventable Deaths

Our estimates for the ranges of potential reductions in HAIs are found in the fifth column of Table 3 and the resulting estimates of preventable infections and deaths are found in the seventh and last columns of Table 3 respectively.

There is nothing novel about trying to estimate the number of infections that could be prevented or lives that could be saved if hospitals followed best practices in infection control. The SENIC project made such an estimate in 1975. They considered 30 to 35 percent of most HAIs preventable with effective surveillance and control programs, and 22 percent of pneumonia cases preventable. In a 1985 follow-up survey, they found that only a fraction of those infections were actually being prevented, because many hospitals still had not implemented recommended infection control measures.(5) This was still the case in the present decade.(6) Our estimated ranges of potential reductions in HAIs is in line with the estimates in Kaye's review.(7)

Table 3. Estimates of preventable infections and deaths

Infection type	Number of HAIs*	Number of deaths*	Case fatality rate	Reduction in infection risk with QI programs†	Projected number of infections with institution of QI programs	Estimated number of preventable infections	Projected number of deaths with institution of QI programs	Estimated number of preventable deaths
BSI	248,678	30,665	12.3%	18%–82%	44,762-203,916	44,762–203,916	5,520–25,145	5,520–25,145
VAP	250,205	35,967	14.4%	38%–71%	72,559–155,127	95,078–177,646	10,430–22,300	13,667–25,537
UTI	561,667	13,088	2.3%	17%–69%	174,117–466,184	95,483–387,550	4,057–10,863	2,225–9,031
SSI	290,485	8,205	2.8%	26%–54%	133,623-204,959	75,526–156,862	3,774–6,072	2,133–4,431

HAI–hospital-acquired infection

QI–quality improvement

*–NNIS 2002 estimates

†–Range from US based QI studies of good or moderate quality in AHRQ report

Limitations

There is considerable uncertainty in our estimate of preventable HAI-related deaths. Uncertainty stems from both the component numbers and the calculation itself. Here we discuss some of those sources of uncertainty.

Number of deaths caused by HAIs

While our estimate of the number of annual deaths caused by HAIs is based on a broad national survey, that survey data is more than five years old. It does not reflect improvements in infection control practice that hospitals have implemented since the time of the survey. The true number of annual HAI deaths at present may be lower. The estimate of HAI-related deaths is also uncertain because there is no definite way to attribute a death to HAI. Patient deaths frequently have multiple causes, and there exists a blurred line between a patient whose death was caused by an HAI and a patient with an HAI whose death was due to another cause.

Proportion of HAIs that are preventable

The key uncertainty in the estimate of preventable HAIs is the limited quality of the HAI reduction studies. In particular, none of the studies are randomized, and few of the studies are controlled, so the validity of the risk reductions reported are limited, and may be exaggerated. For example, most of the studies are of a simple before-after study design, comparing outcomes after the HAI intervention was implemented in a patient population with results from the same population during a time period prior to the HAI intervention. This study design cannot control for other changes in patient care that took place between the control period and the experimental period, making it difficult to attribute the results reported in the study to the study intervention rather than to random variation, patient selection, or other uncontrolled variables, like changes in staffing structures or the implementation of other quality/safety initiatives.

In addition, some of the published studies date back a decade or more, so the infection control practices used in them may have already been implemented at some hospitals, making large HAI reductions less likely in today's hospitals. Another source of uncertainty is generalizing from the results of specialized study populations like the ICU population to more general populations like a general hospital ward.

Number of HAI-caused deaths that are preventable

The key uncertainty here is the fact that we are not estimating preventable deaths from studies that have directly measured death as an outcome. Instead, we are extrapolating reductions in death from the above estimates of reductions in HAIs, and these above estimates have their own limitations. In addition, in multiplying the estimated fraction of HAIs that are preventable by the fatality rate for a given HAI, we assume that the fatality rate for preventable infections is the same as the rate for those infections that weren't prevented. The true effect on deaths could be larger or smaller, depending on the extent to which preventive measures affect the severity of HAIs and the extent to which preventive measures work for the kinds of patients who are more susceptible to fatal HAIs.

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Evidence Tables

Table 4. BSI prevention studies reviewed by AHRQ suggest an 18 to 82% reduction in BSIs depending on the intervention and population examined

Author, Year	Study Design	Setting	Intervention	Comparison	Risk before intervention	Risk after intervention	Risk Reduction
Provonost, 2006	Interrupted time series	ICU patients (United States)	*Preventive:* Hand hygiene; maximum sterile barrier; insertion site selection; chlorhexidine disinfection; removal of unnecessary catheters *QI:* Clinician education, audit and feedback, clinician reminder, organizational change	Previous care	7.7 per 1,000 catheter days	1.4 per 1,000 catheter days	82%
Higuera, 2005	Before-after study	ICU patients (Mexico)	*Preventive:* Hand hygiene *QI:* Clinician education, audit and feedback, organizational change	Previous care	46.3 per 1,000 catheter days	19.5 per 1,000 catheter days	58%
Berenholtz, 2004	Controlled before-after study	ICU patients (United States)	***Intervention**:* *Preventive:* Hand hygiene; maximum sterile barrier; insertion site selection; chlorhexidine disinfection; removal of unnecessary catheters *QI:* Clinician education, audit and feedback ***Control***: Clinician education only	Previous care	Intervention 11.3 per 1,000 catheter days	Intervention 0 per 1,000 catheter days	100%
					Control 5.7 per 1,000 catheter days	Control 1.6 per 1,000 catheter days	82%
Coopersmith, 2004	Before-after study	ICU patients (United States)	*Preventive:* Hand hygiene; maximum sterile barrier; insertion site selection *QI:* Clinician education	Previous care	3.4 per 1,000 catheter days	2.8 per 1,000 catheter days	18%
Warren, 2004	Before-after study	ICU patients (United States)	*Preventive:* Hand hygiene; maximum sterile barrier; insertion site selection *QI:* Clinician education, audit and feedback	Previous care	9.4 per 1,000 catheter days	5.5 per 1,000 catheter days	42%
Warren, 2003	Before-after study	ICU patients (United States)	*Preventive:* Maximum sterile barrier; insertion site selection *QI:* Clinician education, audit and feedback	Previous care	4.9 per 1,000 catheter days	2.1 per 1,000 catheter days	57%
Coopersmith, 2002	Before-after study	ICU patients (United States)	*Preventive:* Hand hygiene *QI:* Clinician education, audit and feedback	Previous care	10.8 per 1,000 catheter days	3.7 per 1,000 catheter days	66%
Eggimann, 2000	Controlled before-after study	ICU patients (Switzerland)	***Intervention**:* *Preventive:* Hand hygiene; maximum sterile barrier; chlorhexidine disinfection; removal of unnecessary catheters *QI:* Clinician education ***Control***: No additional measures	Previous care	Intervention (MICU) 11.3 per 1,000 catheter days	Intervention 3.8 per 1,000 catheter days	67%
					Control (SICU) 10.3 per 1,000 catheter days	Control 11.6 per 1,000 catheter days	–13% (increase)
Sherertz, 2000	Before-after study	ICU patients (United States)	*Preventive:* Hand hygiene; maximum sterile barrier *QI:* Clinician education	Previous care	4.51 per 1,000 catheter days	2.92 per 1,000 catheter days	35%

Table 5. VAP prevention studies reviewed by AHRQ suggest a 38 to 71% reduction in VAPs depending on the intervention and population examined

Author, Year Quality	Study Design	Setting	Intervention	Comparison	Risk before intervention	Risk after intervention	Risk reduction
Good quality							
Babcock, 2004	Before-after study	ICU patients (United States)	*Preventive:* Hand hygiene; HOB>30°; daily interruption of sedation *QI:* Clinician education	Previous care	8.75 per 1,000 ventilator days	4.74 per 1,000 ventilator days	46%
Zack, 2002	Before-after study	ICU patients (United States)	*Preventive:* HOB>30° *QI:* Clinician education	Previous care	12.6 per 1,000 ventilator days	12.6 per 1,000 ventilator days	55%
Moderate quality							
Rosenthall, 2006	Before-after study	ICU patients (Argentina)	*Preventive:* Hand hygiene *QI:* Clinician education, audit & feedback	Previous care	51.3 per 1,000 ventilator days	35.5 per 1,000 ventilator days	31%
Salahuddin, 2004	Before-after study	ICU patients (Pakistan)	*Preventive:* Hand hygiene, HOB>30° *QI:* Clinician education, audit & feedback	Previous care	13.2 per 1,000 ventilator days	6.5 per 1,000 ventilator days	51%
Lai, 2003	Before-after study	ICU patients (United States)	*Preventive:* HOB>30° *QI:* Clinician education, audit & feedback	Previous care	SICU: 45.1 per 1,000 ventilator days	SICU: 27.9 per 1,000 ventilator days	38%
					MICU: 22.4 per 1,000 ventilator days	MICU: 11.6 per 1,000 ventilator days	48%
Kelleghan, 1993	Before-after study	Not reported (United States)	*Preventive:* Hand hygiene, HOB>30° *QI:* Clinician education, audit & feedback	Previous care	17 per 1,000 ventilator days	5 per 1,000 ventilator days	71%

Table 6. UTI prevention studies reviewed by AHRQ suggest a 17 to 69% reduction in UTIs depending on the intervention and population examined

Author, Year	Study Design	Setting	Intervention	Comparison	Risk before intervention	Risk after intervention	Risk reduction
Good quality							
Huang, 2004	Before-after study	ICU patients (Taiwan)	*Preventive:* Removal of unnecessary urinary catheters *QI:* Clinician reminder	Previous care	11.5 per 1,000 catheter days	8.3 per 1,000 catheter days	29%
Greco, 1991	Before-after study	ICU patients (Italy)	*Preventive:* Aseptic insertion and catheter care *QI:* Audit and feedback, clinician education, clinician reminder	Previous care	12.9 per 100 catheters	11.9 per 100 catheters	8%
Moderate quality							
Topal, 2005	Before-after study	Ward patients (United States)	*Preventive:* Reduction in placement of catheters, removal of unnecessary catheters *QI:* Clinician education, clinician reminder, organizational change	Previous care	36 per 1,000 catheter days	11 per 1,000 catheter days	69%
Rosenthal, 2004	Before-after study	ICU patients (Argentina)	*Preventive:* Hand hygiene, aseptic catheter care *QI:* Audit and feedback, clinician education	Previous care	21.3 per 1,000 catheter days	12.4 per 1,000 catheter days	42%
Dumigan, 1998	Before-after study	ICU patients (United States)	*Preventive:* Aseptic insertion and catheter care, removal of unnecessary catheters *QI:* Clinician education, organizational change	Previous care	SICU: 10.3 per 1,000 catheter days	8.6 per 1,000 catheter days	17%
					MICU: 15.8 per 1,000 catheter days	11.2 per 1,000 catheter days	29%
					CICU: 15.1 per 1,000 catheter days	8.3 per 1,000 catheter days	45%

Table 7. SSI prevention studies reviewed by AHRQ suggest a 26 to 54% reduction in SSIs depending on the intervention and population examined

Author, Year	Study Design	Setting	Intervention	Comparison	Risk before intervention	Risk after intervention	Risk reduction
Good quality							
Van Kasteren, 2005	Interrupted time series	Not reported (Netherlands)	*Preventive:* Appropriate use of perioperative antibiotics *QI:* Audit and feedback, clinician education, clinician reminder	Previous care	5.4%	4.6%	15%
Gastmeier, 2002	Controlled study	ICU (Germany)	*Preventive:* Hand hygiene, appropriate use of perioperative antibiotics, decreasing use of preoperative shaving, improving perioperative glucose control *QI:* Audit and feedback, clinician education	Previous care	2.2%	1.6%	26%
Weinberg, 2001	Interrupted time series	Not reported (Columbia)	*Preventive:* Appropriate use of perioperative antibiotics *QI:* Audit and feedback, organizational change	Previous care	Hospital A: 10.5%	0%	100%
					Hospital B: 6.1%	4.4%	28%
Greco, 1991	Before-after study	ICU (Italy)	*Preventive:* Appropriate use of perioperative antibiotics, decreasing use of preoperative shaving *QI:* Audit and feedback, clinician education, clinician reminder	Previous care	7.8%	6.2%	21%
Moderate quality							
Dellinger, 2005	Before-after study	Not reported (United States)	*Preventive:* Appropriate use of perioperative antibiotics, decreasing use of preoperative shaving, improving perioperative glucose control *QI:* Audit and feedback, clinician education, clinician reminder	Previous care	2.3%	1.7%	26%
Borer, 2004	Before-after study	Operating room (Israel)	*Preventive:* Hand hygiene, appropriate use of perioperative antibiotics, decreasing use of preoperative shaving, improving perioperative glucose control *QI:* Clinician education	Previous care	4.2%	0%	100%
Lutarewych, 2004	Before-after study	Not reported (United States)	*Preventive:* Improving perioperative glucose control *QI:* Audit and feedback, clinician education, patient education	Previous care	7.58%	3.47%	54%
Rao, 2004	Before-after study	Not reported (United States)	*Preventive:* Appropriate use of perioperative antibiotics, decreasing use of preoperative shaving, improving perioperative glucose control *QI:* Clinician education, clinician reminder	Previous care	2.1%	1.5%	29%
Won, 2004	Before-after study	Not reported (Taiwan)	*Preventive:* Hand hygiene *QI:* Clinician education, audit and feedback	Previous care	0.33 per 1000 patient days	0.84 per 1000 patient days	–154% (increase)
Larsen, 1989	Before-after study	Operating room (United States)	*Preventive:* Appropriate use of perioperative antibiotics *QI:* Audit and feedback, clinician reminder	Previous care	1.1%	0.7%	36%