A systematic audit of economic evidence linking nosocomial infections and infection control interventions: 1990-2000

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Background: Nosocomial infections (NIs) are a serious patient safety issue. Infection control personnel are responsible for implementing interventions to reduce this risk. The purpose of this systematic review was to audit the published economic evidence of the attributable cost of NIs and interventions conducted by infection control professionals and to evaluate the methods used. Economic evaluation methodology and recommendations for standardization are reviewed.

Methods: A search of MEDLINE and HealthSTAR with medical subject headings or text words "nosocomial infections," "infection control," or "hospital acquired infections" cross-referenced with "costs," "cost analysis," "economics," or "cost-effectiveness analysis" was conducted. Published review articles were also searched. Inclusion criteria included articles published between 1990 and 2000 that contained an abstract and original cost estimate and were written in English. Results were standardized into a common currency.

Results: Fifty-five studies were eligible. Approximately one quarter examined NIs in intensive care patients (n = 13). Most studies were conducted from the hospital perspective (n = 48). The costs attributable to bloodstream (mean = $38,703) and methicillin-resistant *Staphylococcus aureus* infections (mean = $35,367) were the largest.

Conclusions: Increased standardization and rigor are needed. Clinicians should partner with economists and policy analysts to expand and improve the economic evidence available to reduce hospital complications such as NI and other adverse patient/staff outcomes. (Am J Infect Control 2002;30:145-52.)

Nosocomial infections (NIs) are one of the most serious patient safety issues in health care today. The incidence of NIs has been estimated at approximately 2 million cases annually.[1] More than 500,000 of these infections occur in intensive care units (ICUs), and most are associated with the presence of an invasive device (such as a central line or ventilator).[2] Although fewer patients were admitted to US hospitals in 1995 compared with 1975 (36 million vs 38 million) and the average duration of stay decreased (7.9 days to 5.3 days), the national NI rate has risen. In 1975, there were 7.2 NIs per 1000 patient-days compared with 9.8 per 1000 in 1995, an increase of 36%.[3] In addition, it has been estimated that there are approximately 90,000 deaths attributed to NIs annually, ranking it as the fifth-leading cause of death in acute care hospitals.[4] However, the total cost of NIs to society is not clear.

Furthermore, an aim of *Healthy People 2010* is to reduce NIs in ICUs by 10% (objectives 14-20).[5] To meet this goal, it is essential that the effectiveness and efficiency of prevention and control strategies be carefully evaluated so that interventions with demonstrated value can be implemented. Interventions that are the best candidates for widespread implementation must not only work (ie, be associated with reduced infections) but must also be feasible. One important component of feasibility is to ensure that

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Table 1. Types of economic evaluations

Type of study	Definition	Effect measurement
Cost-minimization analysis (CMA)	An analysis that computes the incremental costs of alternatives that achieve the same outcome.	Not measured
Cost-consequences analysis (CCA)	An analysis in which incremental costs and effects are computed, without any attempt to aggregate them.	Natural occurring units*
Cost-effectiveness analysis (CEA)	An analysis in which incremental costs and effects are presented in a ratio.	Natural occurring units
Cost-utility analysis (CUA)	A special type of CEA, in which quality of life is considered.	Quality-adjusted life years
Cost-benefit analysis (CBA)	An analysis in which incremental costs and effects are computed and all benefits and costs are measured in dollars.	Dollars

*Examples of natural occurring units are life-years gained, disability days saved, or cases avoided.

the costs of the intervention (economically and in terms of quality of life) are acceptable and justifiable.

Hence, the purposes of this study were to (1) review the published economic evidence available on the attributable cost of NIs, (2) review the published economic evidence available on interventions conducted by infection control personnel, and (3) evaluate the methods used in these analyses. In addition, a brief review of the economic evaluation methodology and recommendations for the standardization of economic evaluations are presented.

ECONOMIC EVALUATIONS

Economic evaluations of infection prevention and control policies and practices are only meaningful if the new intervention is compared with a realistic comparison policy and practice. Similarly, costs can only be attributable to an NI if there is an adequate control group of similar patients who did not acquire an NI. A simple cost analysis is performed by measuring the costs of a disease or intervention without a comparison group. Although the information from a simple cost analysis is useful as part of an economic evaluation, it is an exercise in accounting and not an economic evaluation.

Five methods of valid economic evaluations commonly used in health care are defined in Table 1.[6] Instrumental and common to all of these analyses is the valuation of the inputs or costs.[7] The methods differ in how effects are measured. Estimating costs is conceptually much easier than estimating effects, although technically it can be more difficult. It is conceptually easier because one doesn't have to search for a measure—the obvious measure is dollars. However, the concept of "cost" takes on concrete meaning only after we specify the perspective from which the evaluation is being conducted.[8,9] Studies may be motivated by policy decisions relevant to specific institutions or individuals. In this case, the perspective of primary interest may be that of a managed care organization, hospital, employer, state health department, or other party. For example, an economic evaluation conducted from the perspective of the hospital may not consider costs (or savings) associated with outpatient health care services or patient or family time. From the third-party payer perspective, the cost of disease and treatments are measured in terms of the dollar volume of claims that need to be paid. Another perspective for defining cost is that of the "society." Operationally, this requires that we attempt to measure the actual economic value (the social opportunity cost) of the resources that are consumed by the disease and by treatments to combat it. In an economic evaluation conducted from the societal perspective, researchers would need to include the cost of implementing the interventions in the hospital; any postdischarge outpatient health care costs; the cost of patient time to receive care; and any other relevant costs, such as social services.

Because of variability in the methods used and a desire to increase quality and comparability of economic evaluations, efforts have been made in recent years to increase the standardization in economic evaluations.[8,10-13] The Panel on Cost-Effectiveness Analysis in Health Care and Medicine convened by the US Public Health Service Department made a number of recommendations and suggested a standard set of methodologic practices intended to improve the comparability of cost-effectiveness evidence, which is called a *reference case*.[8,14,15] Some of the recommendations for an ideal reference case include adopting a societal perspective; reporting results in terms of dollars per quality adjusted life year (QALY) gained (called a cost-utility analysis in Table 1); including downstream net costs (and savings); dis-

Table 2. Characteristics of the studies

Descriptive characteristics	N	%
Geographical region of study		
United States/Canada	31	56.4
Europe	16	29.1
Australia	4	7.3
Asia	2	3.6
South America	2	3.6
Journal		
Infection control	23	41.8
Infection disease/epidemiology	12	21.8
Other clinical specialty	20	36.4
Source of funding		
Government	7	12.7
Industry	6	10.9
Foundation	1	1.8
Not stated	41	74.6
Population/setting		
Intensive care unit	13	23.6
Occupational health	12	21.8
Surgical, nonintensive care	7	12.7
Long-term care	4	7.3
Other hospitalized patients or setting	19	34.6
Nosocomial infection analyzed*		
NIs in general	9	15.5
Body site specific		
Surgical site infection	7	12.1
Bloodstream infection	9	15.5
Pneumonia	7	12.1
Urinary tract infection	1	1.8
Organism specific		
MRSA	8	13.8
Varicella zoster virus	5	8.7
Tuberculosis	2	3.4
Measles	2	3.4
Other	8	13.8
Nosocomial infection definition		
CDC	13	23.2
Other/unspecified	43	76.8
Analytic characteristics		
Cost analysis (no comparison)	21	38.7
Cost-effectiveness analysis	16	29.1
Cost-consequence analysis	15	27.3
Cost-minimization analysis	1	1.8
Cost-benefit analysis	2	3.6
Perspective		
Hospital	48	87.3
Third-party payer	5	9.1
Societal	2	3.6
Costs included†		
Intervention	46	54.8
Hospitalization	29	34.5
Outpatient health services	7	8.3
Non–health care costs	2	2.4
Source of cost data†		
Micro-costing	24	42.9
Estimated	17	30.4
Published	9	16.0
Claims	6	10.7
Source of effectiveness data		
Pre-post	14	25.4
Cohort	10	18.2
Other quasiexperimental design	10	18.2
Case-control	8	14.6
Published	8	14.6
Randomized control trial	5	9
Time horizon		
1 year or less	44	80
More than 1 year	11	20
Sensitivity analysis		
Yes	17	30.9
No	38	69.1

*One study investigating the attributable costs of different MRSA infections had results in 4 categories increasing the sample size (n = 58).[4]
†Categories are not mutually exclusive.

counting future costs and QALYs; and conducting a minimal standard set of sensitivity analyses (ie, analyses in which a parameter is varied and indicates the degree of influence it has on the results of the base analysis).

LITERATURE SEARCH

To understand the state of the published literature regarding economic evidence of NIs and infection prevention and control practices, we conducted a systematic review of the literature. To find the published analyses, we searched MEDLINE and HealthSTAR with the medical subject headings, or text keywords, "nosocomial infections," "infection control," or "hospital acquired infections" cross-referenced with "costs," "cost analysis," "economics," or "cost-effectiveness analysis." In addition, review articles were examined for published articles that met the inclusion criteria as well as published articles that were known to the authors. This search resulted in more than 200 articles. Articles were considered eligible for inclusion if they were published between 1990 and 2000, had an abstract for review, contained an original cost estimate, and were written in English.

THE AUDIT

We developed our audit form on the basis of the Harvard Center for Risk Analysis audit form (http://www.hsph.harvard.edu/organizations/hcra/cuadatabase/intro.html). The following descriptive data were collected from each analysis: geographic region of

Table 3. Summary of results

	Attributable costs (mean [SD])	Intervention costs (mean [SD])	References
NI (in general)	13,973 (17,998)	1138 (1442)	(20-28)
Surgical site	15,646 (13,820)	27*	(4;19;29-33)
Bloodstream	38,703 (3122)	5622 (9066)	(4;18;34-40)
Pneumonia	17,677 (20,455)	Cost-saving†	(4;41-46)
Urinary tract infection	No studies available	1962*	(47)
MRSA	35,367 (2915)	4808 (3368)	(4;48-54)
Varicella zoster virus	No studies available	27,377 (25,312)	(19;55-59)
Tuberculosis	No studies available	61,446 (86,892)	(60;61)
Measles	No studies available	41,087*	(62;63)
Other	No studies available	27,497 (34,568)	(17;28;64-69)

NI, Nosocomial infection; *MRSA*, Methicillin-resistant *Staphylococcous aureus*.
*SD not applicable with 1 study.
†All interventions were found to be cost-saving.

study, publishing journal, sponsorship or funding source, patient population or setting, type of NI analyzed, and use of Centers for Disease Control and Prevention definitions for NIs. The following analytic data were collected from each analysis: type of study, perspective of the study, costs included, source of cost data, source of effectiveness data, time horizon, discounting if time horizon was more than 1 year, and the use of sensitivity analyses. The results of each study were also audited, including the currency used and/or the cost of intervention or cost of infection. All cost estimates were standardized into a common currency with use of the Federal Reserve economic data exchange rates for the year and conversion of the currency into US dollars (http://www.stls.frb.org/fred/data/exchange.html). In addition, all US dollar figures were inflated to equal 2001 values with use of the Bureau of Labor Statistics Consumer Price Index (http://stats.bls.gov/cpihome. htm).

The costs of an intervention or infection vary on the basis of the risk of the target population. Therefore, a published economic evaluation often includes a number of distinct results.[16] When multiple results were presented in a single article for the common NIs (ie, surgical site infection, bloodstream infections, pneumonia, and/or urinary tract infection), each data point was included.

RESULTS

A final set of 55 articles was judged ultimately to contain original cost estimates and became part of our database. Table 2 describes the descriptive and analytic characteristics of the studies. The majority of analyses were conducted in the United States/Canada or Europe (n = 47, 85%). Two infection control journals, the *American Journal of Infection Control* (n = 7) and *Infection Control and Hospital Epidemiology* (n = 16), published more than 40% of the studies. Relatively few studies (n = 14, 25%) reported external funding. Only 22% of the studies stated that they used the Centers for Disease Control and Prevention definitions for NIs.

Cost-effectiveness analyses (CEAs), which include results reported in terms of infection averted, life saved, life-years gained, or QALYs gained, were the most common type of economic evaluations. Of the CEAs, 11 included a time horizon of more than 1 year. However, only 7 of these studies discounted future costs. Although 10 of the CEAs appropriately conducted sensitivity analyses, only 1 study modeling the cost-effectiveness of vaccinating medical students against hepatitis A used the QALYs as the end outcome measure and met the major recommendations for a reference case.[17] Positively, another study assessing the optimal timing of triple lumen catheter changes used life-years gained as the outcome.[18]

Since most of the studies were from the hospital perspective, it is not surprising that only 2 included non—health care costs. Microcosting, a valuation technique that starts with a detailed identification and measurement of all inputs, was frequently used to identify the cost of the resources. However, the use of estimated cost data without clarification of how estimates were obtained was also common. Few of the studies were conducted in conjunction with randomized controlled trials (n = 5).

In the 55 published studies, there were 72 distinct results. Of these, 29 (40%) were considered cost-

saving interventions. Table 3 summarizes the economic evidence from these studies in terms of the infection studied and the attributable and/or intervention costs. Interventions that are cost-saving are not included in the calculation of the mean intervention costs. Bloodstream infections and methicillin-resistant *Staphylococcus aureus* infections had the highest attributable costs. In general, the mean attributable costs of the infections were larger than the mean costs of the corresponding interventions. However, because of the small size of results available and the variability in the results, the standard deviations were often large. The occupational health intervention studies, in general, had higher associated costs than most of the other infection control and prevention interventions.

DISCUSSION

We found the published economic evidence on NI and infection control and prevention to be lacking in rigor. For example, there were a variety of methods used, with only 1 study meeting reference case recommendations. In addition and more troubling, many of the studies were simple cost analyses that did not include a comparison group, which make the results difficult to interpret. Many other audits of economic evidence in health care have also found the evidence to be lacking in terms of standardization, rigor, and breadth.[16,70-72]

The interventions aimed at reducing infections associated with varicella zoster virus, tuberculosis, and measles were all occupational health—focused except for 1 study that investigated the cost-effectiveness of an automated data entry system for surveillance data.[19] In addition, these occupational health interventions had high associated mean costs. However, even though these high costs may have been due to a lower probability of an intervention adverting an infection, they may have also been related to our search strategy, which was focused on NIs and not on occupational health. Therefore, caution is needed when interpreting this result.

There are a number of other limitations to this audit also worth noting. Although a thorough literature search was attempted, some of the published analyses may have been missed. In addition, this systematic review only included published studies; economic evaluations that have found an intervention not to be cost-effective might not be published. Although a comprehensive assessment of the methods used in the various analyses was conducted, no attempt was made to determine the accuracy of the estimates of the effectiveness of the intervention. In addition, no attempt was made to determine the appropriateness of the cost estimates. Therefore, if the analysts assumed a certain adherence rate or level of effectiveness that would not be found in the targeted population or unrealistic or noncomprehensive cost estimates, the validity of the data point must be questioned. Lastly, whenever literature is audited there may be subjectivity in the data collection. Other researchers may have coded some methods differently.

Even when economic evaluations use the same methodology as well as the most reliable and valid estimates of costs and effectiveness available, the results cannot unequivocally show whether a given intervention is worth pursuing. The results of an economic evaluation are just 1 of the inputs in the decision-making process. Other factors and goals, such as equality of services or even increased services for underserved populations, should be considered. For example, just because occupational health–related interventions are more costly does not mean they should not be provided.

The current attributable cost of NIs to society is not known. The total hospital-related financial burden of NIs in the United States was estimated to exceed $4.5 billion in 1992 (with use of the Consumer Price Inflator, this converts to $5.7 billion in 2001 dollars).[1] However, this estimate is made on the basis of data from the Study on the Efficacy of Nosocomial Infection Control (SENIC), which was conducted in the mid-1970s.[73-75] This is despite the fact that NIs are one of the most serious patient safety issues in the US health care system.

Infection prevention and control policies and practices, such as ensuring effective hand hygiene, optimal staffing levels, and care of devices, will lower NI rates. However, these policies and practices use resources. Furthermore, with pressure for shorter lengths of stay and the potential for long-term complications due to the inflammatory response present with an infection, the consequences of acquiring an NI will not always be totally resolved with discharge from the hospital, but little is known regarding the cost of any long-term consequences. Despite rising infection rates and the need to know whether current infection prevention and control practices are cost-effective, there is a gap in the knowledge regarding the cost-effectiveness of these policies and practices.

Demographic trends, the explosion in health care technology, and a changing health care system have focused attention on both the costs and effectiveness of health care services. Although total US health care costs are rising at a slower rate than in the past, national health care spending still accounts for approximately 13.5% of the US gross domestic product, or $1.1 trillion, and the growth rate is expected to rise.[76] Because of this level of spending, it is no longer sufficient simply to assess the efficacy of an intervention. Hence, clinicians and health policy decision-makers are increasingly interested in economic evaluations.

Within this context, there is increased interest in systematically reviewing economic evidence, as has been done with effectiveness evidence, such as the Cochrane collaboration.[77,78] For example, the US Preventive Services Task Force has initiated a process for systematically reviewing cost-effectiveness analyses as an aid in making recommendations about clinical preventive services.[79,80] This evidence will be incorporated into their recommendations for the forthcoming third edition of the *Guide to Clinical Preventive Services*, slated for publication in 2003. As in other audits, only economic evaluations that use standard methods will be included.[81,82]

On the basis of this assessment of the state-of-the-science in economic evaluation related to NI, there is a need for increased standardization and rigor in the economic analyses available. In addition, there is a lack of knowledge regarding the societal costs of many infections. We strongly urge that clinicians partner with economists and policy analysts to expand and improve the economic evidence available on interventions to reduce hospital complications such as NI and other adverse patient/staff outcomes.

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