

POLICY FORUM: PEER-REVIEWED ARTICLE

How Should Economic Analyses Inform Nosocomial Infection Control? Eleftherios Mylonakis, MD and Panayiotis D. Ziakas, MD, MSc, PhD

Abstract

Nosocomial infections are public health threats with often grave human costs. Because implementing screening and best outbreak response practices is costly for health care organizations, allocating resources for interventions requires consensus among stakeholders with a plurality of perspectives about how to weigh prospective interventions' risks and benefits. Economic analysis can facilitate decision making but is relatively new in nosocomial infection prevention and control. This article describes features of and reasons for economic analysis in this specific area and focuses on emerging challenges in antimicrobial stewardship.

To claim one AMA PRA Category 1 CreditTM for the CME activity associated with this article, you must do the following: (1) read this article in its entirety, (2) answer at least 80 percent of the quiz questions correctly, and (3) complete an evaluation. The quiz, evaluation, and form for claiming AMA PRA Category 1 CreditTM are available through the AMA Ed Hub^{TM} .

Nosocomial Infection Costs

Nosocomial infections are a pervasive and costly public health threat. The 5 major health care-associated infections—central line-associated bloodstream infections, ventilator-associated pneumonia, surgical site infections, *Clostridioides* (formerly *Clostridium*) *difficile* infection, and catheter-associated urinary tract infections—add an estimated \$9.8 billion annually in direct US medical costs.¹ If direct, indirect, and societal nonmedical costs are combined, this figure sums up to \$96 to \$147 billion annually.² It has been estimated that, in 2002, approximately 1.7 million patients acquired a health care-associated infection in US hospitals.³ Thereafter, health care-associated infections exhibited a decline,⁴ and later surveys estimated a burden of 721 800 health care-associated infections in US hospitals in 2011.⁵

The notion that nosocomial infections are preventable causes of morbidity has led to the development of dynamic programs to control such infections. It has been estimated that up to 70% of catheter-associated bloodstream and urinary tract infections and up to 55% of ventilator-associated pneumonia and surgical site infections could be prevented, thereby saving thousands of lives and dollars spent.⁶ Modern programs incorporate infection prevention policies, surveillance, outbreak response frameworks, and antimicrobial stewardship. These practices are endorsed by the Centers for Disease Control and Prevention in its compendium of basic infection prevention and control

guidelines, antibiotic resistance guidelines, and device- and procedure- associated guidelines. Moreover, these infection control and antimicrobial stewardship programs can be supported by economic analyses and thereby result in cost-effective improvement of care and significant cost savings. In what follows, we will discuss the critical elements of an economic analysis that can shape changes in policies and practices to control nosocomial infections.

Prevention

Economic analysis is crucial to support the development of infection control programs, despite their implementation cost. Nevertheless, economic analysis is a relatively new area in infection prevention programs. Moreover, even when implemented in this context, economic studies are often limited to simple cost analyses and do not adhere to reporting standards.⁸ For example, such analyses frequently report the gross spending per health care-associated infection on the assumption that savings from preventing a high-cost infection will outweigh the extra costs of expanding infection control programs.^{9,10} Additionally, only a minority of cost analyses (weighted average of 6%) are incorporated in medical guidelines,¹¹ reinforcing disregard for cost-saving interventions.

Only a complete cost-effectiveness analysis can safely guide decisions. Such an analysis requires a core of 3 elements: the cost of the new infection prevention policy (in comparison to other interventions), the cost savings from prevented infections, and the clinical benefit. 12,13 If the measure of clinical benefit includes both duration and quality of life, then a cost-effectiveness analysis is extended to cost-utility analysis, with quality-adjusted life-years (QALYs) being the endpoint. Resulting comparisons of competing strategies are then made based on extra cost per QALY gained instead of extra cost per death averted (or extra cost per infection averted). 8,14 Thus, relative to alternatives, a new strategy may be less effective and either reduce or increase cost or more effective and either reduce or increase cost or more effective and either reduce or increase cost. If a new strategy improves outcomes at an increased cost, which is common, a threshold needs to be established to guide decisions by defining an upper limit of spending to gain one QALY (willingness-to-pay threshold). 15,16

In the specific setting of nosocomial infections, the extraction of cost savings resulting from prevented infections is particularly challenging, especially for seriously ill patients who are already receiving high-cost care, regardless of their infection status. Moreover, apart from direct program implementation costs, there are collateral costs related to suboptimal treatment for nosocomial infections, drug adverse reactions, and the emergence of antibiotic resistance, all of which must be included in cost-savings calculations.¹⁷ Additionally, infection prevention policies are unique in the sense that reducing prescribing of one class of antibiotic may be counteracted by prescribing of and emerging resistance to another class of antibiotic (known as "squeezing the balloon effect"),^{18,19} which might compromise infection control plans and increase associated costs when antimicrobial restrictions are implemented.

Given these considerations, it is often impossible to define the most accurate values for the input variables. While the baseline assumptions can be considered "a best guess," a sensitivity analysis over a range of input variables is necessary to determine the robustness of conclusions, as exemplified by methicillin-resistant *Staphylococcus* aureus infection prevention strategies in intensive-care units.²⁰ Unlike clinical studies, cost-effectiveness analyses until recently lacked a standardized guideline for how they should be conducted and reported. The publication of the Consolidated Health

Economic Evaluation Reporting Standards guidelines,²¹ along with earlier influential recommendations,^{22,23} has provided the framework for analysts to report the key elements of cost-effectiveness analysis, and these guidelines have been adopted in recent studies on health care-associated infections.^{24,25}

Facilitating Decision Making

One challenge in economic analysis and in decision making is the differing perspectives of stakeholders. Clinicians focus mostly on the effectiveness of an intervention and less on the monetary cost. Health care administrators aim to optimize the allocation of resources and, in collaboration with clinicians, to improve health outcomes. For example, although it might be easy for administrators to adopt a universal influenza vaccination program for health care workers,²⁶ in an era of increasing health care complexity (and cost) and constrained budgets, more complex decision making can be a challenging task (see Table).

Table. Decision-Making Goals and Challenges for Health Care Organizations

Goal	Challenge
Fiscal resource stewardship	Optimize anticipated returns from limited resource investments.
	Manage risks of implementing cost- effective interventions that might not be affordable.
Balance different perspectives	Stakeholders have different, sometimes conflicting priorities (ie, organizations focus on cost-benefit analysis, clinicians and patients focus on effectiveness).
Manage lag between implementation and benefit	New interventions have immediate implementation cost but delayed and ambiguous benefits.
Adopt guidelines	Few guidelines adopt economic analyses to support intervention policies.
Manage emerging threats	Outbreaks and epidemics magnify risk aversion tendencies and preclude conducting valid economic analyses early.
Manage fiscal uncertainty	Account for uncertainty about whether pay-for-performance goals will be achieved by interventions implemented.
Forge consensus	Although necessary to optimize decisions, collaboration and forging consensus among policymakers, clinicians, epidemiologists, and other experts might be difficult.

Economic analyses need to focus on costs important to administrators and third-party payers, a task made more challenging by the fragmentation of care. Hospital administrators are interested primarily in costs paid by the hospital, not by the patient. Thus, they are unlikely to support costly interventions that may reduce nosocomial infections but have a worse cost-benefit profile than alternatives, as other hospital functions would be deprived of critical budgetary resources. They opt for a new strategy when it has a large incremental effect and a smaller incremental cost. Even when a cost-effectiveness analysis favors a new intervention, it may be rejected as unaffordable if it pertains to a large inpatient population and another intervention would have minimal impact on the nosocomial budget. From a regional or national perspective, costs have a wider definition, as they include hospital costs, out-of-pocket patient costs, and societal costs. Societal costs include health care utilization, time to seek care, outpatient caregiving, and loss of economic activity.

There needs to be a balance between proven and new strategies in using limited resources to maximize health outcomes. For example, the clinical best care practices to prevent infections, such as hand hygiene, sanitation, and screening, are not questioned and are considered cost-effective. The pertinent savings from such measures can be used to fund human resources, medical equipment and materials, information technology,²⁷ or antimicrobial stewardship programs.²⁸ However, administrators can be reluctant to introduce new interventions, particularly if there is an additional cost without a clear short-term benefit. A new intervention is associated with immediate additional spending on workforce or equipment, while the perceived benefits for an administrator and hospital may arise several years later owing to reductions in morbidity and mortality.^{17,29}

Decision making becomes even more challenging in the setting of outbreaks, either at the local level or during a pandemic, such as the one brought about by the novel coronavirus (SARS-CoV-2).³⁰ High variability and uncertainty of input values arises when defining the economic analysis model. Many unknown components are involved in a new setting—namely, transmission rate, mortality rate and outbreak expected duration, novel surveillance detection tests, and new or repurposed drugs. An economic analysis may not be feasible to guide early decisions, and administrators and policymakers might be more disinclined to take risks.^{31,32,33} To make things more complex, during an outbreak, if multiple interventions are introduced at once, conclusions about each intervention's effectiveness are confounded. As more data become available, revision of implemented strategies can enable selection of more cost-effective strategies.³⁰

Nevertheless, there are hospital infection prevention policies that are nonnegotiable, regardless of any economic analyses. For example, nuclear acid testing of blood products to cover the window period for HIV infection is far from cost-effective, 34 but it is universally required for the zero-risk transfusion practice demanded by society. Moreover, the Centers for Medicare and Medicaid Services ties reimbursement to quality benchmarks using financial incentives (and disincentives), including the Hospital-Acquired Condition Program that comprises 5 major nosocomial infections: central line-associated bloodstream infections, surgical site infections, *Clostridioides* (formerly *Clostridium*) *difficile* infections, catheter-associated urinary tract infections, and methicillin-resistant *Staphylococcus aureus* infections. These infections weigh significantly in hospital reimbursement, and failure to achieve the established goals results in harm to the patient and additional financial cost to the hospital. In other

words, hospitals face both the burden of nosocomial infections and the added financial risks through pay-for-performance systems.³⁵

Conclusion

In conclusion, quantitative and qualitative improvement of economic analysis in the field of nosocomial infection control would facilitate administrators' and policymakers' timely adoption of effective solutions and improve resource allocation for the benefit of health care organizations, physicians, and patients. Close collaboration among administrators, infection control experts, epidemiologists, and those with economic evaluation expertise is necessary to merge the evolving evidence-based guidelines with cost-effective platforms of interventions in a highly competitive health care environment. Such integration across the continuum of health care might optimize the quality of patient care, improve health outcomes, and contribute to patient satisfaction.

References

- 1. Zimlichman E, Henderson D, Tamir O, et al. Health care-associated infections: a meta-analysis of costs and financial impact on the US health care system. *JAMA Intern Med.* 2013;173(22):2039-2046.
- 2. Marchetti A, Rossiter R. Economic burden of healthcare-associated infection in US acute care hospitals: societal perspective. *J Med Econ*. 2013;16(12):1399-1404.
- 3. Klevens RM, Edwards JR, Richards CL Jr, et al. Estimating health care-associated infections and deaths in US hospitals, 2002. *Public Health Rep.* 2007;122(2):160-166.
- 4. Johnson NB, Hayes LD, Brown K, Hoo EC, Ethier KA; Centers for Disease Control and Prevention (CDC). CDC National Health Report: leading causes of morbidity and mortality and associated behavioral risk and protective factors—United States, 2005-2013. MMWR Suppl. 2014;63(4):3-27.
- 5. Magill SS, Edwards JR, Bamberg W, et al; Emerging Infections Program Healthcare-Associated Infections and Antimicrobial Use Prevalence Survey Team. Multistate point-prevalence survey of health care-associated infections. *N Engl J Med.* 2014;370(13):1198-1208.
- 6. Umscheid CA, Mitchell MD, Doshi JA, Agarwal R, Williams K, Brennan PJ. Estimating the proportion of healthcare-associated infections that are reasonably preventable and the related mortality and costs. *Infect Control Hosp Epidemiol*. 2011;32(2):101-114.
- 7. Infection control: guidelines and guidance library. Centers for Disease Control and Prevention. Reviewed August 4, 2020. Accessed September 1, 2020. https://www.cdc.gov/infectioncontrol/guidelines/index.html
- 8. Rennert-May E, Conly J, Leal J, Smith S, Manns B. Economic evaluations and their use in infection prevention and control: a narrative review. *Antimicrob Resist Infect Control*. 2018;7:31.
- 9. Stone PW, Braccia D, Larson E. Systematic review of economic analyses of health care-associated infections. *Am J Infect Control*. 2005;33(9):501-509.
- 10. Stone PW, Larson E, Kawar LN. A systematic audit of economic evidence linking nosocomial infections and infection control interventions: 1990-2000. *Am J Infect Control*. 2002;30(3):145-152.
- 11. Zervou FN, Zacharioudakis IM, Pliakos EE, Grigoras CA, Ziakas PD, Mylonakis E. Adaptation of cost analysis studies in practice guidelines. *Medicine (Baltimore)*. 2015;94(52):e2365.

- 12. Graves N, McGowan JE Jr. Nosocomial infection, the Deficit Reduction Act, and incentives for hospitals. *JAMA*. 2008;300(13):1577-1579.
- 13. Perencevich EN, Stone PW, Wright SB, Carmeli Y, Fisman DN, Cosgrove SE; Society for Healthcare Epidemiology of America. Raising standards while watching the bottom line: making a business case for infection control. *Infect Control Hosp Epidemiol*. 2007;28(10):1121-1133.
- 14. Drummond MF, Davies LM. Evaluation of the costs and benefits of reducing hospital infection. *J Hosp Infect*. 1991;18(suppl A):85-93.
- 15. Fenwick E, O'Brien BJ, Briggs A. Cost-effectiveness acceptability curves—facts, fallacies and frequently asked questions. *Health Econ.* 2004;13(5):405-415.
- 16. Fenwick E, Claxton K, Sculpher M. Representing uncertainty: the role of cost-effectiveness acceptability curves. *Health Econ.* 2001;10(8):779-787.
- 17. Ziakas PD. Economic considerations of antimicrobial stewardship programs. In: LaPlante KL, Cunha CB, Morrill HJ, Rice LB, Mylonakis E, eds. *Antimicrobial Stewardship: Principles and Practice*. Centre for Agriculture and Bioscience International; 2017:322-333.
- 18. Burke JP. Antibiotic resistance—squeezing the balloon? *JAMA*. 1998;280(14):1270-1271.
- 19. Rahal JJ, Urban C, Horn D, et al. Class restriction of cephalosporin use to control total cephalosporin resistance in nosocomial *Klebsiella*. *JAMA*. 1998;280(14):1233-1237.
- 20. Ziakas PD, Zacharioudakis IM, Zervou FN, Mylonakis E. Methicillin-resistant Staphylococcus aureus prevention strategies in the ICU: a clinical decision analysis. *Crit Care Med.* 2015;43(2):382-393.
- 21. Husereau D, Drummond M, Petrou S, et al; CHEERS Task Force. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. *BMJ*. 2013;346:f1049.
- 22. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the Panel on Cost-Effectiveness in Health and Medicine. *JAMA*. 1996;276(15):1253-1258.
- 23. Drummond MF, Jefferson TO; BMJ Economic Evaluation Working Party. Guidelines for authors and peer reviewers of economic submissions to the *BMJ*. BMJ. 1996;313(7052):275-283.
- 24. Pliakos EE, Andreatos N, Tansarli GS, Ziakas PD, Mylonakis E. The cost-effectiveness of corticosteroids for the treatment of community-acquired pneumonia. *Chest.* 2019;155(4):787-794.
- 25. Pliakos EE, Andreatos N, Shehadeh F, Ziakas PD, Mylonakis E. The cost-effectiveness of rapid diagnostic testing for the diagnosis of bloodstream infections with or without antimicrobial stewardship. *Clin Microbiol Rev.* 2018;31(3):e00095-17.
- 26. Yassi A, Kettner J, Hammond G, Cheang M, McGill M. Effectiveness and costbenefit of an influenza vaccination program for health care workers. *Can J Infect Dis.* 1991;2(3):101-108.
- 27. Tchouaket Nguemeleu E, Beogo I, Sia D, et al. Economic analysis of healthcare-associated infection prevention and control interventions in medical and surgical units: systematic review using a discounting approach. *J Hosp Infect*. 2020;106(1):134-154.
- 28. LaPlante KL, Cunha CB, Morrill HJ, Rice LB, Mylonakis E, eds. *Antimicrobial Stewardship: Principles and Practice*. Centre for Agriculture and Bioscience International; 2017.

- 29. Leatherman S, Berwick D, Iles D, et al. The business case for quality: case studies and an analysis. *Health Aff (Millwood)*. 2003;22(2):17-30.
- 30. Branch-Elliman W, Safdar N, Nelson R. Economic considerations in infectious diseases emergency response preparedness: it's all about the point of view. *Clin Infect Dis*. 2021;72(1):148-152.
- 31. Reich NG, Lessler J, Varma JK, Vora NM. Quantifying the risk and cost of active monitoring for infectious diseases. *Sci Rep.* 2018;8:1093.
- 32. Elbasha EH. Risk aversion and uncertainty in cost-effectiveness analysis: the expected-utility, moment-generating function approach. *Health Econ*. 2005;14(5):457-470.
- 33. Zivin JG. Cost-effectiveness analysis with risk aversion. *Health Econ.* 2001;10(6):499-508.
- 34. Jackson BR, Busch MP, Stramer SL, AuBuchon JP. The cost-effectiveness of NAT for HIV, HCV, and HBV in whole-blood donations. *Transfusion*. 2003;43(6):721-729.
- 35. Vokes RA, Bearman G, Bazzoli GJ. Hospital-acquired infections under pay-for-performance systems: an administrative perspective on management and change. *Curr Infect Dis Rep.* 2018;20(9):35.

Eleftherios Mylonakis, MD is the Charles C. J. Carpenter Professor of Infectious Diseases at Brown University in Providence, Rhode Island, where he is also the assistant dean for outpatient investigations and director of the Center for Outpatient and Longitudinal Medical Research at the Warren Alpert Medical School. He is also chief of infectious diseases at Rhode Island Hospital and the Miriam Hospital and director of the COBRE Center for Antimicrobial Resistance and Therapeutic Discovery. Dr Mylonakis studies host and microbial factors of infection, novel antimicrobial compounds, and microbial virulence. He holds 8 patents, has edited 5 books, and published 400 articles and book chapters.

Panayiotis D. Ziakas, MD, MSc, PhD has authored more than 100 peer-reviewed publications in the fields of infections, hematology/oncology, autoimmunity, and epidemiology. He completed medical training in hematology at the University of Athens Medical School and also earned master's and doctoral degrees from the University of Athens. He previously served as a research assistant and instructor in medicine at Brown University's Warren Alpert Medical School. His research focuses on nosocomial infections and the appropriate use of antimicrobial and antifungal agents in immunocompromised individuals and patients with hematologic neoplasia.

Citation

AMA J Ethics. 2021;23(8):E631-638.

DOI

10.1001/amajethics.2021.631.

Conflict of Interest Disclosure

The author(s) had no conflicts of interest to disclose.

The viewpoints expressed in this article are those of the author(s) and do not necessarily reflect the views and policies of the AMA.

Copyright 2021 American Medical Association. All rights reserved. ISSN 2376-6980