

**TECHNOLOGY FOR PATIENT SAFETY
AT VETERANS HOSPITALS**

JOINT HEARING

BEFORE THE
SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY
&
SUBCOMMITTEE ON OVERSIGHT
COMMITTEE ON SCIENCE, SPACE, AND
TECHNOLOGY
HOUSE OF REPRESENTATIVES
ONE HUNDRED THIRTEENTH CONGRESS

SECOND SESSION

JUNE 26, 2014

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**TECHNOLOGY FOR PATIENT SAFETY AT
VETERANS HOSPITALS**

THURSDAY, JUNE 26, 2014

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY AND
SUBCOMMITTEE ON OVERSIGHT,
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY,
Washington, D.C.

The Subcommittees met, pursuant to call, at 9:06 a.m., in Room 2318 of the Rayburn House Office Building, Hon. Larry Bucshon [Chairman of the Subcommittee on Research and Technology] presiding.

LAMAR S. SMITH, Texas
CHAIRMAN

EDDIE BERNICE JOHNSON, Texas
RANKING MEMBER

Congress of the United States
House of Representatives

COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY

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Subcommittee on Research and Technology
and
Subcommittee on Oversight

Technology for Patient Safety at Veterans Hospitals

Thursday, June 26, 2014

9:00 a.m. to 11:00 a.m.

2318 Rayburn House Office Building

Witnesses

Dr. Chetan Jinadatha, Chief, Infectious Diseases, Central Texas Veterans Health Care System

Dr. Elaine Cox, Professor of Clinical Pediatrics, Director of Infection Prevention, Director of Pediatric Antimicrobial Stewardship, Riley Hospital for Children

Dr. Trish M. Perl, Professor of Medicine and Pathology, Johns Hopkins School of Medicine; Professor of Epidemiology, Bloomberg School of Public Health; Senior Epidemiologist, Johns Hopkins Medicine

Mr. Jeff Smith, President, Electro-spec, Inc.

Mr. Morris Miller, Chief Executive Officer, Xenex Disinfection Services

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY

HEARING CHARTER

Technology for Patient Safety at Veterans Hospitals

Thursday, June 26, 2014
9:00 a.m. – 11:00 a.m.
2318 Rayburn House Office Building

PURPOSE

On Thursday, June 26, 2014, the Research & Technology and Oversight subcommittees will hold a joint hearing *Technology for Patient Safety at Veterans Hospitals* starting at 9:00 a.m. The purpose of the hearing is to assess the potential benefits of new technologies to prevent hospital-acquired infections (HAIs), especially given the high percentage of HAI and mortality rates among patients at some Veterans Administration (VA) hospitals. Research supported by the National Science Foundation in robotics, nanotechnology, and other areas of the biological sciences has helped to bring about technological innovations to prevent HAIs.

WITNESS LIST

- **Dr. Chetan Jinadatha**, Chief, Infectious Diseases, Central Texas Veterans Health Care System
- **Dr. Elaine Cox**, Professor of Clinical Pediatrics, Director of Infection Prevention, Director of Pediatric Antimicrobial Stewardship, Riley Hospital for Children
- **Dr. Trish M. Perl**, Professor of Medicine and Pathology, Johns Hopkins School of Medicine; Professor of Epidemiology, Bloomberg School of Public Health; Senior Epidemiologist, Johns Hopkins Medicine
- **Mr. Jeff Smith**, President, Electro-spec, Inc.
- **Mr. Morris Miller**, Chief Executive Officer, Xenex Disinfection Services

BACKGROUND

Hospital acquired infections (HAIs) are the most common complication of hospital care. The Centers for Disease Control (CDC) estimates 1.7 million HAIs per year in the U.S. causing or contributing to up to 99,000 deaths annually.¹

¹ <http://www.ahrq.gov/qual/haiflyer.htm>

A recent series of investigative reports by *The Wall Street Journal* describe significant deficiencies in quality of patient care among VA hospitals, including hospital acquired infections. Although HAIs are a national health care issue, the infection rates at certain VA hospitals exceed the worst-performing private sector hospitals by a factor of ten or more.²

HAIs remain the leading cause of preventable patient injuries and deaths in U.S. hospitals.³ It is also associated with substantial and avoidable costs for health care costs. Studies have shown that the five most common HAIs increase U.S. direct health care costs by at least \$10 billion annually. Both direct and indirect (e.g., post-discharge nursing care) HAI costs are estimated at up to \$45 billion per year. However, this figure understates costs significantly because it omits the costs of resulting long-term disabilities and deaths.⁴

The Veterans Health Administration does not publicly disseminate comprehensive quality and patient safety relevant information, including information on HAIs. According to the CDC, approximately 5% of all U.S. hospital patients contract one or more HAIs during a hospital stay. In the most recent year (2012) for which data is available, there were 703,500 inpatient admissions to VA hospitals.⁵ If the 5% estimate from the CDC also applies to VA hospitals, then approximately 35,000 patients at VA hospitals are affected by HAIs each year.

The CDC considers approximately one-third of all HAIs to be preventable.⁶ Moreover, studies have shown that a large majority of HAIs are preventable if hospital leadership and staff make a sustained commitment to best clinical practices and rigorous patient safety standards.⁷ According to recent reports⁸, the best-performing VA hospitals sustain HAI rates significantly below those found at the best-performing private hospitals.

In the past, many hospital and health care leaders have regarded HAIs as the inevitable consequence of delivering complex health care services. However, the reality that most HAIs can be prevented has changed this view. In order to stimulate improvement, Medicare and many

²<http://online.wsj.com/articles/hai-scherz-doctors-war-stories-from-va-hospitals-1401233147>

<http://online.wsj.com/articles/veterans-affairs-hospitals-vary-widely-in-patient-care-1401753437>

<http://online.wsj.com/articles/political-triage-at-the-va-1402095105>

<http://online.wsj.com/articles/top-lawmakers-call-for-disclosure-of-va-hospital-data-1401810854>

<http://online.wsj.com/articles/visits-to-troubled-hospitals-1402357126>

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 Mar-Apr;122(2):160-6.

⁴ Klevens RM, Edwards JR, Richards CL Jr, et al. Estimating health care-associated infections and deaths in US hospitals, 2002. *Public Health Rep.* 2007 Mar-Apr;122(2):160-6.

<http://consumer.healthday.com/public-health-information-30/health-cost-news-348/hospital-acquired-infections-cost-10-billion-a-year-679761.html>

Umscheid CA, Mitchell MD, Doshi JA et al. "Estimating the proportion of healthcare-associated infections that are reasonably preventable and the related mortality and costs." *J. Infect Control Hosp Epidemiol.* 2011 Feb;32(2):101-14. <http://www.jstor.org/stable/10.1086/657912>

⁵ <http://www.va.gov/vetdata/Utilization.asp>

⁶ http://www.cdc.gov/hai/pdfs/hai/scott_costpaper.pdf

⁷ <http://www.positiveviance.org/pdf/publications/DoWhatYouCan.pdf>

http://www.prhi.org/docs/VA%20long-term_10-1-2005.pdf

http://www.prhi.org/docs/Wiping%20out%20MRSA_10-1-2003.pdf

⁸ <http://online.wsj.com/articles/veterans-affairs-hospitals-vary-widely-in-patient-care-1401753437>

private insurers have instituted direct and indirect payment penalties for hospitals that fail to meet benchmarks for HAIs and other patient safety metrics.⁹

As recently as the 1990s and early 2000s, the Veterans Health Administration hospitals and clinicians pioneering HAI prevention methods indicated that the incidence of the most common HAIs could be reduced dramatically, even among high-risk patients. Experiments at VA hospitals demonstrated significant patient safety benefits from rigorous hospital staff adherence to straightforward infection prevention measures: hand washing, use of gloves and gowns when in contact with patients, cleaning medical equipment, screening new patients for potentially harmful pathogens, and isolating patients who contracted serious infections.¹⁰ In a few VA hospitals, the incidence rates of dangerous types of HAIs was dramatically reduced when these measures were adopted.¹¹

The larger challenge for all U.S. hospitals, including VA institutions, is the need to approach 100% prevention of HAIs. Due to the rapid evolution of antibiotic resistant microbes, including a steadily increasing list of infections that no longer respond to any type of antibiotic, infected patients are at heightened risk of serious injury, permanent disability or death.

Therefore, one focus of research is on new infection prevention technologies. While rigorous compliance with conventional prevention techniques (e.g., hand-washing, isolation of infected patients, etc.) must still be common practice, promising new technologies for sterilizing medical equipment along with “touch” surfaces at hospitals are being developed. Sterilization techniques include: UV light, hydrogen peroxide vapor, and anti-microbial coatings.¹² Self-disinfecting surfaces can be created by coating surfaces with heavy metals (eg, silver or copper), germicides (eg, triclosan), or light-activated antimicrobials. These methods are under active investigation to reduce health care-associated infections. The National Institutes of Health, Centers for Disease Control, National Science Foundation, and other federal agencies fund various research projects for new HAI prevention technologies.

⁹ <http://rds.epi-ucsf.org/ticr/syllabus/courses/68/2009/05/05/Lecture/readings/Dudley.pdf>
<http://www.hci3.org/sites/default/files/files/HCI-IssueBrief-4-2012.pdf>

¹⁰ McBryde ES, Bradley LC, Whitby M, McElwain DL (October 2004). "An investigation of contact transmission of methicillin-resistant *Staphylococcus aureus*". *J. Hosp. Infect.* 58 (2): 104–8. doi:10.1016/j.jhin.2004.06.010. PMID 15474180

¹¹ <http://www.positivedeviance.org/pdf/publications/DoWhatYouCan.pdf>
http://www.prhi.org/docs/VA%20long-term_10-1-2005.pdf

http://www.prhi.org/docs/Wiping%20out%20MRSA_10-1-2003.pdf

¹² Weber, DJ; Rutala, WA (May 2013). "Self-disinfecting surfaces: review of current methodologies and future prospects." *American journal of infection control* 41 (5 Suppl): S31–5. PMID 23622745

Chairman BUCSHON. The joint hearing of the Subcommittee on Research and Technology and the Subcommittee on Oversight will come to order.

Good morning, everyone, and welcome to today's hearing titled "Technology for Patient Safety at Veterans Hospitals."

In front of you are packets containing the written testimony, biographies and Truth in Testimony disclosures for today's witnesses.

Before we get started, since this is a joint hearing involving two Subcommittees, I want to explain how we will operate procedurally so all Members understand how the question-and-answer period will be handled. We will recognize those Members present at the gavel in order of seniority on the full Committee and those coming after the gavel will be recognized in order of arrival. I now recognize myself for five minutes for an opening statement.

This morning's hearing will focus on an important public health issue: the problem of patients contracting dangerous infections while in the hospital. This problem has been in the news lately due to disclosure of unfavorable information about some Veterans Administration hospitals, including high rates of hospital-acquired infections, or HAIs.

We want the highest quality of care and the highest standards of patient safety in all VA hospitals. Big variations among VA hospitals are a cause for concern.

However, as a former cardiothoracic surgeon, I am well aware that HAIs are not a problem unique to the VA Health Care System. Also, it is important to realize that hospital-acquired infection rates will never be zero, but can and should be aggressively minimized.

Rates of hospital-acquired infections appear to have declined in recent years. During the 1990s, estimates hovered around 2 million per year. The CDC's most recent estimate is 1.7 million hospital-acquired infections happen annually. The CDC also calculates this works out to about a one in 25 chance of contracting a serious infection while in the hospital.

The idea a hospital patient, on average, only has a one in 25 chance of getting an infection is certainly not a good thing. Many infections that patients suffer from while hospitalized originate from their own flora—their own bacteria, for non-medical people—i.e., the skin, respiratory, or intestinal bacteria for example, that comes to the hospital with the patient.

That said, research has shown it is possible to prevent a large fraction of hospital acquired infections. For example, simple things like isolating patients who have serious infections, and doctors and nurses washing their hands between each patient, can go a long way toward controlling the spread of potentially lethal infections. One hundred percent adherence to all these best practices by health care personnel won't solve the problem. Hand washing and hand sanitation is just as important for family members and other hospital visitors, too, as they often are unknowingly responsible for spreading bacteria and viruses. Some types of viruses, for example, can survive for months on a tray, a door frame or other surface.

Most people take for granted that antibiotics can ultimately cure all but the most exotic types of infections. Until a few decades ago, antibiotics were, for the most part, an effective backstop against

most hospital-acquired infections. The evolution of antibiotic-resistant superbugs is voiding the assumption that medicine can cure every infection. More than one dozen types of pathogens have developed resistance to most types of antibiotics. In some cases, just one class of antibiotics is still effective, and in a few instances, there are literally no antibiotics that are effective against certain bacteria. Antibiotic overuse and inappropriate use are significantly responsible for the growing number of antibiotic resistant superbugs.

As a personal side note, I believe tort issues surrounding the practice of medicine is partly responsible for this issue and needs reform. Another problem is the slow pace at which new antibiotics are being developed, due to the costly and lengthy approval process.

According to the Infectious Disease Society of America, just one organism, methicillin-resistant *Staph aureus*, better known as MRSA, kills more Americans each year than the combined total of emphysema, HIV/AIDS, Parkinson's disease, and homicide.

The Food and Drug Administration recently approved a new antibiotic for MRSA infections, but that is just one type of bacteria, and the odds are that resistance to the new medicine will develop.

The better news is that there are some promising new, non-pharmaceutical innovations that can help to reduce hospital-acquired infection rates significantly, innovations that don't seem to carry the possibility of eventual antibiotic resistance. These innovations have been developed from research in several scientific fields, including nanotechnology, robotics, computer science, and biology.

We are fortunate to have with us three physicians who are national experts in infectious diseases and the prevention of hospital-acquired infections and two witnesses will describe the anti-infection innovations their companies have brought forward. I look forward to this morning's testimony on this important subject.

[The prepared statement of Mr. Bucshon follows:]

PREPARED STATEMENT OF THE SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY
CHAIRMAN LARRY BUCSHON

This morning's hearing will focus on an important public health issue—the problem of patients contracting dangerous infections while in the hospital. This problem has been in the news lately due to disclosure of unfavorable information about some Veterans Administration hospitals, including high rates of hospital acquired infections, or HAIs.

We want the highest quality of care and highest standards of patient safety in all VA hospitals. Big variations among VA hospitals are a cause for concern. However, as a former cardio-thoracic surgeon, I am well aware that HAIs are not a problem unique to the VA Health Care System. Also, it is important to realize that HAI rates will never be zero, but can and should be aggressively minimized.

Rates of hospital-acquired infections appear to have declined in recent years. During the 1990's, estimates hovered around 2 million per year. The CDC's most recent estimate is 1.7 million HAIs annually. The CDC also calculates this works out to about a one in 25 chance of contracting a serious infection while in a hospital.

The idea a hospital patient, on average, has "only" a one in 25 chance of getting an infection is certainly not a good thing. Many infections that patients suffer from while hospitalized originate from their own flora (ie skin, respiratory, or intestinal bacteria for example.)

That said, research has shown it is possible to prevent a large fraction of hospital infections. For example, simple things like isolating patients who have serious infections, and doctors and nurses washing their hands between each patient, can go a long way toward controlling the spread of potentially lethal infections.

One hundred percent adherence to all best practices by health care personnel won't solve the problem. Hand washing and hand sanitation is just as important for family members and other hospital visitors, too, as they often are unknowingly responsible for spreading bacteria and viruses. Some types of viruses can survive for six months on a tray, a door frame or other type of surface.

Most people take for granted that antibiotics can ultimately cure all but the most exotic kinds of infections. Until a few decades ago, antibiotics were an effective backstop against most hospital-acquired infections.

The evolution of antibiotic-resistant superbugs is voiding the assumption that medicine can cure infections. More than one dozen types of pathogens have developed resistance to most types of antibiotics. In some cases, just one class of antibiotics is still effective. And in a few instances, there is literally no antibiotic that works. Antibiotic overuse and inappropriate use are significantly responsible for the growing number of antibiotic-resistant superbugs. As a personal side note, I believe tort issues surrounding the practice of medicine is partly responsible for this issue and needs reform. Another problem is the slow pace at which new antibiotics are being developed, due to a costly and lengthy approval process.

According to the Infectious Disease Society of America (IDSA), just one organism—methicillin-resistant *Staphylococcus aureus*, better known as MRSA—kills more Americans each year than the combined total of emphysema, HIV/AIDS, Parkinson's disease, and homicide.

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The better news is that there are some promising new, non-pharmaceutical innovations that can help to reduce HAI rates significantly, innovations that don't seem to carry the possibility of eventual antibiotic resistance.

These innovations have been developed from research in several scientific fields, including nanotechnology, robotics, computer science, and biology.

We're fortunate to have with us three physicians who are national experts in infectious diseases and the prevention of HAIs and two witnesses will describe the anti-infection innovations their companies have brought forward. I look forward to this morning's testimony on this important subject.

Chairman BUCSHON. I now yield to the Ranking Member, Mr. Maffei.

Mr. MAFFEI. Thank you very much, Chairman Bucshon. I also want to thank you for holding this hearing and I also want to thank Chairman Broun, who is the Chairman of my Subcommittee, the Subcommittee on Oversight, and I of course want to thank Chairman Smith, the Chairman of the full Committee, and all the Members for being here. This is an important hearing on the technology for patient safety at Veterans Hospitals.

Health care-associated infections are a serious and potentially deadly threat to anyone who spends time in a hospital, any hospital. In fact, overall, not just the VA but all hospitals, there is an average of 200 individuals who die every day as a result of health care-associated infections. This amounts to an estimated 75,000 people a year. Another 650,000 patients become infected each year during their hospital stays, and it can cost as much as \$45,000 per patient to treat these infections. Health care-associated infections in the United States alone cost as much as \$45 billion a year.

I would stress that these infections are not unique to the Veterans Administration's hospitals. I know that health care-associated infections and medical mishaps do not stop at the door of the VA, however. Unfortunately, they are prevalent in all health care facilities, and the tools to combat these infections and to prevent medical errors are the same regardless of where the care is given.

I look forward to hearing from our witnesses today about both proven methods and new technologies that can help play a role in addressing this serious issue. I am particularly interested in hear-

ing from Dr. Trish Perl from Johns Hopkins University, who brings a wealth of experience and expertise to the area of infectious diseases and the role that technology can play in their prevention. She has firsthand experience implementing new technologies to combat hospital infections, some that worked successfully and some that actually increased the rate of infection. I look forward to hearing from her about the possible benefits and potential downsides to implementing unproven technologies in the hospital settings.

Mr. Chairman, I must confess, though, I do have concerns about the testimony of one of our witnesses, however, and that is simply that it wasn't submitted at all in a clear contradiction of this Committee's rules and practices. It is the standard practice of the House Committee on Science, Space, and Technology to have advanced written testimony from witnesses before they testify. Today, the Majority has taken the opposite approach and is willing to sit a witness from the Veterans Administration that has provided no written testimony in advance of this hearing. I am concerned that Majority staff knew about this problem and did not rectify it in a timely manner and agreed to sit this witness without having written testimony prior to the hearing several days ago rather than postponing the hearing or moving forward without this witness.

My understanding is that the failure to have testimony is not the failure of the witness, Dr. Jinadatha, so I apologize to you. I am sorry you are caught in the middle of this. I know that you have provided—you prepared your testimony and it was an approval process that was the issue, but still, I did want to voice these concerns because I do think it is very, very important that we don't set a precedent in this Committee that we do not want to set, that we will have—particularly with the Oversight Subcommittee, that we will have witnesses testifying without having submitted in advance for everybody on the Committee to look at, peruse, develop questions on written testimony.

So with those concerns stated, Mr. Chairman, I yield back.
[The prepared statement of Mr. Maffei follows:]

PREPARED STATEMENT OF THE SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY
RANKING MINORITY MEMBER DAN MAFFEI

Chairman Bucshon, Chairman Broun thank you both for holding this important hearing today on "Technology for Patient Safety at Veterans Hospitals."

The recent disclosures of mismanagement at the VA are deeply troubling. I represent nearly 50,000 veterans in Central New York and I want to ensure they receive the best care possible. Last month, as a result of these revelations about the VA, I personally called for the Secretary of the VA, Eric Shinseki to step down so that the VA could move forward with new management.

But nothing about the substance of this hearing, focused on the threat of Healthcare Associated Infections (HAIs) and potential methods to successfully address them, is isolated to the VA.

Healthcare Associated Infections are a serious and potentially deadly threat to anyone who spends time in a hospital—any hospital. By this time tomorrow 200 individuals at U.S. hospitals will have died as a result of healthcare associated infections. This amounts to an estimated 75,000 people per year. Another 650,000 patients become infected each year during their hospital stay.

It can cost as much as \$45,000 per patient to treat these infections. Healthcare Associated Infections in the U.S. alone cost as much as \$45 billion per year.

I would stress that these infections are not unique to Veterans Administration (VA) hospitals. My home District in Syracuse, New York includes one VA hospital and six public and private hospitals. I know that Healthcare Associated Infections

and medical mishaps do not stop at the door of the VA. Unfortunately, they are prevalent in all healthcare facilities. And the tools to combat these infections and to help prevent medical errors are the same regardless of where the care is given.

The good news is that a recent report released by the Centers for Disease Control and Prevention (CDC) shows steady progress at the national level against Healthcare-Associated Infections. The report found a 44 percent decrease in central line-associated bloodstream infections between 2008 and 2012; a 20 percent decrease in infections related to 10 major surgical procedures between 2008 and 2012; and a 4 percent decrease in hospital-onset MRSA (Methicillin-resistant *Staphylococcus aureus*) bloodstream infections between 2011 and 2012.

But combatting healthcare associated infections is still difficult, often deadly and very costly.

Technologies can help, but I doubt there is a single silver bullet available in this fight to eradicate these troubling and pervasive infections. Simple steps like proper hand-hygiene, appropriate training and clear communication can also have a major impact on the spread of these healthcare associated infections.

I am looking forward to hearing from our witnesses today about both proven methods and new technologies that can help play a role in addressing this serious issue. I am particularly interested in hearing from Dr. Trish Perl from Johns Hopkins University, who brings a wealth of experience and expertise in the area of infectious diseases and the role that technology can play in their prevention. She has first-hand experience implementing new technologies to combat hospital infections, some that worked successfully and some that actually increased the rate of infection. I look forward to hearing from her about the possible benefits and potential downsides to implementing unproven technologies in the hospital setting.

Chairman BUCSHON. Thank you. I would also like to comment on that. Rule 3, Section C says insofar as is practical, no later than 48 hours in advance of his or her appearance, each witness who is to appear before the Committee or any Subcommittee shall file a printed copy in electronic form or written statement of his or her proposed testimony and a curriculum vitae. In this situation, we had some difficulty with the process through the VA getting the written testimony final approval and we felt that the testimony of this witness was very valuable and it was not practical to get the testimony in in time. The delay was unexpected due to the process needing approval and therefore I feel that the witness's testimony is valuable and in no way would prejudice the discussion at this hearing and therefore should be allowed.

Mr. MAFFEI. Would the Chairman yield?

Chairman BUCSHON. I will yield.

Mr. MAFFEI. Mr. Chairman, I appreciate those comments, and I certainly—that is why I would not object to Mr. Jinadatha being a witness here because I do believe that he has a lot of important things to say, but my understanding is that the Majority staff did know about this in enough advance notice to have done something about it. So while I appreciate that at this point of course it couldn't be avoided, there was a point where it could have been, and that is my concern.

The Chairman of my Subcommittee, Mr. Broun, has pressured the Administration many times about the—

Chairman BUCSHON. I take back my time. Thanks for that opinion. I appreciate it. We don't like the situation either but again, feel that the testimony of the witness is very valuable to the context of this hearing, and at this point we will proceed ahead with the hearing.

Chairman SMITH OF TEXAS. Mr. Chairman, could I just add a comment here?

Chairman BUCSHON. I yield to the Chairman of the full Committee, Mr. Smith.

Chairman SMITH OF TEXAS. Thank you. I do want to reassure the Ranking Member, Mr. Maffei, that we actually did try to get the written testimony and we share his sentiments completely. I am as frustrated as anyone else, and I have been frustrated both in this Committee and other Committees when we have had witnesses who because of various governmental rules have not been able to give us the written testimony that we all would like to see ahead of time. So I think we made a good-faith effort to try to get it over the last several days.

I also want to say to the Ranking Member, I very much appreciate his measured remarks, measured comments, and because they were measured, they even have a greater impact than he might think, and we will try to make sure that, as he suggested, this is very much the exception to the rule and not the rule.

Mr. MAFFEI. Would the Chairman yield just so I can thank the gentleman?

Chairman BUCSHON. I will yield.

Mr. MAFFEI. I do want to thank the Chairman of the full Committee and of course, you, Mr. Chairman, for hearing me out on this, and I will just stick with, I just don't want this to be the precedent of the Committee. But thank you very much for hearing us out.

Mr. BROUN. Mr. Chairman?

Chairman BUCSHON. Mr. Broun, I yield.

Mr. BROUN. Thank you, Mr. Chairman.

I just want to remark to my dear friend, good friend, my co-worker on our Oversight Committee, that as he stated in his remarks, it has been something I have been very concerned about and I am extremely concerned just like my friend, Mr. Maffei, is about this very issue, and I would be objecting tremendously except for I think this is an extremely important witness that can give us some insight into the VA, and his testimony has been approved by the VA, from my understanding. It is just some other parts of the Administration that have delayed or dragged their feet, and let me assure my friend, Mr. Maffei, that the staff on this side have been very, very diligent in trying to get this written testimony approved.

His oral testimony—in his oral testimony, he can read his written testimony, and that is okay with the VA. And so what we are trying to do is prevent deaths, and I think this is an emergent situation or I would be objecting very vehemently myself, I assure you, and I don't want this to be a precedent any more than my friend wants it be a precedent. We must have written testimony, but in this case, because of life-threatening situations, I think it is prudent for us to go ahead and hear from the witness, and I appreciate my friend's comments and I agree with wholeheartedly and I appreciate us being able to go forward, and I thank you very much. At this point I will yield back.

Chairman BUCSHON. I will reclaim my time and then with that, I will now recognize the Chairman of the Subcommittee on Oversight, the gentleman from Georgia, Mr. Broun, for his opening statement.

Mr. BROUN. Thank you, Dr. Bucshon. I thank all the witnesses for being here today and going through this little necessary dialogue between us, and I look forward to hearing from you all today.

For those of you all who are not from the South “you all” is singular and plural, so I appreciate all of you all being here.

As both a medical doctor as well as a U.S. Marine, it is deeply troubling to me to hear reports of poor care given to veterans in my home State of Georgia as well as across this country. In January of this year, I returned to Augusta for an oversight visit to the Charlie Norwood VA Medical Center with some of my colleagues. During the trip, I was extremely saddened to see the cavalier attitude expressed by the VA, and the potential implication for hospital-associated infections, or HAIs, and preventable deaths. A recent Wall Street Journal article on VA hospitals cited specifically that, “at Augusta, the in-hospital death rate was 120 percent above that of the best facilities.” This kind of negligence is intolerable and I won’t stand for it.

The principal function of our federal government under the Constitution is to provide for our national defense, and it is imperative that we take care of the men and women who so bravely served our country with dignity and pride. We made promises to veterans, and we must fulfill those promises for those who have sacrificed for all us to keep us free as a nation. Our veterans should receive the best care available anywhere in the country, and there is no question about that.

The Centers for Disease Control and Prevention states that “approximately 1.7 million HAIs occur in United States hospitals each year, resulting in up to 99,000 deaths and an estimated \$20 billion in healthcare costs.” Contributing to these numbers is a wide variation in medical care at VA hospitals with substantially more HAIs and preventable deaths at certain VA hospitals. However, since the VA does not publicly disclose comprehensive details on each of their facilities, it is hard for veterans and their families to receive fair warning that they are walking into a potentially life-threatening situation when they are requesting medical care from those VA facilities.

What is additionally astounding is that the infection rates at some VA hospitals exceed the rates at private sector hospitals by ten times or more. On top of that, the Wall Street Journal article I mentioned earlier notes that, “VA senior management suspended a long-standing program that had sent teams of doctors and monitors to its worst-performing hospitals to try to improve them.” As the Chairman of the Oversight Subcommittee, I consider this lack of oversight, accountability, and due diligence to be totally inexcusable and intolerable.

The treatment of veterans is not only a moral issue, but a national security issue as well. If the federal government fails to fulfill the promises it has made to our veterans, how are we going to recruit the finest men and women to come into the military and stay to be senior NCOs, senior officers, or flag officers? It just will not happen.

I look forward to hearing from our witnesses about technologies that can save veterans from preventable infections and deaths. I also encourage everyone at the VA listening to this hearing today to renew their commitment to our veterans by doing everything in their power and as soon as possible to ensure that our Nation’s heroes are given the care that they deserve and have earned.

I thank you, Chairman Bucshon, Dr. Bucshon, my good friend and medical colleague, for holding this very important hearing, and I yield back the balance of my time.

[The prepared statement of Mr. Broun follows:]

PREPARED STATEMENT OF THE SUBCOMMITTEE ON OVERSIGHT
CHAIRMAN PAUL BROUN

Thank you, Chairman Bucshon, and thank you to all of our witnesses for being here today. I am looking forward to hearing from you all on this very important matter.

As both a medical doctor and a U.S. Marine, it is deeply troubling to hear reports of poor care given to veterans in my home state of Georgia as well as across this country. In January, I returned to Augusta for an oversight visit of the Charlie Norwood VA Medical Center with some of my colleagues. During the trip, I was extremely saddened to see the cavalier attitude expressed by the VA, and the potential implication for hospital-associated-infections—or HAIs—and preventable deaths. A recent Wall Street Journal article on VA hospitals cited specifically that, “at Augusta, the in-hospital death rate was 120% above that of the best facilities.” This kind of negligence is intolerable.

The principle function of our federal government under the Constitution is to provide for our national defense and take care of the men and women who have so bravely served our country with dignity and pride. We have made promises, and we must fulfill those promises for those who have sacrificed for us. Our veterans should receive the best care—there is no question about it.

The Centers for Disease Control and Prevention states that “approximately 1.7 million HAIs occur in U.S. hospitals each year, resulting in up to 99,000 deaths and an estimated \$20 billion in healthcare costs.” Contributing to these numbers is the wide variation in medical care at VA hospitals with substantially more HAIs and preventable deaths at certain VA hospitals. However, since the VA does not publicly disclose comprehensive details on each of their facilities, it is hard for veterans to receive fair warning that they are walking into a potentially life-threatening situation when requesting medical care. What is additionally astounding is that the infection rates at some VA hospitals exceed the rates at private sector hospitals by ten times or more.

On top of that, the Wall Street Journal article I mentioned earlier notes that, “VA senior management suspended a long-standing program that had sent teams of doctors and monitors to its worst-performing hospitals to try to improve them.” As the Chairman of the Oversight Subcommittee, I consider this lack of oversight, accountability, and due-diligence to be inexcusable.

The treatment of veterans is not only a moral issue, but a national security issue as well. If the federal government fails to fulfill the promises it has made to our veterans, how are we going to recruit the finest men and women to come into the military and stay to be senior NCOs, senior officers, or flag officers? It won't happen!

I look forward to hearing from our witnesses about technologies that can save veterans from preventable infections and deaths. I also encourage everyone at the VA listening to this hearing today to renew their commitment to our veterans by doing everything in their power, as soon as possible, to ensure our nation's heroes are given the care that they deserve and have earned.

Thank you again Chairman Bucshon for holding this very important hearing, and I yield back the balance of my time.

Chairman BUCSHON. Thank you, Dr. Broun. I now recognize the Chairman of the full Committee, Mr. Smith, for an opening statement.

Chairman SMITH OF TEXAS. Thank you, Mr. Chairman.

The long delays and unacceptable quality of VA health care for tens of thousands of our veterans has recently become public. Following up on a series of letters to the VA Inspector General and others, I recently met with Acting VA Secretary Gibson at the Audie Murphy Memorial Hospital in my district in San Antonio. I was reassured that he sincerely wants to fix the problems facing

our veterans but we need swift action and strong resolve to fix such a broken system at the VA.

Veterans who live in the 21st Congressional District of Texas and across our country should have the best health care America can provide. American veterans have made tremendous sacrifices to protect and defend our freedoms. They deserve the best health care possible, as soon as possible.

Today's hearing will enable us to understand more about patient safety and how scientific research and new technology can boost efforts to prevent patients from contracting serious infections while they are hospitalized.

A number of VA hospitals are among the worst in the United States in terms of inflicting preventable infections on their patients. Hospital-acquired infections are a serious public health problem that affects patients in hospitals all across the country. In the worst-performing hospitals, which includes some VA hospitals, up to ten percent of patients are harmed by such infections.

A few years ago, a state agency in Pennsylvania analyzed millions of hospital records and found that the in-hospital mortality rate among patients who contracted infections was about five times higher than among patients who were not infected. Research has shown that most of these infections are preventable if hospitals and medical personnel adhere to systematic prevention measures. This starts with essential steps such as thorough, repeated hand-washing and isolation of infected patients. However, hand hygiene and other commonsense measures have been only partially successful.

We are fortunate to have with us this morning three physicians who are experts in the field of preventing hospital-acquired infections. As far as that goes, we have three doctors who are Members of these two Subcommittees this morning, and they are experts in their own right. We also have representatives from two companies that have developed new tools and technologies to prevent infections in hospitals. I look forward to learning more about the science behind fighting harmful hospital-acquired infections, and I am particularly interested in how the VA health care system, the largest integrated health care system in America, could deploy scientifically proven technology and practices with the goal of setting the highest standard of patient safety in all of its hospitals.

Thank you, Mr. Chairman, and I will yield back.

[The prepared statement of Mr. Smith of Texas follows:]

PREPARED STATEMENT OF FULL COMMITTEE
CHAIRMAN LAMAR S. SMITH

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Research has shown that most of these infections are preventable if hospitals and medical personnel adhere to systematic prevention measures. This starts with essential steps such as thorough, repeated hand-washing and isolation of infected patients.

However, hand hygiene and other common-sense measures have been only partially successful. We are fortunate to have with us this morning three physicians who are experts in the field of preventing hospital-acquired infections. We also have representatives from two companies that have developed new tools and technologies to prevent infections in hospitals. I look forward to learning more about the science behind fighting harmful hospital-acquired infections.

I'm particularly interested in how the VA health care system, the largest integrated health care system in America, could deploy scientifically proven technology and practices, with the goal of setting the highest standard of patient safety in all of its hospitals.

Chairman BUCSHON. Thank you, Chairman Smith.

At this time I would like to introduce our witnesses. Our first witness is Dr. Chetan Jinadatha—how did I do—very well—the Chief of Infectious Disease Section at the Central Texas Veterans Health Care System in Temple, Texas. Dr. Jinadatha is also an Assistant Professor of Medicine at Texas A&M University Health Science Center. He is the President of the Texas Infectious Disease Society. Dr. Jinadatha is board-certified in infectious disease. He is also an active researcher in hospital-acquired infections, the role of environment in hospital-acquired infections, and the evaluation of no-touch disinfection technologies. Dr. Jinadatha completed his medical degree in India and his master's in public health at Texas A&M. Welcome.

Our second witness is Dr. Elaine Cox, Professor of Clinical Pediatrics. Dr. Cox trained at Indiana University School of Medicine and has been on the faculty in the section of pediatric infectious disease since 1995. She is currently serving as the Medical Director of Infection Prevention, Medical Director of the Pediatric Antimicrobial Stewardship, and a Safety Officer for Riley Hospital for Children at IU Health. In addition to these and other clinical duties, Dr. Cox has spent much time working on legislation that impacts children's health in the State of Indiana. Dr. Cox earned her undergraduate degree in biochemistry from Indiana University and her medical degree from Indiana University School of Medicine. Welcome.

Our third witness is Dr. Trish Peri. Did I get that right?

Dr. PERL. Perl.

Chairman BUCSHON. Perl. My eyes. I should have put my glasses on, I guess. Dr. Perl is a Professor at the Department of Medicine and Infectious Diseases and Pathology at Johns Hopkins University School of Medicine and in the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health. She is a Senior Epidemiologist for the Johns Hopkins Hospital—John Hopkins Medicine. Dr. Perl received her bachelor of arts and medical

degree from the University of North Carolina at Chapel Hill and a master's of science degree from McGill University in Montreal. She completed her residency in internal medicine at McGill University and a fellowship in infectious diseases and clinical epidemiology at the University of Iowa in Iowa City.

I now recognize Representative Todd Young from Indiana to introduce our fourth witness.

Mr. YOUNG. Thank you, Mr. Chairman. It is an honor to be here with you today. I would just like to say, you are a person of professional competence, high personal integrity and a good friend, so thank you so much for allowing me to introduce our witness, Jeffrey D. Smith, a Hoosier, a resident of Indiana's 9th Congressional District and President and CEO of Electro-spec, which is located in Franklin, Indiana.

Mr. Smith and I had an opportunity to visit briefly yesterday, and it was clear during that brief visit that he cares as deeply as I do about the health of our Nation's veterans and preventing hospital-acquired infections in our Nation's Veterans Hospitals.

He has been with Electro-spec since 1994 and held positions of increasing responsibility beginning as Vice President in 1994. Mr. Smith is also President and CEO of Steriplate LLC, an Indiana corporation he formed in 2013. It focuses on the design, development and implementation of antimicrobial finishes for medical and commercial applications. In May of 1997, Mr. Smith purchased the business from former owner David Yates and assumed the position of CEO and President at that time.

I want to thank you for your presence here today and your testimony about your promising work on potential veteran-saving technology. Thank you, sir.

I yield back.

Mr. BROUN. Would the gentleman yield?

Mr. YOUNG. Indeed.

Mr. BROUN. As a fellow Marine, I would like to correct a statement that you made. There is no such thing as a former Marine. Once a Marine, always a Marine.

Mr. YOUNG. I agree with the gentleman's comments. If the gentleman will yield?

Mr. BROUN. Certainly. Thank you.

Mr. YOUNG. I am told the taxonomy is, there is no such thing as an ex-Marine. There may be a couple of exceptions out there. But whatever. I am proud to be a Marine with you, and thank you. Duly corrected by the senior gentleman on the panel.

Mr. BROUN. Semper fi.

Mr. YOUNG. Semper fi. I yield back.

Chairman BUCSHON. Thank you. I now recognize the Chairman of the full Committee, Mr. Smith, to introduce our final witness.

Chairman SMITH OF TEXAS. Thank you, Mr. Chairman.

Mr. Chairman, I am happy to welcome Morris Miller from San Antonio, who is going to be testifying today.

As CEO of Xenex, Mr. Miller is responsible for the company's business strategy and oversight of day-to-day operations. Under his guidance, the company has grown and established itself as the world leader in UV room disinfection. After starting his career as an attorney, Mr. Morris served as co-founder and President/CEO of

Rackspace Hosting Inc., which now has over \$1 billion in annual revenue and a market cap in excess of \$5 billion. He is an alumnus of Phillips Exeter Academy, the University of Texas at Austin, and the Dedman School of Law at Southern Methodist University, as am I.

Mr. Chairman, I yield back, and we welcome Mr. Miller.

Chairman BUCSHON. Thank you, Mr. Chairman.

As our witnesses should know, spoken testimony is limited to five minutes each after which the Members of the Committee have five minutes each to ask questions.

It is the practice of the Subcommittee on Oversight to receive testimony under oath. Does anyone have a problem with taking an oath? Then if you would please stand and raise your right hand. Do you solemnly swear or affirm to tell the whole truth and nothing but the truth, so help you God? Let the record reflect that all the witnesses participating have taken the oath.

And at this point I will now recognize Dr. Jinadatha for five minutes for his testimony.

**TESTIMONY OF DR. CHETAN JINADATHA,
CHIEF, INFECTIOUS DISEASES,
CENTRAL TEXAS VETERANS HEALTH CARE SYSTEM**

Dr. JINADATHA. Good morning, Chairman Dr. Bucshon, Chairman Dr. Broun, Chairman Smith, Ranking Member Maffei and Members of the Subcommittee. I thank you for the opportunity to participate in this important discussion today. My name is Chetan Jinadatha, and I am the Chief of Infectious Diseases at the Central Texas Veterans Health Care System and an Assistant Professor in the Department of Medicine at Texas A&M University Health Science Center.

I currently serve as the President of Texas Infectious Disease Society. My area of research interest is reduction of hospital-acquired infections using technology including the effectiveness of ultraviolet disinfection.

It is reported that hospital-acquired infections cause 1.7 million infections and 100,000 deaths annually within the United States, costing health care systems \$30 billion to \$40 billion. Methicillin-resistant Staph aureus-related hospital-acquired infections alone cost \$9.7 billion annually. It is hard to predict the percentage of preventable hospital-acquired infections but most facilities aim for zero hospital-acquired infections.

Patients may harbor resistant organisms prior to admission and not have any signs or symptoms. However, the same patient may develop an infection from the organism that they came with or acquire a new organism during their hospital stay, thus resulting in a hospital-acquired infection.

The hospital environment includes surfaces in the patient room, equipment or the hands of health care workers who acquire it from touching other patients or surfaces. An estimated 20 to 40 percent of hospital-acquired infections in the United States have been attributed to cross-contamination by a health care personnel hands, either by direct patient or by touching contaminated environmental surfaces.

Recent literature has indicated that supplementing manual cleaning with disinfection technologies such as hydrogen peroxide systems or UV light technology systems decreased microbial burden on high-touch surfaces such as bed rails, call buttons, toilet seats in patient rooms.

Although the systems add cost and time to the disinfection process, the bacterial load reduction after using these systems effectively complements manual cleaning. Preliminary evidence suggests from a single center study showed a 52 percent reduction of *Clostridium difficile* hospital-acquired infection with the implementation of UV-based protocol. A federally funded, multi-center study in private setting is currently underway to evaluate the effectiveness of UV in reducing hospital-acquired infections.

Similarly, several studies that have shown decreased multi-drug-resistant organism acquisition and reduction in hospital-acquired infection rates after implementation of hydrogen peroxide system across hospitals. In comparing the hydrogen peroxide system to that of an ultraviolet system, hydrogen peroxide requires prolonged exposure time and ventilation system modification for aeration but disinfects better than UV. UV technology disinfection time is shorter than hydrogen peroxide but it has lower bacterial reduction on surfaces.

Hence, technologies such as ultraviolet or hydrogen peroxide have the potential to have an impact on transmission of pathogens in the hospital environment and possibly prevent life-threatening infections. A federally funded study is currently underway to evaluate the effectiveness of UV on hospital-acquired infection rates in four Veterans Affairs Medical Centers, one of which is mine.

In 2013, the Central Texas Veterans Health Care System initiated several patient safety initiatives to decrease the risk of developing hospital-acquired infection including the deployment of ultraviolet disinfection system after manual cleaning.

Reducing hospital-acquired infection requires a multi-prolonged approach. Interventions or technologies such as ultraviolet or hydrogen peroxide do not decrease the importance of rigorous hand-washing, isolation of appropriate patients, and other measures to prevent the spread of pathogens in hospitals. New technologies for prevention do not obviate the need for manual cleaning or antimicrobial stewardship. Health care professionals must work together with the patients to prevent the spread of antibiotic-resistant organisms in health care settings.

Meanwhile, further research is needed to ascertain the generalized ability of our studies and define the specific role of new technologies in hospital-acquired infection prevention. Emergence and spread of antibiotic-resistant bacteria is a significant public health threat. In addition to basic infection prevention and control practices such as hand hygiene and the use of isolation precautions, good antibiotic stewardship and use of supplemental technologies may provide effective and improved strategies to prevent the spread of health care-associated infections and create a safer environment for our patients.

Mr. Chairman, this concludes my testimony. I welcome any questions from the Committee.

[The prepared statement of Dr. Jinadatha follows:]

Dr Chetan Jinadatha is Chief of Infectious Diseases Section at the Central Texas Veterans Health Care System in Temple, Texas. He is also an assistant professor of medicine at Texas A & M University Health Science Center. He is the president of the Texas Infectious Diseases Society. Dr. Jinadatha is a board certified infectious diseases physician. He is also an active researcher in hospital acquired infections, the role of environment in hospital acquired infections and the evaluation of no touch disinfection technologies.

Chairman BUCSHON. Thank you, Doctor.
I now recognize our second witness, Dr. Cox, for five minutes.

**TESTIMONY OF DR. ELAINE COX,
PROFESSOR OF CLINICAL PEDIATRICS,
DIRECTOR OF INFECTION PREVENTION,
DIRECTOR OF PEDIATRIC ANTIMICROBIAL STEWARDSHIP,
RILEY HOSPITAL FOR CHILDREN**

Dr. COX. Good morning. On behalf of Riley Hospital for Children at IU Health, I want to thank all of you here for your continuing commitment to patient safety by focusing on hospital-acquired infections in all patients. Riley Hospital is a self-standing children's hospital with an 85-year history. We see about a quarter of a million patients a year and we are part Indiana University School of Medicine, which gives us a lot of opportunity for research and development of technologies.

So we have heard a lot of statistics this morning: nearly 2 million infections, 100,000 deaths, one in 25 of our hospitalized patients every day having a hospital-acquired infection. This results in about 7.5 million excess hospital days in our country every year, increasing our length of stays by about three to ten times over the expected.

When you look at cost, conservative cost measurements for direct cost are about \$5 billion to \$6 billion, and when you add in total costs, it is certainly upwards of \$30 billion.

But I don't think that these statistics necessarily clarify the entire picture of personal cost. So I work in a children's hospital and I will share with you that recently we had a baby, a newborn, in for heart surgery. Now, that takes two weeks to get out of the ICU and 4 weeks to get out of the hospital, minimum. This family had a 3-year-old at home that they were away from all these weeks. They finally promised their son they would be home for the week-end and they would spend time with him when the baby acquired a central-line-associated bloodstream infection, or a CLABSI. This set that baby's recovery back 6 to 8 weeks and devastated a 3-year-old at home. I think the personal costs suffered by these families that encounter these infections go far beyond the event itself and is not reflected in our statistics.

You know, fighting infection has always relied on prevention, whether it is from vaccination or the development of the bundle, which we now all use to prevent infections, as the Chairman said. We have used it at Riley. We have cut our CLABSI rate by 65 or 70 percent. But the question is, is that enough? Is that enough for any of our patients, our veterans all the way to our babies?

I think the other problem is that we have plateaued. What are our other strategies? Well, certainly we have a reaction position we can take. We can treat with antibiotics. That is kind of the horse already being out of the barn. By then, infection is already set up.

You know, antibiotics have changed the face of infectious-disease treatment in America, which has been great, but it has also led to the development of resistance. This is accelerating in our time, and it is directly due to antibiotic overuse and use, and there is no antibiotic we have currently that is impervious to the development of

resistance. These are important players in HAIs. They occur in about 16 percent of the events, and over infections that have susceptible organisms they increase length of stay by an additional 20 percent and cost by an additional 30 percent.

We use antimicrobial stewardship, we use isolation and we have slowed the development and spread of resistance but we haven't eradicated it, and CDC just recently came out and said that infection with these multi-drug-resistant organisms is an emerging threat to health care in the United States.

In light of all that, I think we do need to look at new technologies. We have used some things in the environment. Can we expand that? Can we get beyond 55 to 65 percent safe for our patients? I think we have known the effects of metals for years. Why can't we expand their use in the environment? And can we look at the patient level? Can we coat things like orthopedic rods and ventriculoperitoneal shunts and cardiac implants so that we can prevent infections at the patient level?

We have known about the germ theory since the mid-19th century. We have the Institute of Medicine report, "To Err Is Human," on patient safety since 1999 and yet we are still struggling. We are still only 55 to 65 percent safe for the patients in our environment who trust us to care for them.

The impact financially on the health care budget is severe and negative, and I think if we could whip this problem as much as possible, we could turn those resources to other initiatives for patient safety and patient quality of care and, above all, do no harm, as is our oath.

I thank you for this hearing.

[The prepared statement of Dr. Cox follows:]

Testimony for the of the United States Committee on Science, Space, and Technology
Subcommittee on Research and Technology

June 26, 2014

On behalf of Riley Hospital for Children at IU Health, let me begin by thanking you for your continued commitment to improving patient safety by focusing on hospital acquired infections (HAIs). For more than 85 years, Riley Hospital at IU Health has been one of the nation's leading children's hospitals. In fact, Riley was once again distinguished this year as the only nationally ranked children's hospital in Indiana by *U.S. News & World Report*. Each year, Riley provides care, support and comfort to 215,000 inpatients and outpatients from across Indiana, the nation and the world. Part of Indiana University Health, Riley enjoys a unique partnership with the Indiana University School of Medicine, giving our highly skilled physicians access to innovative treatments using the latest research and technology.

I am sure you are quite familiar with the statistics on HAIs: CDC estimates that there are 2 million infections every year in the United States with 100,000 attributable deaths. Every day, 1 out of every 25 patients in the US has a hospital acquired infection, resulting in at least 7.5 million excess hospital days and 3-10 times increase in length of stay. The conservative cost estimate is \$5-6 billion for direct costs and total costs calculated by the National Nosocomial Infection Surveillance System (NNIS) could range from \$30-100 billion per year. Whether the HAI is due to a blood or urinary catheter infection, surgical site infection, ventilator associated pneumonia, or clostridium difficile (c. difficile) from antibiotic therapy, there is tremendous cost to patients and families beyond any of the dollar figures noted above. Every day in America, families suffer from preventable events during hospitalization. Last spring, there was a newborn at our facility who had undergone heart surgery. His 3 year old brother was being cared for by extended family so that the parents could be at the bedside of their critically ill baby. All week, the parents had been promising big brother that they would come home on the weekend and take him to the zoo so he could spend time with them. Two days before the scheduled visit home, the baby got a central line associated bloodstream infection. He decompensated giving his parents more sleepless nights of fear and continued time away from the older child. The ripples felt by our patients due to these events are significant and have long lasting effects far beyond one admission.

The keystone in fighting infections has always been prevention. Vaccines have changed the practice of infectious diseases since the first endeavors by Edward Jenner and smallpox. Further advancements in infection prevention in the hospital occurred in 2006 with the Michigan Keystone project led by Drs. Berenholtz and Pronovost and their colleagues. By describing what is commonly known as the "the bundle"—a series of easy interventions used in combination that can decrease infection risk—and linking it to traditional prevention efforts such as hand hygiene and isolation, hospitals have succeeded in decreasing their HAI rates by 55-65%. At Riley, we have employed the bundle and since 2007, have decreased our central line associated bloodstream infection rate by close to 70% and have been steady at that rate for the last 3 years. And while these foundational pieces of care can never be abandoned, we appear to have reached a plateau on prevention with these techniques alone. There is a multitude of factors that contribute to our inability to further prevention: endogenous flora, human factors including non-compliance, recovery time, and need for ongoing devices to support life-saving technologies that have changed the face of medicine in America.

Our only other defense is a reactive position—to treat infections once they have already set up. While antibiotics have been critical over the last century to treat infectious diseases, their use has stimulated the development of multidrug resistant organisms. While this is not a new problem, considering methicillin resistance was first described in 1968, one year after the drug was introduced to the market, the rate of resistance development has been accelerated. This is directly due to antibiotic overuse and there is not a single antibiotic that has shown the ability to avoid resistance. While research continues, there is agreement by all parties that there are not enough antibiotics in the drug pipeline to effectively battle organisms like methicillin resistant staphylococcus aureus, vancomycin resistant enterococcus, vancomycin resistant staphylococcus aureus, and c difficile. These organisms are prominent players in HAIs occurring in about 16% of cases. These infections account for 20% longer length of stay and 30% increased costs over infections without resistance and the resultant mortality is high. Our current strategies of antimicrobial stewardship and isolation practices have slowed development and spread of resistance but have not eradicated it and the CDC considers MDRO infections as an emerging threat to United States healthcare.

In light of all these factors and the knowledge that many microbes come from the translocation of one's own bacterial flora, we need additional weapons in our arsenal to thwart the infections that pose significant danger to our hospitalized patients. To do that, we will need to consider new and innovative approaches to infection prevention that, although will not replace our traditional strategies, can potentially augment them and take us to the next level from where we are currently plateaued. UV light and metal coatings such as copper and silver have been used as disinfectants in water and on surfaces for years and their success has been clear. If we can take these technologies and look for additional clinical applications for patients, more infections could be prevented which would have additional downstream effects to slow the development of resistance. For example, the use of nanoparticle metal ions could be used to coat implantable devices in patients. These charged ions would act like a sword, piercing the cell membrane of organisms that land on the devices looking for an opportunity to cause infection. Once pierced, the cell becomes incapable of replication and dies, thereby disallowing infection to set up. Advantages over antimicrobial impregnated devices include no loss of activity over time since the antibiotic effect wanes over a period of weeks and no contribution to the development of resistance. Device related infections are major cause of morbidity and mortality as well as cost in surgical site infections. For infections such as spinal fusions, ventriculoperitoneal shunts (VPS), and cardiac repairs, the potential benefits are significant. If we take the case of one VPS infection, infection can go right into the central nervous system, an area where it could do massive damage. Management requires 2 surgeries and generally 3 or more weeks of antibiotics in the hospital for therapy. Opportunities to prevent the spread of infection up the catheter and across the valve into the central nervous system could potentially protect brain function in our most vulnerable of patients.

Despite the fact that the germ theory was described by Pasteur in the mid-19th century and the Institute of Medicine first published the *To Err is Human Report* in 1999, we continue to struggle with HAIs and their effects on the patients who trust us to care for them. Healthcare costs are severely and negatively impacted by infections that to a large degree should be preventable. To make further strides in our war on germs, we need to support new technologies permitting us to turn our resources toward other initiatives to meet our patients' needs and, above all, do no harm.

Bio

Elaine Cox M.D., Professor of Clinical Pediatrics, trained at Indiana University School of Medicine and has been faculty in the section of pediatric infectious disease since 1995. Her areas of clinical interest have included HIV, cardiovascular surgery and related infections, and device related infections. She is currently serving as the medical director of infection prevention, and medical director of pediatric antimicrobial stewardship, as well as Safety Officer for Riley Hospital for Children at IU Health. In addition to these and other clinical duties, Dr. Cox has spent much time working on legislation that impacts children's health in the State of Indiana.

Chairman BUCSHON. Thank you.
I now recognize Dr. Perl for your testimony.

**TESTIMONY OF DR. TRISH M. PERL,
PROFESSOR OF MEDICINE AND PATHOLOGY,
JOHNS HOPKINS SCHOOL OF MEDICINE;
PROFESSOR OF EPIDEMIOLOGY,
BLOOMBERG SCHOOL OF PUBLIC HEALTH;
SENIOR EPIDEMIOLOGIST, JOHNS HOPKINS MEDICINE**

Dr. PERL. I will start by turning on the microphone.

Chairmen Bucshon and Broun, Chairman Smith, Ranking Members Maffei and Lipinski, and distinguished Members of this Subcommittee, thank you for the opportunity to appear today.

I will share lessons learned from hospital attempts to integrate technology into clinical care and highlight the importance of using scientific assessment to ensure hospitals make cost-effective and evidence-based decisions to improve patient outcomes.

I am a Physician and a Professor at Johns Hopkins University and their Senior Epidemiologist, and I am also the former President of the Society of Health Care Epidemiology of America, which is the professional society that works around health care-associated infections and multi-drug-resistant organisms.

That aside, my job has allowed me to study novel technologies including no-touch technologies and to investigate outbreaks associated with new products and devices, i.e., in other words, the unintended consequences of using these devices in the health care environment.

The Committee should be aware that I am doing a large research study that is partially funded by the VA, and my husband is employed by the University of Maryland and the VA.

Health care-associated infections, as everyone has mentioned, are common and actually cause about half of the untoward events that occur in health care affect approximately four percent of all patients. As we have heard, they are costly to patients and to the health care system, and to prevent these health care-associated infections, we encourage hand hygiene, vaccination, isolation, and more and more integrating technology. Many novel technologies are introduced into the market every year. It is commonly difficult to determine the merit of each device or idea without independent, well-designed studies that look at their efficacy.

I would actually like to review two personal experiences of why we need to be thoughtful about using technology and how we need to approach our efforts to protect patients. Approximately eight years ago, we began a study at our institution and looked at a technology that vaporized hydrogen peroxide, an excellent disinfectant, into the environment. The goal is to disinfect surfaces that were potentially contaminated with bacteria despite terminal cleaning. The technology was intriguing and expensive yet there were unknowns including around patient safety and the impact on our other expensive equipment. Ultimately, we developed a study, and after testing in our intensive care units, we significantly decreased the risk of acquiring a multi-drug-resistant organism in the patients in those units. No risk to patients, damage to equipment or

the facility was identified. Hence, our recommendation to our leadership was to continue using this technology, and it was based on scientific evidence. We have subsequently showed that we can use this technology to disinfect surfaces of supplies that are in these rooms, they can be reused, and it leads to cost savings that help pay for this technology.

Another story is in mid-October 2004, our institution introduced a new mechanical valve needleless device, which is used on IV tubing. These are devices that decrease needle sticks among health care personnel. By April of 2005, approximately six months later, the catheter-associated bloodstream infection rate in our children's hospital had increased by 60 percent. Using fluorescent dye, we determined that these devices could not be cleaned using standard techniques. When we removed the device from our institution, our rate returned to normal. What seemed to be a very benign introduction of a nursing product turned into significant patient safety issue for our patients.

So in summary, health care-associated infections are a significant challenge for health care despite strides to date, there are huge opportunities to improve patient safety and we should begin and insist upon the basic infection prevention. However, there is a role for technology that can improve our processes and protect patients. This technology, while often tantalizing, can have unexpected consequences and we must be vigilant in our approach to its introduction.

Congress should continue its long history of supporting science, and this is an area where science needs to guide decisions so we are thoughtful about how to introduce and use technology. The health care community should develop standards to measure the effectiveness of new technologies like this new touch disinfection that are being discussed today so we can measure their efficacy in a standard fashion. Congress should consider funding learning labs or centers of excellence to evaluate these exciting products in the context of patient care using trained scientists. These labs consider the multiple issues that impact patients to assure we do not do harm. There is not a one-size-for-all solution, and this effort needs the expertise that will translate science into effective patient care.

Thank you.

[The prepared statement of Dr. Perl follows:]

Statement by Trish M. Perl, MD, MSc

Professor of Medicine, Pathology and Epidemiology, Johns Hopkins University
Senior Epidemiologist, Johns Hopkins Medicine

Hearing on the

Technology for Patient Safety at Veterans Hospitals

June 26, 2014

Subcommittee on Research and Technology and the Subcommittee on Oversight

Committee on Science, Space and Technology

United States House of Representatives

Chairmen Bucshon and Broun and Ranking Members Maffei and Lipinski and distinguished members of the Subcommittees, thank you for the opportunity to testify today and share my perspective on the use and limitations of technology to prevent hospital acquired infections and improve care. Today I will share some of the lessons learned from hospitals' attempts to integrate technology into clinical care with the goal of reducing hospital acquired infections and through these examples I will highlight the importance of using scientific assessment to ensure hospitals are making cost effective decisions that ultimately improve patient outcomes.

My name is Trish Perl and I am a physician and a Professor in the Departments of Medicine (Infectious Diseases) and Pathology at Johns Hopkins University School of Medicine and in the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health. I am currently the Senior Epidemiologist for Johns Hopkins Medicine. I am the former President of the Society of Healthcare Epidemiology of America. In my current role I am in charge of helping the institution have mechanisms in place to measure and prevent potential healthcare-associated infections or infections that result because of medical care or problem organisms or pathogens and multidrug resistant organisms (such as *Staphylococcus aureus*, methicillin resistant *Staphylococcus aureus*, *C. difficile*). The strategies to prevent infections or infectious complications from occurring include education of healthcare providers, developing best practices, facilitating behaviors, using technology including vaccination, novel products, and new design. In my role as a healthcare epidemiologist I have been involved in the study of novel technologies and investigating outbreaks associated with new products, i.e. the unintended consequences of the use of these devices. My comments will be focused on healthcare associated infections, epidemiologically significant organisms and the role of technology in their prevention.

1. Frequency and impact of healthcare-associated infections

Healthcare associated infections cause approximately half of all untoward events that occur to patients. A recent study by the Centers for Disease Control in Atlanta and published in the *New England Journal of Medicine* surveyed 183 hospitals (36% small, 44% medium and 20% large) and found that 4% of the 11,282 patients investigated had a healthcare associated infection.¹ These infections were more likely to be seen in large hospitals like the one where I practice. Pneumonia and infections after surgery (surgical site infection) were the most common and caused 22% each of the total number of infections. Gastrointestinal infections were the third most common infection and caused 12.1% of all infections. Infections associated with devices including intravenous catheters, bladder catheters and pneumonias related to intubation accounted for close to 26% of these infections. Translated into a national statistic, in 2011, over 648,000 patients had close to 722,000 healthcare-associated infections. Most interesting about

¹ Magill et al. Multistate Point-Prevalence Survey of Healthcare-Associated Infections. *NEJM* 2014; 370:1198-1208

this study and not surprising is that many of the patients with healthcare-associated infections were more likely to have a device (intravenous catheter, bladder catheter, endotracheal tube) in place on the day the infection was identified.

Another recent study that included close to 2 million patients admitted to hospitals in Pennsylvania in 2010 noted that the mortality of these patients with healthcare-associated infections was approximately 9% versus 1.7% in patients without a healthcare-associated infection.² Similarly, the average length of stay was 21.9 days in patients with healthcare-associated infections and 5 days in patients without a healthcare-associated infection.

This study is one among many that has looked at costs associated with these infections and found that the estimated average Medicare fee-for-service for hospitalizations among patients with a healthcare-associated infection was \$21,378 versus \$6,709 for a patient without a healthcare-associated infection. More importantly, 40% of patients were readmitted for any reason and 30.5% were readmitted for a complication or infection. In total, the average payment for a readmission was between \$8,940 and \$9,483 per patient for a total payment of between \$23 and \$28 million. Another group estimated the total, annual costs to the US for five major infections to be \$9.8 billion with infections.³

2. Measurement

I would like to make one comment about measurement of healthcare-associated infections. The CDC and professional organizations like the Society for Healthcare Epidemiology of America and the Association for Professionals in Infection Control and Epidemiology have partnered to develop and implement standard definitions and case finding strategies. These definitions have been in use since the 1970's and while they have evolved over time, this partnership between the CDC, professional organizations and healthcare personnel in hospitals has led to a robust system to identify these infections. Almost every acute care hospital in the US employs trained infection preventionists to use these definitions to identify infections. This provides us with data to follow trends, benchmark and identify problems. Why is this important? These systems have provided the healthcare epidemiology community with a powerful tool to assess the impact of our interventions.

3. Prevention Strategies

Prevention of healthcare-associated infections requires a team of trained professionals who have a "bundle" of strategies. In general, these include education of healthcare

² <http://www.phc4.org/reports/hai/10/docs/hai2010report.pdf>

³ Zimlichman et al. *Healthcare-associated infections: a meta analysis of costs and financial impact on the US healthcare system. JAMA Intern Med* 2013; 173:2039-46

personnel, development of policies to assure best practices to prevent infections, surveillance for infections and epidemiologically significant organisms and use of strategies to modify behaviors and instill a safe culture with strong leadership. This backbone requires interventions and practices that all healthcare personnel are expected to perform or comply with and include: hand hygiene, vaccination, use of isolation and barrier precautions and the use of technology in all forms. The use of basic infection control strategies has led to a significant decrease in healthcare-associated infections. The CDC's HAI Progress report published in 2012 reports progress between 2008 and 2012. The report reveals a 44% decrease in central line catheter associated infections and a 20% decrease in surgical site infections or infections occurring after 10 types of operations. Despite having many "tools" to prevent infections we have further progress to be made. Our challenge is to assure that we facilitate best practice by ensuring healthcare providers know what to do and why to do it; to insure that institutions have the proper equipment that is placed to facilitate appropriate behaviors and to provide them with data so they know how they are doing.

4. Novel Technologies

However, the healthcare environment is becoming increasingly complex and if one goes into patient rooms they are filled with monitors and complicated equipment. We also work in an environment where we are asked to do more with less. Hence, the infection control community is challenged to rely on standard infection prevention strategies and has introduced different types of technology to facilitate work and improve patient safety.

One of the most notable technologies has been the use of electronic surveillance systems that concatenate data from patient medical records and facilitate surveillance for healthcare-associated infections and can provide alerts to infection preventionists when there is an organism of concern or a potential problem. These technologies are used in addition to the patient medical record. At my institution it has allowed us to decrease the time doing surveillance and send practitioners to the wards to educate and plan interventions.

Beyond the electronic surveillance systems, many novel technologies are introduced into the market every year to protect either patients or healthcare personnel or to facilitate the work. There are three separate areas of particular interest in the current market—one is the use of technology to improve compliance.

- A. Compliance with basic practices such as hand hygiene, use of gowns and gloves when needed is commonly poorer than we would like for many reasons including poor knowledge, limited supplies, and inconvenience. Hence, technology that can automate measurement such as hand hygiene use is very intriguing.

- B. Second, the contribution of the environment to transmission of resistant or significant organisms is now recognized so there are a myriad of products and equipment that attempt to improve cleaning and even disinfect the environment because even in the best of circumstances traditional cleaning is not perfect. In fact, in addition to some of the issues associated with complex surfaces with many nooks and crannies that are difficult to clean, there is also the need for rapid turn over to assure patient access to beds in a high turnover job that is not viewed as prime. Plus, materials with antimicrobial properties are being applied to high touch surfaces or products that may be reused to decrease the risk of cross contamination to assist with this effort.
- C. The third is to sort through the myriad of products many of which are conceptually exciting and to assess them in a scientific fashion to assure that there are no unintended consequences as they are introduced into a clinical environment. Because of this dynamic environment, integrated solutions are needed to assure that we do no harm. For example, in a patient room we could potentially introduce copper clad surfaces and then coat other surfaces with silver nanoparticles. Soft surfaces such as linens could be impregnated with substances and novel cleaning disinfectants could be used leading to an untoward event.

Two personal experiences:

Approximately eight years ago we were approached by a company and asked to integrate a novel technology into our cleaning processes. This technology vaporized hydrogen peroxide, a very good disinfectant, into the environment. It in theory would help disinfect surfaces that remained with organisms despite what is called a terminal cleaning when a room turned over. The technology was intriguing, yet there were many unknowns including its limited use in healthcare and there were questions about patient safety but also the impact on the environment and other equipment. At the time Johns Hopkins had a much older facility and the rooms were small and cramped and we knew that in this imperfect physical environment, we could decrease the risk of acquisition of resistant organisms by additional means. Furthermore, the technology was extremely expensive so in this setting it was not possible to make a business case to our administration.

We proposed a study, after partnering with our clinical colleagues and brought in this technology into 3 of our intensive care units with the sickest and most high-risk patients. We did this because the science did not support the use of this technology except in the settings of outbreaks. This enabled us to address the concerns about patient risks and potential damage to equipment and the environment and to assure that our recommendations to leadership were based on scientific evidence. The trial lasted three years and was a true partnership between clinicians, infection prevention and the company. We demonstrated that this technology was particularly helpful when used in

rooms where the occupant was colonized or infected with a resistant organism.⁴ In this setting we reduced environmental contamination by 35% and more importantly the risk of transmission to patients from environmental contamination by 64%. We subsequently showed that we could use this technology to disinfect the surfaces of supplies. This allowed us to stop the practice of throwing out supplies that were in a room of a patient colonized or infected with an epidemiologically significant organism.

In Mid October 2004, our institution introduced a new mechanical valve needless device with positive pressure. These devices reportedly decrease needlestick injuries among healthcare personnel and facilitate nursing care.⁵ By April of 2005, the catheter associated bloodstream infection rates in the Children's Center had increased by 60%. Using fluorescent dye we demonstrated that these devices could not be cleaned using standard techniques and after discussion among various experts elected to remove the product from the healthcare environment. When we removed the device our rates returned to normal. Since this time multiple institutions have reported similar findings with these devices and most of these have been re-engineered without "positive-pressure" and have not been found to increase infections. Nonetheless, what seemed to be a benign introduction of a nursing product turned into a significant patient safety issue for the Johns Hopkins Hospital and our patients. The literature is replete of examples of this type of technology that lead to increased catheter associated bloodstream infections at other institutions and in their patients.

5. Summary

In summary, healthcare-associated infections are a significant challenge for healthcare and represent a portion of patient safety issues in hospitals and healthcare settings.

We know about these complications because we have a robust process to survey these infections and use trained professionals to measure them. This system provides people, congress and healthcare professionals with a barometer to measure our performance.

Despite the challenges in healthcare, there are huge opportunities to improve patient safety and like all professionals I will tell you that the basic processes of hand hygiene and evidence based practice are paramount. However, there is a role and need for technology to improve our processes and protect patients. This technology, while often tantalizing can have unexpected consequences and we must be vigilant in our approach.

Congress has a long history of supporting science and this is an area where science needs to guide our decisions. We need to be thoughtful about how to introduce and

⁴ Passaretti et al. *An Evaluation of Environmental Decontamination With Hydrogen Peroxide Vapor for Reducing the Risk of Patient Acquisition of Multidrug-Resistant Organisms. Clin Infect Dis* 2013;56:27-35
⁵ Maragakis et al. *Increased Catheter-Related Bloodstream Infection Rates After the Introduction of a New Mechanical Valve Intravenous Access Port. Infect Control Hosp Epidemiol* 2006;27:67-70

use technology to assure we protect patients. Congress can help in this and I strongly recommend that it help fund learning labs or centers of excellence to evaluate these exciting products in the context of patient care using trained scientists and consider the multiple issues that impact patients to assure that we do not do harm. This effort is complicated and needs expertise that will translate science into effective patient care.

Examples of different cleaning technologies for healthcare that are currently used, being evaluated or proposed⁶

Disinfectants & Cleaning tools:

- Demand-release chlorine disinfectants :
 - Chlorine dioxide
 - Sodium dichloroisocyanurate
 - Chloramine-t7
- Superoxideized water
- Microfiber mops
- Microfiber wipes

Soft Surface Technologies:

- Copper oxide impregnation
- Citric acid impregnation
- Organosilane-based quaternary ammonium impregnation
- Silver-impregnated yarn

Hard Surface Technologies:

- Copper and copper alloy cladding
- Silver iodide and modified polyhexamethylene biguanide coating
- Silver nanoparticle incorporation
- Triclosan incorporation
- Quaternary ammonium salt surfactant coating
- Microtopography surface
- Light-activated antimicrobial coatings
 - Cellulose acetate-containing toluidine blue O and rose Bengal
 - Silicon polymer-containing methylene blue and gold nanoparticles
 - Titanium dioxide coating

Whole room technologies:

- UV light
- Combination of ozone/uv light/hepafiltration
- Hydrogen peroxide vapor or aerosolization
- Titanium dioxide spary

⁶ Currie, B. (2013), Revisiting Environmental Hygiene and Hospital-Acquired Infections, IDSE, http://www.idse.net/download/HAI_IDSE13_WM.pdf

Trish M. Perl, MD, MSc

Dr. Perl is a Professor in the Departments of Medicine (Infectious Diseases) and Pathology at Johns Hopkins University School of Medicine in Baltimore, Maryland, and in the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health. She is Senior Epidemiologist for The Johns Hopkins Medicine.

Dr. Perl received her Bachelor of Arts and medical degree from the University of North Carolina at Chapel Hill and a Master of Science degree from McGill University in Montreal, Canada. She completed a residency in internal medicine at McGill University and a fellowship in infectious diseases and clinical epidemiology at the University of Iowa in Iowa City, Iowa.

She has extensive practical and research experience in the field of healthcare associated infections and resistant and epidemiologically significant organisms and is recognized globally for her innovation and research in the field and the use of research knowledge in the healthcare setting. Dr. Perl is the former President of the Society of Hospital Epidemiologists of America (SHEA) and has served on advisory panels for the IOM, the CDC and WHO and been a consultant to the NIH and ARHQ. She was the Courage Fund Visiting Professor in 2008-10. An active researcher, Dr. Perl has been a principal and co-principal investigator on multiple studies funded by the CDC, the Veteran's Affairs Administration over the years. She has authored or coauthored over 200 peer-reviewed articles. In addition, she has written multiple chapters and contributed to guidelines and policies relevant to healthcare associated infections at the institutional, state and federal level. She has been asked to help with management of international outbreaks including SARS and MERS CoV and consults with international governments on guideline development and strategies to prevent healthcare associated infections and antimicrobial resistance.

Chairman BUCSHON. Thank you, Dr. Perl.
I now recognize Mr. Smith for five minutes to present his testimony.

**TESTIMONY OF MR. JEFF SMITH,
PRESIDENT, ELECTRO-SPEC, INC.**

Mr. SMITH. Thank you, Chairmen Bucshon, Broun and Smith, Members of the Committee, and Congressman Young for that nice introduction. I am not nearly as eloquent as my doctors are on the panel so I might sneak a "y'all" into my testimony. We will see.

I am President of Electro-spec and Steriplate. What we do, we specialize in high reliability and highly functional electroplating of devices for the military, aerospace, medical and automotive industries, and the reason I am here today is to talk about a new technology that we have developed called Steriplate. Steriplate was designed specifically for medical applications, antimicrobial situations hopefully to make a dramatic impact in the transmission of HAIs.

But first I want to draw kind of an analogy to what the statistics that were shared with you previously. Imagine a Boeing 737 crashing every single day in the United States with 200 people on board and there are no survivors. Can you imagine what the general public would be? Can you imagine what the FAA would be dealing with? That is what we are dealing with with HAIs, just to put things in perspective. The Department of Health and Human Services has made this an agency priority goal for HAIs. They have new metrics in place with goals hopefully to be achieved by the year 2020. So it is a big issue obviously. Copper and copper alloy as well as antimicrobial metal coatings are the one continuous, sustainable method for reducing the bacterial burden that you have on surfaces, whether they are in body or out of body. Our Steriplate process, which I have some examples here for you, employs copper as one of the metals as well as another antimicrobial metal in the process, and it is designed specifically for again antimicrobial functionality but also by alloying in other metals, we designed a metal that has more tarnish resistance, corrosion resistance and wear resistance than traditional copper. The antimicrobial testing that we have done thus far specifically on the traditional HAI bacteria, E. coli, for example, we had a 99.9998 percent reduction. With MRSA, we had a 99.998 percent reduction, and similar results against C. diff and B. subtilis bacteria.

Another aspect of Steriplate that we have designed is using nanotechnology in the process to impart hydrophobic or hydrophilic surface. The hydrophilic surface is designed to provide an antimicrobial that is on touch surfaces outside the body. We are currently using this technology for surfaces that typically can be contaminated by touch or translocation as well. The hydrophobic aspect of Steriplate really was designed for in body, and what we are trying to do is repel typical solution in terms of blood, urine, cerebral fluid, whatever it may be, and the applications that we are working on right now in terms of implantable devices are everything from VP shunts to Baclofen pumps for cerebral palsy, scoliosis rods, access ports for dialysis, just to name a few, the traditional types of devices that have a high rate of infection associated with them.

Another aspect of this is also to potentially have a surface that is antithrombotic to prevent clotting as well, so an antimicrobial and antithrombotic surface.

But to summarize today for you, the time, cost and complexity associated with developing this technology is huge. You know, we are geared specifically to try to provide an answer to not just the Veterans Hospitals but hospitals across the United States. We are a small company. We have 85 employees. But we have reinvested about 30 percent of our net profit back into developing this technology. So it is really critical for us to be able to be here today to present our technology to share with you our findings as well as hopefully be able to solicit help from federal agencies like NIH, CDC, National Science Foundation, Veterans Affairs as well or any other federal agencies that might be able to help us continue to develop the technology behind Steriplate and hopefully antimicrobial surfaces in general.

Thank you very much.

[The prepared statement of Mr. Smith follows:]

Testimony of

Jeffrey D. Smith

President/CEO of Electro-Spec, Inc. and President of Steriplate, LLC

Submitted to the Subcommittee on Research and Technology

& the Subcommittee on Oversight

Committee on Science, Space and Technology

For the hearing entitled

Technology for Patient Safety at Veterans Hospitals

U.S. House of Representatives

Washington, D.C.

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Electro-Spec is a company engaged in the field of electroplating utilizing precious and semi-precious metal on devices and components in the aerospace, automotive, telecommunication, military and medical industries. Steriplate is a wholly owned subsidiary of Electro-Spec that is engaged in developing specialty metal alloys that have been shown to be antimicrobial in testing against specific types of bacteria known to cause Hospital Acquired Infections (HAI's). I would like to thank you for the invitation to present our exciting and potentially life-saving technology. In my testimony, I will address the following key points:

- 1.) The serious threat that is posed in the United States, concerning HAI's and the need for newer methods and technology to help combat the cost associated with treatment and prevention of the spread of infectious diseases.
- 2.) The ability of copper and copper alloys (**specifically Steriplate**) to provide a continuous antimicrobial surface to help prevent the spread of HAI's.
- 3.) The time, expense and complexity that exist in trying to engineer and develop new technologies that will address the ongoing issues in veterans hospitals and hospitals across the United States and the barriers associated with commercialization and market success.

A brief summary of the key points highlighted and emphasized in my testimony can be found at the end of this document.

My testimony today is based upon my metallurgical knowledge and background, as a business owner of Electro-Spec and Steriplate, and the infinite possibilities of utilizing metal as an antimicrobial finish in a variety of applications inside and outside the human body.

Electro-Spec (an Indiana company) specializes in high reliability and highly functional electroplating. Electro-Spec utilizes precious and semi-precious metal on ferrous and non-ferrous materials for the aerospace, military, medical, automotive and telecommunication industries. Electro-Spec utilizes state-of-the-art chemistries and equipment to electroplate some of the most demanding devices and components for its customers. Devices and components that go into space, military defense, implantable (life sustaining and life altering) or various telecommunication equipment, are just a few of the items that Electro-Spec is recognized as the preferred plating supplier for. With a customer base of Lockheed Martin, Raytheon, Boeing, Medtronic, Smiths Group, Energizer, Northrop Grumman, Honeywell and TRW, Electro-Spec is viewed as a strategic partner in the advancement of innovative equipment, devices and technologies.

Problem Statement

The United States is viewed as one of the most technologically advanced, innovative and forward thinking countries in the world. In fact, the United States is considered the global leader in medical innovation. Yet despite all of these advances in technology, the 4th leading cause of death in the United States is Hospital Acquired Infections (HAI's), something that plagues every nation in the world. The CDC reports in their most recent study that 1 out of every 20 patients treated in a hospital, will become infected with a Hospital Acquired Infection. Unfortunately, the most recent statistics of 183 hospitals showed 648,000 patients nationwide suffered 721,000 infections which lead to 75,000 deaths in 2011. This is equivalent to over 200 deaths per day (more than AIDS and Breast Cancer combined), associated to infection from various forms of bacteria, of which some are particularly resistant to antibiotic therapy and treatment. Hospital Acquired Infections result in a net increase in cost of \$43,000 per patient and an additional 19 days of hospitalization and result in 2.5 x increased likelihood of readmission within 30 days. The financial impact to the nation is estimated at over \$45 billion in trying to deal with infectious diseases.

HAI's are various types of infections that patients acquire while they are receiving care or treatment for another condition in a health care environment. HAI's can be spread or acquired anywhere care is being administered. The information referenced above through the CDC is specific to hospitals, but obviously HAI's can be acquired from inpatient acute care facilities, ambulatory surgical centers, outpatient centers, long term care facilities or even field hospitals. These infections are associated with various risk factors with the patient and the medical services rendered. Transmission of communicable diseases between patients and healthcare workers or even overuse of antibiotics, are other ways of acquiring HAI's. The U.S. Department of Health and Human Services (HHS) has identified the reduction of HAI's as an "Agency Priority Goal" for the Department. HHS has stated

that it is committed to reducing the national rate of HAIs by demonstrating significant, quantitative and measurable reductions in hospital acquired central line-associated bloodstream infections and catheter-associated urinary tract infections. Newly established goals for the reduction of HAI's have a target date of 2020 (HAI National Action Plan) and these goals are being supported by the U.S. Department of Labor, U.S. Department of Defense and the U.S. Department of Veterans Affairs, along with scientists, clinicians and health leaders.

Emerging Technologies

Many emerging technologies to help control HAI's have been developed and implemented in recent years. Everything from bleach wipes, to UV Light Disinfection machines, to hydrogen peroxide vapor machines have been utilized to control the spread of infectious disease and cross contamination. However, these methods are used to "treat" the source of contamination and do not pose a permanent and continuous method to controlling the HAI's. In certain situations, the surfaces can become immediately re-contaminated through human contact or contact with contaminated equipment. Microbes have the ability to reproduce rapidly in the right environment and can exist on surfaces for days, weeks or even months in the right environment. However, in order for the microbe to transition to a pathogen, it must be able to survive on surfaces for a sufficient amount of time while retaining its ability to be virulent or colonize a susceptible host after removal from the surface it was contacted with – thus resulting in inadvertent transmission. Many current methods for the removal of these pathogens treat the surface once, but don't provide continuous treatment or prevention. To date, the only recognized method for permanent, continuous and sustainable reduction in the bacterial burden of surfaces is copper.

In 2008 the United States Environmental Protection Agency (EPA) registered five families of copper-containing alloys as antimicrobial, establishing that products manufactured from one of these registered alloys can make public health claims wherein the label indication states that the alloys kill 99.9% (\log_{10} 3.0) of bacteria within two hours of exposure (1). It is anticipated that the solid antimicrobial copper surfaces will remain microbiocidal for the life of the product (>10 years). A variety of controlled studies have looked at the antimicrobial activity of copper surfaces against specific human pathogens (2,3,4,5,6,7,8). In fact solid copper surfaces have been found to be microbiocidal to well over 30 bacteria, fungi and viruses. Of the microbes listed in Table 1, five were evaluated in the studies used to grant the public health registration by the United States EPA. The public health claims granted illustrate the robust nature of the antimicrobial activity (9). Alloys granted registration contain greater than 60% metallic copper and were found to continuously kill greater than 99.9% of Gram-negative and Gram-positive bacteria within two hours of exposure even after repeated contamination illustrating how solid copper surfaces will inhibit the buildup of microorganisms between routine cleaning and sanitizing steps.

<i>TABLE 1</i>		
<i>MICROORGANISMS SENSITIVE TO THE ANTIMICROBIAL PROPERTIES INTRINSIC TO SOLID METALLIC COPPER</i>		
<i>Microbe</i>	<i>Reference(s)</i>	<i>EPA</i>

		<i>Registered</i>
<i>Acinetobacter baumannii</i>	(47)	
<i>Aspergillus flavus</i>	(96)	
<i>Aspergillus fumigatus</i>	(96)	
<i>Aspergillus spp.</i>	(96)	
<i>Campylobacter jejuni</i>	(28)	
<i>Candida albicans</i>	(47, 96)	
<i>Clostridium difficile</i>	(97)	
<i>Clostridium difficile</i> spores	(97)	
Carbapenem-Resistant <i>Enterobacteriaceae</i> (CRE)	(84)	
<i>Enterobacter aerogenes</i>	(87)	*
<i>E. coli</i> O157:H7	(87, 104)	*
<i>Escherichia coli</i> -NDM1	(93)	
<i>Fusarium culmonium</i>	(96)	
<i>Fusarium oxysporium</i>	(96)	
<i>Fusarium solani</i>	(10)	
<i>Fusarium spp.</i>	(96)	
Influenza A (including H1N1)	(53)	
<i>Klebsiella pneumoniae</i>	(47)	
<i>Klebsiella pneumoniae</i> -NDM-1	(93)	

<i>Legionella pneumophila</i>	(65, 66)	
<i>Listeria monocytogenes</i>	(105)	
Methicillin Resistant <i>Staphylococcus aureus</i> (MRSA)	(87)	*
<i>Methylobacterium spp.</i>	(76)	
<i>Mycobacterium tuberculosis</i>	(47)	
Norovirus	(94)	
<i>Penicillium chrysogenum</i>	(96)	
<i>Penicillium spp.</i>	(96)	
<i>Pseudomonas auriginosa</i>	(87, 96)	*
Rhinovirus	(11)	
Rotavirus	(11)	
<i>Salmonella enterica</i>	(28)	
<i>Salmonella typhi</i>	(79, 80)	
<i>Spingomonas spp.</i>	(76)	
<i>Staphylococcus aureus</i>	(87)	*
<i>Serratia marcescens</i>	(11)	
Vancomycin Resistant Enterococci (VRE)	(87)	*
<i>Vibrio cholerae</i>	(79, 80)	

(9) Information provided by Michael Schmidt, Ph.D – Dept. of Microbiology and Immunology – Medical University of South Carolina

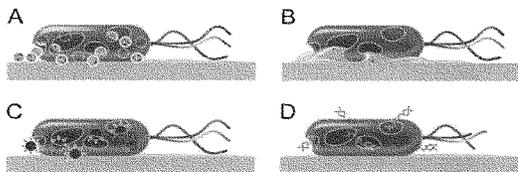
The public health claims attributed to solid copper have been evaluated to limit the bacterial burden found on commonly touched surfaces and objects in active healthcare environments.

What makes copper so effective?

The metal destroys bacteria by coaxing the organism to donate electrons to it, resulting in the production of free radicals within the cell. The result is damage to bacterial DNA and cell proteins.

The metal is also effective against viral and fungal pathogens. The entire process occurs quickly resulting in the collapse of a

population within minutes. **Thus, the likelihood that the population will develop resistance to this multifaceted mechanism of death is unlikely.**



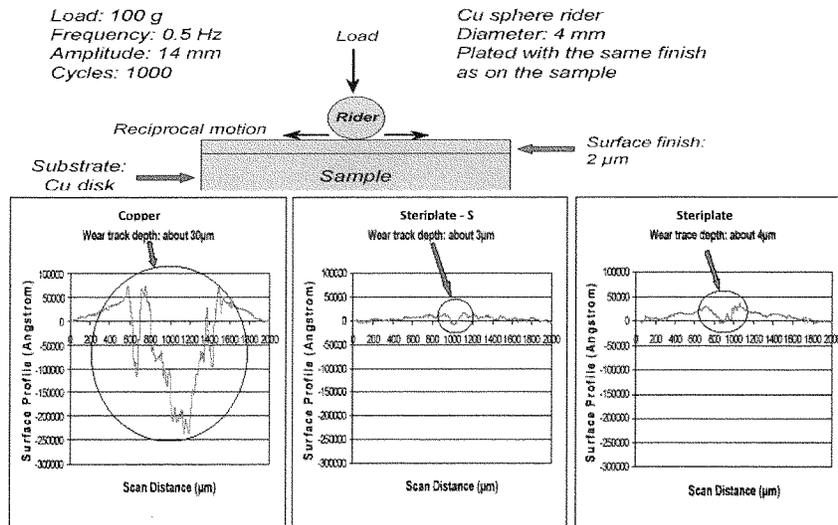
Antimicrobial Metal Technology

STERIPLATE™

What is Steriplate and how has it been shown to be antimicrobial? Steriplate is a tertiary alloy specifically designed for medical applications. Comprised of three distinctly different metals, Steriplate is an electroplated alloy that can be plated on numerous types of surfaces to impart antimicrobial properties on the surface and shown to provide the same benefits of copper. At the same time it gives better wear, corrosion, and tarnish properties than conventional copper can provide.

Wear Resistance: Steriplate exhibits excellent lubricity and wear properties

Sliding Wear Test Setup

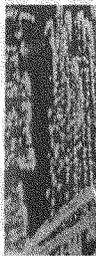


Corrosion Resistance: Steriplate exhibits exceptional corrosion and tarnish resistance in a variety of environments

- Artificial sweat (ISO 3160) : < 24 h
- Thioacetamide: >24 h
- NSS: Brass: 48 H to white rust, >122 H
- Humid atmosphere (85°C – 85% RH): >72Hrs
- Thermal Cycles: -50°C/+85°C, RH=70% for 10 days (1000 cycles):no discoloration
- Tarnish resistance: no color change after 4 H exposure at 150°C.

Antimicrobial Testing: Steriplate demonstrated antimicrobial properties in various efficacy testing

E. coli (CRE)



Escherichia coli BAA-249 (CRE)

This bacteria is a Gram-negative, rod shaped, facultative anaerobe commonly found in the gastrointestinal tract of mammals. Although most serotypes of this microorganism are harmless there are pathogenic groups of *E. coli* such as enterohemorrhagic (EHEC), verocytotoxin producing (VTEC) and Shiga-like toxin producing (STEC) that can cause a multitude of illnesses. *E. coli* is relatively susceptible to disinfection when dried on a surface, yet it can be a challenging microorganism to mitigate in solution.

**ANTIMICROBIAL
TEST LABORATORIES**

Page 1 of 2

Study Location: NIG4980
04APR2014

E. coli (CRE) BAA-249 JS.Z.2901 Study Results

Test Microorganism	Contact Time	Carrier Type	CFU/Carrier	Percent Reduction Compared to Control at Contact Time	Log ₁₀ Reduction Compared to Control at Contact Time	
E. coli (CRE) BAA-249	Time Zero	ATL Control	2.25E+05		N/A	
	2 Hours	ATL Control	1.00E+05			
		Steriplate w/ SAM - Petal Bow	4.35E+04	71.00%	0.54	
	24 Hours	ATL Control	2.45E+04			N/A
		Steriplate w/ SAM - Petal Bow	<5.00E+00	>99.9998%	>5.69	
		Steriplate w/ SAM - Petal Bow	<5.00E+00	>99.9998%	>5.69	

- Results showed that Steriplate demonstrates antimicrobial functionality against *E. coli* (CRE) at greater than 99.9998% reduction in 24 hours.

S. Aureus (MRSA):



Staphylococcus aureus 33592 (MRSA)
 This bacterium is a Gram-positive, spherical-shaped, facultative anaerobe. Staphylococcus species are known to demonstrate resistance to antibiotics such as methicillin. S. aureus pathogenicity can range from commensal skin colonization to more severe diseases such as pneumonia and toxic shock syndrome (TSS). S. aureus is commonly used in several test methods as a model for gram positive bacteria. It can be difficult to disinfect but does demonstrate susceptibility to low level disinfectants.

Results of the Study

Test Microorganism	Contact Time	Carrier Type	CFU/Carrier	Percent Reduction Compared to Control at Contact Time	Log ₁₀ Reduction Compared to Control at Contact Time
S. aureus (MRSA) 33592	Time Zero	ATL Control	3.20E+05	N/A	
		ATL Control	4.60E+05		
	6 Hours	Steriplate w/ SAMs - Nickel Base	1.00E+01	99.999%	4.66
		Steriplate w/o SAMs - Nickel Base	2.00E+01	99.996%	4.36

- **Results showed that Steriplate demonstrates antimicrobial functionality against MRSA at an 99.99% reduction in just 6 hours of exposure**

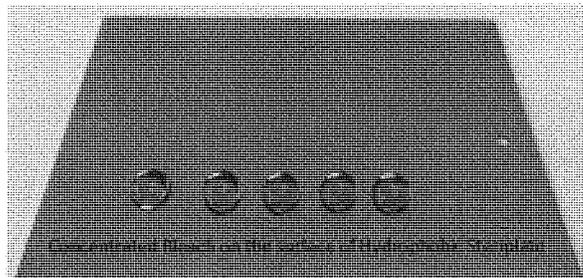
Biocompatibility Testing – Independent testing by a current medical customer

- Based upon the conservative assumption of patient exposure to a 2.5 gram component, these levels were below the levels of toxicological concern.
- MEM Cytotoxicity – Not cytotoxic

Not only does Steriplate have excellent metallurgical properties that can provide unique medical and environmental properties, the most unique property about Steriplate is that it can be made to be “hydrophobic” or “hydrophilic”. These properties provide a unique metallic surface that has antimicrobial properties, with even more unique capabilities outside or potentially inside the body.

One of the most critical aspects of making a surface resistant to microbial “loading”, is to ensure that the surface is dry. By making Steriplate hydrophilic (readily absorbing liquid), the surface will have a propensity to dry quicker, rather than “pooling” in certain areas of the surface. Most surfaces will dry unevenly due to this pooling of liquid and result in continued loading of microbes in these areas. Outside the body, Steriplate is designed to provide maximum antimicrobial efficacy through its alloy composition and hydrophilic properties.

Steriplate with hydrophobic (repel liquid) surfaces, has been designed for clinical trials on devices that are short term or long term implantable or semi-implantable devices traditionally susceptible to infection.



The additional benefit of having a hydrophobic surface that is antimicrobial, is the ability to repel blood, mucous, saliva, urine, perspiration and other contaminated “liquids” that obviously have the ability to transmit tremendous amounts of bacteria to various surfaces instantly. A secondary hypothesis that has not yet been trialed clinically, is that Steriplate in its hydrophobic state, may be able to act as an antimicrobial surface while imparting an additional benefit of being anticoagulant in preventing clotting and strokes. One of the current trials being discussed is to see if Steriplate can provide an antimicrobial surface that prevents thrombosis.

Electro-Spec and Steriplate are currently working with the IU School of Medicine on potential clinical trials on the following applications:

Application #1.)

Ventriculo-peritoneal shunts are commonly used devices in pediatric patients for hydrocephalus or intraventricular hemorrhages. The shunts remain in place for prolonged periods, sometimes for life, and must be tapped periodically for a variety of reasons. A certain percentage of these patients develop an infection at the site where the shunts interface with the cerebrospinal fluid. If the valve at the interface is coated with Steriplate this should reduce the incidence of infection, especially since data shows excellent bactericidal results with organisms that commonly infect pediatric shunts.

Application #2.)

For patients with severe scoliosis, the standard treatment is to install one or more metal rods in the spine for several months to years until the curvature is corrected. Sometimes the patient develops an infection around one of the rods. This type of infection can be very difficult to clear with a foreign body such as a rod in place and if it cannot be cleared, the only viable option may be to remove the rod. This may result in an incomplete fusion or instability of the spine and often creates further complication for the scoliosis treatment plan. If the rods were coated with Steriplate, this could reduce the incidence of infections, again with data that shows efficacy against the common organisms implicated in such infections.

Application #3.)

Baclofen pumps are used to administer Baclofen in a controlled dose to help patients suffering from spasticity from certain diagnoses like cerebral palsy. The pumps are implanted under the skin in a pocket in the abdominal area. Sometimes the pocket site around the pump becomes infected, necessitating surgical removal and prolonged antibiotic therapy. If the pump casing is coated with Steriplate, this could potentially reduce the incidence of infection in these patients.

Application #4.)

Adult dialysis patients are often fitted with a graft with an access port that is used to administer their hemodialysis treatment. Infection of these ports is quite common. The ports are currently made of plastic. If the grafts could be made of a metal and coated with Steriplate it could potentially cause a reduction in infections at the port site.

Where do we go from here?

In the United States, a high degree of statistical significance is needed to provide a convincing argument to U.S. federal government healthcare authorities, such as the Centers for Disease Control and Prevention (CDC), regarding the effectiveness of copper alloys in reducing microbial loads and cross infection in healthcare environments. For this reason, clinical trials at three major US hospitals were conducted between July 2010 and June 2011 with the intent of examining environmental bacterial loads, infection rates, and impacts on cross-contamination in intensive care unit (ICU) rooms retrofitted with copper touch surfaces versus rooms without copper surfaces (10).

The trials were funded by the U.S. Department of Defense (DOD) under the Telemedicine and Advanced Technology Research Center (TATRC), a subordinate element of the United States Army Medical Research and Materiel Command (USAMRMC). DOD has extraordinary interests in the potential for antimicrobial copper surfaces to reduce hospital-acquired infections because it wants to prevent hospital-acquired infections among thousands of its enlisted armed forces servicemen and servicewomen who have been injured in recent conflicts. TATRC, which funds a Military Infectious Disease Program was granted funds by the United States Congress to evaluate the antimicrobial effectiveness of copper, brass and bronze alloys. The studies were coordinated through the Advanced Technology Institute in Charleston, South Carolina (10).

Four-year clinical studies, published in 2013, were conducted at the intensive care units (ICUs) at Memorial Sloan-Kettering Cancer Center in New York City, one of the world's most prestigious cancer facilities, the Medical University of South Carolina, and the Ralph H. Johnson VA Medical Center in Charleston, South Carolina.

The studies revealed that the use of antimicrobial copper surfaces in the ICU's reduced the number of healthcare-acquired infections (HAIs) by 58% compared to patients treated in ICUs with non-copper touch surfaces. The antimicrobial copper surfaces were proved to work continuously.
 (*US Army Medical Research and Materiel Command under Contract No. W81XWH-07-C-0053. The views, opinions and/or findings presented here are those of the author(s) and should not be construed as an official US Department of the Army position.)

Concluding Thoughts:

Every day over 200 people die due to hospital acquired infections. To borrow an analogy from Dr. Michael Schmidt (Director of Office of Special Programs and Professor and Vice Chair – Dept. of Microbiology and Immunology at The Medical University of South Carolina), if a jet plane carrying 200 passengers crash every single day of the year killing everyone on board, there would be public outrage. The entire fleet of planes throughout the country would be grounded and there would be significant investigations by the FAA, Aircraft manufacturers, Dept. of Defense and many more public and private entities. It would lead to questions of national security and would probably put the nation's economy in a tailspin. This is happening in a different manner and it is happening at an alarming pace. However, this is preventable and the technology is emerging to support the National Action Plan developed by the Dept. of Health and Human Services. Companies like Electro-Spec and Steriplate have the technology, but lack the financial resources necessary to further promote and market this technology. If we continue to invest wisely and work in a collaborative environment, where promotion and support of these emerging technologies is established at all levels (public and private), there is no doubt that the United States could not only save precious lives, but dramatically reduce the incidence of infectious disease and continue to lead the world in medical innovations. The time is now, however, as antibiotics are becoming less and less effective. Bacteria are continuing to mutate and become less and less resistant to antibiotics. Scientists worldwide continue to try and decode the defense mechanisms of various types of bacteria in an attempt to slow these mutations. Providing an environment where these bacteria are constantly being "attacked" and cannot reproduce and multiply, is the foundation of control in an effort to prevent the spread of HAI's. Copper and Copper alloys have been proven to be antimicrobial and provide a continuous way to control and limit the environmental burden, found in all medical facilities.

Thank you for your interest and support in this exciting and life-changing technology to address HAI's. I welcome your comments and questions.

Summary of Testimony:

- The United States is the unquestioned leader in the world in terms of medical innovation and technology. This is predominantly due to a system that rewards innovation and fosters collaboration to facilitate life-changing, life-sustaining and life-altering technologies to improve our lives. Unfortunately, one of the leading causes of death in the United States and one of the most expensive to treat, are hospital acquired infections. The U.S. Department of Health and Human Services (HHS) has identified the reduction of HAI's as an "Agency Priority Goal" for the Department. HHS has stated that it is committed to reducing the national rate of HAIs by demonstrating significant, quantitative and measureable reductions in hospital acquired central line-associated bloodstream infections and catheter-associated urinary tract infections. A new National Action Plan has been established this past year with significant goals to achieve by the year 2020. Federal and private funding will be necessary to meet these goals. The task will be difficult, but innovation is the backbone of small businesses, research institutions and the American people.
- Many emerging technologies to help control HAI's have been developed and implemented in recent years. Everything from bleach wipes, to UV Light Disinfection machines, to hydrogen peroxide vapor machines have been utilized to control the spread of infectious disease and cross contamination. **However**, these methods are used to "treat" the source of contamination and do not pose a permanent and continuous method to controlling the HAI's. In certain situations, the surfaces can become immediately re-contaminated through human contact or contact with contaminated equipment. Microbes have the ability to reproduce rapidly in the right environment and can exist on surfaces for days, weeks or even months in the right environment. However, in order for the microbe to transition to a pathogen, it must be able to survive on surfaces for a sufficient amount of time while retaining its ability to be virulent or colonize a susceptible host after removal from the surface it was contacted with – thus resulting in inadvertent transmission. Many current methods for the removal of these pathogens treat the surface once, but don't provide continuous treatment or prevention. To date, the only recognized method for permanent, continuous and sustainable reduction in the bacterial burden of surfaces is copper. In 2008 the United States Environmental Protection Agency (EPA) registered five families of copper-containing alloys as antimicrobial, establishing that products manufactured from one of these registered alloys can make public health claims wherein the label indication states that the alloys kill 99.9% (\log_{10} 3.0) of bacteria within two hours of exposure(1). It is anticipated that the solid antimicrobial copper surfaces will remain microbiocidal for the life of the product (>10 years).
- Steriplate is a tertiary alloy specifically designed for medical applications. Comprised of three distinctly different metals, Steriplate is an electroplated alloy that can be plated on numerous types of surfaces to impart antimicrobial properties on the surface and provide the same benefits of copper. It provides better wear, corrosion, and tarnish properties than conventional copper. Additionally, Steriplate can be made to be hydrophobic or hydrophilic to impart additional properties to a variety of surfaces, devices and products (inside or outside the body).

- Antimicrobial surfaces offer a continuous way to control the environmental burden associated with various types of pathogens. Through the Surgical Care Improvement Project and the National Action Plan through HHS, hospitals and medical facilities have increased their level of hygiene and adopted best practices to levels previously unseen. However, it is intuitive to argue that any process or technology that augments or supplements the effectiveness of patient hygiene and routine cleaning will most definitely lead to lower rates of HAI's. The continuous antimicrobial effect of copper and copper alloys only enhance and complement the best cleaning practices required of medical facilities.

End Notes:

- 1.) **United States Environmental Protection Agency.** 2008. EPA registers copper-containing alloy products. <http://www.epa.gov/opp00001/factsheets/copper-alloy-products.htm>.
- 2.) **Noyce, J. O., H. Michels, and C. W. Keevil.** 2006. Potential use of copper surfaces to reduce survival of epidemic methicillin-resistant *Staphylococcus aureus* in the healthcare environment. *J Hosp Infect* **63**:289-97.
- 3.) **Quaranta, D., T. Krans, C. Espirito Santo, C. G. Elowsky, D. W. Domaille, C. J. Chang, and G. Grass.** 2010. Mechanisms of contact-mediated killing of yeast cells on dry metallic copper surfaces. *Appl Environ Microbiol* **77**:416-26
- 4.) **Warnes, S. L., S. M. Green, H. T. Michels, and C. W. Keevil.** 2010. Biocidal efficacy of copper alloys against pathogenic enterococci involves degradation of genomic and plasmid DNAs. *Appl Environ Microbiol* **76**:S390-401
- 5.) **Weaver, L., J. O. Noyce, H. T. Michels, and C. W. Keevil.** 2010. Potential action of copper surfaces on methicillin-resistant *Staphylococcus aureus*. *J Appl Microbiol* **109**:2200-5.
- 6.) **Wheeldon, L. J., T. Worthington, P. A. Lambert, A. C. Hilton, C. J. Lowden, and T. S. Elliott.** 2008. Antimicrobial efficacy of copper surfaces against spores and vegetative cells of *Clostridium difficile*: the germination theory. *The Journal of antimicrobial chemotherapy* **62**:522-5.
- 7.) **Wilks, S. A., H. Michels, and C. W. Keevil.** 2005. The survival of *Escherichia coli* O157 on a range of metal surfaces. *Int J Food Microbiol* **105**:445-54.
- 8.) **Wilks, S.A., H.T. Michels, and C.W. Keevil.** 2006. Survival of *Listeria monocytogenes* Scott A on metal surfaces: implications for cross-contamination. *Int J Food Microbiol* **111**:93-8.
- 9.) **MICHAEL G. SCHMIDT, PH.D, ANDREA L. BANKS, M.D., AND CASSANDRA D. SALGADO, M.D. M.S.** 2014. Role of the Microbial Burden in the Acquisition and Control of Healthcare Associated Infections: The Utility of Solid Copper Surfaces **4**:23-25.
- 10.) **MICHAEL G. Schmidt, Cassandra D. Salgado, Kent Sepkowitz, Joseph John, Robert Cantey, Hubert Attaway, Katherine Freeman, Peter Sharp Harold Michels** 2013. Copper Surfaces Reduce the Rate of Healthcare-Acquired Infections in the Intensive Care Unit – **Chicago Journals**
- 11.) (Agency for Healthcare Research and Quality August 2010. Adult Hospital Stays with Infections due to Medical Care. HCUP (Healthcare Cost and Utilization Project) statistical brief #94; Martin, J. 2011. Pennsylvania Health Care Cost Containment Council, February 2011. (<http://www.phc4.org/reports/hai/09/docs/hai2009report.pdf>)

Jeffrey D. Smith

Jeffrey D. Smith is president and CEO of Electro-Spec, Inc., an Indiana corporation located in Franklin, Indiana. Electro-Spec has been in business since 1959 and is an employee-owned company which emphasizes teamwork and collaboration in every aspect of its operation.

Smith holds a Bachelor's Degree in Government and Professional Administration from the University of Notre Dame and has been with Electro-Spec since 1994. He has held positions of increasing responsibility, beginning as Vice President in 1994. In May of 1997, Smith purchased the business from former owner David Yates and assumed the position of CEO/President at that time. In 1994, Electro-Spec employed eight people and had approximately \$1 million in revenue. By 2002, Electro-Spec grew to employ 40 people with revenue of approximately \$5 million. In 2003, Electro-Spec suffered a devastating fire that destroyed the entire facility. Unfortunately, there was nothing salvageable and everything was lost in the fire. Smith decided that it was time to reinvent the company and invested millions of dollars in new equipment and automation to build the most state-of-the-art plating facility in the United States. Because of efforts to recover from the fire, Electro-Spec was awarded the Indiana Blue Chip Business Award in 2004, and Smith was awarded Businessman of the Year by the City of Franklin in 2004. In 2012, Electro-Spec purchased the plating division of Interconnect Devices located in Kansas City, KS and relocated its operations to Franklin, IN.

Today, Electro-Spec is a multi-national company employing 85 employees with sales over \$12 million. The company recently purchased a new 50,000 square foot facility in 2012 and completed its relocation in 2013. Through reinvestment and innovation, Electro-Spec is committed to helping restore Indiana to its historic position as a leader in precision manufacturing.

Electro-Spec is recognized as one of the leading specialty plating companies in the United States. The company offers services throughout North America and has enlarged its customer base to include companies in Asia and Europe. Electro-Spec is a supplier to a wide range of high-tech industries including RF/microwave, aerospace, military, medical and automotive.

Jeff Smith is also president and CEO of Steriplate LLC, an Indiana corporation he formed in 2013, which focuses on the design, development and implementation of antimicrobial finishes for medical and commercial applications.

Smith currently holds a provisional patent application for the Steriplate technology (US Serial No. 61/895,644) and is in the process of filing a utility patent application for the Steriplate technology, once additional testing has been completed.

Under the leadership of Jeff Smith, Electro-Spec has received state and national awards and recognition for the quality of its products. Among these awards are:

- Indiana Industrial Operators Association – Manufacturer of the Year 2014
- Indiana Dept. of Environmental Management – Environmental Stewardship Award
- Indiana Dept. of Environmental Management – Partners for Pollution Prevention
- Numerous awards and recognition from Lockheed Martin, Raytheon, Medtronic, NASA

Electro-Spec is a member of:

- National Association of Surface Finishers
- Indiana Industrial Operators Association
- Indiana Manufacturers Association
- Indiana Chamber of Commerce
- US Chamber of Commerce

Chairman BUCSHON. Thank you very much, Mr. Smith.
I now recognize Mr. Miller for five minutes to present his testimony.

**TESTIMONY OF MR. MORRIS MILLER,
CHIEF EXECUTIVE OFFICER,
XENEX DISINFECTION SERVICES**

Mr. MILLER. Good morning. Thank you, Chairman Smith, Chairmen Broun and Bucshon and other distinguished Committee Members. It is an honor to be here today.

Every year, HAIs cost \$20 billion and kill 100,000 Americans, more than breast cancer, auto accidents and HIV combined. This is a devastating problem, so I wanted to share some good news with the Committee. Hospitals that use our germ-zapping robot kill pathogens and drug-resistant superbugs and their infection rates have dropped more than 50 percent. I am joined today by Dr. Mark Stibich, who along with his Xenex co-founder, Julie Stachowiak, both hold Ph.D.'s in epidemiology from Johns Hopkins. They founded Xenex to stop hospital-associated infections.

Just two years ago, scientists were unsure the role of the environment in the passage of the infections from patient to patient. Over the past two years, we know without a doubt that these pathogens and superbugs exist on bed rails, remote controls, nurse call buttons, telephone handsets. These superbugs are microscopic. We have spent—I have spent a lot of time with housekeepers over the past two years. These are some of the hardest-working Americans you have ever met. They cannot do the task that is assigned to them in the time that they have. They clean but they cannot disinfect every surface, and they never know whether they have eliminated the microscopic superbugs. Now in our hospitals, they clean and then they use our Xenex robots. We call them housekeeping heroes.

My written testimony has every detail of our proven, peer-reviewed outcome studies in journals like American Journal of Infection Control. To summarize, we have seen a sustained 53 percent reduction in C. diff infections. We have seen a sustained 56 percent reduction in MRSA, also known as staph infections. Just this week, two VAs told us, Muskogee, 50 percent drop in overall infections, Iowa City, 30 percent drop in C. diff. This is the only technology of its kind that has shown this ability to impact rates.

Now, since 1901, we have known that we can use ultraviolet light put out by low-intensity narrow-spectrum mercury bulbs to disinfect things like water. In the hospital where room turnover time is critical, they are too slow. The Xenex robot uses full-spectrum, high-intensity pulsed xenon bulbs to create UV light and destroy the DNA of bacteria in four ways. The light is 25,000 times brighter than sunlight. Disinfection takes about five minutes. The pathogens have no defense.

At the end of 2013, more than 200 hospitals including 26 VA Hospitals now utilize the technology. How do we know the results that have been peer-reviewed and published? Because our customers purchase the devices, they achieve the results. They were so excited that they decided to publish them.

Just recently, a new customer, an infection preventionist from a California hospital, came to me. They had an outbreak in their labor and delivery suites. Sixty mothers and their newborns, didn't ask for it, all got MRSA. They were fighting it. They were following all of the CDC guidelines. They couldn't stop it. In desperation, they called us. We sent over one of our employees. The employee began disinfecting the rooms. Within three days, the outbreak stopped. There have been no more infections since.

So the next logical question I would think is, well, what is the cost of technology like this? It is about \$1 per patient day. And the return on the investments for a 36-month use of the robot, the hospitals tell us it pays for itself in about four months.

So one of the questions you asked was, what can Congress do? On Hospital Compare, which is a Web site that you all insisted on sharing data, insist on more data, specifics on MRSA, C. diff, VRE and the other infection rates that we know are preventable. To the extent that you can, don't pay for preventable infections, and a little bit outside the box, incentivize hospitals. If you gave them \$1 to \$1.50 per patient day that they could bill through to use this advanced disinfection, this would give patients the disinfection they need and don't know to request.

In 1968, Congress mandated that automakers install seatbelts. In 2012, seatbelts saved over 12,000 lives. If Congress mandated the proper disinfection of these hospital rooms, we could save that many lives in two months.

I feel pressure every day because 5,000 Americans are infected and 273 die. We have the technology to save them. If you or a loved one ever has to go to a hospital, you would like to know that your hospital or procedure room would not make you sick.

Let us work together to prevent millions of infections and save 50,000 lives a year. Our veterans, their families and all Americans deserve no less.

Thank you.

[The prepared statement of Mr. Miller follows:]



Testimony of

Morris Miller, CEO

Xenex Disinfection Services

"Technology for Patient Safety at Veterans Hospitals"

Before the U.S. House of Representatives
Committee on Science, Space, and Technology
Subcommittee on Research and Technology
Subcommittee on Oversight

June 26, 2014

Technology for Patient Safety at Veterans Hospitals -- Summary

1. Healthcare Associated Infections are a significant national problem when measured by cost (\$20 billion per year), infections (2 million per year) and lives lost (10,000 per year). Many of these HAIs are caused by "Superbug" pathogens that are antibiotic-resistant and lack known cures.
2. Xenex has provided an effective response to HAIs through the development of its "Germ-Zapping" Robot, which disinfects rooms using pulsating broad spectrum ultraviolet (UV) light technology.
3. The Xenex robot emits pulsating light that destroys the DNA of the pathogens so they cannot reproduce or spread. The germ-zapping robot uses xenon gas to produce intense bursts of UV light which destroys the most difficult to kill pathogens (e.g. *C. diff.*) in four minutes.
4. Xenex represents a significant advancement in UV disinfection technology, which has historically relied upon mercury bulbs requiring significantly greater exposure times to disinfect (as long as 45 minutes for *C. diff.*).
5. Six (6) peer-reviewed studies have been published supporting the efficacy of the Xenex germ-zapping robot, including three where Xenex customers reported significantly reduced HAI rates after implementing the robot. No other UV technology has peer-reviewed studies demonstrating the impact of the technology on actual patient infection rates.
6. The Xenex germ-zapping robot is cost-effective and produces a significant ROI.
7. Congress has an opportunity to meaningfully improve the health of its veterans and citizens by promoting policies that accelerate the adoption of technologies that can effectively disinfect the hospital environment.

Testimony of Morris Miller, CEO

Xenex Disinfection Services

Thank you Chairman Smith, Chairmen Broun and Bucshon, Ranking Members Maffei and Lipinski and other distinguished Committee Members. It is an honor to be here today.

My name is Morris Miller. I am the CEO of XENEX DISINFECTION SERVICES, headquartered in San Antonio, Texas. With me today is Mark Stibich, one of our Co-Founders. Both Mark and Xenex co-founder Julie Stachowiak earned their Ph.D.s in epidemiology from the Johns Hopkins Bloomberg School of Public Health.

We are here today to present testimony about our Germ-Zapping Robot™ that kills the deadly pathogens that annually cause an estimated 2 million Healthcare Associated Infections, 100,000 deaths and \$20 billion in cost to the U.S. healthcare system. (<http://www.cdc.gov/HAI/surveillance/index.html>)

As requested, I will address how our company developed this technology and how it works to enable hospitals to prevent healthcare acquired infections known as HAIs. I will discuss the results of the usage of our robot and peer-reviewed studies explaining how more than 200 hospitals including 26 VA facilities use our technology with favorable cost-effective results. I will also discuss how Congress can motivate both VA and all hospitals to use this new cost-effective technology to eliminate pathogens that cause infections.

I will do so through 5 points:

1. The Problem
2. How Xenex Kills the Pathogens that Cause Infections
3. Proven Results of Xenex
4. Cost Savings and Return on Investment
5. Mandating Room Disinfection

1. THE PROBLEM

The Environment Matters

Over the past 2 years the evidence has become overwhelming that pathogens in the hospital environment cause the passage of infections from patient to patient. The scientific community now accepts as fact, that pathogens in the hospital environment cause infections. These germs are found on "High Touch" surfaces like bedrails, doorknobs, tray tables, remote controls, telephones and nurse call buttons, where they are easily transmitted to the patient.

These pathogens include "Staph" like MRSA (Methicillin-resistant Staphylococcus aureus), *C. diff* (*Clostridium Difficile*), VRE and new pathogens like MERS (Middle Eastern Respiratory Syndrome). These microorganisms are increasingly antibiotic resistant, and are commonly referred to as "superbugs." The resulting infections from these pathogens frequently involve significant pain and suffering, and many end in death.

Infections typically occur when hospitals place patients in patient and treatment rooms where a previous occupant was infected. Extensive cleaning with mops, buckets and wipes doesn't eliminate the germs. Some of these pathogens, like *C.diff*, can live up to 6 months on a hospital surface.

2. HOW XENEX KILLS THE PATHOGENS THAT CAUSE INFECTIONS

Xenex was founded to develop technology to stop the HAI epidemic by the fastest, most effective and most economical means possible. Our Germ-Zapping Robot™ has been repeatedly proven through peer-reviewed studies, trials and real-world usage to stop the spread of the pathogens that cause HAIs.

Ultraviolet (UV) light disinfection, using mercury lamps, has been around for decades. It can be an effective but often impractical disinfection tool, as the lamps must be used for a lengthy period of time. Our technology uses xenon gas to produce intense bursts of UVC light, resulting in a significantly faster disinfection cycle when compared to mercury disinfection systems. For example, Xenex kills *C.diff* spores in 4 minutes, as compared to 40 minutes for leading mercury products.

Xenon is an environmentally friendly inert gas. All other UV companies – and there are many – use toxic mercury bulbs. Every one. Hospitals are trying to eliminate the use of mercury in their facilities. Of the mercury providers, we cannot find a single provider, not a single one who has

published outcome studies demonstrating the effectiveness of their devices. We contend that is because the mercury systems take far too long to disinfect a single room and therefore it is not possible to disinfect enough rooms to bring down the bacterial load when you are using a mercury system.

The Xenex robot utilizes pulsed xenon to create UVC light – this flashing, germicidal light is 25,000 times brighter than sunlight. The bright light destroys the DNA of the microorganisms in 4 ways so they can't reproduce or mutate – they become harmless and unable to infect the next patient in that room.

Our device is simple to operate. A hospital employee wheels the robot into an empty patient room, places it on one side of the bed and turns it on. They return 5 minutes later, flip over the remote control, phone and other items to expose the surfaces to the light and run it for another 5 minutes. In just 5 to 10 minutes we have destroyed the microorganisms lurking in that room. That's it!

We developed this protocol in conjunction with MD Anderson and published our results in *ICHE (Infection Control & Hospital Epidemiology)*. That study showed that our robot was 20 times more effective in disinfecting the room than traditional cleaning.

3. XENEX RESULTS ARE PROVEN

Today I am presenting to you the results of 6 peer-reviewed and published studies proving the efficacy of our device. These studies were performed at world-class hospitals. Before and after implementing Xenex, the hospitals followed standard CDC and professional society guidelines for infection prevention – a bundled approach of hand hygiene, antibiotic stewardship, and cleaning with bleach when appropriate. **IT WASN'T ENOUGH**. When they incorporated our germ-zapping robots into their cleaning protocol, they experienced significant reductions in their infection rates. 3 of the peer reviewed studies show dramatic improvements in patient satisfaction and superior environmental disinfection of VRE and MRSA when Xenex is used in hospitals.

- HCAHPS improved by 2 quartiles at Trinity Hospital (*Risk Management & Healthcare Policy*)

- **MRSA Reduced by 99% in 22% faster time** period than manual cleaning (Biomed Central Infection Diseases)
- **Xenex 20x better than standard cleaning at removing VRE** from patient rooms (*Infection Control & Hospital Epidemiology*)

In the last year we have had 3 peer-reviewed studies demonstrating the effectiveness of our robots. These studies reported that fewer patients contracted *C.diff* and MRSA infections when our robots were used to clean patient rooms. These studies were:

- Cooley Dickinson Hospital Reduced **C.diff Infections 53%**: *American Journal of Infection Control (AJIC)*
- Cone Health Reduced **MRSA Infections 56%**: *Journal of Infection Prevention*
- Westchester Medical Center Saw **20% Drop in HAI Rates** (despite only treating a portion of rooms): *American Journal of Infection Control (AJIC)*

Most of our customers use our robots to disinfect their patient rooms, intensive care units, operating rooms, equipment rooms, procedure rooms, emergency rooms, public restrooms, nurse stations and changing rooms. The data shows that the more widespread use of the germ-zapping robots the better the results.

Our customers' stories are inspiring and show what is possible when dedicated people on the front lines of infection control are supported by their administration. An Infection Preventionist at a customer facility recently told me about a MRSA outbreak at her labor and delivery unit. They had 60 victims (women and their newborns who contracted MRSA infections) and didn't know what to do/how to stop it. On an emergency basis, we loaned the facility our robots, and three days later, the outbreak was halted.

The use of our robot in the Operating Room is producing very exciting results. A facility recently told us they went from 7 Surgical Site Infections (SSIs) to 0. That's meaningful. A study performed at Cambridge, a Harvard teaching facility, showed that our robot reduced surface contamination in the OR by 81%. It also showed that between-case contamination in the OR

continued to rise from case to case but was reduced to almost zero when the Xenex device was used between cases.

These reductions are not theoretical or in a lab. They are in real hospitals and have been peer reviewed.

4. BOTTOM LINE ON COST SAVINGS AND RETURN ON INVESTMENT

Treating a single HAI can cost \$4,000 - \$30,000. If just 2-3 infections are avoided per year the robot pays for itself. Another way to look at it: using our device costs approximately \$1.50 per occupied patient room day.

Hospitals using our device typically report a return on investment (ROI) in just 3 or 4 months and that's just the financial impact of reducing HAIs. Consider also the quality of life impact of the pain and suffering avoided by victims and their families.

Xenex has a direct impact on hospital financials including a shorter length of stay, an increase in revenue generating bed days, reduced re-admission, improved HCAHPS (Hospital Consumer Assessment of Healthcare Providers and Systems) scores, reduced chance of CMS penalties and reduced cost of care.

Dr. Jinadatha briefed you on his research that shows that our robot is significantly better than manual cleaning and we have a number of VA facilities reporting fewer infections. Dr. Jinadatha is also conducting numerous studies on the efficacy of the technology as well as other benefits such as room turnover time. We believe germ-zapping robots should be used system wide in the VA. Our Veterans deserve the highest quality care and state of the art technology. Especially when it saves both lives and taxpayer dollars.

5. INCENTIVIZING ROOM DISINFECTION

How can we motivate hospitals and VA patient care facilities to adopt new infection prevention technology?

Two potential starting points

First, some HAI data can be found online at the Hospital Compare website, which is a good starting point. Patients and their families can go online and see infection rates at the hospitals in

their areas. Requiring hospitals to report with greater infection specificity will result in an increased focus and effort by the hospitals to eliminate preventable infections.

Second, While CMS penalties are motivational; we don't think they are sufficient to force a change in infection control protocols. Value based purchasing can be effective. For example, if *C.diff* and MRSA infections were included in the value based purchasing criteria today, which they are not, we could stop a majority of the cases for about 20 times less than what it costs to treat them.

We believe the most effective means of combating HAIs is for Congress to provide an incentive for hospitals to adopt the strategies and technologies necessary to eliminate these infections. If hospitals are allowed to bill \$1.50 per occupied patient room day for advanced disinfection, you would quickly see a nationwide drop in the occurrence of HAIs. The ROI on this investment to the healthcare system could be 20-50 to 1 for each dollar spent.

Congress CAN incentivize hospitals to make room disinfection part of their standard of care. In 1991, Congress mandated automakers to include airbags, which to date has saved more than 14,000 lives. Stopping HAIs could save more lives than 23 years of airbags in less than 4 months.

Xenex brings you a proven solution to the problem of healthcare associated infections. We are working hard to deploy our robots nationwide and throughout our VA system. This solution would save money, destroy superbugs that cause infections, prevent suffering and save lives.

Every day delayed means another 274 people die in the U.S. and another 5,000 become infected! We have the technology, it is made in America, it has been used in U.S. hospitals and it is proven to work!

If you or your loved one ever has to go to the hospital I hope you will insist on the proper disinfection of your hospital room or procedure room with a germ-zapping robot. I hope you will support this initiative to get germ-zapping robots in use throughout our VA system and the entire federally supported healthcare system. Our veterans, their families and your constituents nationwide deserve no less.

Thank you.

Relevant Media Coverage

<https://www.youtube.com/watch?v=BOYhFE0rPKo> (CNN feature on Cooley Dickinson *C.diff* reduction)

http://www.salisbury.va.gov/SALISBURY/features/Xenex_UV_robot_enhancing_sanitizing_procedures.asp

<https://www.youtube.com/watch?v=yGJYAlYsUQM> (Xenex robot credited for reducing infections at Jack C. Montgomery Muskogee VA)

Published Studies

Implementation and impact of ultraviolet environmental disinfection in an acute care setting – *American Journal of Infection Control*

[http://www.ajicjournal.org/article/S0196-6553\(13\)01432-6/fulltext](http://www.ajicjournal.org/article/S0196-6553(13)01432-6/fulltext)

The effect of portable pulsed xenon ultraviolet light after terminal cleaning on hospital-associated *Clostridium difficile* infection in a community hospital – *American Journal of Infection Control*

[http://www.ajicjournal.org/article/S0196-6553\(13\)00249-6/fulltext](http://www.ajicjournal.org/article/S0196-6553(13)00249-6/fulltext)

Implementation of innovative pulsed xenon ultraviolet (PX-UV) environmental cleaning in an acute care hospital – *Risk Management & Healthcare Policy*

http://www.dovepress.com/articles.php?article_id=15602

Impact of a multi-hospital intervention utilising screening, hand hygiene education and pulsed xenon ultraviolet (PX-UV) on the rate of hospital associated methicillin resistant *Staphylococcus aureus* infection – *Journal of Infection Prevention*

<http://bjj.sagepub.com/content/early/2013/06/05/1757177413490813.abstract>

Evaluation of a Pulsed-Xenon Ultraviolet Room Disinfection Device for Impact on Hospital Operations and Microbial Reduction – *Infection Control & Hospital Epidemiology*

<http://www.jstor.org/stable/10.1086/658329>

Evaluation of a pulsed-xenon ultraviolet room disinfection device for impact on contamination levels of methicillin-resistant *Staphylococcus aureus* – *BMC Infectious Diseases*

<http://www.biomedcentral.com/1471-2334/14/187>

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As CEO, Morris Miller is responsible for Xenex's business strategy and oversight of day-to-day operations. Under his leadership, the company has grown quickly and established itself as the world leader in UV room disinfection. He is also the founder of Sequel and Cutstone Ventures, where he invests in and acts as an advisor to technology companies. After starting his career as an attorney, Morris was co-founder and President/CEO of Rackspace Hosting, Inc. which now has over \$1 billion in annual revenue and a market cap in excess of \$5 billion. He is an alumnus of Phillips Exeter Academy, The University of Texas at Austin and The Dedman School of Law at Southern Methodist University.

Chairman BUCSHON. I would like to thank the witnesses for their testimony, and reminding Members that the Committee rules limit questioning to five minutes. At this point the Chair will open the round of questions. I recognize myself for five minutes.

I want to start with Dr. Perl because one of my areas—I mean, I was a cardiovascular and thoracic surgeon, and other than orthopedists, probably the most infection-averse people in the hospital. It is obviously a disaster when it happens.

I have always been interested in when people come in how to, you know—what the patient themselves are bringing into the hospital and what the effect not just on hospital-based antibiotic use but outpatient antibiotic use as on the development of resistant bacteria, and I can say this because I have four kids and they have all kinds of ear infections and everything, and I have parents who are seniors who get antibiotics for all kinds of things that they probably shouldn't. Can you just discuss a little bit about maybe some of the things we might do in training infectious-disease professionals or internists about really how to manage that on an outpatient basis because I do think that has a significant impact on inpatient hospital infection.

Dr. PERL. Yes. Thank you for the question, and I think you are absolutely correct. The reality is that we don't have all the answers but what we can tell you is, even actually after one dose of antibiotics, you can develop resistant organisms. It has been best studied actually in the perioperative surgical setting where they have looked at that. So the challenge really is to really make sure that we use antibiotics appropriately, and to do that, we really have to enhance diagnostics. When we can differentiate whether somebody has a bacterial infection versus a viral infection, you can direct your therapy much more appropriately to limit the use of antibiotics, to define duration, course durations, and also to make sure that we simplify the antibiotic and really use one that we don't go more broadly than we need to.

So in terms of what we can do in the outpatient setting, it is almost like it is really common sense. Just make it simple. Make sure it is for the right thing and—

Chairman BUCSHON. And I think, don't you also think that it is a public education process? I mean, how many—every practicing physician has had a patient come in and they clearly have a viral infection but it keeps going and they just have a hard time believing that it is not something that needs to be treated with antibiotics. It is probably a multipronged approach, right? I mean, all of us that practice medicine know that phenomenon, right? And what happens is, the patient will ultimately get antibiotics from someone, and so how do we solve that problem? Maybe we can—is there a way we can bring this more to the public attention than we already are?

Dr. PERL. I don't have all of the answers but I would certainly tell you that there have been very effective public health campaigns that we could look to. I mean, we have been able to reduce smoking. We have been able to get people to use car seats. We have been able to get people to use seatbelts. So I think that there are clearly examples out there but it requires directed, concerted effort

from multiple groups, as you know, not only directed at health care professionals but also, as you point out, the public.

Chairman BUCSHON. Thank you. That is a big problem to solve.

Dr. Cox, are there different or more significant risks resulting from hospital-acquired infections at pediatric hospitals, such as IU Health, comparing children to adult hospitals? Is there a difference?

Dr. COX. So there is a difference. Children are not just short adults, certainly, but I think it is sort of interesting if you look at the two ends of the spectrum, sort of what you have at this end of the table, very young infants and very elderly patients. Their immune systems do not function quite as well as they do in the peak times of their life and so they are both at risk. I also think when you look at self-standing children's hospitals, there is a lot of referral patients, the very complicated problems. They require a lot of instrumentation. So you are a cardiovascular surgeon. All cardiovascular open hearts who have been on the pumps require a lot of instrumentation, no matter your age, and those are the risks that occur everywhere, even beyond children.

Chairman BUCSHON. Okay. Thank you.

And are there—at Riley, what is your review process you identify a hospital-acquired infection and do you think—has that morphed over time to change or improve the process to try to retrospectively find out why exactly that happened? Do you have information on that?

Dr. Cox. We do. So I think it is pretty typical, I think, of what is becoming the norm across the country. So it used to be nobody worried about this, it is just a little bit of extra antibiotic, until that became clear that that is not appropriate, and so now what hospitals do, including ours, is we have a standardized work flow. Every single infection in our hospital that is hospital-acquired is investigated. There is a form. Our nursing staff, our clinical nurse specialists who are advanced practitioners, sort of lead the information gathering. We review the chart. We interview everybody who took care of the patient in that 48 hours prior to the onset of the infection. Then we sit down as a multidisciplinary group, RTs, physical therapists, nurses, doctors, everybody, pharmacists, that we can get and we look at every piece of that puzzle.

What has happened over time is initially we had all these aha moments, right—oh, this shouldn't have happened, we should have used this technique, we didn't do that. I think over time as we have gotten better, we have sort of picked that low-hanging fruit, if you will, and we have cleared up those things that are easily done and so we have seen our infection rates go down. What becomes the challenge then, right, as we review these cases, the solutions get harder and harder and so we need to come up with new strategies that don't replace what we have always done but just augment them.

Chairman BUCSHON. Thank you very much, and my time is expired so I will recognize Mr. Swalwell for his questioning.

Mr. SWALWELL. Thank you, Chair, and good morning to our witnesses.

I wanted to start by first comparing our VA Hospitals to non-VA Hospitals across the country, and I just want to go witness by wit-

ness. Yes or no, to your knowledge, is there any known difference in any studies that you are aware of or anecdotally in hospital-acquired infections at VA Hospitals as compared to non-VA Hospitals. I will start with Dr. Jinadatha. Yes or no?

Dr. JINADATHA. No.

Mr. SWALWELL. Dr. Cox?

Dr. COX. No.

Mr. SWALWELL. Dr. Perl?

Dr. PERL. No.

Mr. SWALWELL. Mr. Smith?

Mr. SMITH. No.

Mr. SWALWELL. Mr. Miller?

Mr. MILLER. Don't know.

Mr. SWALWELL. And Dr. Jinadatha, are you aware of any studies underway or in your own experience working with patients in central Texas who are veterans with regard to HAIs?

Dr. JINADATHA. Yes, sir. As I mentioned in my testimony, we have a multicenter study where we are looking at how does implementation of UV technology affect outcomes such as hospital-acquired infections so we have two intervention sites and two control sites so we are comparing standard practice versus enhanced cleaning to see if that makes a difference.

Mr. SWALWELL. Great. And certainly in the last six months, we have learned a lot about Veterans Hospitals. Over the last four to five years, we have learned a lot about the veterans' claims disability backlog and most on this panel, I assume, would agree and most of my colleagues would agree that what we promise our veterans and how we treat our veterans is not matching up and that we promised them that we will take care of them and right now we have unacceptable backlogs in the care in some of these hospitals that have been highlighted like in Phoenix, for example, is outrageous and not what they deserve.

However, I am concerned that by having this hearing, we may be alluding to or implying that a problem exists that does not exist, and we could further hurt confidence that our veterans have in our health care system by implying that HAIs exist or occur at a greater rate at VA Hospitals than they do elsewhere, and so Dr. Jinadatha, is it your experience that you are not seeing at least in the central Texas system anything that would exceed your area, community or private hospitals?

Dr. JINADATHA. We are a very small facility, sir. We have 90 operating beds. So our infection rates when we compare it to our hospitals of our similar size, we are at national average or below national average on some of the measures.

Mr. SWALWELL. And Mr. Smith called for to study this not just for our Veterans Hospitals but for non-Veterans Hospitals additional federal funding for the CDC, for the NIH, for the National Science Foundation, and just going again across with the witnesses, would you agree that when we are making our budgeting priorities we should be increasing funding for those programs or cutting funding? So would you say increase or cut, Dr. Jinadatha?

Dr. JINADATHA. Since I am a researcher, increase.

Mr. SWALWELL. Okay. And Dr. Cox?

Dr. COX. Increase.

Mr. SWALWELL. And Dr. Perl?

Dr. PERL. Increase.

Mr. SWALWELL. Mr. Smith?

Mr. SMITH. Yeah, definitely increase.

Mr. SWALWELL. And Mr. Miller?

Mr. MILLER. Increase with incentives.

Mr. SWALWELL. And actually I am glad you brought up those incentives because Dr. Perl, starting this fall Medicare is set to impose penalties on hospitals that have poor infection control rates as an incentive to improve quality of care. Do you believe that this is a reasonable policy that will help reduce hospital infection rates? And then Mr. Miller, if you could follow up on that?

Dr. PERL. I am not a public policy researcher but I think that if it does go ahead, and in your opinion, that is the way the country should go, that we absolutely need to make sure that we don't have untoward consequences as a result of that. I mean, I think the risk is that we lose resources that may be supporting some of the practices that all of us have been talking about.

Mr. SWALWELL. Great. And Mr. Miller, is that an incentive you would support, and could you give us examples of others that you might support?

Mr. MILLER. So I think the—I am in support of including more in Hospital Compare data and increasing the penalties on value-based purchasing, making sure that things like MRSA, C. diff, VRE, Gram-negative staph, that those are all included in there so that the hospitals absolutely know they are not going to make money by making the patients sick. Is that responsive?

And then the second thing is, the other idea is, that's the stick, and then providing them with an incentive that enables them to say okay, I have got 20,000 patient days coming up, I can afford to buy the technology that is going to save you 20 to one on your spend, that is more direct.

Mr. SWALWELL. Thank you, Mr. Miller, and Mr. Chair, I yield back the balance of my time.

Chairman BUCSHON. I want to take a personal privilege and just comment briefly on what has happened at hospitals when Medicare decides not to pay for infections, for example, in cardiovascular surgery when you have a sternal wound infection. They decide not to pay for it. Now the hospitals that I have worked at now culture everybody when they come into the hospital and it is flooding our microbiology labs with nasal swab cultures and others to try to prove that indeed the infection came to the hospital with the patient. So your comment on unintended consequences of public policy is well taken.

I now recognize Dr. Broun for five minutes.

Mr. BROUN. Thank you, Dr. Bucshon.

By the way, Mr. Swalwell, there are some studies that show that some VA hospitals have higher infection rates than others, so there is data.

Back to my question. Dr. Jinadatha, as I alluded to in my remarks, the Veterans Health Care Administration executives in Washington apparently have access to detailed information about quality care and patient safety at individual VA hospitals all across the system but a lot of this information is not available to the pub-

lic. As the Chairman of the Oversight Subcommittee, I am a huge proponent of transparency and accountability. So when I hear that some VA hospitals exceed the infection rates of private-sector hospitals by 10 times or more, it seems especially important to alert veterans to the kind of medical treatment that they should expect to receive.

So why isn't the VA more forthcoming in providing objective information and data about individual patient outcomes in VA hospitals?

Dr. JINADATHA. Mr. Chairman, I am a frontline clinician and I usually focus on what I can do for the veteran that is at my hospital. Unfortunately, I will have to take it for the record and see what I can get back.

Mr. BROUN. Well, if you would, please, because I think it is imperative that patients know what the infection rates are, et cetera, as well as all patient outcomes at various hospitals.

I will ask all witnesses this. If the two technologies represented here today were implemented properly at all VA hospitals, how much would that improve current conditions? In addition to highlighting technologies that can help improve vet infections and death, what more can Members of this Committee, Members of Congress do to improve care for our veterans? And Mr. Miller, I know you offered some suggestions in your testimony so let us start over here on the other side with Dr. Jinadatha.

Dr. JINADATHA. Generalizing one center experience and applying it across all VAs, I don't know whether it will decrease or not because I believe every hospital is different. The patient population is different. The procedure done is different. The culture is different. So I don't know whether that will solve the problem. It might help some institutions and it may hurt some institutions, depending on the local conditions.

Dr. COX. You know, it is a difficult thing. I think first and foremost, people should know the kind of care they are entitled to get and what they should expect. I think accountability comes from knowledge, and I think educating the consumer as well to the role that they pay is critically important. We don't need an antibiotic for everything, and you know, you don't need a line in longer just because it is more convenient, and we need to consider how we prepare the entire care team, which includes not only the hospital-based personnel but the patient and family themselves, and I think that can go a long way. I think all of these strategies can augment it. The question is, are we ever going to get to zero, and I think that is a question we think probably not but can we be closer.

Mr. BROUN. Dr. Perl, if you would answer quickly, I have got some more questions and I want to go forward so I am about to run out of time in another minute and a half.

Dr. PERL. Well, just to sort of add to what has been said, we actually don't know. There have been not been any head-to-head studies, and I think this Committee needs to really recognize that there are incremental potential benefits or incremental potential detriments with any of these technologies, and they must be studied in a very rigorous way so that we make good choices.

Mr. BROUN. Thank you. And I will just—Mr. Smith, if you don't mind, I have got another question that I would like to ask Dr. Cox and Dr. Perl.

Both of you referred to the concept of the bundle and you referenced that in your testimony. It is an approach that appears to have helped in you all's own hospitals to decrease infection rates significantly. So what specifically does the bundle entail, and do you see this is something that can be implemented in the VA Hospitals? Dr. Cox?

Dr. COX. Yes. So the bundle is just a series of very easy things—wash your hands, scrub the hub, let it dry, access with aseptic technique, review every day if you need this device in place, and it is tweaked a little from device to device but that is the basic premise, and the beauty of it is, it is very inexpensive and it is very quick and it is very easy to do, and it should be able to be done not only in all hospitals and VA hospitals but in resource-limited countries as well.

Mr. BROUN. Dr. Perl, any addition to that?

Dr. PERL. No, I would agree with what the witness said. I would just add that actually there have been some data in VA hospitals looking at implementation of these bundles that have actually shown they are effective. So they are device-specific but they can actually give people very structured processes that facilitate good care.

Mr. BROUN. Thank you all.

Mr. Chairman, if I may take a point of personal privilege?

Chairman BUCSHON. Sure.

Mr. BROUN. As a family-care doctor, I just want to state that something I fought my whole medical career is overutilization of antibiotics in patients, and I have had patients come to my office, as all primary-care physicians do, for every earache, for every child or every sore throat, every cough, even bronchitis, most of these are due to viral illnesses or allergies, and antibiotics are not appropriate in that treatment modality for taking care of those patients. Patients have to be responsible too.

I have spent a career trying to educate my patients and my patients' moms and dads that antibiotics are not the solution to every fever, and whatever we can do, whatever you can do, whatever the medical community can do to try to help stop this overutilization of antibiotics is something that I focused upon my whole medical career and it is absolutely imperative that we continue to do that.

And one other final comment, Mr. Chairman, is that these hospital-acquired infections just—they are a whole plethora of things, whether it is a nosocomial pneumonia, as you very well know, whether it is Legionella that develops from a faulty air conditioning system, whether it is a catheter or an IV set or anything else or whether it is a heart valve, the problem has a whole wide variety of potential causes and so it is not a very simple thing to say the bundle is going to protect our patients from infections, and it is just absolutely—I thank you for helping us put together this hearing, and I yield back. I thank you for the leeway.

Chairman BUCSHON. Thank you, Mr. Broun. I now recognize the Chairman of the full Committee, Mr. Smith.

Chairman SMITH OF TEXAS. Thank you, Mr. Chairman, and let me direct my initial questions to Mr. Miller.

Mr. Miller, in your oral testimony today, you gave us the good news that on the whole, you felt like your device, your technology has reduced infections by about 50 percent, sometimes a little bit more, sometimes a little bit less. That is a phenomenal drop and has incredible consequences if you can reduce the infections by half. To take it to the next step, that means you are saving a lot of lives as well.

My question is merely—I would like for you to expand a little bit more on how effective your technology is in creating a bacteria-free environment, particularly compared to other methods that are used.

Mr. MILLER. Thank you. So I think this also responds to Dr. Broun as well. Before we ever released the product, we did testing at M.D. Anderson, and at M.D. Anderson, comparing post-cleaning rooms versus rooms that were cleaned with Xenex, we found that the cleaning didn't make a statistically significant difference. In other words, whether you clean the room or didn't clean the room, if you ran the robot, there ended up being 20 times less bacteria. This is on a colony-per-square-inch count at the end of the day, and where manual cleaning could never get rid of VRE in the environment, the robot was able to basically because it doesn't miss surfaces. It is always hitting it with its high-intensity UV light, and as a result of having a less bacterial count in the room, then the patient isn't subject to getting infection even if perhaps somebody forgets to wash their hands, maybe they won't infect the patient anyway. So getting that bacterial load way down, 20 times lower, is part of the key of the success of the device.

Chairman SMITH OF TEXAS. And Mr. Miller, also, what impediments have you encountered in trying to persuade others to use your technology and have a wider spread use of your technology?

Mr. MILLER. Overwhelmingly, the primary objection is, they say well, we just don't have enough budget to do that, we understand the benefit to the patients but we just can't afford it.

Chairman SMITH OF TEXAS. You said it paid for itself, I believe, in four months. How did you calculate that?

Mr. MILLER. That is what the hospitals report back to us, so our very—one of our very first hospitals said they got a 50 to 1 payback on the investment. They saved almost 1,100 patient days just after starting to use it in their ICUs.

Chairman SMITH OF TEXAS. What is the typical cost of this device?

Mr. MILLER. It costs about \$104,000 for the device and then it can treat somewhere between 30 and we have hospitals treating as many as 65 patient rooms per day, so on a per-room basis, it ends up being somewhere between \$2 and \$3.50 on the discharge of that patient.

Chairman SMITH OF TEXAS. That is amazing, and I appreciate your putting that in the record.

My next question is, what kind of obstacles have you encountered in developing even new processes or new technology?

Mr. MILLER. We are working as fast as we can. Dr. Stibich spends the Majority of his time thinking about what is the next iteration.

Chairman SMITH OF TEXAS. Have there been any regulatory problems that you have encountered?

Mr. MILLER. Not so far.

Chairman SMITH OF TEXAS. Okay. I am glad to hear that. I thought maybe you had. Okay.

The other question I have is, are there any other similar products like yours available on the market?

Mr. MILLER. As Dr. Perl referred to, there is hydrogen peroxide gas. It can absolutely work. It takes about three and a half to four hours including sealing the room, disinfecting it, but it does a good job. There is also the—there is devices that are built on mercury bulbs, and if you had two and a half hours, approximately two hours and fifteen minutes to disinfect a hospital room, those work as well. So basically it is a time difference, four hours, two hours and fifteen minutes, or about ten minutes.

Chairman SMITH OF TEXAS. Okay. Thank you.

And let me ask whatever panelist might be the best one to answer this question, and that is, is there any danger that bacteria will develop a resistance to these types of methods that are trying to create a bacteria-free environment? Mr. Miller, if you want to respond first, it looks like you are eager to.

Mr. MILLER. Yeah. We know of a—there is a recent study that showed that the bacteria do not develop a resistance to this kind of treatment.

Chairman SMITH OF TEXAS. Let me just see if any of the doctors on the panel have a comment on that as well. Is there any danger that bacteria would develop a resistance to this type of technology?

Dr. JINADATHA. We in central Texas evaluated the risk of developing resistance to mercury-based and xenon-based technologies, and in our preliminary report—and I want to disclose that it is not peer-reviewed yet. We did present this data at the APIC meeting that there was no development of resistance in our experiment.

Chairman SMITH OF TEXAS. That sounds to me like more good news, not only for you all but, more importantly, for patients in the hospitals themselves.

Thank you, Mr. Miller. Thank you all for your expert testimony today, and Mr. Chairman, I will yield back.

Chairman BUCSHON. Thank you, Mr. Smith. At this point I will ask unanimous consent to introduce the Wall Street Journal investigative articles about VA health care into the record, and note that in those articles, within the VA system itself, there does appear to be a wide variance on the incidence of hospital-acquired infections.

[The information appears in Appendix II]

Chairman BUCSHON. At this point I will recognize Mr. Lipinski for five minutes.

Mr. LIPINSKI. Thank you Mr. Chairman. I want to thank you and all the chairmen for holding this hearing. Although the issues we are talking about today are not unique to VA hospitals, we do owe it to our veterans to do all we can to take care of them for what they have given to us, for us, the sacrifices they have made. So I want to thank of our witnesses for coming to testify today.

The first thing I wanted to ask is, I wanted to ask Dr. Perl, I just wanted to get your thoughts—I know you are not an expert on the specific technology but the Xenex’s pulse xenon ultraviolet technology, do you believe this technology has been proven or do you believe more research is needed to test its potential benefits for reducing the rate for infections?

Dr. PERL. So I would actually say that there is preliminary evidence suggesting that it does decrease the microbial contamination in the environment. There is limited evidence that is not as rigorous as we would like looking at the impacts in the clinical setting—does it actually decrease infections—and that is really that translation that is needed.

Mr. LIPINSKI. Okay. I just wanted to get clarification there.

Something else I wanted to bring up. I know it has been discussed a little bit, and it was also in written testimony. Dr. Perl, I think many of us would like to think that there is a single solution for this problem; if only we adopted the right technology, health care-associated infections would be eliminated, and I am not talking just specifically on this issue but on all issues that we get here, that we discuss here in Committee. We are looking for that one breakthrough that is going to solve everything, and we know it is more complicated than that, especially an issue that I talk about very often here on this Committee is the aspect of human behavior. We could have the best technology in the world, if it not being used correctly or may be not used at all or we are just doing things that are bad, that human behavior can undermine the best technology that we have in place.

So Dr. Perl, can you speak of the importance of low-tech applications or processes such as training, clear communication and proper hand hygiene that would help in efforts to eliminate infections? Before you go, I just want to say everyone on the Committee knows I am always talking about the importance of having research in behavioral sciences, and behavior—we need to understand people’s behavior or else the best technology is not going to do us any good. So what can you add on that?

Dr. PERL. I think you have actually really stated the big challenge. Human factors, which is really this behavior is a huge challenge for us in health care. We are asking people to do multiple tasks with critically ill patients commonly, and including a lot of different things simultaneously, and so what you are always challenged with is making sure that people are doing everything that they need to do and that you facilitate those kinds of behaviors. So we could have all of the technology in the world but if people don’t know how to use it or how to integrate it into their work flow or they don’t have time to integrate it, then we are back to square one. So this whole issue of not only bringing in the technology but actually figuring out how to operationalize it once we know what works is going to be critical, and having done clinical trials in this arena, I can just tell you, it is much more difficult than it looks at face value. So it is a huge challenge as well as issue to think through.

Mr. LIPINSKI. Would you like to add something, Mr. Miller?

Mr. MILLER. Just two things. We agree with that. As part of a bundle, we never just deliver a robot. There is always robust train-

ing that goes to the people. That is number one. And then number two, three of the studies out of the six that I have shown you are actually outcome studies showing the reduction peer-reviewed in the published journal so not just showing reductions in pathogens in the environment.

Mr. LIPINSKI. Thank you. I will yield back.

Mr. JOHNSON. [Presiding] I thank the gentleman for yielding back. The Chairman has stepped out for a minute, and I have taken his place, so I will yield myself five minutes, Representative Bill Johnson from Ohio, and first of all, Dr. Jinadatha, thank you for being here today, and the entire panel. I recognize that you specifically did not have—you are not the reason why we didn't get written testimony. It was the bureaucracy, and quite honestly, I must state for the record that that is exactly what is causing so many Members here and so many Americans across the country concern is the bureaucracy in the VA that is not looking out for the best interest of our veterans, and I am not speaking about you specifically. But clearly, we have some major issues, and this attitude of, we will get to you when we get to you, and a lack of sense of urgency in addressing the concerns of the voice of the American people, which is the United States Congress, that is very, very concerning to me, but I do want to thank you for being here today.

And with that, let me ask just a few basic questions. What suggestions do you—and this is for the entire panel and we will just go left to right if that is okay. What suggestions do you have to prevent the outbreaks and the spread of diseases, for example, such as Legionnaire's?

Dr. JINADATHA. My belief is, it is about people, process and products, and I think if we master all the three, we probably could prevent a lot of our infections including Legionella.

Mr. JOHNSON. Okay. Dr. Cox?

Dr. COX. I think you have to go both from an environmental approach, particularly for things like Legionella. I think you have to take what Dr. Perl said and get rapid diagnostics so that you can intervene earlier because outcomes will be better, and then I think you have to keep looking at the individual patient level, what can you do there as well.

Mr. JOHNSON. Okay. Thank you. Dr. Perl?

Dr. PERL. You have asked actually a very loaded question, and it really requires a comprehensive approach, and I think we have identified the people issues. There are technologic solutions but there is also implementation that is critical in all of this, and it has got to be multidisciplinary and really involve everyone from front-line staff to leadership to really be effective.

Mr. JOHNSON. Thank you. Mr. Smith?

Mr. SMITH. Yeah, my belief is really, is it kind of two things. It is mindset, getting people to understand that HAIs are not inevitable, they are preventable. That is the big thing initially. The second thing, as Dr. Perl said, implementation or practice, and it is a collaborative effort. There is no one specific solution. It is going to take a collaborative effort of multiple technologies to be able to make the impact that we all want.

Mr. JOHNSON. Okay. Mr. Miller?

Mr. MILLER. And what we have seen is when the hospital administration makes a concrete commitment to patient safety, it is amazing what you can see.

Mr. JOHNSON. It kind of starts at the top, doesn't it?

Mr. MILLER. Absolutely.

Mr. JOHNSON. And we see that in many instances. That seems to be the key.

Dr. Jinadatha, do you know if the VA has specifically implemented any procedures to prevent Legionnaire's outbreaks like the one that happened in Pittsburgh? Has Legionnaire's been addressed specifically within the VA?

Dr. JINADATHA. I will start with my facility. We have a water safety Committee, and the chair is led by the top leaders from the front office, and we take every precaution to do whatever we can within our powers to make sure our veterans are safe from the Legionnaire's perspective at our facility.

As to the VA, I am not sure. I probably can get back to you. But I know it is a concentrated effort that is going on to do whatever we can to take care of that.

Mr. JOHNSON. Shifting gears just a little bit, kind of a different subject. You know, we have read stories about millions of dollars in performance bonuses paid to VA hospital managers even as patient wait times for appointments and other problems including HAIs festered. Should the VA explicitly and primarily base performance pay to health care managers on objective measures of care that our veterans receive? I would just like your opinions, and we will go left to right again. Dr. Jinadatha, do you have an opinion?

Dr. JINADATHA. No, sir.

Mr. JOHNSON. You don't have an opinion, or your answer is "no"?

Dr. JINADATHA. I don't have an opinion.

Mr. JOHNSON. Okay. Dr. Cox?

Dr. COX. I think with all the benchmarking data that we have now and accountability, I think that performance measures can be instituted in a lot of varieties including for bonuses.

Mr. JOHNSON. Okay. Dr. Perl?

Dr. PERL. I think there is a risk, and you have to really actually decide what you are looking for. The risk is that if it is a performance-related measure, that there is strategy to game the system, and so perhaps if you include those, you also want to have process measures that are a little bit harder to game, so I think that is the risk, and there are people who are much smarter than I that are thinking about those things.

Mr. JOHNSON. Got you. Mr. Smith?

Mr. SMITH. As a small-business owner, my life revolves around risk-reward and accountability, and so while I can't specifically comment to your question, in any situation, reward and accountability, I think, is a good thing.

Mr. JOHNSON. Mr. Miller?

Mr. MILLER. And I am cognizant of what Chairman Bucshon said earlier about unintended consequences. On the other hand, in all the companies that I have grown, we have 6,000 employees, there is nothing like incentives that are properly put in place to get them focused on what the administration of that entity wants to see hap-

pen, and then you measure it and then you re-measure it and then you adjust the incentives constantly.

Mr. JOHNSON. Well, thank you all, and as a 26-1/2-year veteran, I can tell you that I am concerned about the care that our veterans get. I appreciate the edification on this particularly interesting and critical subject that you brought to us today, and I agree, there is no such thing as a former Marine. Semper fi. I am Air Force, but thank you for your service. I yield back to the Chairman.

Chairman BUCSHON. I yield now to Ms. Esty for five minutes.

Ms. ESTY. Thank you, and I want to thank the Chairman again for holding this important hearing today, and I want to thank all our witnesses. We certainly all have a shared commitment to serving those who have served us, and some of the issues we have seen are a microcosm of what we see more broadly in hospitals. As one whose father sat in a prominent university hospital in 2005 where he had a staph infection induced in the hospital that greatly accelerated his demise, this is of particular concern to me and something I am aware of the consequences that happens.

A couple of things just at the outset. I think we have heard over and over again, and as I serve on the Transportation and Infrastructure Committee as well and on the Rail Subcommittee and I live in Connecticut, the importance is a safety culture because this has to do with human element of any of these technologies, any of these procedures are ultimately going to depend on human beings to implement them and so we are going to need to create a safety culture at each and every institution and we also need to frankly make it easy for people to do the right thing, and that is to be able to use the technology well for everybody involved in the situation to be able to do the right thing most easily and not force them to adapt to what we think they ought to do but actually recognize the reality of human behavior. So that being said, I think the best technology in the world, as we would all agree, is not going to do any good if people won't use it properly.

So to that end, I wanted to turn to you, Dr. Perl, to talk about how we do currently test technologies because in order to have appropriate testing, you want to reduce the number of variables but at the end of the day, we also have to look at human behaviors. Could you talk a little bit about that?

Dr. PERL. So I probably recognize one end of that spectrum, but in general, there are different kinds of technologies and what happens for drugs, for example, may be different than what happens for devices and could be different than some of the disinfectants that are being talked about and actually the current technology that has been discussed today as far as I understand is somewhat unregulated and there are no standards. So in general, there is a process that is usually run at the government level where the device or the drug is regulated. What happens in the FDA is a little different than what will happen in, say, the EPA for disinfectants. Once that goes through that process, then products are generally brought into the marketplace and commonly people will approach you and say I have this new device, I would like you to look at it, or I have this new product I would like you to look at it, and then how you approach it will be very different. What I do may be different a little bit than what Dr. Cox does, and we try and look at

the technology not only from a safety point of view but from an infectious risk point of view, from an engineering point of view, and if we think it is interesting, you can either pilot it or commonly you may say look, there are some risks and benefits and we would actually like you to go ahead—we would like to do a study, and then you try and determine sources of funding to go ahead and do these kinds of studies. Sometimes these are done under the rubric with IRBs, or institutional review boards, and sometimes they are actually done as quality projects. So that is in general the process.

It has been relatively difficult for us to get funding to test this kind of technology in a much more what I would call rigorous scientific way.

Ms. ESTY. And I can follow up on exactly that point, who currently is funding the research on these technologies, and if you have thoughts about who ought to be, whether we need a dedicated federal funding stream to deal with technologies. Obviously we do in the drug category. We have separate ones for medical devices. Is this something, given the importance of HAIs, that we ought to be looking at a funding stream dedicated to that in and of itself?

Dr. PERL. So I think that funding for HAIs has actually been—it has been greatly underfunded, given its importance, and we really do not have a good home. The NIH will say this is really not our area. They might fund resistance at a very basic science level. The CDC really does not have that much research funding, and what they have is minimal. Traditionally, we haven't gone a lot to the EPA, et cetera, and AHRQ has not been necessarily quite as interested in technologies but more implementation science. So there is not a good home, and I think that—I am not sure that another infrastructure needs to be created but certainly there needs to be an infusion into this arena to assure that we are studying things appropriately.

Ms. ESTY. And if I may, could I ask all five you if I can follow up afterwards, if you have thoughts about just deciding a home. I agree with you, it makes no sense to create a new agency. That would be foolish. But someone needs to take ownership of this issue clearly. It makes no sense to have no dedicated stream, given the expense, the mortality, the human expense, as well as the cost to our system. Someone needs to wrap their arms around this, take ownership, start developing metrics and have a funding stream that it gets the respect and resources it deserves.

Thank you all very much.

Chairman BUCSHON. I would agree with that.

I now recognize Mr. Collins for five minutes.

Mr. COLLINS. Thank you, Mr. Chairman.

Dr. Jinadatha, as Chief of Infectious Diseases, do you run your own blood testing lab and so forth in your hospital?

Dr. JINADATHA. We have our own pathology, microbiology and hematology lab, and of course, I have my own research lab.

Mr. COLLINS. So using PCR and molecular diagnostic equipment? If a patient comes in, you will do your own blood tests?

Dr. JINADATHA. Yes, we have.

Mr. COLLINS. Now, one thing I have been concerned about is—and I know you are not in Buffalo, but in Buffalo, our VA hospital was—it was discovered by the IG a year and a half ago. They were

reusing insulin pens. A very basic, you can't make this stuff up, reusing insulin pens. We had to test many thousands of patients to see if they had contracted HIV or hepatitis through the reuse of these insulin pens. We just discovered through a whistleblower that they were not properly sterilizing their instrumentation, I mean, not just by a little bit, and so the whistleblower contacted the Office of Special Counsel and now it just came out two days ago about instrumentation within the hospital not being sterilized, almost, again, something you can't imagine.

So what I really discovered is, coming out of the private sector, best practices are the heart and soul of quality, but in many cases, that means benchmarking. We have three great hospital systems in western New York: the Kaleida Health System, Catholic Health System and Erie County Medical Center. The VA was not benchmarking with any of them, and I can only use the word "arrogance." The arrogance of the VA system was, we are the best, we are the biggest. Well, they are anything but, and if you don't benchmark, how do you know what others are doing? Because, you know, not to say for sure but I can assure you, the other systems weren't reusing insulin pens on several patients. They were sterilizing their instrumentation.

So a real quick question. Do you do and do you have someone that does proficiency programs testing out your technicians on your molecular diagnostic equipment?

Dr. JINADATHA. We have a certification process, the CAP, which is the—

Mr. COLLINS. College of American Pathology?

Dr. JINADATHA. Yes.

Mr. COLLINS. So CAP is running your program?

Dr. JINADATHA. They come and inspect us, so does, I believe, IG and—

Mr. COLLINS. So with CAP, they are sending you the samples two or three times a year, influenza, whatever, and then they are scoring you?

Dr. JINADATHA. Yes. I believe we undergo CAP certification.

Mr. COLLINS. How is your score?

Dr. JINADATHA. Since that is not something I run, I don't know but—

Mr. COLLINS. Well, I am glad because that is an outside agency. CAP does a very good job.

Dr. JINADATHA. They kept us working, so I believe we are good on their benchmarks.

Mr. COLLINS. So does your system benchmark? I mean, are you making sure you have got best practices?

Dr. JINADATHA. We have a national infectious disease office that is located in Cincinnati, and we get directives, we get handed down best practices that we should be implementing, some of the examples that have been alluded to by the panelists are MRSA bundle, the MDRO program. We have a CLABSI reduction program and an antimicrobial stewardship program.

Mr. COLLINS. But is that coming down from on high to you or is your hospital reaching out to the others even in your area just to share information?

Dr. JINADATHA. Absolutely, sir. One of that would have been an example of how we instituted UV disinfection technology at our facility. So in our facility, which I can speak for, we do both. We take some of the best practices that are given to us from the national office. We also initiate on our own some best practices that I follow the literature and bring it into—try to bring it into practice.

Mr. COLLINS. Again, in Buffalo, I just don't—I wonder if any other panelist has a comment, not as a physician, but how could you reuse insulin pens? How could they be doing that? Or in the case of instrumentation, not sterilizing it. And it was really—the technicians didn't seem to care. They were going through the motions. I mean, does anyone else—it is almost rhetorical. Mr. Smith?

Mr. SMITH. Just a quick comment. You know, one of the questions before was practice, implementation, training people and so forth, and again, it is going to take a collaborative effort to have the favorable impact that we all want.

With our technology, it is not—it does not require training people. It is just simple implementation, whether it is in the touch surfaces outside the body or potentially inside the body. So this is a continuous type of technology that does not require training. And so thankfully, you take the human element out of that, the decision making—the poor decision making out of that aspect.

Mr. COLLINS. Thank you. I just would conclude by saying it is obvious our veterans deserve the best care. It has been very disappointing in the Buffalo area with a very large hospital, we have not delivered the best care, and I go back to—you know, I have sensed a level of arrogance within the VA that they just know best, and then when you show them they don't, they still say they know best.

So anyway, thank you, Mr. Chairman.

Chairman BUCSHON. Thank you. We need to bring this more to the public's attention. It does get out there some into the mass media. When we discuss funding for a lot of medical research, obviously there is a disparity between different disease processes within the funding stream, many of which is related to, in my view, for political reasons and for the fact that some things are on the front page and some things are not. This is one area that we have heard today that the dramatic impact on the people that we take care of in health care and how it most likely is very clear that we need more research and more public awareness of this problem because the impact, I think, can be dramatic.

So I would like to at this point thank all the witnesses for their valuable testimony and the Members for their questions. The Members of the Committee may have additional questions for you, and we will ask you to respond in writing. The record will remain open for two weeks for additional comments and written questions from the Members.

At this point the witnesses are excused and this hearing is adjourned. Thank you.

[Whereupon, at 10:49 a.m., the Subcommittees were adjourned.]

Appendix I

ANSWERS TO POST-HEARING QUESTIONS

ANSWERS TO POST-HEARING QUESTIONS

Responses by Dr. Chetan Jinadatha

**HOUSE COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY
SUBCOMMITTEE ON OVERSIGHT**

“Technology for Patient Safety at Veterans Hospitals”

Questions for the Record, Dr. Chetan Jinadatha, Chief, Infectious Diseases, Central Texas Veterans Health Care System

Questions submitted by Rep. Larry Bucshon, Chairman, Subcommittee on Research and Technology and Rep. Paul Broun, Chairman, Subcommittee on Oversight

1. The Veterans Health Administration) apparently has methicillin resistant staph (MRSA) prevention studies underway at four hospitals. UV light disinfection is the focus of at least one of them. Please supply details of the studies, including summary and objectives, description of any technology employed, target date for completion, (any) interim results, and plans to implement/follow up on the studies. For instance, if interim or final results indicate an effective means for preventing infections, will the methods be implemented at all Veterans Health Administration hospitals?

VA Response: Attached is the abstract which details the requested study. There are no reported findings to date. The study ends in April 2016.



zeber IIR 12-347.pdf

2. What is the Veterans Health Administration’s plan to reduce hospital-acquired infection (HAI) rates? Apart from the four studies alluded to above, what other technological or systems-based improvements is the Veterans Health Administration considering to prevent HAIs?

VA Response: The Veterans Health Administration (VHA) has developed and implemented various initiatives to reduce healthcare-associated infections (HAI), with prioritization of efforts in alignment with the Department of Health and Human Services National Action Plan. In fact, VHA has been at the forefront of implementing large-scale HAI prevention programs, most notably for prevention of MRSA (see below for a list of publications highlighting MRSA prevention program successes). For example, there has been a 72 percent reduction of MRSA HAIs in intensive care units (ICU) and 66 percent in non-ICU acute care settings since the initiative began in 2007. These published system-wide results contribute to the field of knowledge on HAI prevention in the U.S.

Select Publications:

a) Jain R, Kralovic SM, Evans ME, Ambrose M, Simbartl LA, Obrosky DS, Render ML, Freyberg RW, Jernigan JA, Muder RL, Miller LJ, Roselle GA. Veterans Affairs Initiative to

Prevent Methicillin-Resistant *Staphylococcus aureus* Infections *New England Journal of Medicine* 364:15; 1419, 2011.

b) Kralovic SM, Evans ME, Simbartl LA, Ambrose M, Jain R, Roselle GA. Zeroing in on MRSA: U.S. Department of Veterans Affairs' MRSA Prevention Initiative. *American Journal of Infection Control* 41; 456-8, 2013.

c) Evans ME, Kralovic SM, Simbartl LA, Freyberg RW, Obrosky DS, Roselle GA, Jain R. Veterans Affairs methicillin-resistant *Staphylococcus aureus* prevention initiative associated with a sustained reduction in transmissions and health care-associated infections. *American Journal of Infection Control* 41; 1093-5, 2013.

d) Evans, M., Kralovic, S., Simbartl, L., Obrosky, D.S., Hammond M., Goldstein, B., Evans, C., Roselle, G., Jain, R. Prevention of methicillin-resistant *Staphylococcus aureus* infections in spinal cord injury units. *American Journal of Infection Control* 41; 422-6, 2013.

e) Evans, M., Kralovic, S., Simbartl, L., Freyberg, R., Obrosky, D.S., Roselle, G., Jain, R. Nationwide reduction of healthcare-associated methicillin-resistant *Staphylococcus aureus* infection in Veterans Affairs long-term care facilities. *American Journal of Infection Control* 42; 60-62, 2014.

3. Has the Veterans Health Administration studied increased costs, lengths-of-stay, and in-hospital mortality rates associated with HAIs? If so, what are the numbers associated with those studies?

VA Response: No, VA has not specifically studied the impact of HAIs on mortality, length of stay, or costs within VA hospitals. The existing literature is quite robust regarding the critical importance of prevention, early recognition, and management of these events. However, our ongoing research focuses on how to best implement programs to reduce HAIs, with particular emphasis on catheter-associated urinary tract infections, multi-drug resistant organisms (antibiotic stewardship), surgical site infections, and ICU-associated infections.

4. Has Veterans Health Administration studied increased litigation/settlement costs emanating from HAIs? If so, please provide this information to the Committee.

VA Response: No, VA has not specifically studied the increase in either litigation/settlement costs as a result of HAIs.

5. Please provide institution-specific HAI rates for Veterans Health Administration hospitals for the most recent year.

VA Response: Infection rates in VA hospitals can be viewed and compared on the following publically available website: <http://www.hospitalcompare.va.gov/index.asp>.

6. Several references were made during our hearing to the need for more research into HAI prevention, ranging from biocidal technology to social/behavioral studies. Which research areas do you think are most important to address?

VA Response: Some research areas that are important to address include: 1) rapid diagnostics; 2) clinical effectiveness and improved patient outcomes of prevention modalities beyond the initial demonstration of the effect of the modalities on pathogens; and 3) development of large scale studies and/or reproducible results in multiple settings to assure validation and generalizability of any single center study.

Additionally, the VA Office of Research and Development is involved in several projects that address MRSA and other HAIs, including a dedicated Collaborative Research to Enhance and Advance Transformation and Excellence (CREATE) initiative on MRSA (<http://www.hsrdr.research.va.gov/centers/create/mrsa.cfm>).

Recently, the Society for Healthcare Epidemiology of America (SHEA) authored a paper outlining the major research areas in dire need. These are outlined in the table below and the paper is attached as a reference.

Table 1. Examples of High priority topics in infection prevention research identified by the SHEA Research Committee

Topic	Examples of specific areas for investigation
Healthcare-associated infections (HAIs)	Evaluate HAI prevention across the spectrum of healthcare especially non-acute care settings
	Evaluate approaches for dissemination and implementation of HAI prevention methods such as human factors research
Device-associated infections (CLABSI, CAUTI, VAE)	Examine the epidemiology of device-associated infections (DAIs) in non-ICU settings
	Test novel technology and strategies for DAI prevention such as impregnated devices and maintenance bundles
	Examine the reliability and validity of surveillance definitions in different patient populations and their impact on outcomes and practices
Surgical site infections (SSIs)	Compare various postoperative wound care strategies for reducing SSIs
	Assess the impact of an operating room checklist on SSI rates
	Evaluate patient-specific risk factor modification (such as smoking cessation) strategies for reducing SSIs
Multidrug-resistant organisms (MDROs) and <i>Clostridium difficile</i>	Assess transmission dynamics and novel interventions to prevent transmission in acute and non-acute care settings
	Evaluate the role of the environment and the impact of environmental disinfection on transmission
	Examine the role of laboratory technology to identify MDROs and guide infection prevention measures

Respiratory Viruses	Evaluate the effects of barrier precautions on respiratory virus transmission Assess the acceptability of N-95 masks for prevention of respiratory virus transmission Evaluate the role of novel diagnostics in preventing nosocomial respiratory viruses and identifying emerging respiratory viruses
Antimicrobial Stewardship	Evaluate the impact of antimicrobial stewardship programs on emergence of resistance, patient outcomes, and cost Explore the benefits of alternative methods for antimicrobial stewardship such as post-prescription review Assess the use of performance metrics for antimicrobial stewardship
Environment	Compare available touchless cleaning technologies for efficacy and acceptability Assess favored methods for surveillance of environmental cleaning Assess the role of hospital epidemiologists and infection preventionists in changing policy related to environmental cleaning



7. Do you find there to be management problems in the Veterans Health Administration system that contribute to increased HAIs and mortality rates? Is there something being done to change this?

VA Response: VHA recognizes that there may be local considerations of staffing, space, and infrastructure that could be optimized to enhance HAI prevention. However, at this time, VHA is unaware of management issues that could contribute to HAIs or mortality rates.

8. Do managers at the Veterans Health Administration get paid bonuses? If so, does the bonus system take into account the patients that have been cared for at the hospital, the HAI rate, and the mortality rate? If not, how are bonus amounts calculated?

VA Response: In accordance with VA policy, all employees who are covered under VA's performance appraisal program or proficiency rating system are eligible to receive performance awards for sustained performance on job responsibilities over the period of a rating year. The performance award amount is determined by a process which considers the performance rating attained, which includes many aspects of patient care. Performance plans are individualized, and senior executives are expected to look across a broad range of patient care indicators and identify areas where improvement effort is needed. This may include specific efforts to reduce HAI or to address underlying factors that may increase

mortality, but HAI and mortality rate targets have not been explicit elements of senior executive plans for the purpose of calculating bonuses.

Recommendations for Senior Executive award criteria are developed by VA's Corporate Senior Executive Management Office (CSEMO) based on the distribution of final ratings and available budget dollars. The Secretary makes final decisions on all Senior Executive award criteria to include rating levels eligible for awards, dollar amounts or percentage of salary amounts for awards, and organizational performance results eligible for awards.

9. Who do Veterans Health Administration managers report to? How often do they have to check in and what do they report? What standards are they held to?

VA Response: Senior Executives are VHA leaders who are either in the Senior Executive Service (SES) or Title 38 equivalent pay grades including Veterans Integrated Service Network (VISN) Directors and Medical Center Directors. All SES employees are covered by the Senior Executive Performance System. All Medical Center Directors report to an assigned VISN Director. Each of the 21 VISN Directors reports to the Deputy Under Secretary for Health for Operations and Management and meets at least once quarterly to review VISN performance.

10. A lot of knowledge about how to prevent hospital-acquired infections has been developed in the last decade. But hundreds of thousands of hospital patients are still injured each year by infections that are considered by many experts to be preventable. Why is this problem so difficult to solve?

VA Response: While it is true that a lot of knowledge has been gained in the last decade, consensus on the best practices for prevention of HAIs is not always available and knowledge from small studies is not necessarily generalizable to all situations. Furthermore, translating science into actionable, effective prevention programs needs to address the complexity of real-world settings such as hospitals that may not be an issue in controlled experiments. Another important barrier to solving the problem is that microbes evolve new antimicrobial resistances and new pathogens emerge. Regardless of all these issues, it does not mean that nothing can/should be done to reduce HAIs. (See the response to Question 2 above for examples of VA progress.)

11. Medicare has implemented financial penalties on hospitals that do not exceed thresholds for hospital acquired infections, with the thresholds and penalties increasing over time. State Medicaid programs and private sector insurance companies are also turning to financial incentives and disincentives to drive improvements in patient safety. Do you think these payment changes are constructive? Do you think these changes have been at least partly responsible for recent years' incremental improvements in infection rates?

VA Response: VA does believe that it is important to know if these major financial incentive/disincentive programs are effective at reducing actual HAI rates in the United States (as opposed to, for example, reducing the reporting or assessment of infections as health care-associated). It is difficult, however, for VA to comment specifically on the effectiveness of programs implemented by other entities on improving HAI rates.

Furthermore, attribution of improvement to one particular program is challenging when multiple additional factors may be associated with the outcome.

12. Based on your clinical experience, what do you think are the most serious deficiencies in how we are approaching the problem of antibiotic resistant infections? Where would you put the emphases in new research? Are you aware of any promising research or new ideas that might make a difference in combating antibiotic resistant infections?

VA Response: Areas such as the following should be considered for research and development: 1) antibiotic stewardship; 2) rapid diagnostics; 3) new antimicrobials; 4) new vaccines; 5) public and health care provider education relating to appropriate use and limitations of antibiotics, such as the Centers for Disease Control and Prevention (CDC) website: <http://www.cdc.gov/getsmarthcare/>.

The greatest deficiency is the scant antimicrobial pipeline against multidrug-resistant strains. This is especially true for gram-positive organisms. In addition to finding new antimicrobial agents, it is equally important to better understand bacterial resistance mechanisms so work-around can be built into the drug discovery process. Another possible approach is the development of inhibitors of specific resistance mechanisms, such as was done to combat beta-lactamase-mediated resistance with tazobactam/ clavulanate, sulbactam. These agents rejuvenated many penicillin-like drugs and the same may be true for drugs subject to other resistance mechanisms (e.g. fungal infections). Efflux inhibitors have been studied sporadically but none have advanced very far. Most of this work has been done by small biotech companies or academia, resulting in stagnation. Mechanisms that would be amenable to inhibitor development would be enzymatic resistance (i.e. aminoglycoside modifying enzymes), efflux (competitive or non-competitive blockade of the pump proteins), or any other specific protein-related mechanism.

Additionally, the lack of rapid diagnostic tests, lack of understanding of reservoirs or transmission, especially for new and emerging resistant bacteria, is a major issue. Some emphasis should be placed on gut microbiome research, the role of dietary manipulation for reducing colonization, probiotics or healthy bacteria to reduce colonization and as potential therapeutic choices and comparative effectiveness of combinations of antibiotics to explore synergy. Because we now know the genome sequence of many of these organisms there is no shortage of drug targets but mounting a medicinal chemistry program against a bacterial target is expensive in terms of dollars as well as personnel needed for success.

Examples of promising research or new ideas that could make a difference in combating antibiotic resistant and supported by the Office of Research and Development (ORD) include:

- An environmental disinfection intervention to prevent *C. difficile* transmission: Dr. Curtis Donskey at the Cleveland VA Medical Center and his research team are developing evidence-based strategies to prevent transmission of healthcare-associated pathogens, including antibiotic-resistant bacteria and *Clostridium difficile*. The work include a) monitoring and

feedback to improve environmental cleaning –the use of environmental cultures to provide monitoring and feedback to environmental services personnel was highly effective in improving disinfection of hospital rooms without the need for new disinfection technologies, b) patient hand hygiene – patient hand hygiene is an important patient safety measure, but limited efforts have been made to engage patients in hand hygiene interventions. A patient-centered, provider-facilitated approach that markedly improved patient hand hygiene has been developed, and c) targeted antimicrobial prophylaxis to prevent infections after procedures – infections with antibiotic-resistant *E. coli* are an increasingly common complication after prostate biopsy. An intervention involving screening for carriage of resistant *E. coli* with targeted modification of prophylaxis was very effective in preventing infections.

- The Continuing Challenge of Carbapenemases in *K. pneumoniae*: KPC-2 & NDM-1: In the VA Health Care system, *Klebsiella pneumoniae* is among the most resistant bacteria infecting Veterans, especially the elderly and infirm. At present the two most important threats to penicillin-and cephalosporin-type antibiotics against *K. pneumoniae* are the KPC and NDM beta-lactamases, enzymes in bacteria that inactivate these lifesaving drugs. Dr. Robert Bonomo of the Cleveland VA Medical Center is investigating how these inactivating enzymes destroy these potent antibiotics using tools from genetics, biochemistry, and structural studies. His investigation could potentially lead to developing strategies to halt the spread of resistance mediated by these enzymes and promote novel antibiotics that are able to treat patients infected with these bacteria and restore health.
 - *E. coli* ST131 and Intestinal Colonization: Dr. Robert Johnson of the Minneapolis VA Medical Center and colleagues identified a single, recently emerged *Escherichia coli* strain (the H30 sub-clone within *E. coli* sequence type ST131) as the main cause of antibiotic-resistant *E. coli* infections among Veterans across the U.S., evidence that this strain is causing an epidemic of drug-resistant infections among Veterans. The strain appears to spread extensively within households and can persist for a long time in colonized individuals, often causing repeated infections. It tends to be associated with older, more debilitated individuals, which makes the aging Veteran population a prime target. Dr. Johnson and his team are developing rapid tests that can detect this strain when infected patients present for care, which could allow better-targeted initial antimicrobial therapy, avoiding the 48+ hour delay associated with current culture-based testing methods. Additionally, efforts are underway to examine ways to block intestinal colonization by this strain, which could help interrupt the invisible web of transmission that likely underlies the current ST131 epidemic.
13. The FDA pipeline contains very few new antibiotics. The pharmaceutical industry asserts there is relatively less profit in developing new classes of antibiotics. Also, there is an ongoing spate of corporate takeovers of U.S. pharmaceutical companies, usually accompanied by reductions in research and development. Federally-funded basic research already underpins most pharmaceutical research and development. Do you think the federal government should get directly involved in developing new antibiotics?

VA Response: While VA has helped with advancing the approval of new indications for medications, VA alone is not in a position nor has the resources to develop new antibiotics for Food Drug Administration (FDA) approval. The involvement of the Federal government

may be the quickest way forward, but whether or not it is financially feasible is another question. Perhaps there are better ways rather than direct involvement, such as tax benefits for companies willing to invest the resources. Alternatively, close collaboration between industry and academia in centers for drug discovery dedicated to this problem, with funding from both industry and the Federal government, is one possible model. Again, it might be better to look for inhibitors of known resistance mechanisms to revitalize already existing antibiotics. Inhibitors of gram-negative resistance-nodulation-division (RND) pumps would probably have the greatest immediate impact. Ultimately, development of a broad-spectrum inhibitor that includes RND, major facilitator, and multidrug and toxic compound extrusion (MATE) efflux pumps across gram-positive and gram-negative species would be desirable but may not be possible. Ideally this approach would involve bioinformatics specialists, structural biologists, medicinal chemists, and microbiologists working together.

Another alternative model worth pursuing could be studying existing antibiotics that are in use in other countries but not approved in the U.S. for novel indications and possible therapeutic applications. In such cases, the pharmaceutical industry is often not interested in pursuing this route because of the low return on investment for them. However, the payoff in combating antibiotic-resistant infections could be huge—thus the federal government could invest in this area. It is clear that a comprehensive approach supported by governmental agencies is seen as critical: drug discovery, chemical optimization, delivery/reformulation, pharmacokinetics, treatment, preclinical models of infection, and safety.

14. The first line of defense against hospital acquired infections is to prevent transmission by touch. To prevent person to person transmission, all of the protocols for preventing infections stress thorough, frequent hand washing by doctors and nurses and others who come into contact with patients. But nothing near 100% adherence has been attained. Why is it so difficult to get trained health care providers to maintain high standards of hand sanitization?

VA Response: Transmission by hand contact is only a part of the issue regarding HAIs. Data are sparse regarding the reasons for less than 100 percent adherence. More research is needed on implementation science and human factors. VHA has issued guidance based on CDC and World Health Organization (WHO) guidelines for establishing the basic requirements for hand hygiene practices in VHA facilities (VHA Directive 2011-007 published February 16, 2011).
http://vaww.va.gov/vhapublications/ViewPublication.asp?pub_ID=2367
http://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=2367

15. Are you aware of significant social/behavioral research into how to stimulate higher rates of compliance with infection prevention protocols?

VA Response: There are numerous research articles on the study of infection prevention protocols such as hand hygiene, but little exists on how to increase and sustain compliance

behaviors. Few interventions to influence hand hygiene have had a measurable, prolonged effect on hand hygiene behavior. Reasons for poor adherence to infection prevention protocols are multifactorial and require a multifaceted approach to change behavior. Both the WHO and CDC have comprehensive programs available for use by health care facilities to assist in improving adherence to infection prevention protocols.

Additionally, the VA Office of Research and Development, Health Services Research and Development Service, is engaged in several areas of social/behavior research in HAI prevention, specifically related to hand hygiene and surgical/device-related infections.

For hand hygiene, social/behavioral research falls into two categories: surveillance and interventions. We conducted a national survey of hand hygiene practices in VA (Reisinger et al, 2013, AJIC) for the VA Office of Public Health's National Center for Occupational Health and Infection Control, in response to an Office of Inspector General (OIG) report on infection prevention. The survey covered both surveillance and interventions currently being conducted in VA facilities. A hand-hygiene Collaborative Research to Enhance and Advance Transformation and Excellence (CREATE) study grew out of this work, as well as a meta-analysis of hand hygiene interventions (Schweizer et al, 2014, CID) and a study (Perencevich IIR 09-099) of theoretically-informed hand hygiene signs (Reisinger et al, 2014, ICHE).

The objective of the hand-hygiene CREATE is to test the effectiveness of three bundled social/behavioral interventions and to disentangle their individual effectiveness. It also includes multiple site visits to understand current and evolving hand hygiene practices.

For surveillance, we have conducted a systematic review of automated hand hygiene surveillance systems (Ward et al, 2014, AJIC), which found little evidence in support of automated systems for improving compliance. In addition, we conducted a study (Perencevich IIR 09-099) on best practices to minimize the Hawthorne effect with directly observed monitoring of hand hygiene compliance (Yin et al, in press, ICHE).

For surgical/device-related infection prevention, VA researchers were involved with a surgical-site infection (SSI) prevention study with the University of Iowa, including a meta-analysis of a staphylococcus aureus prevention bundle (Schweizer, Perencevich, et al, 2013, BMJ). This meta-analysis informed an ongoing SSI CREATE study, which focuses on the implementation issues of integrating the surgical bundle into clinical practice (gathering data on several social/behavioral issues during site visits for this study).

Additionally, VA researchers in the VISN 10 Tele-ICU program are working to spread a quality improvement initiative they have conducted to reduce central line-associated bloodstream infections.

16. In some other developed countries and areas of the world (Scandinavia, for instance), HAI rates are much lower than in the U.S. To your knowledge, are different infection fighting technologies or protocols used in these places?

VA Response: A direct comparison between HAI rates in countries with very different demographics (population size, health factors, age, etc.) and social services (universal health care, etc.) is complex, and many factors not seemingly directly related to HAI prevention would also need to be considered. For example, Scandinavia has better control of antibiotic use in animals than in the U.S. and other parts of the world, which may be a factor in the differences in prevalence of HAIs between countries.

17. The Veterans Health Administration runs the largest integrated health care system in the world. How can there be so much variation among Veterans Health Administration hospitals in mortality rates, infection rates, and other key measures of patient outcomes?

VA Response: Geographic variations in health care outcomes has been a perplexing and persistent problem throughout health care, and, within VHA, continued variation is evident despite system-wide progress in reducing mortality, infections, and other complications. Some of the variation is attributable to differences in health determinants across different regions of the United States (e.g., lower incomes and poorer social support contribute to higher readmission rates). A certain portion of variation, particularly in standardized mortality rates (SMR) is the result of methodological problems such as residual confounding (i.e., patient factors that are not corrected by the risk adjustment models); missing data; and measurement error. Finally, physician practice itself is variable, because gaps still exist in medical knowledge especially the comparative effectiveness of different treatments.

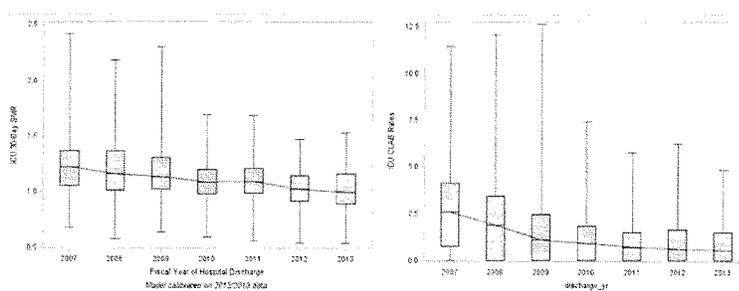


Figure 1: 30 Day ICU mortality rates across VA (trend lines depict overall decline in rate; blue boxes indicate interquartile range (25th percentile to 75th percentile) and upper/lower bars depict high and low outliers.

Figure 2: Central Line infection rates across VA

18. VA executives in Washington, D.C. apparently receive detailed information about quality of care and patient safety at individual Veterans Health Administration hospitals. Much of this information is not available to the public. Do you believe public access to this information could spur improvement? Should the Veterans Health Administration release more information as a matter of ethical responsibility to its patients and their families?

VA Response: VHA agrees that increased public access to information concerning quality of care and patient safety is desirable and is currently testing approaches to generate and report additional patient safety and quality indicators including Agency for Healthcare Research & Quality (AHRQ) Patient Safety Indicators and CDC Standardized Infection Rates. Our intent is to make these data public via VA and external websites, including Medicare Hospital Compare. The Veterans Choice Act of 2014 authorizes VHA to expand its public reporting, using its own websites as well as Medicare Hospital Compare, and we are taking the necessary steps to add those additional indicators.

19. Patient safety in hospitals emerged as a national health care issue in the 1990s. Veterans Health Administration hospitals and health care professionals were at the forefront in reducing hospital acquired infections and other threats to patient safety. Today, some Veterans Health Administration hospitals are still among the best and safest in the nation, but patient safety at other Veterans Health Administration hospitals lags far behind. Why isn't learning and best practices standardized across all Veterans Health Administration hospitals and within integrated private healthcare systems?

VA Response: VHA has a variety of standardized best practices that crosswalk all facilities. These include clinical team training, patient safety alerts, tool kits that help improve infection control issues, and others. However, in some cases the ability to spread change may be limited by lack of similarity across all hospitals; this limit the number of examples of clearly proven best practices.

In instances when best practices are clearly proven, and when opportunities of shared learning are optimal, VHA still can show system-wide improvements. However, opportunities to improve exist by increasing our understanding of how to ensure that some best practices can be adapted across the entire system regardless of the size or complexity of facilities.

20. What other (other than high intensity UV light) materials and technological innovations has the Veterans Health Administration studied or considered in order to prevent hospital-acquired infections? Biocidal coatings? High quality single use surgical instruments? Hydrogen peroxide vapor? Other? Among the innovations considered by the Veterans Health Administration, what advantages and disadvantages have been encountered?

VA Response: VHA relies on evidence-based guidance groups (e.g., CDC) and the published body of literature/evidence for the validity and feasibility of new technologies, and for implementation guidance.

21. What steps have been taken or considered since the completion of the report, “NCPS Lessons Learned—Reusable Medical Equipment in VHA?” In what instances are sterile, traceable, single use instruments or implants not an advantage over reusable locally sterilized products?

VA Response: In November 2011, representatives from VHA program offices (Environmental Program Service, National Center for Patient Safety (NCPS), Office of the General Counsel, National Sterile Processing Services (SPS), Surgery, Environmental Protection, Office of Acquisition, Logistics, and Construction) participated in a work group to revisit the possibility of reprocessing and reusing single-use devices (SUD). In 2008, VHA had previously conducted an in-depth evaluation regarding reprocessing and reuse of SUDs and made recommendations on VA policy regarding reprocessing and reuse of SUDs. After careful consideration, the work group unanimously agreed, for the safety of our patients, to not permit reprocessing or reuse of any medical device labeled as single-use. The 2011 SUD work group again came to the same conclusion.

There has been ongoing education and training for VHA employees (e.g., leadership training for SPS Chiefs; Level 2 training for SPS Chiefs) provided by the National Office of Sterile Processing, prior to and since the release of the NCPS lessons learned Reusable Medical Equipment (RME) report. In addition, there are monthly calls with the sterile processing service field to inform the field of issues and training and to address any issues the field is having. Standard Operating Procedures and competency assessments continue to be required at the facility level.

Finally, with the assistance of the ISO Consultation Division, a lease program for endoscopes was initiated to assist facilities in the standardization of endoscopes and reprocessing equipment. This standardization helps ensure consistent reprocessing. VA instituted an annual inspection/audit program for each facility that includes mandatory facility-led inspections as well as VISN level inspections to SPS area as well as areas outside SPS that store, transport and/or reprocess critical and semi-critical RME.

Additionally, sterile, traceable single instruments would not be an advantage over reusable products when: 1) the quality of the disposable device is not anywhere comparable to the reusable device (e.g., this can be an issue with some eye instruments); 2) where physicians can't get comfortable using the disposable products (e.g., they are going to do best with devices they feel comfortable with); 3) where disassembly/reassembly and reprocessing are simple processes; 4) when cost is a significant factor (i.e., it costs a lot of money to control biohazard waste with disposable devices); and 5) where efforts are strongly focused on green/environmental sustainability.

Single-use instruments are typically designed for use in a clinic setting and are acceptable to use with clinician approval. However, surgical instruments require precision and surgical-quality stainless steel. Therefore, these instruments are not normally designed for single patient use. Implantable devices are traceable and most often are single patient use.

22. What other technologies, besides those discussed in depth at the hearing, are currently being used to mitigate or prevent hospital acquired infections? How do they compare in cost and efficacy to the technologies discussed in depth at the hearing?

VA Response: In addition to standard methods to prevent HAIs, new technologies are emerging that may advance the ability to actually prevent them. In addition to technology mentioned in the hearing, additional promising technologies include hydrogen peroxide gas sterilization. Many of these new technologies have not had head-to-head comparative testing to determine their clinical value, which could be the most efficacious, or in which areas of the hospital they would be most useful. VHA will continue to monitor these technologies for the best opportunities to decrease rates of HAIs.

Rep. Eric Swalwell
Member, Subcommittee on Oversight
Committee on Science, Space & Technology
Questions for the Record (QFRs)

-Joint Hearing-
Subcommittee on Research & Technology and
Subcommittee on Oversight
“Technology for Patient Safety at Veterans Hospitals”
Thursday, June 26, 2014

Question for **Dr. Chetan Jinadatha**, Chief, Infectious Diseases,
Central Texas Veterans Health Care System

QFR #1: Earlier this year, you were the lead author of a study that evaluated the use of a pulsed xenon ultraviolet light (PPX-UV) disinfection device manufactured by Xenex Healthcare Services, LLC based in San Antonio, Texas.¹ Under “competing interests” the article said: “This study’s laboratory activity including use of the PPX-UV machine was supported by a grant from Xenex Healthcare Services, LLC. No author has identified a competing interest regarding the study beyond working for the institution studied (Department of Veterans Affairs, Veterans Health Administration).” In addition, under “funding” you acknowledged: “This study’s laboratory activity including use of the PPX-UV machine was supported by a grant from Xenex Healthcare Services, LLC.” Please indicate the size of each individual grant provided by Xenex Healthcare Services, LLC related to this study.

VA Response: The study was performed under a Cooperative Research and Development Agreement (CRADA) executed between the Central Texas Veterans Health Care System (CTVHCS) and Xenex Healthcare Services under the authority of 15 U.S.C. 3710a. This type of agreement permits Federal agencies to set up collaborations with non-Federal entities for sharing of resources, personnel, intellectual properties, and materials. VA may accept funds, but may not provide funds. VA can set-up CRADAs with an entity so long as it is within the Department’s mission, research and development committee concurs, and a willing investigator is available to co-ordinate the collaboration.

In the initial study referred above, Dr. Chetan Jinadatha was the principal investigator who collaborated under the CRADA. The grant size was \$21,840 (including indirect to Research foundation). The money was given to the Central Texas Veterans Research Foundation (Non-Profit wing that operates under the CTVHCS umbrella) for study-related expenses as mentioned in the study disclosures.

QFR #2: Please also provide a list of any and all other studies or evaluations in which you have participated or you are participating in that involve Xenex’s pulsed xenon ultraviolet light (PPX-

¹ Chetan Jinadatha, et. al., “Evaluation of a pulsed-xenon ultraviolet room disinfection device for impact on contamination levels of methicillin-resistant *Staphylococcus aureus*,” *BMC Infectious Diseases*, April 7, 2014, accessed here: <http://www.biomedcentral.com/1471-2334/14/187>.

UV) technology. For each of these cases please indicate the specific amount of financial compensation provided by Xenex Healthcare Services, LLC, whether in the form of a grant or some other form. Please also include any studies or evaluations you anticipate engaging in regarding Xenex's PPX-UV and the grant amount or other financial compensation that you anticipate receiving.

VA Response: Dr. Chetan Jindatha is involved in the following studies that include pulsed xenon UV light technology:

- *Evaluation of a Pulsed-xenon Ultraviolet Room Disinfection Device for impact of contamination levels of MRSA*
- *Can Multidrug-Resistant Organisms Become Resistant to UV Light After Serial Exposures? An Experiment*
- What is a good pre-clean routine prior to use of Pulsed Xenon UV device in a time limited and time unlimited setting?
- Reference lab for other centers doing Pulsed xenon on mercury based UV work.

The total grant amount for these above studies was \$129,548, including Central Texas Veterans Research Foundation indirect costs. The devices used in the studies are owned by the VA except for the Evaluation of a Pulsed-Xenon Ultraviolet Room Disinfection Device (HR 12-347, PI: John Zeber) study. It is a fully-funded merit study by the VA's Health Services Research and Development Service.

Dr. Jindatha also anticipates submitting grants where he will be the Principal Investigator (PI) or Co- investigator that might involve pulsed xenon or mercury based UV or hydrogen peroxide systems. These could be funded by industry or from the VA funding or other federal funding mechanisms. If industry is involved it will be funded under a CRADA between the VA and industry. Dr. Jindatha also plans to participate in a cooperative studies program related to pulsed xenon.

Dr. Jindatha has not received any compensation from Xenex or any other industry directly or indirectly. Dr. Jindatha has never received any financial compensation, gifts or meals from Xenex Healthcare Services or any other industry where he has served as a PI or investigator of a study.

Rep. Elizabeth Esty
Member, Subcommittee on Research & Technology
Committee on Science, Space & Technology
Questions for the Record (QFRs)

-Joint Hearing-
Subcommittee on Research & Technology and
Subcommittee on Oversight
“Technology for Patient Safety at Veterans Hospitals”
Thursday, June 26, 2014

Question for **ALL WITNESSES**

QFR #1: Hospital Associated Infections (HAIs) (also known as Healthcare Acquired Infections (HAIs) take a significant toll on public health and lead to serious financial repercussions for the healthcare industry and the U.S. economy. Despite the significant impact of HAIs, the federal government does not have a dedicated funding stream to help combat these infections nor a dedicated entity in charge of overseeing efforts to scientifically evaluate technologies, procedures or policies to help prevent and eliminate these potentially lethal infections. What organizational measures do you believe the federal government should take to help combat Hospital Associated Infections, including rigorous evaluation of potential preventive technologies, so that there is a single entity in charge of spearheading efforts to address this important issue?

VA Response: The recent Presidential Executive Order dated September 18, 2014, “Combating Antibiotic-Resistant Bacteria”, establishes detecting, preventing, and controlling antibiotic resistance as a national security priority and directs the newly-created Task Force for Combating Antibiotic-Resistant Bacteria to facilitate and monitor both the implementation of the executive order and the National Strategy for Combating Antibiotic-Resistant Bacteria. This new structure and high-level focus will help to define direction and leadership for addressing this important issue. Implementation science of adapting a new technology is another key area that is poorly studied. Existing funding is designated to help understand technology and challenges in a more robust manner. However, we recognize that health care dollars are precious and have competing interests. Hence incentives for VA hospitals to adapt such technology would be an ideal way where the Federal government can direct health care industry to take up implementing such technology earlier than they normally would.

Responses by Dr. Elaine Cox

**HOUSE COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY
SUBCOMMITTEE ON OVERSIGHT**

“Technology for Patient Safety at Veterans Hospitals”

Questions for the Record, Elaine Cox, M.D., Professor of Clinical Pediatrics, Director of Infection Prevention at Riley at IU Health, Director of Pediatric Antimicrobial Stewardship, Riley Hospital for Children

Questions submitted by Rep. Larry Bucshon, Chairman, Subcommittee on Research and Technology and Rep. Paul Broun, Chairman, Subcommittee on Oversight

1. Several references were made during our hearing to the need for more research into hospital-acquired infection prevention, ranging from biocidal technology to social/behavioral studies. Which research areas do you think are most important to address?

There are several areas for overlap of research with regard to HAIs. While I think socio-behavioral research is critical to understanding and then modifying human behavior, I suspect that the ability to overcome human factors in behavior is limited. Therefore, I think it is imperative to consider other options for research to improve the rate of HAIs. While we can never give up trying to improve the performance of human beings, it is clear that there are several areas like environmental cleaning, antibacterial coatings, and different disinfectant techniques that may be more beneficial and sustainable than attempts to modify human behavior.

2. A lot of knowledge about how to prevent hospital-acquired infections has been developed in the last decade. But hundreds of thousands of hospital patients are still injured each year by infections that are considered by many experts to be preventable. Why is this problem so difficult to solve?

Caring for patients is complex. It is very difficult to diagnose and treat patients without some degree of invasive monitoring or maintenance. These interventions, while life-saving in many ways, can also be a risk from the standpoint of infection. Certainly the advent of devices have changed the face of healthcare. For example, use of central lines has revolutionized medicine but any foreign body poses a risk for infection. As our technology has increased, we have not maintained aseptic practices and protective mechanisms to meet that evolution. In addition, the landscape of healthcare has changed requiring care ratios for staff that have ever increasing numerators which decreases the ability to be compliant with known protective techniques and increases the risk of infection with higher ratios of patients to caregivers.

3. Medicare has implemented financial penalties on hospitals that do not exceed thresholds for hospital-acquired infections, with the thresholds and penalties increasing over

time. State Medicaid programs and private sector insurance companies are also turning to financial incentives and disincentives to drive improvements in patient safety. Do you think these payment changes are constructive? Do you think these changes have been at least partly responsible for recent years' incremental improvements in infection rates?

I think that there has been increased awareness on the part of providers and hospital systems of HAIs secondary to potential penalties. Data would show that hospitals have changed behavior to decrease such infections by up to 55% in the case of CLABSIs. However, the external financial penalties can only elevate behavior to a certain point. Beyond that point, personal engagement and commitment are necessary to get beyond that sticking point.

4. Based on your clinical experience, what do you think are the most serious deficiencies in how we are approaching the problem of antibiotic resistant infections? Where would you put the emphases in new research? Are you aware of any promising research or new ideas that might make a difference in combating antibiotic resistant infections?

The most serious deficiencies in approaching resistant infections is the continued overuse of antibiotics. There are several issues surrounding antibiotics that need to be adequately addressed. Using the right drug at the right time at the right dose is critical to managing both the primary infection and minimizing collateral damage from the use of antibiotics. All too often we under dose drugs based on our concerns for adverse events. This allows germs to continue to grow but to also figure out methods of resistance. Even worse is when we expose patients to antibiotics for illnesses or conditions that do not require antibiotics (trauma, viral infections, etc.) allowing them to be exposed, changing their endogenous flora and rendering a memory for resistance that will last years if not a lifetime. Over that last decade, many studies have shown that judicious use of antibiotics can at least stabilize if not decrease antibiotic resistance. We need to have more support for antimicrobial stewardship programs throughout the US and reward people who have demonstrated appropriate use of antibiotics. In addition, we need to continue to educate the public on not requesting or expecting medication at every visit. The American public needs to be empowered to question if they need medication and to ask all the right questions when receiving a prescription, taking the medication exactly as prescribed, and not saving leftover medication.

5. The FDA pipeline contains very few new antibiotics. The pharmaceutical industry asserts there is relatively less profit in developing new classes of antibiotics. Also, there is an ongoing spate of corporate takeovers of U.S. pharmaceutical companies, usually accompanied by reductions in research and development. Federally-funded basic research already underpins most pharmaceutical research and development. Do you think the federal government should get directly involved in developing new antibiotics?

Antibiotic development has slowed significantly over the last two decades. The dollars that are required to do the R&D as well as the marketing for new drugs is staggering and very difficult to recoup. However, there need to be incentives to encourage drug companies to pursue new antibiotic research. While the federal government needs to be very cautious about involvement in pharma and respect independent entrepreneurial activities, tax breaks for such research and

other incentives need to be explored and supported/funded by federal government entities so that they can be realized.

6. The first line of defense against hospital acquired infections is to prevent transmission by touch. To prevent person to person transmission, all of the protocols for preventing infections stress thorough, frequent hand washing by doctors and nurses and others who come into contact with patients. But nothing near 100% adherence has been attained. Why is it so difficult to get trained health care providers to maintain high standards of hand sanitization?

Hand hygiene should always remain the first line of defense against infection. The beauty of hand hygiene as an infection prevention strategy is that it is effective and inexpensive. The addition of alcohol based hand gels has made the time commitment minimal. So why is there not 100% compliance? I suspect that there is not 30% of the healthcare workforce that never washes their hands. Rather, everyone likely misses 30% of their own opportunities to wash their hands. It may be as simple as they do not intend to touch anything in the patient space or they just do not realize the opportunities in front of them or the times they contaminate themselves on their way to the patient. It is not malicious neglect in my opinion, but rather an obliviousness to the vast number of opportunities to be compliant. We need to consider creative ways to give people a new lens like doing hand hygiene observations on their own so that they increase their awareness of opportunities.

7. Are you aware of significant social/behavioral research into how to stimulate higher rates of compliance with infection prevention protocols?

While people have studied a number of interventions related to hand hygiene, the most successful studies have been related to types of cleaner available and their kill rates rather than to the human behavioral elements related to compliance. There are some studies that show behavioral modeling can be effective. For example, if the first caregiver to enter the room of a patient out of a group washes their hands and dons appropriate personal protective equipment (PPE), the rest of the group is significantly more likely to emulate the desired behavior. Studies have also shown it is not a lack of acknowledgement that hand hygiene is important but rather putting that practice into action that is the major factor in non-compliance.

8. In some other developed countries and areas of the world (Scandinavia, for instance), hospital-acquired infection rates are much lower than in the U.S. To your knowledge, are different infection fighting technologies or protocols used in these places?

I am not aware of specific interventions in Scandinavia and other such areas that result in lower HAIs in those areas. However, there are a few questions that come to mind: does a national health system result in lower infection rates? Is that related to less use of devices and technology, less elective care? Are there incentives built into the reimbursement system that act as key drivers to push behavior toward handwashing and prevention of HAIs such as bonuses or other incentives?

9. The Veterans Health Administration runs the largest integrated health care system in the world. How can there be so much variation among Veterans Health Administration hospitals in mortality rates, infection rates, and other key measures of patient outcomes?

There is great variability in patients and how they present as well as in caregiver styles. We cannot control the unintended variation in patient presentation. It is a difficult question to know how much we should decrease variation in practice by caregivers. Physicians spend a very long time and lots of personal resources to hone their critical thinking skills to problem solve at the patient level. There are truly many ways to treat and care for patients. Many physicians are always the product of the way they were trained. It is incumbent upon them to keep up with changing standards of care and technology. However, what we should keep in mind is that only the patient should inject variability into the equation. The systems should run with standard work and standards of care in the background and allow the practitioners to use critical thinking to problem solve at the level of the individual in front of them requiring care. Our approach to the central line, urinary catheter, ventilator, surgical wound should not vary and should be according to the well-defined, published standards.

10. Veterans Health Administration executives in Washington, D.C. apparently receive detailed information about quality of care and patient safety at individual Veterans Health Administration hospitals. Much of this information is not available to the public. Do you believe public access to this information could spur improvement? Should the Veterans Health Administration release more information as a matter of ethical responsibility to its patients and their families?

Transparency in health care is a somewhat new and complex phenomenon. While I think that aggregate data should be available to consumers, it is clear that without the appropriate context, information can be misconstrued. There are also significant issues around patient privacy that must be taken very seriously. However, competition frequently motivates people to strive for higher standards so ranking systems like US News and World Report rankings can be very effective in stimulating hospitals to work toward improvement. Appropriate reports given with applied context would be very useful to disclose to the public. I agree that our patients should have access to information regarding the safety of their hospital.

11. Patient safety in hospitals emerged as a national health care issue in the 1990s. Veterans Health Administration hospitals and health care professionals were at the forefront in reducing hospital-acquired infections and other threats to patient safety. Today, some Veterans Health Administration hospitals are still among the best and safest in the nation, but patient safety at other Veterans Health Administration hospitals lags far behind. Why isn't learning and best practices standardized across all Veterans Health Administration hospitals and within integrated private healthcare systems?

Every institution has its own culture. If each and every VA Hospital has not put a focus on development of a culture of safety, there will be variation. A major detriment to US hospitals attaining the culture of safety has been the fear of litigation and retaliation, making true transparency a frightening possibility. I work in a state with good malpractice laws that are fair.

This has helped Indiana achieve new heights of transparency in healthcare in the last decade. In addition, the sharing between different institutions on best practice and sharing stories of harm that occurred has not been completely utilized. I think we need more networks and collaboratives such as the pediatric Solutions for Patient Safety group that is an “all teach, all learn” effort. This helps the practice of sharing and adopting best practices surge so that everyone’s patients benefit from lessons learned in medicine despite what facility led the charge. In addition, internally we need to be very intentional in defining patient harm and action plans to combat it rather than totally speaking in terms of patient safety.

12. Have hospitals studied increased costs, lengths-of-stay, and in-hospital mortality rates associated with hospital-acquired infections? If so, what are the numbers associated with those studies?

There are many studies related to hospital acquired infections. One in 25 patients on any given day in a US hospital is suffering from a hospital acquired infection. Estimates in multiple studies show that costs of HAIs are between \$2-10 billion per year in the United States. These are green dollars. In addition length of stay, mortality, and cost have been shown in multiple other studies to be at least doubled in patients whose stay was complicated by an HAI vs. those who were uninfected. These numbers are vastly increased in patients who have an MDR (multidrug resistant) organism causing their infection. These numbers reflect beds, resources, and healthcare dollars that are not available for other key initiatives in healthcare including acute care, vaccines, lifestyle improvement, and research to further the healthcare agenda.

13. Have hospitals studied increased litigation/settlement costs emanating from hospital-acquired infections?

The number of litigation cases surrounding HAIs is definitely on the increase and likely will go up by 1% per year for the foreseeable future. Recent information from the Hospital Professional Liability and Physician Liability Benchmark Analysis states that 1 out of 4 claims and 24% of hospital liability costs are related to HAIs. With the new spotlight of public attention on the subject, these numbers are not likely to decline.

14. Do you find there to be management problems in the hospital system that contribute to increased hospital-acquired infections and mortality rates? Is there something being done to change this?

I think that every level of hospital management has become more aware of the collateral and direct damage done by HAIs. Many efforts and resources are being directed at this issue. Many factors contribute and while I do not think there is management malfeasance, getting the clear priorities for management and employment strategy is taking time. For example, finding the exact patient to caregiver ratio continues to be a challenge in the current economic landscape of healthcare.

15. Are managers at hospitals paid bonuses? If so, does the bonus system take into account the patients that have been cared for at the hospital, the hospital-acquired infections rate, and the mortality rate? If not, how are bonus amounts calculated?

Managers and executives are usually on a bonus or contribution management scheme. These bonuses are predicated on meeting certain quality metrics in the hospital and include HAI rates, LOS, etc. This has stimulated interest in improvement although financial incentives seem to only take initiatives so far.

16. Who do hospital managers report to? How often do they have to check in and what do they report? What standards are they held to?

Everyone has a boss. Managers report to directors who report to the C suite who reports to the board. Generally, metrics for their area or team are pulled from decision support and placed on a dashboard monthly. Generally they are held to various percentages of national benchmarks to receive bonus money or to be put in remediation.

17. What other technologies, besides those discussed in depth at the hearing, are currently being used to mitigate or prevent hospital acquired infections? How do they compare in cost and efficacy to the technologies discussed in depth at the hearing?

There are some practices that are currently being used in many institutions across the country. The most recent effort involves daily bathing of patients with chlorhexidine gluconate to decrease skin colonization. A study in the *New England Journal of Medicine* showed a decrease in staph infections by 30% with this technique. Implementation across hospital units has proven to be expensive and challenging for some institutions. Other hospitals are trialing various other interventions such as metal coatings of furniture, trays, and other items. Hospitals are also looking at different ways to evaluate hand hygiene. Electronic monitoring has been piloted in various settings. This gives many points of observational data although it is expensive and requires the ability to enforce accountability. In addition, it still may not give data that can pinpoint hand hygiene at the critical point of interaction with the patient as opposed to entry/exit from the room. I am very certain that there are many other initiatives in the pipeline and I hope that one or several can improve the incidence and outcomes of HAIs in the people that depend upon us and trust us to care for them.

Rep. Elizabeth Esty

Member, Subcommittee on Research & Technology

Committee on Science, Space & Technology

Questions for the Record (QFRs)

-Joint Hearing-

Subcommittee on Research & Technology and

Subcommittee on Oversight

“Technology for Patient Safety at Veterans Hospitals”

Thursday, June 26, 2014

Question for **ALL WITNESSES**

QFR #1: Hospital Associated Infections (HAIs) (also known as Healthcare Acquired Infections (HAIs) take a significant toll on public health and lead to serious financial repercussions for the healthcare industry and the U.S. economy. Despite the significant impact of HAIs, the federal government does not have a dedicated funding stream to help combat these infections nor a dedicated entity in charge of overseeing efforts to scientifically evaluate technologies, procedures or policies to help prevent and eliminate these potentially lethal infections. What organizational measures do you believe the federal government should take to help combat Hospital Associated Infections, including rigorous evaluation of potential preventive technologies, so that there is a single entity in charge of spearheading efforts to address this important issue?

Funding remains an ongoing challenge for everyone in medical research. While dollars are critical for research and development of new technologies to prevent infection and new modalities to treat them, there is no cohesive force to streamline those efforts. This results in having to build infrastructure to support research at each institution which increases the funding needs further. The result is more healthcare expenditures with less data. If there was a single entity acting as the gatekeeper, efforts could be coordinated rather than just repeated and more dollars could be used for actual studies rather than being used over and over to cover indirect costs for multiple institutions to put the research infrastructure into place. In addition, a national agenda could be put into place regarding HAIs by groups with extensive expertise culled from areas such as CDC, WHO, and leading academic universities, and an action plan with a timeline could be developed. This would result in accountability to achieve improvements and allow for monitoring and accountability of those funded. This would also take out any bias from having corporate sponsors.

Responses by Dr. Trish M. Perl

**HOUSE COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY
SUBCOMMITTEE ON OVERSIGHT**

"Technology for Patient Safety at Veterans Hospitals"

Questions for the Record, Dr. Trish M. Perl, Professor of Medicine and Pathology, Johns Hopkins School of Medicine, Professor of Epidemiology, Bloomberg School of Public Health, Senior Epidemiologist, Johns Hopkins Medicine

Questions submitted by Rep. Larry Bucshon, Chairman, Subcommittee on Research and Technology and Rep. Paul Broun, Chairman, Subcommittee on Oversight

1. Several references were made during our hearing to the need for more research into hospital-acquired infection prevention, ranging from biocidal technology to social/behavioral studies. Which research areas do you think are most important to address?

Among the areas discussed at this hearing the areas that are most important to address include 1) how do we measure efficacy of novel technologies ie what are the standards so that we can compare the technologies; 2) how effective are the technologies in the clinical setting--ie moving beyond the laboratory; 3) which technologies are needed in what settings ie how do we marry the technology with the risk of the clinical setting and 4) how to enhance the implementation (behaviors).

2. A lot of knowledge about how to prevent hospital-acquired infections has been developed in the last decade. But hundreds of thousands of hospital patients are still injured each year by infections that are considered by many experts to be preventable. Why is this problem so difficult to solve?

Healthcare settings are complicated environments and the investment in research has not matched the investment in for other diseases. Investment in research from the basic sciences to the clinical setting to support innovation, behavioral change and measurement is needed to develop strategies to decrease this infection. The CDC has sponsored Centers of Excellence to study healthcare associated infections but the funding is minimal and there are not enough of these centers to tackle the problem. To put this in perspective, millions of dollars have been invested to study cancer and HIV and we have not seen this investment in the field of healthcare associated infections or antimicrobial resistance.

3. Medicare has implemented financial penalties on hospitals that do not exceed thresholds for hospital-acquired infections, with the thresholds and penalties increasing over time. State Medicaid programs and private sector insurance companies are also turning to financial incentives and disincentives to drive improvements in patient safety. Do you think these payment changes are constructive? Do you think these changes have been at least partly responsible for recent years' incremental improvements in infection rates?

These changes – what we call pay for performance—have clearly heightened the focus of institutions on healthcare associated infections. The incentives have helped provide infection prevention with the needed attention to provide support to the groups

charged in hospitals with prevention efforts. This being said, we need to enhance measurement systems to assure that the system remains focused on performance improvement and not improvement for payment. There are increasing reports of institutions that "game the system" which is not the goal of these efforts. This is another area where research to measure the impact of this public policy change will be important to help guide congress and regulators.

4. Based on your clinical experience, what do you think are the most serious deficiencies in how we are approaching the problem of antibiotic resistant infections? Where would you put the emphases in new research? Are you aware of any promising research or new ideas that might make a difference in combating antibiotic resistant infections?

This is a terrific question and would need a thesis to answer it. There are needs at multiple levels including understanding the mechanisms of resistance but also how these translate into patient outcomes, how to prevent them and what/which of the efforts are most important. As an epidemiologist, the work I see as most important is determining if antimicrobial stewardship programs do make a difference, determining if community based interventions decrease antimicrobial resistance and determining whether novel diagnostics can improve identification of syndromes like influenza so that fewer antimicrobials are use. Centers of Excellence and grants supporting this type of infrastructure to do these studies would be an important step forward. This entire area is ripe for interventions.

5. The FDA pipeline contains very few new antibiotics. The pharmaceutical industry asserts there is relatively less profit in developing new classes of antibiotics. Also, there is an ongoing spate of corporate takeovers of U.S. pharmaceutical companies, usually accompanied by reductions in research and development. Federally-funded basic research already underpins most pharmaceutical research and development. Do you think the federal government should get directly involved in developing new antibiotics?

I am not an expert in how to drive economic development in this arena but I can say that the European Union has developed a multi-million dollar project to develop public, private partnerships and this is a very interesting model. It is clear that we need to do something and in the past federal support of research has facilitated many innovations.

6. The first line of defense against hospital-acquired infections is to prevent transmission by touch. To prevent person to person transmission, all of the protocols for preventing infections stress thorough, frequent hand washing by doctors and nurses and others who come into contact with patients. But nothing near 100% adherence has been attained. Why is it so difficult to get trained health care providers to maintain high standards of hand sanitization?

Changing behavior and culture requires years of interventions that are focused on improving knowledge, changing behaviors and attitudes. These changes need to be facilitated by making sure that we have access to the equipment or products that we need. The percentage of people aware that hand hygiene is important has increased dramatically and this is a testimony to many in public health, academics, industry and the media. I think of the changes that have been required to implement car seats, decrease smoking and encourage seat belt use. We need all hands on deck so that we provide people with the knowledge and tools they need and then set the expectation of the

behaviors that should be in place.

7. Are you aware of significant social/behavioral research into how to stimulate higher rates of compliance with infection prevention protocols?

Yes, there is research to understand what motivates healthcare workers and families to improve compliance. There is always the need for more research and this would be an area where research support can be enhanced.

8. In some other developed countries and areas of the world (Scandinavia, for instance), hospital-acquired infection rates are much lower than in the U.S. To your knowledge, are different infection fighting technologies or protocols used in these places?

There are some variations in practice in some areas of the developed world, however, much of the difference is related to behavior and attitudes.

9. The Veterans Health Administration runs the largest integrated health care system in the world. How can there be so much variation among Veterans Health Administration hospitals in mortality rates, infection rates, and other key measures of patient outcomes?

I do not have access to this information. What data I have seen is that the outcomes from the VHA are similar to those for other US health systems.

10. Veterans Health Administration executives in Washington, D.C. apparently receive detailed information about quality of care and patient safety at individual Veterans Health Administration hospitals. Much of this information is not available to the public. Do you believe public access to this information could spm improvement? Should the Veterans Health Administration release more information as a matter of ethical responsibility to its patients and their families?

Answering this type of question is always difficult because not all information is meaningful. I do believe that transparency is important but public reporting is complicated in that the data released needs to be understandable to the public. I do think having a group of experts coming together to make recommendations may help congress determine how to approach this. One way or another a scientifically driven process will enhance the public trust.

11. Patient safety in hospitals emerged as a national health care issue in the 1990s. Veterans Health Administration hospitals and health care professionals were at the forefront in reducing hospital-acquired infections and other threats to patient safety. Today, some Veterans Health Administration hospitals are still among the best and safest in the nation, but patient safety at other Veterans Health Administration hospitals lags far behind. Why isn't learning and best practices standardized across all Veterans Health Administration hospitals and within integrated private healthcare systems?

Many people share this concern and agree that this is a huge conundrum. Understanding what leads to this variation whether it is leadership, incentives, quality of staff will be very important.

12. Have hospitals studied increased costs, lengths-of-stay, and in-hospital mortality rates associated with hospital-acquired infections? If so, what are the numbers associated with those studies?

There are many studies that have looked at this type of data. I am happy to provide you with those studies. The caveat is that these studies all use different strategies to capture the data so this is an area where standardization is important.

13. Have hospitals studied increased litigation/settlement costs emanating from hospital-acquired infections?

I am not sure.

14. Do you find **there** to be management problems in the hospital system that contribute to increased hospital-acquired infections and mortality rates? Is there something being done to change this?

There is a fair amount of variation that in practices and to answer this question, one would need to do a well designed study that could 1) measure the management structure and 2) try to establish an association so that the hypothesis could be further tested.

15. Are managers at hospitals paid bonuses? If so, does the bonus system take into account the patients that have been cared for at the hospital, the hospital-acquired infections rate, and the mortality rate? If not, how are bonus amounts calculated?

The use and calculation of bonuses varies from hospital to hospital and health system to health system. You would need to ask individual hospitals and hospital systems whether this is done and how it is done.

16. Who do hospital managers report to? How often do they have to check in and what do they report? What standards are they held to?

This is another example of a practice that varies from hospital to hospital and health system to health system. You would need to ask individual hospitals and hospital systems whom managers report to and what standards are in place.

17. What other **technologies**, besides those discussed in depth at the hearing, are currently being used to mitigate or prevent hospital-acquired infections? How do they compare in cost and efficacy to the technologies discussed in depth at the hearing?

There are a myriad of technologies that are being developed to clean the environment such as UV light and hydrogen peroxide vaporization, to improve the coating of surfaces in healthcare settings, to enhance patient care and to enhance the diagnosis of diseases etc. There is a lot of innovation and very entrepreneurial work—we need to make sure that these technologies are tested with appropriate and adequately designed studies to assure they are safe and effective.

Rep. Elizabeth Esty
Member, Subcommittee on Research & Technology
Committee on Science, Space & Technology
Questions for the Record (QFRs)

-Joint Hearing-
Subcommittee on Research & Technology and
Subcommittee on Oversight
"Technology for Patient Safety at Veterans Hospitals"
Thursday, June 26, 2014

Question for ALL WITNESSES

QFR #1: Hospital Associated Infections (HAI's) (also known as Healthcare Acquired Infections (HAI's)) take a significant toll on public health and lead to serious financial repercussions for the healthcare industry and the U.S. economy. Despite the significant impact of HAI's, the federal government does not have a dedicated funding stream to help combat these infections nor a dedicated entity in charge of overseeing efforts to scientifically evaluate technologies, procedures or policies to help prevent and eliminate these potentially lethal infections. What organizational measures do you believe the federal government should take to help combat Hospital Associated Infections, including rigorous evaluation of potential preventive technologies, so that there is a single entity in charge of spearheading efforts to address this important issue?

This question gets at the heart of the issue of how to best study this important area of science. It is a fundamental and key question. The study of healthcare associated infections encompasses antimicrobial resistance, environmental contamination, and behavioral qualities. Because this is a subject that translates from basic science to implementation the research efforts are fragmented. I believe that a partnership between the CDC, AHRQ and the NIH with pooling of monies dedicated to research will help develop a strategic research agenda that is less fragmented and more targeted. Developing a cadre of program officers that could manage such a portfolio will advance the science in a way that was successfully done for both HIV and cancer which are examples of diseases that have as much impact as HAIs and resistant organisms.

Responses by Mr. Jeff Smith

U.S. House of Representatives

Washington, D.C.

June 26th, 2014

House Committee on Science, Space, and Technology

Subcommittee on Research and Technology

Subcommittee on Oversight

“Technology for Patient Safety at Veterans Hospitals”

Questions for the Record, Jeff Smith (President of Electro-Spec, Inc. and Steriplate LLC)

Questions submitted by Rep. Larry Bucshon, Chairman, Subcommittee on Research and Technology and Rep. Paul Broun, Chairman, Subcommittee on Oversight

1.) Several references were made during our hearing to the need for more research into hospital-acquired infection prevention, ranging from biocidal technology to social/behavioral studies. Which research areas do you think are most important to address?

- a. While I can only speak specifically to our technology (Steriplate), the key word in the question above is “Prevention”. In the past, the key word has been “Treatment” and in order for us to make a sizable and meaningful impact on HAI’s, it will be necessary to focus research on technologies that are easy to implement and educate that prevent HAI’s. In my opinion, social and behavioral education is already underway with the general public and health institutions, agencies and various entities. The education of HAI’s is something that has been slow to hit the “mainstream” in my opinion as many people initially felt that HAI’s were simply something that was an inevitable byproduct of healthcare. Only within the last five years, has the Dept. of Health & Human Services, CDC and NIH really focused squarely on calculating and substantiating the statistics behind HAI’s and their economic and mortality burden on patients well enough to provide data to educate us with. There are all kinds of new initiatives associated with the Affordable Care Act now, but there honestly needs to be more. Most people do not know that HAI’s

Testimony of Jeffrey D. Smith before the House Subcommittee on Research and Technology, June 26, 2014

are the 4th leading cause of death in the United States, when you ask them. HAFs are not “inevitable” and are definitely preventable. Focusing on technology that is easy to implement and easy to educate, provides the best approach to addressing the question above.

- b. Steriplate is a technology that is designed for a number of applications and uses that meet the needs of “ease of education and ease of use”. Not specific to “touch” surfaces or surfaces that are typical sites for the translocation of bacteria and germs, Steriplate can also be utilized on semi-implantable or even implantable surfaces and devices. These are the kinds of surfaces that have the highest rate of infection that obviously require a much higher rate of sterilization effectiveness and practice. Unlike other types of technology that focus on either treatment or sterilization of surfaces in the environment, Steriplate works continuously without human intervention and thus the need for exhaustive and expensive training and education is not necessary. So, these kinds of technologies are the easiest to implement and conversely, present the biggest impact in terms of research dollars and investment in my opinion.

2.) Would you please give a thumbnail sketch of how your company was created? Where did the technology come from, and what was the inspiration for commercializing it? Did you have direct or indirect government assistance at the outset or along the way?

- a. Steriplate LLC is a wholly owned subsidiary of Electro-Spec, Incorporated. Electro-Spec specializes in utilizing precious and semi-precious metals for medical, automotive, aerospace and telecommunication devices and equipment. Through ongoing research and development of the antimicrobial benefits of metals in certain applications, Steriplate was formed. Steriplate is the principal research arm of Electro-Spec for antimicrobial coatings in a variety of applications. Steriplate processes include metal electroplating and unique surface treatments for environmental, semi-implantable and permanent implantable devices.
- b. Using the natural ability of certain types of metals to be antimicrobial, Steriplate is a super alloy that continuously kills bacteria when exposed to its surface. Having the additional properties of high corrosion resistance, wear resistance and hydrophobicity, another level of performance can be achieved in a variety of devices and applications that have traditionally been susceptible to failure for contamination. There are many tests that still need to be conducted for appropriate fit, use and function for Steriplate and to date, there has been no federal or state assistance in the validation and possible commercialization of Steriplate. The research to date has been solely funded through Electro-Spec and has been private in nature.

3.) Following on the preceding question, do you have any thoughts about how to make a more effective and efficient process for commercialization of new scientific knowledge?

- a. You really have to start with the definition of “commercialization” to understand what is involved to get to that point. Commercialization is the point that you can effectively introduce a product or production process into the appropriate market. Because of the issues associated with testing and validation of new technologies for medical applications (FDA approval, EPA approval, etc.), it is not only difficult for a small company to navigate the approval process without appropriate expertise and legal counsel, but it is incredibly expensive and a long, arduous process as well. The issue that we have with Steriplate is that it potentially will require FDA and EPA approval and this requires an inordinate amount of time and expense that either our company simply cannot afford or potential investors don’t want to entertain. There are so many new and emerging medical technologies out there, that unless you have the in-house talent and expertise or the financial resources necessary to get it through the approval process, it will never make it to commercialization. The United States is recognized as the world leader in medical innovation and technology. However, the process to commercialize that innovation and technology is very cumbersome and expensive and there really needs to be some agency or entity that can facilitate the approval process for these innovations, rather than abandoning the idea due to the expense or time associated with getting the approvals. Whether that assistance comes in the form of incentives, resources or representation, something needs to be done to facilitate the commercialization of new technologies for those companies that cannot financially afford it. All too often the proving ground for some of these new medical technologies ends up being overseas, before the technology makes it back to the United States. This simply needs to change, so that U.S. medical technology and innovation stays where it originated.

4.) A lot of knowledge about how to prevent hospital-acquired infections has been developed in the last decade. But hundreds of thousands of hospital patients are still injured each year by infections that are considered by many experts to be preventable. Why is this problem so difficult to solve?

- a. As I had indicated earlier, part of this is an education on not only what HAI’s are, but how they can be prevented as well. The overwhelming sentiment until recently was that HAI’s were an inevitable consequence of medical treatment and hospitals frankly had little incentive to do anything about it. In some cases, HAI’s were viewed as additional revenue for some treatment facilities sadly. It is my belief that only within the last five years, have the Dept. of Health & Human Services, the CDC, the National Health Institute and the World Health Organization really identified the true mortality and morbidity rates associated with HAI’s and also what their socioeconomic impacts are. It is only within the last few years (2008-2010) that

HHS has made HAI's an "agency priority goal" by establishing steering committees to develop national action plans on education and prevention of HAI's. In 2011, the "Partnership for Patients" initiative was established to help with these efforts with goals to be achieved through 2013. This plan expired in 2013 and a new National Action plan was adopted at a conference in Washington DC in September of 2013 with goals through 2020. As of 2013, only 50% of the goals from this plan had been achieved.

Metric	Source	National 5-year Prevention Target	On Track to Meet 2013 Targets?
Bloodstream infections	NHSN	50% reduction	Yes
<i>Clostridium difficile</i> (hospitalizations)	HCUP	30% reduction	No
<i>Clostridium difficile</i> infections	NHSN	30% reduction	No
Urinary tract infections	NHSN	25% reduction	No
MRSA invasive infections (population)	EIP	50% reduction	Yes
MRSA bacteremia (hospital)	NHSN	25% reduction	No
Surgical site infections	NHSN	25% reduction	Yes
Surgical Care Improvement	SCIP	95% adherence	Retired

Statistics for 2014 have yet to be published for the National Action Plan and are due this summer. HHS has decided to use 2015 statistics to adopt the goals for 2020. So as you can see, it is only recently that a concerted effort has been made on a federal level, to provide meaningful data, statistics, action plans and goals to combat HAI's. The question as to why it is difficult to solve is due to the inability of people to understand that this is not only a serious problem, but that it is a preventable problem. CMS administrator Donald Berwick, M.D. stated the issue perfectly when he said, "any potentially preventable complication of care is unacceptable". Only within the past few years are we starting to understand that HAI's are preventable and the fact that they occur is unacceptable.

- 5.) **Medicare has implemented financial penalties on hospitals that do not exceed thresholds for hospital-acquired infection, with the thresholds and penalties increasing over time. State Medicaid programs and private sector insurance companies are also turning to financial incentives and disincentives to drive improvements in patient safety. Do you think these payment changes are constructive? Do you think these changes have been at least partly responsible for recent years' incremental improvements in infection rates?**
- a. I definitely think this is necessary and has been one of the most effective initiatives to date. The only way to drive change in accountability and focus, is to effect change in responsibility for the quality of care provided. Thankfully, the federal government has recognized that on several levels now. The Centers for Medicare and Medicaid Services (CMS) has implemented policies to not pay for additional costs associated with HAI's which forces the hospitals to absorb the cost of treating these patients. By employing quality-centric standards for reimbursement, the hospitals have no choice but to improve their overall quality of care. Eventually, the "quality of care" needs to be transparent to the public, in terms of infection rates and readmission rates. Reputation can play a large role in not just education of the public about the ability of a hospital to provide services, but to also enforce the necessary changes to prevent HAI's in general. I think you will see private institutions follow suit very quickly on this, because infections not only cause loss of life potentially, but they also cost in excess of \$80 billion per year to treat. Establishing a "score card" system is vital and tying that system to financial incentives and disincentives is the only way that you will have a meaningful change in the way HAI's are viewed and handled.
- 6.) **What do you think are the most serious deficiencies in how we are approaching the problem of antibiotic resistant infections? Where would you put the emphasis in new research? Are you aware of any promising research or new ideas that might make a difference in combating antibiotic resistant infections?**
- a. Part of the problem starts with overprescribing antibiotics to people as well as the use of antibiotics on animals. We are seriously jeopardizing the effects of antibiotics in general, by the rampant use of antibiotics in our society. Couple this with the sheer costs associated with getting new drugs to market and the time frame necessary for approvals and it is frankly a recipe for disaster. Additionally, bacteria are developing resistance at an alarming rate, by mutating into "nightmare bacteria" or "super bugs" by producing enzymes that easily break down antibiotics. Getting back to my central argument about prevention vs. treatment, I think that the emphasis on new research needs to be on technologies that prevent colonization of surfaces and possible contamination or translocation of bacteria vs. new ways to treat infections that are already in place. Treating infections with drugs is not only expensive, but it is a reactive response to the problem vs. a proactive response in trying to provide a sterile environment in the first place. While drug therapy has its obvious place and

importance, I don't believe that we can stay ahead of the pace that "nightmare bacteria" or "super bugs" can. Technologies that continuously kill and eliminate the bacteria on the surface of devices or equipment are the fool proof way of dramatically reducing HAI's in general. I believe that Steriplate is one of those technologies that would be easy to implement, quick to implement and has a low cost associated to it as compared to other types of technologies.

7.) Are you aware of significant social/behavioral research into how to stimulate higher rates of compliance with infection prevention protocols?

- a. I think what is being proposed on a federal level (specifically through CMS) is a good start. Anything that can be done to educate the public in terms of infection performance rates and readmission rates, is critical to holding hospitals accountable and providing decision making tools to the general public. The CMS Hospital Compare website will have a huge impact on the transparency of HAI rates at various facilities. With these kinds of practices in place, consumers will be able to compare performance and results and hospital leaders will have no choice but to draw the connection between clinical care outcomes and patient selection of services. Additionally, it is critical that better methods are put in place to capture the statistics behind HAI's. The CDC needs to do a better job of capturing the various rates of infections at not just hospitals, but inpatient acute care facilities, ambulatory surgical centers, outpatient centers, long term care facilities and field hospitals as well. I believe the issue of HAI's is far greater in number than what is being reported. There needs to be a better system in place for tracking HAI's and I am surprised that the Affordable Care Act does not address this or provide for this, in its requirements.

8.) In some developed countries and areas of the world (Scandinavia, for instance), hospital-acquired infection rates are much lower than in the U.S. To your knowledge, are different infection fighting technologies or protocols used in these places?

- a. There are definitely varying rates of infection in certain countries as compared to others. The United States, Canada, Europe (UK, France particularly), Japan and Mediterranean countries have a surprisingly higher rate of infection as compared to Scandinavian countries or even the Netherlands. While it can be argued that they have developed different technologies for prevention of HAI's, the real reason that there is a difference is due to the antibiotics in the food supply. The "advanced" countries have very aggressive requirements and policies in place on a federal level to minimize the use of antibiotics in livestock and poultry. These countries also do a better job at educating health professionals on the dangers of overprescribing antibiotics through their federal health programs. It can be argued that by policing the use of antibiotics throughout the food chain and through controls in

prescriptions in Scandinavia, their immune systems are not as compromised and can effectively fight off traditional bacterial loads that other nationalities cannot.

9.) What other technologies, besides those discussed in depth at the hearing, are currently being used to mitigate or prevent hospital-acquired infection? How do they compare in cost and efficacy to the technologies discussed in depth at the hearing?

- a. The three main technologies currently used are bleach wipes, UV light and Hydrogen Peroxide Vapor units. Each of these technologies works, but has their limitations. Bleach wipes have been used for many years, but require not only constant use, the surfaces can easily be recontaminated shortly after disinfection. Additionally, bleach wipes require human intervention in that there could be a significant difference in how one person uses the bleach wipe to disinfect a surface from another person who may not be as thorough. There are far too many variables in using bleach wipes and the continued results in the rates of infection support this. Finally, they are obviously a consumable product as they can only be used once and then have to be properly disposed of.
- b. “No Touch” technology like UV light does an excellent job of disinfecting a surface that is exposed to the light. However, it requires training in the use of the device, maintenance of the device and is susceptible to “shadowing” on surfaces where the light cannot effectively penetrate the surfaces intended to be exposed. In other words, there is no residual method for treatment beyond those areas that aren’t exposed, other than bleach wipes. UV light cannot remove stains from a surface that may absorb some of the light. Also, all hospital personnel and patients must be removed from the room during the treatment cycle, as they cannot be exposed to the radiation. Additionally, the UV light over time, can dramatically affect materials and surfaces exposed in terms of brittleness and discoloration.
- c. Vapor phase is another type of “No Touch” technology. Hydrogen Peroxide Vapor is effective, but requires the room to be completely sealed and off limits for a cycle time up to 2 ½ hours for effective treatment. The ventilation of the room must also be controlled or limited for the entire duration of the treatment. Training and maintenance of the equipment is essential to the effectiveness of the units as well. Unlike UV Light technology, VHP equipment requires personal protective equipment and exposure limitations. Due to the recognized hazards of hydrogen peroxide, OSHA, ACGIH and NIOSH have all set average daily exposure limits of 1 ppm. Concentrations higher than that either requires respirators or no exposure due to health hazards. Some decontamination levels reach 1,000 ppm with VHP units. Most VHP equipment suppliers offer not only training on the use of the equipment but operator safety training as well, due to the associated hazards.
- d. All of the previous “no touch” technologies do not offer continuously active disinfection. They are “treatment based” and site specific and require their

antimicrobial activity to be dispersed through the atmosphere. In stark contrast to this technology, antimicrobial metals like Steriplate simply require the fugitive microbe come in contact with the surface of Steriplate, in order to begin the disinfection cycle. Steriplate does not require any human intervention or interaction as it is surface based, irrespective of the location of the bacteria. Steriplate is not only antimicrobial, but it is tarnish, corrosion and wear resistant and can be applied on a variety of devices either outside the human body (touch surfaces) or inside the body. The other technologies treat a surface once and can become recontaminated over time, depending upon the activity. These technologies are also exclusive to touch surfaces outside the body. Steriplate does not exhibit the same rapid restoration of the bacterial burden associated with other “No Touch” technologies like UV Light and HPV. Steriplate’s ability to continuously kill bacteria will also typically match or exceed the useful life of the device or surface that it is applied to.

e. It is important to note though that all of these “No Touch” technologies are used to augment good hygiene, in order to effectively minimize the spread of infectious bacteria and germs. These technologies will still require good hygiene practices in health settings and are not meant to replace these practices. Proper training and procedures in cleaning to prevent the spread of infectious bacteria or the colonization of surfaces, will always be vital in the attempt to prevent HAI’s.

Questions for the Record, Jeff Smith (President of Electro-Spec, Inc. and Steriplate LLC)

Question submitted by Rep. Elizabeth Esty

Hospital Associated Infections (HAI's)(also known as Healthcare Acquired Infections) take a significant toll on public health and lead to serious financial repercussions for the healthcare industry and the U.S. economy. Despite the significant impact of HAI's, the federal government does not have a dedicated funding stream to help combat these infections nor a dedicated entity in charge of overseeing efforts to scientifically evaluate technologies, procedures or policies to help prevent and eliminate these potentially lethal infections. What organizational measures do you believe the federal government should take to help combat Hospital Associated Infections, including rigorous evaluation of potential preventative technologies, so that there is a single entity in charge of spearheading efforts to address this important issue?

- a. The facts are that the incidence of HAI's has only decreased a negligible amount over the past (20) years. According to the CDC, there are approximately 1.7 million long-term care beds in which 1.6 to 3.8 million infections are estimated to occur each year. The best literature that I have found that addresses the question above in detail can be found on the CDC's website (http://www.cdc.gov/hai/pdfs/toolkits/toolkit-hai-policy-final_01-2012.pdf
 - i. The above toolkit puts the issues in perspective in terms of responsibility and accountability. It is imperative that the Department of Health and Human Services work with the states on developing policies for prevention, reporting, training, and incentives for new technology.
- b. On a federal level, the Department of Health and Human Services needs to continue to promote its "Health Care Innovation Awards" program to incentivize new medical technologies that could have a dramatic effect in the reduction of infections in healthcare institutions and clinics.

Responses by Mr. Morris Miller

HOUSE COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
SUBCOMMITTEE ON RESEARCH AND TECHNOLOGY
SUBCOMMITTEE ON OVERSIGHT

"Technology for Patient Safety at Veterans Hospitals"

Questions for the Record, Morris Miller, CEO, Xenex Disinfection Services

Questions submitted by Rep. Larry Bucshon, Chairman, Subcommittee on Research and Technology and Rep. Paul Broun, Chairman, Subcommittee on Oversight

1. Several references were made during our hearing to the need for more research into hospital-acquired infection prevention, ranging from biocidal technology to social/behavioral studies. Which research areas do you think are most important to address?

Morris Miller:

Screening and detection: The detection, documentation and tracking of colonized individuals are areas that require further research. Existing evidence shows that non-infected, colonized patients can contaminate the environment, creating risk for other patients and health care workers. The health care system must strike a balance between burdening patients with screening and the identification of risks to uninfected patients in facilities. As an increasing number of individuals become colonized with organisms such as *C. difficile* in their healthcare encounters (for example, in a nursing home). These colonizations pose a risk not only to the individual, but also a risk to other people. **Result: Colonized but uninfected people won't infect uninfected and uncolonized patients.**

Prevention: More research and support should go into identifying and applying technologies that prevent the transmission of organisms within the healthcare sector. There is a reluctance in the scientific community to investigate multiple simultaneous interventions because of the added statistical complexity. While study design is important, investigating interventions and new technologies in a staggered manner results in significant delays. Increased sophistication in the research design and data collection mechanisms must allow for multi-site investigations to more rapidly determine the impact of new technologies and interventions. **Result: By identifying and applying multiple technologies in multi-site investigations the scientific community can determine ways to stop the transmission of organisms in the healthcare environment.**

Antimicrobial resistance: Antimicrobial resistance is resulting in the emergence of infections for which no effective treatments are available. Antimicrobial stewardship has been in place for a number of years, but compliance to guidelines remains a problem. Additional research into both the prescribing behaviors of physicians and means to encourage and/or enforce antimicrobial stewardship is needed. This is especially important on an international scale as resistance created elsewhere in the world will eventually travel globally. Additionally, funding should be made available for alternative treatment mechanisms, as well as the development of new antibiotics. **Result: Superbugs result from poor use of antibiotics and are a worldwide threat greater than any war we may face. Stopping the transmission of pathogens in the environment and ensuring proper antimicrobial stewardship are as important as the governments military spend for the health and welfare of US citizens.**

2. Would you please give a thumbnail sketch of how your company was created? Where did the technology come from, and what was the inspiration for commercializing it? Did you have direct or indirect government assistance at the outset or along the way?

Morris Miller: Epidemiologists Dr. Mark Stibich and Dr. Julie Stachowiak (Both - Ph.D. Johns Hopkins) were conducting public health interventions when they learned of air disinfection technology being used to combat airborne tuberculosis. Recognizing that the technology, with significant adaptations, had the potential to solve a

major global health issue – HAIs -- they began evaluating its efficacy and potential for commercial applications. They founded Xenex Technologies in Houston in August 2008.

Xenex was accepted to the Houston Technology Center (HTC), the largest technology business incubator in Texas. HTC provided introductions to consultants and potential investors, which ultimately led to Stibich and Stachowiak to Morris Miller, one of the co-founders of Rackspace Hosting. Understanding the financial impact of HAIs on hospitals and the cost of HAIs to society (2,000,000 people suffering infections in the US annually and 100,000 US deaths/year), Miller was intrigued by the potential of Xenex's pulsed xenon ultraviolet-C (UVC) room disinfection system and became involved in growing the company. The company was re-incorporated as Xenex Healthcare Services in April 2009 and relocated to Austin. The first prototype of Xenex's pulsed xenon UV room disinfection system became commercially available in 2010. The company relocated in 2012 to San Antonio and was renamed Xenex Disinfection Services in 2013.

Beginning in 2012, Xenex entered into a rapid growth phase. During this time, Morris Miller became CEO and assembled a highly experienced senior management team to rapidly expand the company's sales force, manufacturing capabilities and develop additional products. Xenex continues to innovate and develop new solutions to save lives and reduce suffering by destroying the deadly pathogens that cause HAIs.

Nearly 250 hospitals across the U.S. have used Xenex's room disinfection system. Many of the hospitals consider their Germ-Zapping Robots™ part of their infection prevention team and hospital employees have bestowed names such as Rosie, Mr. Clean, Violet, Ray and Germinator on their devices.

The company did not have at the outset. However, after proving the efficacy of its Germ-Zapping Robots, in the Temple VA the company has participated in research with the VA and the Robots are used in more than 30 VA facilities around the country.

3. Following up on the preceding question, do you have any thoughts about how to make a more effective and efficient process for commercialization of new scientific knowledge?

Morris Miller: The question is very open-ended and broad. Having said that, you can perhaps think of the current structure that exists in the US and formulate more efficient ways for the various organizations to work together. For example:

CDC. The CDC should meet with companies with innovative technology no less than twice a year and the CDC should update its recommendations to improve best practices on a more frequent basis.

Commercial Insight. Industry needs to work more closely with universities and funders to establish stronger connectivity between academic research and defined commercial needs and the implications of changing payment models.

- When discoveries occur in the laboratory, most researchers are not responding to a specific market opportunity or considering the requirements for commercial success. The result is a high probability of misalignment and inefficiency as early-stage technologies attempt to find their way to market and industry seeks innovations. Commercial pathways may be even less clear in the case of new technologies. As we investigate technologies, it is important to increase awareness about how convergence across the healthcare, life sciences, and telecommunications industries can affect development requirements and regulatory processes.
- It is important for developers of early-stage health technologies to understand changing payment and business models. As the industry shifts toward more integrated and accountable care delivery models, new health technologies will need to integrate with a range of health information technologies, including electronic health records. The days of creating a business model around a CPT code are gone. With greater direction and defined commercial opportunities, entrepreneurs will be more inclined to help researchers develop their technologies, and the inventions will have better odds of success.

National Referral Network. We should consider creating an actively managed national referral network that connects new technologies to funding, investment, and commercial opportunity.

- All stakeholders could benefit from a large-scale referral network for early-stage health technologies. An actively managed national network that engages universities, investors, government organizations and commercial leaders as partners would create additional opportunity for promising research to find funding and commercial pathways beyond the bounds of a single program.

Regional Program Models. Universities and funders of acceleration programs should consider the value of regional models and how unique requirements will affect program development. Multi-university models can offer significant value by reducing the cost of developing acceleration programs. They also foster ecosystems of support for researchers and entrepreneurs that extend beyond the contacts and resources of any single university.

All the while finding ways to make more efficient the FDA/EPA and USPTO to allow technology a faster pathway.

Patent Reciprocity. The US should offer patent reciprocity to other nations around the world to allow young companies to protect their patents internationally without the tremendous filing fees and time required in every foreign jurisdiction. A reciprocal patent system would streamline the introduction of technology worldwide and would allow companies to invest more money in R&D instead of filing fees.

4. A lot of knowledge about how to prevent hospital-acquired infections has been developed in the last decade. But hundreds of thousands of hospital patients are still injured each year by infections that are considered by many experts to be preventable. Why is this problem so difficult to solve?

Morris Miller:

My opinion and discussions with IPs and Safety Officers

Despite numerous programs on Patient safety, preventable patient injuries (including HAIs) occur every year for several reasons: There is a general lack of accountability for noncompliance – includes staff, hospital leaders, license independent professionals, physicians etc.

1. Inconsistency when addressing the occurrence of an injury (HAI or other) and action plan for correction
2. Race to stay under budget creates dangerous staffing ratios (nursing, EVS etc.)
3. Lack of proper training for new employees as well as existing employees expected to perform a new task
4. Lack of appropriate mentoring for new professionals
5. Profit margin does not include cost of claims paid out for the injuries - profit and claims are kept in separate buckets
6. Lack of sustainability on projects –knee jerk approach without thoughtful consideration of presenting issue, potential solution and desired long term outcome

This Executive Summary during the NPSF Leadership Day PreConference session speaks volumes: Gerald Hickson, MD, chair of the National Patient Safety Foundation Board of Directors, provided insight from his work at the Center for Patient and Professional Advocacy (CPPA) at Vanderbilt University. According to Dr. Hickson, one of the reasons patient safety and quality improvement initiatives fail is because there is no plan to deal with noncompliance, and true leadership commitment is lacking. To be successful, patient safety initiatives require not just a good idea and sound science, but people, processes, and technology.

The CPPA team has developed a tiered intervention strategy for managing what they refer to as "unreasonable variation in human performance." This standardized method is used to address noncompliance, with agreement from leadership at the start that people will be treated the same across all departments and disciplines—even if that means firing a high-volume clinician.

According to Dr. Hickson, analysis of reports of noncompliance – and comparison with other organizations – shows that 40% of reports concern only 2% of clinicians.

Dr. Hickson proposed a number of elements required for success of safety initiatives:

1. Leadership commitment not just to the project, but to the methods of enforcing codes of conduct
2. Understanding by all of the need and the impact
3. Measurement tools and plans
4. Multilevel training
5. Alignment of the project with the organizational goals, vision, or core values
6. Resources for the project
7. A dedicated project team
8. A project champion
9. The will to address unnecessary variation in human performance

Gregg Meyer, MD, MSc, vice chair of the NPSF Board of Directors, closed the program by asking attendees to think about "What are you going to do differently based on what you heard today?" He summarized the major points of the day:

1. Data plus anecdote equals action. Make the best use of storytelling and metrics.
2. Talk about the outcomes that matter. Instead of talking about hand hygiene, show MRSA and VRE rates. Show: "This is the impact it had on us financially."
3. Search for positive deviance. We spend too much time on the lower end of performance. Understanding what is going on at the positive end is a powerful opportunity.
4. Expose biases and seek to understand naysayers.
5. Never waste a crisis: use a serious safety event to effect change.
6. Patient safety professionals have the opportunity to be seen as part of the solution. By investing in safety, organizations will see a return on that investment.
7. Be flexible with execution. Keep a single promise: It's going to get better (not perfect)

<http://www.npsf.org/>

<http://reginaholiday.blogspot.com/2011/04/walking-gallery.html>

5. Medicare has implemented financial penalties on hospitals that do not exceed thresholds for hospital-acquired infections, with the thresholds and penalties increasing over time. State Medicaid programs and private sector insurance companies are also turning to financial incentives and disincentives to drive improvements in patient safety. Do you think these payment changes are constructive? Do you think these changes have been at least partly responsible for recent years' incremental improvements in infection rates?

Morris Miller: Yes and yes. Initial HAI incentives or disincentives have focused primarily on device associated infections (Catheter Associated Urinary Tract Infections – CAUTI and Central Line Associated Blood Stream Infections – CLABSI). More recently, the programs added measures for Surgical Site Infections (SSIs) *Cdiff* and MRSA. We believe these programs will encourage adoption of new processes and technology that will have a dramatic, favorable impact on the cost and outcomes of our health system.

The sooner the measures include the environment (which we know we can disinfect!) the sooner you will see dramatic drops in infection rates. A patient should not occupy a room that has not received 3 (5 minute – 15 minutes total) Xenex robot disinfection cycles or 3 (45 minute – 2 hours 15 minutes total) Mercury bulb disinfection cycles.

6. What do you think are the most serious deficiencies in how we are approaching the problem of antibiotic resistant infections? Where would you put the emphases in new research? Are you aware of any promising research or new ideas that might make a difference in combating antibiotic resistant infections?

Morris Miller: I think we need better control of prescription practices in hospitals, specifically, making sure that the bug/drug matches are appropriate. Every hospital has a different microbial population, and we should be more diligent in making sure patients are getting the right dose of the right drug, administered by the right route. Failure of one of these three items can lead to low level exposure of the microbe to the antibiotic, and induce resistance. I think a good focus for research would be effective methods of encouraging behavior change among physicians prescribing antimicrobials, and the implementation of multidisciplinary teams to assess antimicrobial use in hospitals.

7. Are you aware of significant social/behavioral research into how to stimulate higher rates of compliance with infection prevention protocols?

Morris Miller: Many interventions have been implemented to improve the compliance with infection prevention practices. These interventions cover a wide-range of practices including hand hygiene, disinfection, sterilization, use of personal protective equipment and antimicrobial prescribing. To date, there has been difficulty sustaining a long-term impact on behavior. Typically, the level of compliance at a facility is a representation of the culture of that facility. Recent changes on CMS reimbursement seems to have helped in raising the awareness of infection control with the hospital leadership and has likely contributed to recent improvements in compliance.

Disinfecting the environment may be the best way to reduce infections because even poor compliance will not result in the passage of a pathogen that is not in the environment. Thorough environmental disinfection, like safety belts and airbags in cars, assumes that operators will do their best but will make mistakes. In most instances, the safety belts, airbags and environmental disinfection will protect the occupants of the car or the hospital room.

8. In some other developed countries and areas of the world (Scandinavia, for instance), hospital acquired infection rates are much lower than in the U.S. To your knowledge, are different infection fighting technologies or protocols used in these places?

Morris Miller: The differences in infection rates can be largely attributed to the differences in the population dynamics. Countries with lower rates tend to have different patterns of movement among the population as well as different levels of access to medical care.

9. What other technologies, besides those discussed in depth at the hearing, are currently being used to mitigate or prevent hospital acquired infections? How do they compare in cost and efficacy to the technologies discussed in depth at the hearing?

Morris Miller: There are numerous technologies available in the marketplace with claims and targets surrounding HAI reduction. When considering these products, one must consider the entire infection control bundle at a facility. Some of the products may provide an incremental increase in patient safety while other products could provide a new means or method of creating patient safety. Comparing products directly is not possible without knowing the full context of the facility and the problems that are being addressed.

Rep. Eric Swalwell

Member, Subcommittee on Oversight
Committee on Science, Space &
Technology Questions for the Record
(QFRs)

-Joint Hearing-

Subcommittee on Research & Technology
and

Subcommittee on Oversight

"Technology for Patient Safety at Veterans Hospitals"

Thursday, June 26, 2014

Question for Mr. Morris Miller, Chief Executive Officer, Xenex Disinfection Services

QFR #1: Your company produces a pulsed xenon ultraviolet light (PPX-UV) disinfection device to help eliminate Hospital Associated Infections (HAIs) (also known as Healthcare Acquired Infections). In some cases your associated companies, such as Xenex Healthcare Services, LLC, based in San Antonio, Texas, have provided grants or other compensation to individuals or entities conducting evaluations or assessments of the effectiveness and efficiency of this device. In one case Xenex Healthcare Services, LLC provided a grant to researchers at the Central Texas Veterans Health Care System, for instance.¹

- **Please provide a list of any and all grants or other compensation provided to researchers or institutions involved in studies or evaluations related to assessing the effectiveness or efficiency of Xenex's pulsed xenon ultraviolet light (PPX-UV) technology.**

Morris Miller:

Xenex has funded three institutions to investigate the pulsed xenon technology it produces.

1. Cooperative Research and Development Agreement with the Central Texas Veterans Research Foundation entitled: "Central Texas Veterans Healthcare System (CTVHCS)"
2. A research agreement and grant to the University of Texas, MD Anderson Cancer Center, to support a research fellow and laboratory costs in the exploration of the impact of pulsed xenon disinfection on HAI risk.
3. A grant to Cambridge University entitled "The effects of pulsed xenon ultraviolet (PX-UV) disinfection on environmental contamination in operating rooms"
4. Honorarium to Dr. Roy Chemaly for educational presentations.
5. A research grant to Wayne State University entitled: ""The effects of pulsed xenon ultraviolet (PX-UV) disinfection on environmental contamination in operating rooms"

Rep. Elizabeth Esty

Member, Subcommittee on Research & Technology

Committee on Science, Space & Technology

Questions for the Record (QFRs)

-Joint Hearing-

Subcommittee on Research & Technology and

Subcommittee on Oversight

"Technology for Patient Safety at Veterans Hospitals"

Thursday, June 26, 2014

Question for ALL WITNESSES

QPR #1: Hospital Associated Infections (HAIs) (also known as Healthcare Acquired Infections (HAIs) take a significant toll on public health and lead to serious financial repercussions for the healthcare industry and the U.S. Economy. Despite the significant impact of HAIs, the federal government does not have a dedicated funding stream to help combat these infections nor a dedicated entity in charge of overseeing efforts to scientifically evaluate technologies, procedures or policies to help prevent and eliminate these potentially lethal infections. What organizational measures do you believe the federal government should take to help combat Hospital Associated Infections, including rigorous evaluation of potential preventive technologies, so that there is a single entity in charge of spearheading efforts to address this important issue?

Morris Miller: The federal government should create an entity, possibly within the NIH, that is committed to evidence-based patient safety and HAI prevention. This entity would consolidate information from other entities such as professional societies and the CDC to create standardized guidelines and regulations. The entity would also fund researchers to investigate promising new technologies and interventions. It is important to note that the entity must be structured in such a way to assist the healthcare sector in "catching up" to other sectors in terms of technology adaptation while retaining high standards of evidence. Currently, HAI prevention guidelines are updated too infrequently, leaving the public exposed to risk because of the long scientific publishing cycle and journal editorial priorities. The entity created should contemplate creating a new scientific journal in the field committed to rapidly publishing case studies, best practices and scientific articles in an open access format. This sharing of information is critical to accelerate the rate of adoption of solutions within the healthcare sector.

Appendix II

ADDITIONAL MATERIAL FOR THE RECORD

PREPARED STATEMENT OF FULL COMMITTEE RANKING MEMBER EDDIE BERNICE
JOHNSON

OPENING STATEMENT

Ranking Member Eddie Bernice Johnson (D-TX)
Committee on Science, Space, and Technology

Joint Subcommittee Hearing
"Technology for Patient Safety at Veterans Hospitals"

June 26, 2014

Thank you, Mr. Chairman.

As the Chairman is aware, yesterday I formally requested that the VA not send their witness to testify without having written testimony in advance. I want to emphasize that I do not believe this is the fault of the VA or the witness. They were given little time to prepare his testimony and informed the Majority days ago that written testimony would not be available before the hearing. But regrettably the Majority made no efforts to reschedule the hearing to allow for written testimony. Having a witness testify before this Committee without a written statement is highly unusual and sets a bad precedent. It also puts the witness in a difficult position, testifying under oath without his testimony being cleared by his Agency or OMB. I wish the Majority had chosen a different path.

This morning we are discussing how technology can be used to increase patient safety at Veterans Hospitals.

I worked in a VA Hospital in Dallas where I eventually became Chief Psychiatric Nurse for 15 years. I loved my work and the people I was privileged to serve. I know personally how the VA system can provide our nation's men and women in uniform with health care that they more than earned by protecting our freedom. I also saw the hard-working and loyal culture that exists at VA Hospitals.

Unfortunately, there is some work to be done to ensure that all of our nation's heroes have access—and timely access—to medical care. I have heard from many veterans in my district who have had to wait long periods of time to get an appointment at a VA hospital, including some who never end up seeing a doctor. This is inexcusable and must be fixed.

But this hearing is not about fixing the VA. The Committees on Veterans' Affairs in both the House and Senate have worked on bills that were passed out of their respective bodies and the House voted to convene a conference committee to work out the differences between those two bills just last week.

As the Science, Space, and Technology Committee, we should be focusing on research and technology that can increase patient safety at *all* hospitals, public and private.

One big issue of patient safety at all healthcare facilities is healthcare-associated infections. An estimated 75,000 patients die each year from healthcare-associated infections. It is clear that these infections add significantly to the cost of healthcare and as a result burden our economy.

Healthcare-associated infections are largely preventable and we must work to eliminate them as much as possible. As a former nurse, I know that stopping the spread of any infection begins with proper hand hygiene. Since healthcare workers are the most common vehicle for transmitting healthcare-associated pathogens, hand hygiene is a leading measure for preventing and reducing the transmission of healthcare-associated infections.

I am also excited at the promise technology offers to reduce or eliminate healthcare-associated infections, but do want to mention that this is an area that still needs more fundamental research. In order to work on eliminating healthcare-associated infections, we need to understand things like the biology of healthcare-associated infections, specific mechanisms responsible for transmission, and the variation in implementation of policies and processes across hospitals. Any conversation about ways to reduce healthcare-associated infections must include the need for research into these questions and funding to support that research.

It is exciting to think that if we just had the right gadget, then we could eliminate healthcare-associated infections completely. However, as our witnesses can discuss, technology is not guaranteed to reduce or prevent healthcare-associated infections. In fact, some technologies may actually increase healthcare-associated infections. It is vital that we conduct proper testing and evaluation of potential new technologies before adopting them into a healthcare environment.

Finally, I look forward to hearing from the witnesses about the role the federal government can play in funding research into healthcare-associated infections as well as providing funding to properly test and evaluate new technologies that could dramatically reduce or eliminate these infections.

I want to thank all the witnesses for being here today. I yield back the balance of my time.

ARTICLES SUBMITTED BY SUBCOMMITTEE CHAIRMAN LARRY BUCSHON

VA reportedly stopped sending teams to try to improve underperforming hospitals

Published June 10, 2014
FoxNews.com

The Department of Veterans Affairs suspended a program that sent teams of doctors and monitors to try to improve its worst-performing facilities for approximately two years, according to a published report.

The Wall Street Journal, citing agency doctors and internal records, reported that the visits were "paused" beginning in early 2011. Dr. Carolyn Clancy, the head of the agency's quality and safety program, said the VA had begun to revive the program about a year ago.

The Journal report specifies seven VA hospitals that have consistently received a rating of one star out of a possible five from the VA since at least 2011. Those hospitals are located in Augusta, Ga.; Little Rock, Ark.; Providence, R.I.; Murfreesboro, Tenn.; Oklahoma City; Phoenix; and Puget Sound (Seattle), Wash. The star rating system measures hospitals according to key performance standards, including death rates among acute-care patients and among patients suffering from congestive heart failure and pneumonia. Length of stays and readmission rates are also taken into consideration.

It is not clear why the agency halted the visits, though the Journal report cites current and former VA doctors who claim that top managers of the agency played down the utility of basing the ratings system on specific medical outcomes.

Dr. Clancy claimed to the Journal that each of the hospitals with the poorest rating "has gotten at least one visit in the last year or year and a half."

The report comes as a government report released Monday found that more than 57,000 veterans have been waiting 90 days or more for their first VA medical appointments, and an additional 64,000 appear to have never gotten appointments at all after enrolling.

"This behavior runs counter to our core values," the report said. "The overarching environment and culture which allowed this state of practice to take root must be confronted head-on."

Richard Griffin, the VA's acting inspector general, said his office was investigating 69 VA medical facilities nationwide for possible wrongdoing, up from 42 two weeks ago. The investigations could result in criminal charges, which Griffin said may be needed to combat senior VA leaders who have allowed and even encouraged fraudulent scheduling practices often referred to as "gaming" the system.

"Once someone loses his job or gets criminally charged for doing this, it will no longer be a game. And that will be the shot heard around the system," Griffin said Monday night at a hearing of the House Veterans Affairs Committee.

Acting VA Secretary Sloan Gibson said earlier Monday that VA officials have contacted 50,000 veterans across the country to get them off waiting lists and into clinics and are in the process of contacting 40,000 more.

The controversy forced VA Secretary Eric Shinseki to resign May 30. Shinseki took the blame for what he decried as a "lack of integrity" through the network. Legislation is being written in both the House and Senate to allow more veterans who can't get timely VA appointments to see doctors listed as providers under Medicare or the military's TRICARE program. The proposals also would make it easier to fire senior VA regional officials and hospital administrators.

House Speaker John Boehner, R-Ohio, said the report demonstrated that Congress must act immediately.

"The fact that more than 57,000 veterans are still waiting for their first doctor appointment from the VA is a national disgrace," Boehner said.

The new audit said a 14-day agency target for waiting times was "not attainable," given poor planning and a growing demand for VA services as Vietnam-era vets age and younger veterans from the Iraq and Afghanistan wars enter the system. The 2011 decision by senior VA officials to set the target, and then base bonuses on meeting it, was "an organizational leadership failure," the report said.

A previous inspector general's investigation into the troubled Phoenix VA Health Care System found that about 1,700 veterans in need of care were "at risk of being lost or forgotten" after being kept off an official, electronic waiting list.

The report issued Monday offers a broader picture of the overall system. The audit includes interviews with more than 3,772 employees nationwide between May 12 and June 3. Respondents at 14 sites reported having been sanctioned or punished over scheduling practices.

Wait times for new patients far exceeded the 14-day goal, the audit said. For example, the wait time for primary care screening appointment at Baltimore's VA health care center was almost 81 days. At Canandaigua, New York, it was 72 days. On the other hand, at Coatesville, Pennsylvania, it was only 17 days and in Bedford, Massachusetts just 12 days. The longest wait was in Honolulu — 145 days.

But for veterans already in the system, waits were much shorter.

For example, established patients at VA facilities in New Jersey, Connecticut and Battle Creek, Michigan, waited an average of only one day to see health care providers. The longest average wait for veterans already in the system was 30 days, in Fayetteville, North Carolina, a military-heavy region with Fort Bragg Army Base and Pope Air Force Base nearby.

It was not clear whether all 64,000 veterans who did not get appointments remained interested in being seen by the VA.

Despite the long waiting list, the audit said most veterans seeking care are able to get timely appointments. About 96 percent of the 6 million appointments scheduled at VA facilities as of May 15 were slated within 30 days, the report said.

That reassuring statistic came with a warning, however. Under VA guidelines that have since been rescinded, veterans were supposed to be seen within 14 days of their desired date for a primary care appointment. The inspector general described a process in which schedulers simply selected the next available appointment and used that as the purported desired date. That practice allowed numerous — and false — zero-day wait times, the IG said.

Gibson, the acting VA secretary, said the department is hiring new workers at overburdened clinics and other health care facilities across the nation and is deploying mobile medical units to treat additional veterans.

The VA believes it will need \$300 million over the next three months to accelerate medical care for veterans who have been waiting for appointments, a senior agency official said in a conference call with reporters. That effort would include expanding clinics' hours and paying for some veterans to see non-VA providers. The official said he could not say how many additional health providers the VA would need to improve its service.

The report said 112 — or 15 percent — of the 731 VA facilities that auditors visited will require additional investigation, because of indications that data on patients' appointment dates may have been falsified, or that workers may have been instructed to falsify lists, or other problems.

Boehner said the House would act on legislation this week to allow veterans waiting at least a month for VA appointments to see non-VA doctors, and said the Senate should approve it, too. An emerging bipartisan compromise in the Senate is broader than that, but senators have yet to vote on it.

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The Associated Press contributed to this report.

Doctors' War Stories From VA Hospitals

Administrators limited operating time so that work stopped by 3 p.m.

By Hal Scherz
May 27, 2014 7:26 p.m. ET

With the recent revelations about the disgraceful treatment of patients by the Veterans Affairs hospitals, the public is discovering what the majority of doctors in this country have long known: The VA health-care system is a disaster. Throwing more money at the system, or demanding the scalps of top bureaucrats—Washington's reflexive response to any problem of this sort—won't repair the mess. What's needed is a fundamental rethinking of how to provide medical care for America's veterans.

The federal government runs two giant health-care programs—Medicare and the VA system. Medicare is provided by private physicians and other providers. Its finances are a mess, but the care that seniors receive is by and large outstanding. The VA health-care system is run by a centrally controlled federal bureaucracy. Ultimately, that is the source of the poor care veterans receive.



The Phoenix VA Health Care Center. Associated Press

U.S. doctors are well aware of the problems with VA hospitals because many of us trained at them. There are 153 VA hospitals. Most of them are affiliated with the country's 155 medical schools, and they play an integral role in the education of young physicians. These physicians have borne witness to the abuses and mismanagement, and when they attempt to fight against the entrenched bureaucracy on behalf of their patients, they meet fierce resistance.

Most doctors have their personal VA stories. In my experience at VA hospitals in San Antonio and San Diego, patients were seen in clinics that were understaffed and overscheduled. Appointments for X-rays and other tests had to be scheduled months in advance, and longer for surgery. Hospital administrators limited operating time, making sure that work stopped by 3 p.m. Consequently, the physician in charge kept a list of patients who needed surgery and rationed the available slots to those with the most urgent problems.

Scott Barbour, an orthopedic surgeon and a friend, trained at the Miami VA hospital. In an attempt to get more patients onto the operating-room schedule, he enlisted fellow residents to clean the operating rooms between cases and transport patients from their rooms into the surgical suites.

Instead of offering praise for their industriousness, the chief of surgery reprimanded the doctors and put a stop to their actions. From his perspective, they were not solving a problem but were making federal workers look bad, and creating more work for others, like nurses, who had to take care of more post-op patients.

At the VA hospital in St. Louis, urologist Michael Packer, a former partner of mine, had difficulty getting charts from the medical records department. He and another resident hunted them down themselves. It was easier for department workers to say that they couldn't find a chart than to go through the trouble of looking. Without these records, patients could not receive care, which was an unacceptable situation to these doctors. Not long after they began doing this, they were warned to stand down.

There are thousands of other stories just like these.

In my experience, the best thing that a patient in the VA system could hope for was that the services he needed were unavailable. When that is the case, the VA outsources their care to doctors in the community, where their problems are promptly addressed. But these patients still need to return to the VA system for other services and get back on a long waiting list.

Proponents of the Affordable Care Act have long used the VA to showcase the benefits of federally planned and run health care. Doctors know otherwise—and it is no surprise that a majority of them have opposed a mammoth federal regulatory apparatus to control health care in this country. The systemic problems with the VA bureaucracy are a harbinger of things to come.

The best solution for veterans would be to wind down the VA hospitals. The men and women who have served in our armed forces should be supplied with a federally issued insurance card allowing them to receive their care in the community where it can be delivered better and more efficiently.

The veterans who receive their care at VA hospitals are the kindest and most grateful patients that I have had the privilege to care for in my career. Unfortunately, they are getting shortchanged. The time to repair this national embarrassment is long past.

Dr. Scherz is a pediatric urological surgeon at Georgia Urology and Children's Healthcare of Atlanta and serves on the faculty of Emory University Medical School.

Veterans Affairs Hospitals Vary Widely in Patient Care

Internal Records Show Facilities Such as Phoenix Have Far Higher Death Rates Than Peers

By Thomas M. Burton and Damian Paletta

Updated June 3, 2014 8:05 a.m. ET

According to internal Veterans Affairs records, wide variations have emerged in the quality of medical care offered at VA hospitals, with death rates and lethal infections far higher in some facilities than in others. WSJ's Tom Burton explains on the News Hub. Photo: AP

The Phoenix facility at the heart of the crisis at the Department of Veterans Affairs is among a number of VA hospitals that show significantly higher rates of mortality and dangerous infections than the agency's top-tier hospitals, internal records show.

The criticism that precipitated last week's resignation of VA Secretary Eric Shinseki has focused largely on excessive wait times for appointments across the VA's 150-hospital medical system.

But a detailed tabulation of outcomes at a dozen VA hospitals made available to The Wall Street Journal illustrates a deeper challenge; vastly disparate treatment results and what some VA doctors contend is the slippage of quality in recent years at some VA facilities.

Some of the discrepancies are stark, especially for an agency known for offering high-quality care in 50 states.

Care Gaps

An internal database of medical outcomes at select Veterans Affairs hospitals shows a wide discrepancy in quality across the 150-hospital system.

	☆☆☆☆☆ PHOENIX rated one-star (lowest) in quality by VA	★★★★★ BOSTON rated five-star (highest) in quality by VA	VA five-star hospitals' average
Acute care 30-day death rate (1.0 is expected rate)	1.13	0.83	0.86
IV line bloodstream infection	3.80 per 1,000 cases	0.12 per 1,000 cases	0.32 per 1,000 cases
Pneumonia 30-day death rate	11.39%	8.40%	9.53%

Source: VA SAIL database, 12 months through first quarter 2014. Results are risk-adjusted.

The Wall Street Journal

The rate of potentially lethal bloodstream infections from central-intravenous lines was more than 11 times as high among patients at the Phoenix facility than it was at top VA hospitals, data from the year ended March 31, 2014, show.

Those infections, called sepsis, can quickly cause multiple organ failure and kill an otherwise relatively healthy patient within days or even hours. The data don't show what percentage of patients died as a result.

Among patients admitted to the hospital for acute care, the Phoenix VA Health Care System had a 32% higher 30-day death rate than did the top-performing VA hospitals, a finding flagged as statistically significant by the agency's medical analysts.

By contrast, Boston's VA hospital, considered among the system's best, had a central-IV-line, bloodstream-infection rate that was 63% below the average of the top-performing hospitals. It also had a slightly better-than-average, 30-day mortality rate for acute care.

Scott McRoberts, spokesman for the Phoenix VA Health Care System, said on Monday the database "is an internal measurement system to benchmark our improvement, and is not for public consumption."

Variations in the quality of health care exist outside the VA system as well, though it is difficult to measure because relatively small numbers of hospital groups report a range of medical outcomes. But some experts in medical-quality measurement say the VA discrepancies stand out.

"Wide variations are a problem at both the VA and private hospitals. But I would expect to see much smaller variations in a national, integrated delivery system like the VA," said Ashish Jha, a professor at the Harvard School of Public Health and a physician in the VA system.

In all, the data point to VA hospitals in Phoenix, Atlanta, Houston and Dublin, Ga., as among the system's lower-rated facilities, while those in Boston, Cleveland and Minneapolis rank among the top performers, according to VA officials and internal documents.

The findings come from a nonpublic VA database called Strategic Analytics for Improvement and Learning, known as SAIL. SAIL tracks procedure outcomes and ranks VA hospitals on a scale of five stars, the best, to one star, the lowest.

The SAIL data tabulate hospital performance across a wide range of safety measures, such as acute-care death, death from congestive heart failure and pneumonia, and deaths from avoidable causes like urinary-tract infections and ventilator-associated pneumonia.

A VA spokesman said SAIL has emerged as a useful barometer for the agency, but is "still very much a work in progress" whose efficacy will increase as the agency "gains more experience with it and refines its development and use."

On Tuesday morning, the spokesman said the VA's Veterans Health Administration targets "facilities that fail to demonstrate improvement" and subjects those hospitals "to increasing degrees of scrutiny and oversight by VHA leadership."

The VA spokesman didn't identify specific hospital centers that might be subject to higher scrutiny.

The Veterans Administration's inspector general found systemic scheduling problems in its review of 42 hospitals across the country, according to an interim report. How did schedulers in Phoenix cook the books? WSJ's Jason Bellini has #TheShortAnswer.

The VA's inspector general in recent months has publicly used the SAIL data to point out significant problems at individual hospitals, illustrating how valued the information has become when identifying health-care problems.

VA hospitals in Atlanta, Houston and Dublin, Ga., declined to comment or referred questions to the national VA office. The VA spokesman wouldn't address variations in care.

In other examples of variations in care, the Atlanta VA Medical Center, a two-star hospital for quality, has more than three times the rate of central-IV infections than the average of five-star VA hospitals. Houston's VA hospital, ranked as a two-star hospital, had a 47% higher acute-care mortality rate than the five-star hospital rate.

The VA has disclosed a variety of health-care quality data for its hospitals, often including more information than the great majority of private hospitals make public.

It has built several Internet portals that allow the public to see information about infection rates, among other things, and how it compares with agency goals.

But the database published by the VA is less detailed and offers less ability to compare hospitals than SAIL.

For example, the Phoenix VA doesn't appear to be an outlier on the VA's main comparison website, www.hospitalcompare.va.gov.

By comparison, Pennsylvania has published hospital-specific medical outcomes from private and other hospitals for decades. They showed great variations initially, but a look at the current data set appears to show less variability among institutions.

The VA has long been on the cutting edge of medical advances, including in its gathering and disseminating of data.

It pioneered a national surgery quality-improvement program in recent decades that rigorously measured its own surgeons' performance. By 2011, it also took the extraordinary step of beginning to publish some of its hospitals' medical-complication and surgical death rates, with an eye toward ratcheting up excellence.

At the same time, the wide variation in outcomes among facilities sparked an internal battle over how much detailed data should be made public, said current and former VA doctors.

William E. Duncan, who supervised publication of medical outcomes until his 2012 departure, said in an interview that he urged that more data be posted regardless of the impact.

But his superior, VA Under Secretary for Health Robert Petzel, argued that the more detailed outcomes should stay private at the VA, senior VA doctors say.

Efforts to reach Dr. Petzel, who was forced out of office recently, weren't successful.

Amid the spat, Dr. Duncan was forced out of the agency in 2012, he said. The VA spokesman didn't answer questions about Dr. Duncan's departure.

Dr. Duncan, now living in the Maryland suburbs of Washington, said the VA system of measuring and publishing outcomes was designed with lofty aspirations: "The goal was not for hospitals to be average performers. The goal was to be in the top 10%."

He is upset by the recent complaints about the VA.

"Our patients have little recourse, and they rely on our staff to tell them the truth," he said. "We can't forget that medical quality is not just access to care."

As for the relatively poor results from Phoenix, this was no secret within the department, he said. "It was in their own data."

Top Lawmakers Call for Disclosure of VA Hospital Data

Congressmen Say Agency Should Make Available to Public the VA's Metrics on Mortality, Infection

By Damian Paletta And Thomas M. Burton

Updated June 3, 2014 12:10 p.m. ET

WASHINGTON—Two top lawmakers leading Congress's probe of the Department of Veterans Affairs called on Tuesday for the agency to disclose internal analyses that measure treatment outcomes at VA hospitals.

The request came after a [Wall Street Journal article](#) revealed significantly higher rates of mortality and dangerous infections at some VA hospitals compared with others.

The finding was based on internal VA data called Strategic Analytics for Improvement and Learning, or SAIL. The data, which the VA doesn't make public, rank and score more than 100 VA hospitals according to a variety of metrics, including infection and mortality rates.

"Every veteran seeking care at a VA hospital deserves to know exactly what he is walking into," said Rep. Jeff Miller (R., Fla.), chairman of the House Committee on Veterans' Affairs. "That's why all of VA's SAIL data should be available to the public."

"We need to pull the covers off of this," said Rep. David Scott (D., Ga.). "The VA has covered up long enough. We have to restore the public's confidence."

A VA spokesman didn't immediately respond to a request for comment on Tuesday.

The SAIL reports contain analyses that measure the outcomes of health-care treatment. For example, the SAIL data reveal that the rate of potentially lethal bloodstream infections from central-intravenous lines was more than 11 times as high among patients at the Phoenix facility than it was at highest-rated VA hospitals.

The VA is facing a firestorm of bipartisan criticism following revelations that a number of medical centers held secret waiting lists for veterans in order to mask how long people had to wait for care. VA Secretary Eric Shinseki [resigned last week](#).

There are roughly 150 medical centers within the VA system, and a rising number of veterans seek health care from the VA each year. SAIL data reviewed by the WSJ found that the outcomes of several hospitals varied widely, with higher rates of mortality at the VA in Phoenix, for example, than the VA in Boston.

"While most veterans receive quality medical care from VA facilities, some VA medical centers are lagging painfully behind," Mr. Miller said.

The data are risk-adjusted to remove the confounding effect of factors like age, smoking, diabetes and other diseases that could skew the results and bias them for or against a given hospital.

While the VA hasn't disclosed the SAIL data, the VA's inspector general has cited it in numerous reports as a way to spotlight problems with different hospitals.

Political Triage at the VA

For veterans on the wait list, the Senate fires a three-committee salute.

Updated June 8, 2014 7:00 p.m. ET

Washington's attention span on the Veterans Affairs scandal seems to be expiring. Though 42 of the VA's 152 major campuses (27%) are still under investigation for falsifying wait-time records, the Senate is converging on a bipartisan deal that claims to solve the problem. The pity is that the price of so little reform is another layer of political enamel on the VA status quo.

At least Vermont Independent Bernie Sanders and Arizona Republican John McCain are moving slightly beyond the standard trumpet summons of a blue-ribbon commission—though of course their compromise appoints not one, or even two, but three of those. The bill loosens the civil-service rules so the VA brass can demote or fire senior employees for cause such as negligence or incompetence. This is what counts as a reform breakthrough in Washington these days.

The Senate's best idea is a safety valve that would allow patients to escape the VA when the treatment queues exceed the bureaucratic scheduling targets. The target for a phantom if not a real appointment is now an absurd 14 days, which would try even the best U.S. hospitals. The bill adopts a proposal from Mr. McCain, Oklahoma's Tom Coburn and several GOP colleagues that would issue veterans a "choice card" to seek care outside the VA if the wait is longer than the two-week max, an incentive to set more realistic goals. Alas, this partial privatization is only a trial that runs out in two years.

In return for this workforce concession, Mr. Sanders was able to extract from Republicans \$500 million in emergency spending to expedite hiring for new doctors, nurses and other staff. This is on top of this year's \$57.3 billion VA budget, which is 106% more than in 2003 though patients have increased by only 30%.

The bill also gives the VA \$236.9 million to lease or build 27 new major medical facilities in 18 states and Puerto Rico. And the Phoenix VA will be rewarded for its dissembling and dysfunction that resulted in preventable deaths with a new \$20,757,000 "community-based outpatient clinic." In the world of government, when you fail you get *more* money. Then everyone expresses outrage and surprise when we get more failure.



Arizona Sen. John McCain, center, with Sen. Jeff Flake, left, and North Carolina Sen. Richard Burr during a press conference about veterans affairs on Tuesday. EPA

The White House is leaking that it may nominate Toby Cosgrove of the Cleveland Clinic to be the next VA secretary, and we're not sure what he did to deserve that punishment. But if he and Congress want to do something to end the VA's failing culture, they could do worse than read the remarkable lead editorial in this week's *New England Journal of Medicine*.

Kenneth Kizer led a VA-improvement wave in the 1990s and Ashish Jha of Harvard is a staff physician at the Boston VA. They describe the VA's "toxic milieu" as the result in part of "increasingly centralized control of care delivery and associated increased bureaucracy." Those qualities are usually why liberals tout the VA as a health-care model, with government experts trumping individual physician discretion.

Drs. Kizer and Jha observe that the performance measurement programs of the 1990s have swollen from two dozen metrics to "hundreds of measures with varying degrees of clinical salience" whose use "not only encourages gaming but precludes focusing on, or even knowing, what's truly important." The central-office management in Washington has grown to 11,000 workers from a mere 800 two Presidents ago, and the vast bureaucracy has taken over decisions that used to be made in autonomous regional centers.

After the Senate deal, look for the politicians in both parties to drop this issue and move on. The Kizer-Jha diagnosis is merely one among many showing that the VA's problems run far deeper than a new hospital building or more spending can solve, which means that the Senate's non-reform reform betrays veterans one more time.

VA Halted Visits to Troubled Hospitals

Change Came as Growing Number of Facilities Had High Death Rates

By Thomas M. Burton
June 9, 2014 7:42 p.m. ET

The Department of Veterans Affairs stopped sending teams of turnaround experts to underperforming hospitals at the same time a growing number of VA facilities showed consistently high death and complication rates, internal agency records and interviews reveal.

Starting in 2011, when the VA instituted a new system to track performance standards, five VA hospitals notched consistently poor scores on a range of critical-care outcomes, including mortality and infection rates. By the first quarter of this year, that bottom-performing group had expanded to at least seven hospitals, records show.

During most of that time, VA senior management suspended a long-standing program that had sent teams of doctors and monitors to its worst-performing hospitals to try to improve them, agency doctors said.

The VA has come under intense criticism for prolonged waiting times for veterans to obtain care, a crisis that prompted VA Secretary Eric Shinseki to resign last month. An internal VA audit released Monday found some 60,000 veterans are experiencing long wait times for health care, while 70% of VA facilities auditors visited had used an alternative to official appointment schedules to make wait times appear much shorter.

The intense focus on patient wait times has obscured what appear to be lingering, and in some cases worsening, quality issues at a number of the agency's 127 acute-care medical and surgical hospitals.

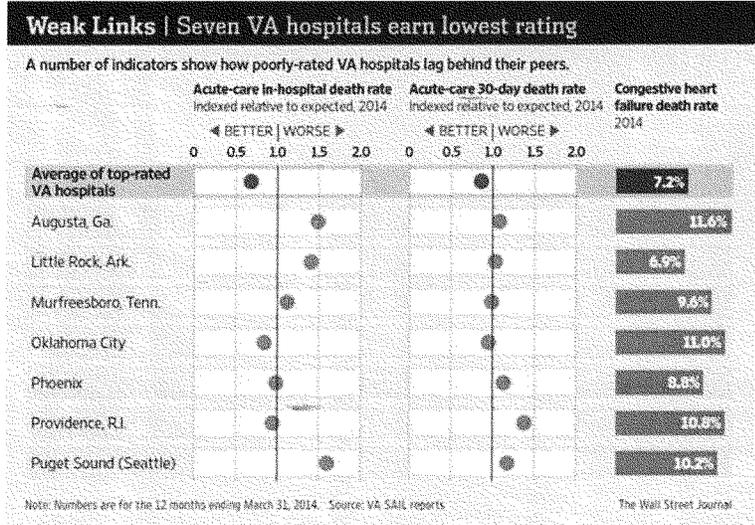
Carolyn M. Clancy, a national medical-quality expert recently appointed to run the agency's quality and safety program, said there is no simple explanation for the persistent failings at some VA hospitals.

"The 'why' question is hard," Dr. Clancy said in an interview Monday. "Sometimes it's about leadership" at individual facilities.

She said the VA began to revive the hospital site-visit program about a year ago. "Every one of these hospitals" with the poorest outcomes "has gotten at least one visit in the last year or year and a half," she said. And if a death occurs in a hospital's heart-catheterization center, she added, "there's a team in there within 24 hours."

The new scrutiny follows a period, beginning in early 2011, when such visits "were paused," according to Joseph Francis, the VA's director of clinical analytics. Current and former VA doctors say the lag in scrutiny came at a time of turmoil when top managers of the agency, some of whom since have been ousted, played down the utility of measuring specific medical outcomes.

The post Dr. Clancy now holds had been vacant for more than two years.



Five VA hospitals scattered across the country have consistently ranked at the bottom of the VA's quality rating—one star out of a possible five—since at least 2011. The stars measure hospitals according to key performance standards, such as death rates among acute-care patients and among patients suffering from congestive heart failure and pneumonia.

That roster of underperforming hospitals has recently expanded to at least seven, in Augusta, Ga., Little Rock, Ark., Providence, R.I., Murfreesboro, Tenn., Oklahoma City, Phoenix and Puget Sound (Seattle), Wash., VA documents show.

The low ratings resulted principally from poor scores on measures involving deaths and complications, though other factors such as length of stay and readmission rates played a role. All the measures relate to quality of care, experts say. The quality numbers were "risk adjusted" to account for factors such as patient age, smoking history and poor health.

Five of the low-ranking hospitals didn't respond to requests for comment. A spokeswoman for the Phoenix hospital said, "We continue to look at [the data] to identify opportunities for improvement." A spokesman for the Central Arkansas VA Healthcare System in Little Rock said it accepts especially complex cases from six surrounding states, so its length-of-stay numbers make the total-quality picture look worse.

As of March 31, six VA hospitals—in Ann Arbor, Mich., Boston, Cleveland, Minneapolis, Wichita, Kan., and the VA's Connecticut campuses in West Haven and Newington—scored in the top, five-star tier in quality.

Medical-quality experts at the VA and elsewhere said that a given hospital may receive a poor numerical rating occasionally without being of much significance. But poor results across the board, and over an extended period, are far more serious, they said.

The VA's one-star hospitals appear to exist in a different world from those at the top, and veterans appear to receive far worse care there as a result.

For instance, compared with an average of the top VA hospitals, Little Rock's had a 108% higher rate of in-hospital mortality for acute care. At Augusta, the in-hospital death rate was 120% above that of the best facilities. At the Oklahoma City VA, there were 122% more cases of ventilator-associated pneumonia, which can prove fatal.

The Charlie Norwood VA Medical Center in Augusta stood out on a number of measurements. Beyond its overall death rate, it had a congestive heart failure death rate of 11.56%, significantly higher than the 7.2% rate at the best VA facilities. It also had twice the rate of septic infections in patients who had central intravenous catheters.

At the five-star-rated Minneapolis facility, by contrast, the in-hospital and 30-day acute-care death rates were both better than the top hospitals' average, and it had a lower rate of in-hospital complications as well.

The VA system on a national-average basis has performed roughly as well as a broad sample of national private hospitals, according to internal VA documents. But the one-star VA hospitals ranked worse than their poorly performing peers in private medicine, documents show.

One VA doctor familiar with the agency's quality efforts said that between about 2005 and 2011, the VA dispatched its quality-improvement team to hospitals whenever they produced consistently poor results.

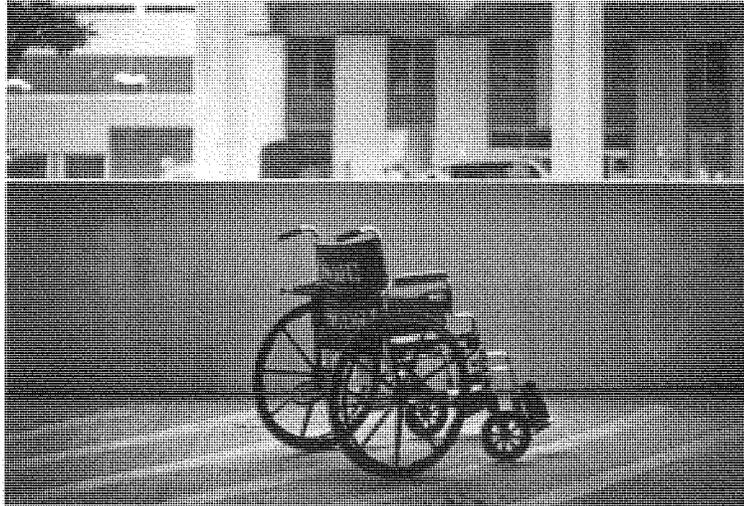
The apparent drop in quality at a range of VA hospitals is surprising, given that the agency historically has been known for medical excellence. For decades, VA doctors have been measured on their surgical outcomes. The agency was at the forefront of medical-outcome transparency when it began publishing a range of surgical and medical outcomes measures in 2011.

Veterans Affairs Watchdog Downplayed Medical Care Problems, Probe Finds

Report Claims Legitimate Whistleblowers' Critiques Were Ignored

By MICHAEL M. PHILLIPS and BEN KESLING

Updated June 23, 2014 7:33 p.m. ET



A wheelchair sits outside the Atlanta VA Medical Center late last month as Department of Veterans Affairs continues to be embroiled in controversies surrounding the medical care the department provides. *David Goldman/Associated Press*

WASHINGTON—A Department of Veterans Affairs internal watchdog created to safeguard the medical care provided to former service members instead routinely played down the effect of treatment errors and appointment delays, a federal special counsel alleged Monday.

In a letter to President [Barack Obama](#), U.S. Special Counsel Carolyn Lerner said the VA Office of the Medical Inspector has repeatedly undermined legitimate whistleblowers by confirming their allegations of wrongdoing, but dismissing them as having no impact on patient care.

The strongly worded critique adds a new layer to the [veterans-care scandal](#) that has rocked the VA and the Obama administration in recent months.

Among the cases that whistleblowers reported to the special counsel:

A veteran wasn't given his first comprehensive psychiatric evaluation until he had spent eight years as a resident of a Brockton, Mass., VA psychiatric unit, in 2011.

Drinking water at the VA facility in Grand Junction, Colo., was tainted with elevated levels of Legionella bacteria, which can cause a form of pneumonia, and standard maintenance and cleaning procedures weren't performed.

A VA pulmonologist in Montgomery, Ala., portrayed past test readings as current results in more than 1,200 patient files, "likely resulting in inaccurate patient health information being recorded," Ms. Lerner wrote.

In Buffalo, N.Y., VA staff sometimes mishandled sterile surgical instruments and failed to wear required protective gear.

In each of these cases, VA whistleblowers brought the information to the special counsel, an independent federal entity that is charged with enforcing whistleblower-protection laws. The special counsel passed it along to the Office of the Medical Inspector.

The VA medical inspector concluded that the hospitals' failings, while accurately reported by the whistleblowers, didn't threaten veterans' health or safety, even when the VA inspector general had concluded that similar faults compromised care in other cases, according to the letter from Ms. Lerner.

Referring to the Brockton psychiatric unit, the Office of the Medical Inspector wrote, "OMI feels that in some areas [the veterans'] care could have been better, but OMI doesn't feel that their patient's rights were violated," according to OMI documents cited in Ms. Lerner's letter. Ms. Lerner called such statements "a serious disservice to the veterans who received inadequate patient care for years after being admitted to VA facilities."

"This approach has prevented the VA from acknowledging the severity of systemic problems and from taking the necessary steps to provide quality care to veterans," wrote Ms. Lerner.

Acting VA Secretary Sloan Gibson said the VA accepts the Office of Special Counsel's recommendations, and ordered a full review of the VA's Office of Medical Inspector's operation to be completed in two weeks.

"I am deeply disappointed not only in the substantiation of allegations raised by whistleblowers, but also in the failures within VA to take whistleblower complaints seriously," he said in a written statement.



The Brockton, Mass., VA facility. *Scott Eisen/The Enterprise*

The special counsel's allegations are the latest blow to the VA, which was rocked this spring by revelations that some employees doctored records to make appointment wait-times appear far shorter than they were. The disclosure prompted then-Secretary Eric Shinseki and other top VA officials to resign.

"There are many instances where there have been whistleblowers that have resulted in investigations," Sen. Jerry Moran (R., Kan.), a member of the Senate Committee on Veterans' Affairs, said Sunday. "We have no idea if anything has come from those investigations or reports."

Since the scheduling scandal surfaced, the VA inspector general, a separate internal watchdog, has examined operations at dozens of medical VA facilities across the nation. The VA has conducted its own reviews. Federal investigators have said they are working to determine whether criminal charges will be brought in any of the cases.

Though the Office of Special Counsel has the authority to refer whistleblower-retaliation cases to the Justice Department for criminal prosecution, the agency said its current findings don't involve such potentially criminal retribution.

Mr. Gibson has been battling to control the crisis, traveling to VA facilities around the country and making appearances to reassure veterans, the public and Congress. He said Thursday that the VA had contacted 70,000 veterans to get them quick appointments.

In an internal message this month to the VA's 341,000 staff, Mr. Gibson promised protection for those who reported misdeeds in agency operations.

"Relatively simple issues that front-line staff may be aware of can grow into significantly larger problems if left unresolved," Mr. Gibson said. "In the most serious cases, these problems can lead to and encourage improper and unethical actions."

Joe Davis, a spokesman for the Veterans of Foreign Wars, a veterans-advocacy group, welcomed the special counsel's report. "What we want is more scrutiny," Mr. Davis said. "The more eyes that are looking at this means more scrutiny, and that leads to more accountability," he said.

Clinical Impact of Antimicrobial Resistance in European Hospitals: Excess Mortality and Length of Hospital Stay Related to Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infections[†]

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Antimicrobial resistance is threatening the successful management of nosocomial infections worldwide. Despite the therapeutic limitations imposed by methicillin-resistant *Staphylococcus aureus* (MRSA), its clinical impact is still debated. The objective of this study was to estimate the excess mortality and length of hospital stay (LOS) associated with MRSA bloodstream infections (BSI) in European hospitals. Between July 2007 and June 2008, a multicenter, prospective, parallel matched-cohort study was carried out in 13 tertiary care hospitals in as many European countries. Cohort I consisted of patients with MRSA BSI and cohort II of patients with methicillin-susceptible *S. aureus* (MSSA) BSI. The patients in both cohorts were matched for LOS prior to the onset of BSI with patients free of the respective BSI. Cohort I consisted of 248 MRSA patients and 453 controls and cohort II of 618 MSSA patients and 1,170 controls. Compared to the controls, MRSA patients had higher 30-day mortality (adjusted odds ratio [aOR] = 4.4) and higher hospital mortality (adjusted hazard ratio [aHR] = 3.5). Their excess LOS was 9.2 days. MSSA patients also had higher 30-day (aOR = 2.4) and hospital (aHR = 3.1) mortality and an excess LOS of 8.6 days. When the outcomes from the two cohorts were compared, an effect attributable to methicillin resistance was found for 30-day mortality (OR = 1.8; *P* = 0.04), but not for hospital mortality (HR = 1.1; *P* = 0.63) or LOS (difference = 0.6 days; *P* = 0.96). Irrespective of methicillin susceptibility, *S. aureus* BSI has a significant impact on morbidity and mortality. In addition, MRSA BSI leads to a fatal outcome more frequently than MSSA BSI. Infection control efforts in hospitals should aim to contain infections caused by both resistant and susceptible *S. aureus*.

The emergence of resistant bacteria is a natural consequence of antibiotic use and complicates the treatment of

infected patients. *Staphylococcus aureus* resistant to isoxazolyl penicillins (methicillin-resistant *S. aureus* [MRSA]) is one of the most frequent pathogens causing resistant infections in hospitals worldwide (14, 21, 53). The questions are whether and to what extent resistance affects survival and the duration of hospital admission in patients with bacterial infections. Previous studies compared patients with MRSA infections to those infected by methicillin-susceptible *S. aureus* (MSSA), using mortality as one of the main endpoints. New insights challenge this approach for a number of reasons.

Several studies have shown that patients with MRSA bloodstream infection (BSI) differ in many ways from those with MSSA BSI; they are older, have more comorbidities, and experience longer hospital admissions before the onset of infection (6, 22, 37). If these two groups of patients are compared directly, bias is introduced, compromising the validity of the results. Of all hospitalized patients at risk of acquiring MRSA BSI, the younger, relatively more healthy MSSA patients are selected as the control group, magnifying the possible impact of resistance (20). Moreover, time-dependent distortions are introduced, as patients staying in the hospital for a shorter period, like MSSA patients, have a smaller chance of acquiring MRSA BSI than patients hospitalized for longer periods, who for many reasons are more likely to die, thus leading to overestimation of the clinical impact of resistance (36).

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It has also been shown that MRSA BSIs are not replacing infections caused by MSSA but adding to the existing burden (3, 15, 43). For this reason, MRSA-specific mortality needs to be measured against mortality in patients free of *S. aureus* BSI. A parallel matched-cohort design (23) allows this comparison. MRSA and MSSA patients are compared separately to controls who have chances to acquire an MRSA or MSSA BSI equal to those of the case patients to whom they are matched. At the same time, this design provides the means to determine the impact attributable to resistance *per se* and minimizes bias.

Different mortality outcomes are used in the literature. Some studies have focused on hospital mortality (10, 35, 37), while others determined mortality within a predefined interval (29, 32). Each outcome measure requires a distinct analytical approach, as well as correct interpretation. Since previous investigations often ignored this subtle distinction, subsequent analysis often resulted in flawed conclusions (31).

There is thus a need for more robust estimates of the impact of methicillin-resistant *S. aureus* BSI on unambiguously defined mortality and morbidity endpoints using the appropriate control groups and correct analytical methods. In the present study, the excess 30-day mortality, hospital mortality, and length of stay attributable to MRSA BSI were determined by collecting data from a large sample of European hospitals, using a parallel-cohort design and appropriate statistical approaches.

MATERIALS AND METHODS

Setting. Thirteen tertiary care centers (WHO definition [2]) from as many European countries were selected from hospitals participating in the European Antimicrobial Resistance Surveillance System (EARSS) (12). For EARSS, the National Representatives are responsible for the selection of hospitals on the basis of gendemoepidemiological representativeness. EARSS requires that a minimum of 20% of hospitals participate per country. We are therefore well aware of the distribution of resistance in the participating countries and chose hospitals representative of the national level of methicillin resistance. The selected hospitals also showed good diagnostic accuracy, according to the results of the external quality assessment exercise carried out annually by EARSS.

Study design. A prospective parallel matched-cohort design was chosen. Cohort I consisted of patients with MRSA BSI (MRSA cohort), cohort II consisted of patients with MSSA BSI (MSSA cohort), and both cohorts included controls free of *S. aureus* BSI. Any episode of MRSA or MSSA BSI in an adult patient (≥ 18 years old) was identified by daily laboratory liaison. Blood cultures were taken on clinical indication, and all hospital patients with a laboratory-confirmed diagnosis of *S. aureus* BSI were included. Susceptibility was determined by a cefoxitin or oxacillin screen test and confirmed by a PCR *mecA* test or a PBP2a agglutination test, according to consensus protocols published in the EARSS manual (11). The day of enrollment was defined as the date the first positive blood culture was obtained. Each patient with an *S. aureus* BSI was matched to two controls. Since taking into account the time dependency of nosocomial infections is more important than adjusting for other confounding factors (7, 42), controls were matched on the length of hospital stay (LOS) before enrollment of a patient with BSI (± 3 days). Other matching variables were not included, because that would reduce the number of cases eligible for the study, thereby diminishing the representativeness of the cases for all patients with *S. aureus* bacteremia in the participating hospitals. If more than two patients were eligible as controls, the patients closest to the patient with *S. aureus* BSI in the ward registry were selected.

Data reporting and training of on-site investigators. For each hospital, a dedicated on-site investigator was recruited. They were trained in consistent enrollment and data collection in two workshops, using anonymized patient records provided by one of the authors (P.G.D.). Patients were enrolled for 12 months between July 2007 and June 2008. Anonymized data were recorded using a Web-based and password-protected data submission tool hosted by the Netherlands National Institute of Public Health and the Environment. Built-in data checks secured data validity. To further ensure uniform application of study definitions, one author (M.E.A.D.K.) provided continuous help desk support.

The data sources were patient records, the electronic hospital information system, the laboratory information system, and nursing notes. Postdischarge surveillance to determine survival 30 days after enrollment was carried out by telephone contact with patients or their general practitioners.

The pre-enrollment data recorded were transfer from a long-term care facility, nursing home, or another hospital; admission diagnosis; type of admission (emergency or elective); comorbidities in the Charlson Comorbidity Index (9); previous surgery; and frequent hospital exposure, defined as two or more hospital admissions in the previous 12 months. At enrollment, the following variables were recorded: demographic data (age and gender), the anatomical source of *S. aureus* BSI, the susceptibility profile of the causative pathogen, and poly- or monomicrobial bacteremia, as well as the presence of indwelling devices (tracheal tube, central venous catheter, arterial vascular access, peripheral vascular access, urinary catheter, tracheostomy, nasogastric tube, or wound drainage tube), where the presence of a tracheal tube was used as a surrogate marker for an intensive care unit (ICU) stay. The main outcomes were mortality 30 days after enrollment, hospital mortality, and LOS after enrollment.

Crude mortality was defined as the proportion of MRSA and MSSA patients who died. Attributable mortality was defined as the ratio between the risk of dying among patients with MRSA or MSSA BSI and that of their matched controls, taking into account matching and additional explanatory variables that influenced effect estimates by multivariate analysis. This was expressed as the odds ratio (OR) for 30-day mortality and the hazard ratio (HR) for hospital mortality.

This study complied with the Dutch patient confidentiality regulations and ethical standards (28) and was approved by local institutional ethical committees when required.

Statistical analysis. Statistical analyses were performed using SAS 9.1 and R 2.8.1. Univariate comparisons of patients with *S. aureus* BSI (either MRSA or MSSA) and unexposed patients were performed using Cochran's Q statistic for categorical variables. For continuous variables, Friedman's rank sum test was used.

Analyses of outcomes (30-day or hospital mortality and LOS after enrollment) were performed separately for the MRSA and MSSA cohorts. All collected variables, other than LOS before infection (the matching criterion), that could influence the relationship between MRSA or MSSA and the outcome were tested for confounding in bivariate regression. Variables were included in multivariate analyses if they changed the effect estimate by more than 5%. Collinearity was assessed by generating a correlation coefficient matrix. A robust sandwich covariance matrix estimator was used to account for the matched design. The effect attributable to methicillin resistance was determined by the ratio of the adjusted effect measures for MRSA BSI and MSSA BSI from the parallel cohorts, and the confidence intervals were determined as described by Altman and Bland (4).

Thirty-day mortality and hospital mortality. The effect of *S. aureus* BSI on mortality was determined by logistic regression for 30-day mortality and by Fine and Gray's extended Cox's regression for competing events for hospital mortality (13, 41). For hospital mortality, cumulative incidence graphs were created using a cause-specific hazard model in which both discharge alive and hospital mortality were included as competing endpoints (25, 30).

Length of hospital stay after enrollment. A generalized linear model (GLM) with gamma distribution and log link function for positively skewed data was used to determine the impact of *S. aureus* BSI on LOS after enrollment (5, 16). The excess LOS was calculated by comparing the mean outcomes predicted by the multivariate model for all patients in each group. Confidence intervals for the difference in LOS in days were obtained by parametric bootstrapping.

Data heterogeneity. To test for group effects at the hospital level, multilevel models for hierarchical data were used for logistic regression and the GLM models. Stratified analyses were used for the Fine and Gray model.

RESULTS

The participating hospitals reported 1,000 *S. aureus* bloodstream infections, 310 (31%) of which showed methicillin resistance (range, 7 to 65%) (Table 1). For 134 (13%) of the patients with BSI, no appropriate match (equal LOS before enrollment ± 3 days) could be identified, and they were excluded. For 111 (13%) of the included patients with *S. aureus* BSI, only a single control could be matched. Therefore, the analyses were based on 248 patients with MRSA BSI matched

TABLE 1. Activity data for participating hospitals from July 2007 to June 2008

Hospital no.	Country	No. of beds	No. of admissions	No. of bed days	No. of infected ^a /controls	National % MRSA ^b	MRSA hospital mortality (%)
H1	Austria	2,137	99,761	657,268	50/99	8	50
H2	Belgium	856	26,337	290,790	32/64	21	50
H3	Croatia	1,724	63,804	479,528	72/143	35	43
H4	England	1,210	104,680	292,030	117/239	31	44
H5	Germany	1,234	56,193	391,258	81/126	19	30
H6	Greece	949	44,214	293,632	56/66	41	25
H7	Ireland	819	22,418	238,166	95/187	33	28
H8	Italy	912	55,600	292,150	67/133	34	38
H9	Latvia	1,029	46,343	307,006	54/108	13	33
H10	Malta	835	48,504	252,488	80/151	56	29
H11	Romania	1,109	72,739	427,666	37/70	33	52
H12	Scotland	877	53,276	255,215	132/257	31	13
H13	Slovenia	2,344	83,161	614,353	127/249	7	65
Total		16,035	777,030	4,791,550	1,000/1,882	30	36

^a Infected, number of first episodes of *S. aureus* BSI.

^b Proportion of MRSA according to EARSS 2008 (12).

to 453 controls and 618 patients with MSSA BSI matched to 1,170 controls.

The excluded patients had longer periods of hospitalization between admission and enrollment ($P < 0.01$), excluded MSSA patients also had a longer hospitalizations after enrollment ($P < 0.01$), and excluded MRSA patients had higher hospital mortality ($P < 0.01$). Otherwise, there were no significant differences.

Irrespective of methicillin susceptibility, the included patients with *S. aureus* BSI were more often male, more likely to have had frequent hospital exposure, more often had an emergency admission, had a higher number of comorbidities, frequently suffered from severe renal disease or diabetes with end organ damage, and had more indwelling devices than controls. Taking into account methicillin susceptibility, patients with MRSA BSI were older, more likely to have had two or more hospital admissions in the previous year, more often received antibiotics and more often had surgery before enrollment, had more comorbidities and higher prevalence of diabetes, and were more often exposed to indwelling devices at enrollment than patients with MSSA BSI. A similar difference in risk profiles was found for the controls in the MRSA versus the MSSA cohort. As expected, MRSA patients had a longer hospital stay before enrollment (median, 4 days; interquartile range [IQR], 0 to 12) than MSSA patients (median, 1 day; IQR, 0 to 6) (Table 2).

30-day mortality. After the onset of MRSA BSI, 74 of the 242 (31%) exposed patients died within 30 days, whereas 36 of the 429 (8%) controls died within 30 days after enrollment. Most patients died in the hospital, but four (5%) of the MRSA patients and six (17%) of the controls died after discharge. Of 585 patients with MSSA BSI, 126 (22%) died, whereas out of 1,082 controls, 83 (8%) died within 30 days after enrollment. Six (5%) of the MSSA patients and 17 (20%) of the control patients died after discharge (Table 2).

Table 3 shows the results of the univariate and multivariate regression analyses. Since multilevel analysis showed that group effects at the hospital level did not influence the coefficients for *S. aureus* exposure, the numbers are based on regular logistic regression. Compared to controls without *S. aureus* BSI, expo-

sure to MRSA BSI remained significantly associated with mortality after all potential confounders were adjusted for; the adjusted OR (aOR) for dying 30 days after enrollment was 4.4 (confidence interval [CI], 2.8 to 7.0). For patients exposed to MSSA BSI, the aOR for mortality 30 days after enrollment was 2.4 (CI, 1.7 to 3.3).

Comparison of the aORs from the MSSA and MRSA cohorts showed an increased risk of death within 30 days, attributable to methicillin resistance, with an OR of 1.8 (CI, 1.04 to 3.2).

Hospital mortality. Eighty-five of 239 (36%) MRSA patients died in the hospital, whereas only 41 of 446 control patients (9%) died during their hospital stay. Among patients with MSSA BSI, 138 of 604 (23%) died, whereas only 76 of 1,166 (7%) control patients died during their hospital stay (Table 2).

Figure 1 illustrates the dynamics of hospital mortality and discharge over time for both cohorts. Figure 1A shows that for patients with MRSA BSI, LOS till discharge alive varied widely, whereas most MRSA patients died in the hospital within 1.5 weeks after enrollment. Figure 1B reveals a similar pattern for MSSA patients, although a higher proportion of patients was discharged alive within a much shorter time interval.

Table 4 illustrates the impact of MRSA and MSSA BSI on hospital mortality using a subdistribution proportional hazards model. Since the stratified analysis did not show a group effect at the hospital level, the hospital level was not taken into account in these analyses. After all potential confounders were adjusted for, the hazard rate for dying in the hospital was 3.5 times higher for patients with MRSA BSI than for control patients. Patients with MSSA BSI had a 3.1-times-higher adjusted hazard rate for dying in the hospital than the matched control patients.

Comparison of excess hospital mortality for patients with MRSA BSI and MSSA BSI resulted in an HR for hospital mortality of 1.1 (CI, 0.7 to 1.8) associated with methicillin resistance.

Length of stay after enrollment. Patients with MRSA BSI stayed in the hospital for a median of 16 days (IQR, 6 to 32 days) after enrollment. Control patients had a median LOS of

TABLE 2. Characteristics of patients in the MRSA and MSSA cohort. *P* values correspond to Cochran's Q statistic or Friedman ranks sum test, whenever appropriate

Characteristic	Value ^a									
	MRSA cohort					MSSA cohort				
	BSI	N	Controls	N	P value	BSI	N	Controls	N	P value
Female	96 (39)	248	230 (51)	453	<0.05	231 (37)	618	543 (46)	1,170	<0.01
Age (yr) ^b	69 (58–77)	248	67 (54–79)	453	0.42	66 (53–76)	618	67 (54–77)	1,170	0.36
Transfer from another institution	38 (18)	211	44 (11)	391	<0.05	87 (16)	539	114 (11)	1,021	<0.05
>2 hospital stays in previous yr	80 (38)	211	90 (23)	391	<0.01	131 (24)	539	177 (17)	1,021	<0.01
Emergency admission	181 (73)	248	283 (62)	453	<0.01	496 (80)	618	784 (67)	1,168	<0.01
Antibiotic therapy before enrollment	148 (60)	248	239 (53)	453	0.27	195 (32)	618	467 (40)	1,170	<0.01
Surgery before enrollment	60 (24)	248	110 (24)	453	0.10	106 (17)	618	210 (18)	1,170	0.65
Length of stay before enrollment ^b (days)	4 (0–12)	248	3 (1–11)	453	0.06	1 (0–6)	618	2 (0–6)	1,170	0.07
Admission diagnosis										
Cardiovascular disease	38 (15)	248	81 (18)	453	0.54	111 (18)	618	266 (23)	1,170	<0.01
Connective tissue disease	4 (2)	248	1 (0)	453		12 (2)	618	14 (1)	1,170	0.50
Dermatological causes	3 (1)	248	6 (1)	453	1.00	11 (2)	618	16 (1)	1,170	0.21
Endocrine/metabolic causes	8 (3)	248	12 (3)	453	0.75	13 (2)	618	41 (4)	1,170	0.16
Gastrointestinal causes	36 (15)	248	79 (17)	453	<0.05	50 (8)	618	155 (13)	1,170	<0.01
Genitourinary causes	28 (11)	248	53 (12)	453	0.96	42 (7)	618	85 (7)	1,170	0.25
Gynecologic causes	0	248	3 (1)	453		2 (0)	618	10 (1)	1,170	0.26
Hematologic causes	3 (1)	248	19 (4)	453	<0.05	21 (3)	618	24 (2)	1,170	0.08
Infectious disease	55 (22)	248	23 (5)	453	<0.01	149 (24)	618	87 (7)	1,170	<0.01
Neurological causes	9 (4)	248	39 (9)	453	<0.05	48 (8)	618	103 (9)	1,170	0.23
Oncologic causes	22 (9)	248	43 (9)	453	0.61	47 (8)	618	91 (8)	1,170	0.98
Orthopedic causes	8 (3)	248	18 (4)	453	0.10	26 (4)	618	61 (5)	1,170	0.38
Pulmonary causes	21 (8)	248	32 (7)	453	0.89	34 (6)	618	108 (9)	1,170	0.05
Trauma	5 (2)	248	16 (4)	453	0.07	29 (5)	618	39 (3)	1,170	0.28
Undetermined	8 (3)	248	28 (6)	453	0.19	23 (4)	618	70 (6)	1,170	<0.05
Charlson Comorbidity Index										
Charlson score ^b	3 (2–5)	248	2 (1–3)	453	<0.01	2 (1–4)	618	2 (0–3)	1,170	<0.01
Myocardial infarct	37 (15)	248	40 (9)	453	<0.05	71 (11)	618	125 (11)	1,170	0.93
Congestive heart failure	57 (23)	248	90 (20)	453	0.54	103 (17)	618	167 (14)	1,170	0.14
Cerebrovascular disease	41 (17)	248	48 (11)	453	<0.05	63 (10)	618	139 (12)	1,170	0.48
Chronic pulmonary disease	43 (17)	248	59 (13)	453	0.26	67 (11)	618	155 (13)	1,170	0.10
Mild liver disease	10 (4)	248	22 (5)	453	0.96	26 (4)	618	30 (3)	1,170	0.11
Severe liver disease	22 (9)	248	20 (4)	453	0.06	28 (5)	618	34 (3)	1,170	<0.05
Severe renal disease	68 (27)	248	76 (17)	453	<0.01	133 (22)	618	157 (13)	1,170	<0.01
Peripheral vascular disease	35 (14)	248	47 (10)	453	0.45	67 (11)	618	128 (11)	1,170	0.30
Connective tissue disease	37 (15)	248	40 (9)	453	0.06	71 (11)	618	125 (11)	1,170	0.28
Peptic ulcer	12 (5)	248	24 (5)	453	0.90	31 (5)	618	61 (5)	1,170	0.26
Diabetes	82 (33)	248	78 (17)	453	<0.01	125 (20)	618	214 (18)	1,170	0.84
Diabetes with end organ damage	33 (13)	248	19 (4)	453	<0.01	44 (7)	618	45 (4)	1,170	<0.01
Hemiplegia/paraplegia	20 (8)	248	15 (3)	453	0.06	21 (3)	618	48 (4)	1,170	0.25
Cancer/leukemia	47 (19)	248	98 (22)	453	0.47	113 (18)	618	195 (17)	1,170	0.76
Metastatic solid tumor	17 (7)	248	36 (8)	453	0.97	42 (7)	618	61 (5)	1,170	0.64
AIDS	0 (0)	248	2 (0)	453		4 (1)	618	5 (0)	1,170	0.72
Dementia	12 (5)	248	16 (4)	453	0.88	19 (3)	618	46 (4)	1,170	0.72
Indwelling device at enrollment										
Intubation	33 (13)	248	41 (9)	453	0.13	55 (9)	618	53 (5)	1,170	<0.01
Central venous catheter	112 (46)	248	108 (24)	451	<0.01	209 (34)	617	146 (12)	1,169	<0.01
Arterial vascular access	40 (16)	248	45 (10)	453	<0.05	71 (11)	618	78 (7)	1,170	<0.01
Peripheral vascular access	181 (73)	247	296 (67)	444	<0.05	448 (73)	616	759 (65)	1,162	<0.01
Urinary catheter	126 (51)	245	161 (36)	451	<0.01	215 (35)	618	263 (23)	1,165	<0.01
Tracheostomy	9 (4)	248	11 (2)	453	0.48	19 (3)	618	11 (1)	1,170	<0.01
Nasogastric tube	54 (22)	247	60 (13)	453	<0.01	74 (12)	618	71 (6)	1,168	<0.01
Wound drainage tube	41 (17)	248	53 (12)	450	0.08	43 (7)	618	72 (6)	1,169	0.90
Characteristics of the BSI										
Polymicrobial BSI	22 (9)	245				54 (9)	607			
Hospital onset of BSI (>48 h)	139 (56)	248				275 (44)	618			
Source										
Bone/joint	5 (2)	248				22 (4)	618			

Continued on following page

TABLE 2.—Continued

Characteristic	Value ^a									
	MRSA cohort					MSSA cohort				
	BSI	N	Controls	N	P value	BSI	N	Controls	N	P value
CNS ^b foci	0	248				12 (2)	618			
Intervention	2 (1)	248				7 (1)	618			
Ear-nose-throat	6 (2)	248				7 (1)	618			
Intra-abdominal	10 (4)	248				11 (2)	618			
Intravascular	59 (24)	248				156 (25)	618			
Lower respiratory tract	28 (11)	248				63 (10)	618			
Skin/soft tissue	53 (21)	248				126 (20)	618			
Urinary-genital	12 (5)	248				22 (4)	618			
Unknown	73 (29)	248				192 (31)	618			
Outcome										
Died in hospital	85 (36)	239	41 (9)	446	<0.01	138 (23)	604	76 (7)	1,166	<0.01
Died within 30 days after enrollment	74 (31)	242	36 (8)	429	<0.01	126 (22)	585	83 (8)	1,082	<0.01
Length of stay after enrollment ^c (days)	16 (6–32)	240	7 (3–18)	447	<0.01	15 (7–26)	604	8 (4–14)	1,166	<0.01

^a Percentages are in parentheses.

^b Median and interquartile range are shown.

^c CNS, central nervous system.

7 days (IQR, 3 to 18 days) after enrollment (Table 2). The univariate regression model showed that MRSA patients stayed 1.6 times (CI, 1.4 to 2.0) longer from enrollment to discharge (alive or dead) than the matched control patients (Table 5).

Patients with MSSA BSI stayed in the hospital for a median of 15 days (IQR, 7 to 26 days) after infection. Control patients had a median LOS of 8 days (IQR, 4 to 14 days) after enrollment (Table 2). The univariate regression model showed that MSSA patients stayed 1.7 times (IQR, 1.5 to 1.9 times) longer from enrollment to discharge than the matched control patients, as presented in Table 5.

Multilevel analysis showed that group effects at the hospital level did not change the coefficients for *S. aureus* BSI exposure, and therefore, the results presented are based on regular GLMs. After adjustment for potential confounders, MRSA patients stayed 1.6 times longer in the hospital after enrollment, which resulted in an excess length of stay of 9 days (IQR,

5 to 14 days). For the MSSA cohort, only the number of indwelling devices was an important confounder. The adjusted excess length of stay for patients with MSSA BSI was 1.6 times the length of stay of the matched controls, resulting in 9 excess days (IQR, 7 to 10 days).

Comparison of the excess lengths of stay for MRSA and MSSA patients showed that there was no difference in length of stay after enrollment (ratio, 1.0 [CI, 0.8 to 1.3]; excess days, 0.6 [CI, –4 to 5]) (Table 5).

DISCUSSION

Acknowledging the need for accurate and precise estimates of the clinical impact of methicillin resistance in *S. aureus*, we set out to determine the patient mortality at day 30 and the instantaneous risk of dying during the hospital stay, as well as the extra length of stay attributable to MRSA BSI, by conducting the largest prospective cohort study designed for this pur-

TABLE 3. Impacts of MRSA and MSSA BSI on 30-day mortality^a

Type of analysis	N	OR for effect measure (CI)	Effect measure and potential confounders in model
MRSA vs controls			
Univariate	661	4.8 (3.2–7.1)	BSI with MRSA
Multivariate	533	4.4 (2.8–7.0)	BSI with MRSA, central venous catheter, peripheral vascular access, urinary catheter, >2 admissions in the previous yr, Charlson Comorbidity Index, and no. of indwelling devices
MSSA vs controls			
Univariate	1,614	3.3 (2.5–4.3)	BSI with MSSA
Multivariate	1,590	2.4 (1.7–3.3)	BSI with MSSA, emergency admission, central venous catheter, urinary catheter, nasogastric tube, no. of indwelling devices
MRSA cohort vs MSSA cohort, comparison of multivariate effect estimates		1.8 (1.04–3.2)	Methicillin resistance of <i>S. aureus</i> BSI

^a Univariate and multivariate logistic regression and comparison of multivariate effect estimates from both cohorts.

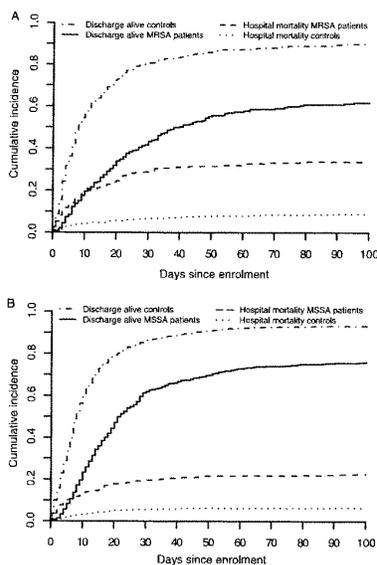


FIG. 1. Cumulative-incidence functions for the competing risks, discharge alive and hospital mortality, for patients with, and their matched controls without, *S. aureus* BSI. (A) MRSA BSI. (B) MSSA BSI.

pose. An effect attributable to methicillin resistance could be discerned only for mortality within 30 days, which was increased by 80% (OR, 1.8; CI, 1.04 to 3.2), but not for hospital mortality (HR, 1.1; CI, 0.7 to 1.8) or length of hospital stay

(excess days, 0.6; CI, -3.7 to 5.3). Irrespective of the methicillin resistance trait, *S. aureus* BSI alone increased mortality, as well as LOS, and infected patients died 2 to 4 times more often within 30 days, the instantaneous probability for dying during the entire hospital admission was 3 to 4 times higher, and the patients stayed on average 9 days longer in the hospital than their controls. These findings were consistent among all participating hospitals.

Although mortality as a study endpoint seems straightforward, different measures can lead to different conclusions. It is important to realize that mortality within a predefined interval is a static measure indicating excess mortality within that interval (proportion), while hospital mortality is a dynamic measure that provides insight into the temporal dynamics of dying during the entire hospital stay (rate). Since mortality during hospital admission is easier to determine than mortality within a certain period of follow-up, hospital mortality is regularly used as a measure for the impact of resistance. For reasons of comparability, we included the same measure, despite the complexities related to time-to-event analyses and difficulties when interpreting the resulting hazard ratios. Although not statistically significant, we found that the mortality rate (deaths/hospital day) was higher for MRSA than for MSSA patients; at the same time, statistical tests confirmed that in absolute numbers, more MRSA than MSSA patients died within 30 days.

In comparison with previously published research, three important characteristics of this study stand out. The parallel matched-cohort design made it possible to match infected patients to controls with similar hospital exposure, thereby increasing the comparability of the risk profiles of infected and control patients and, as a consequence, diminishing time-dependent bias (40), as well as severity-of-illness bias (20). Furthermore, two explicitly defined mortality measures were included, of which hospital mortality was analyzed by appropriate analytical methods, taking into account the duration of hospital admission, as well as competing events, i.e., the fact that patients who are discharged alive will not die in the hospital and vice versa (31). Finally, the generalizability and precision of the estimates were improved by sampling from 777,030 patients treated in 13 tertiary care centers from as

TABLE 4. Impacts of MRSA and MSSA BSI on hospital mortality^a

Type of analysis	N	HR for effect measure (CI)	Effect measure and potential confounders in model
MRSA vs controls			
Univariate	695	4.5 (3.2-6.3)	BSI with MRSA
Multivariate	566	3.5 (2.4-5.2)	BSI with MRSA, no. of indwelling devices, Charlson Comorbidity Index, central venous catheter, urinary catheter, frequent hospital contact, diabetes
MSSA vs controls			
Univariate	1,787	3.8 (2.9-5.0)	BSI with MSSA
Multivariate	1,765	3.1 (2.3-4.2)	BSI with MSSA, intubation, central venous catheter, urinary catheter, no. of indwelling devices
MRSA cohort vs MSSA cohort, comparison of multivariate effect estimates		1.1 (0.7-1.8)	Methicillin resistance of <i>S. aureus</i> BSI

^a Univariate and multivariate Fine and Gray proportional hazards regression and comparison of multivariate effect estimates from both cohorts.

TABLE 5. Impacts of MRSA and MSSA BSI on length of stay after enrollment^a

Type of analysis	N	Ratio of median length of stay for effect measure (CI)	Extra length of stay in days for effect measure (CI)	Effect measure and potential confounders
MRSA vs controls				
Univariate	669	1.6 (1.4–2.0)	9.6 (5.7–13.8)	BSI with MRSA
Multivariate	558	1.6 (1.3–2.0)	9.2 (5.2–13.5)	BSI with MRSA, emergency admission, peripheral vascular access, frequent hospital contact, transfer from another institution, diabetes with end organ damage
MSSA vs controls				
Univariate	1741	1.7 (1.5–1.9)	8.4 (6.6–10.3)	BSI with MSSA
Multivariate	1721	1.6 (1.5–1.8)	8.6 (6.8–10.4)	BSI with MSSA, no. of indwelling devices
MRSA cohort vs MSSA cohort, comparison of multivariate effect estimates		1.0 (0.8–1.3)	0.6 (–3.7–5.3)	Methicillin resistance of <i>S. aureus</i> BSI

^a Univariate and multivariate analysis (generalized linear model with gamma distribution and loglink function) and comparison of the multivariate effect estimates from both cohorts.

many different European countries for a total of 4.8 million bed days.

The possible limitations of this study include the potential distortion of results due to discrepancies between hospitals, such as variation in blood culture frequencies or local differences in clinical management. However, multilevel analyses, which were used to test for heterogeneity, indicated that differences between participating centers did not modify the results. Nevertheless, as with any observational study, residual bias or confounding can never be completely ruled out. Second, the nature of the matched-cohort design and our stringent matching criteria meant that we had to exclude exposed patients with excessive length of hospitalization before infection, because we were unable to find appropriate controls. These patients differed in a systematic manner from those enrolled, as they had a higher mortality (MRSA patients) or extra length of stay (MSSA patients). To impute the direction of impact of counterfactual controls is difficult, but due to the low number of excluded patients, the magnitude of the impact is expected to be small.

The differences in study design make this study unique and less amenable to a direct comparison with previously published results. Nonetheless, several studies lend support to our findings. A recent study focusing specifically on 30-day mortality but directly comparing MRSA and MSSA patients found a similarly increased ratio (OR, 2.2; CI, 1.0 to 5.0) (3). Three other studies (17, 19, 27) analyzing the impact of methicillin resistance on hospital mortality using time-to-event methods, but ignoring competing events, also found no impact on the instantaneous risk of dying. Finally, another study (6) supported our finding that patients with MRSA and MSSA infections have equal durations of hospitalization after enrollment. Others who made claims to the contrary ignored the influence of the duration of hospital exposure before infection (1, 8).

There are four intuitive explanations for the 80% excess mortality of MRSA patients over MSSA patients in our study: (i) increased vulnerability of the host, (ii) inappropriate empirical antibiotic treatment, (iii) delayed appropriate therapy, and (iv) inferior effectiveness of reserve antibiotics. In this prospective study, great efforts were undertaken to control for

important host factors through matching for length of hospital admission prior to the onset of infection and adjusting for important confounders, like the severity of disease, making increased vulnerability an improbable explanation. Although it seems likely that administration of inappropriate therapy could lead to higher mortality in MRSA patients (18, 39), a recent systematic review (26) argues that this has never been adequately assessed, since detailed analyses that take into account timeliness and drug levels of empirical therapy are still lacking. Moreover, poor interrater agreement on the multiple factors that influence judgments about appropriateness make it difficult to measure (34). *A priori*, one would also assume that inappropriate empirical therapy should have had a different impact in each participating center due to distinct local prescribing practices. However, we found no evidence of heterogeneity between hospitals. The most likely reason for the increased mortality among MRSA patients is the delay in administration of appropriate therapy and the fact that conventional MRSA treatment, consisting of vancomycin, is not as effective as beta-lactams against MSSA (24, 38).

In conclusion, data from 13 tertiary care centers from different European countries showed that mortality and LOS attributable to *S. aureus* BSIs are significant. MSSA infections increased mortality more than 2-fold, and methicillin resistance contributed an additional 80% excess mortality at day 30 after infection. These results emphasize the clinical importance of invasive *S. aureus* infections but unequivocally underline the additional burden imposed by resistance, which not only aggravates the clinical outcome, but adds to the overall caseload of patients with *S. aureus* BSI. Ideally, interventions should be targeted at prevention or improved management of both resistant and susceptible *S. aureus* BSI.

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Estimating the impact of healthcare-associated infections on length of stay and costs

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Abstract

Healthcare-associated infections (HAIs) unquestionably have substantial effects on morbidity and mortality. However, quantifying the exact economic burden attributable to HAIs still remains a challenging issue. Inaccurate estimations may arise from two major sources of bias. First, factors other than infection may affect patients' length of stay (LOS) and healthcare utilization. Second, HAI is a time-varying exposure, as the infection can impact on LOS and costs only after the infection has started. The most frequent mistake in previously published evidence is the introduction of time-dependent information as time-fixed, on the assumption that the impact of such exposure on the outcome was already present on admission. Longitudinal and multistate models avoid time-dependent bias and address the time-dependent complexity of the data. Appropriate statistical methods are important in analysis of excess costs and LOS associated with HAI, because informed decisions and policy developments may depend on them.

Keywords: Burden, economics, infection, methodology, multistate, review

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The Economic Burden of Healthcare-Associated Infections (HAIs)

Healthcare-associated infections (HAIs) are additional burdens on individual hospitals and healthcare systems [1]. They can increase the costs of patient care from several economic perspectives, including those of hospital administrators, third-party payers and patients. In healthcare systems relying on fixed per diem accounting systems, the presence of an HAI does not necessarily decrease reimbursement revenue for hospitals, as added bed-days can be charged to third-party payers (e.g. health insurance companies). However, after the introduction of prospective payment mechanisms based on diagnosis-related groups and similar classifications, the full costs of HAI are most frequently borne by hospitals themselves. Recently, the decision of the American Centers for Medicare to stop reimbursement for HAI has increased the attention paid to this topic and the need for careful interpretation of surveillance data [2].

Excess costs of HAI are related to additional diagnostic tests and treatment, additional hospital days, and postdischarge complications, among others. Quantifying the exact economic burden attributable to HAI still remains a challenging issue [3–5]. Over the last two decades, a number of studies with different designs have attempted to estimate the excess burden of HAI [6,7]. Earlier data from the UK provide a telling picture. Some individual Trusts within the National Health System have attempted to estimate the costs of individual outbreaks of specific infections. An outbreak of methicillin-resistant *Staphylococcus aureus* (MRSA) in Kettering, for example, was estimated to cost the individual hospital involved approximately £400 000. [8]. The biggest cost drivers were those related to the set-up of isolation wards for infected patients, with other costs mostly being associated with cleaning and replacement of materials. The limited knowledge among policy-makers about the true financial burden of HAI, such as MRSA infection, led to a commissioned study at the London School of Hygiene and

Tropical Medicine. On the basis of the results of this investigation, HAI was estimated to cost approximately £1 billion per year, approximately £56 million of which was spent outside the hospital by general practitioners and outpatient centres [9]. Patients with HAI incurred costs that were 2.8 times higher than those for patients free from infection, with an average incremental cost of approximately £3000. With respect to length of stay (LOS), patients with HAI spent approximately 2.5 times more time in hospital, equivalent to an excess LOS of 11 days. Notably, approximately 19% of patients in the study showed signs and symptoms of HAI manifesting after discharge. These postdischarge costs associated with HAI are likely to have been underestimated, given the limitations of the available data on outpatient utilization and indirect costs related to HAI [9].

Since the completion of this landmark study, there have been several attempts to estimate the excess costs of HAI. Two systematic reviews of the literature by Stone *et al.* have summarized the evidence on this topic between 1990 and 2004; they evaluated a total of 125 studies, 70 of which were published between 2001 and 2004 [6,7]. This recent increase in the number of publications highlights the growing interest in the economic implications of HAI over the last 10 years. However, these reviews revealed wide variation in the cost estimates, as well as in the methods used to estimate costs. Another review of the literature, analysing 45 randomized controlled trials reporting cost data and covering a wide variety of clinical areas, reported that only 56% of them gave results for statistical comparisons between randomized groups, only 36% gave rational conclusions, and none of them reported a sample size calculation for cost analyses [10].

The basic framework used by many of these studies is to first identify the additional time that patients spend in the hospital as a result of HAI, as well as the specific healthcare utilization relating to the treatment and management of the infection. These additional days and specific interventions are then monetized for calculation of the specific costs attributable to a single infection. Generally, studies that have followed this basic approach suffer from three limitations. First, the estimation of healthcare utilization, and more specifically LOS in hospital, that can be attributed to HAI is often biased. Several factors other than infection may be associated with patients' excess LOS and healthcare utilization. Second, the approaches used to measure the costs of healthcare resource use are often biased when researchers fail to account for important differences between true costs, charges and reimbursement levels, for example. In addition, financial accounting systems may not always allow for appropriate identification of fixed and variable costs, leading to

inaccurate estimates. Third, many studies on the excess costs of HAI are not explicit in their selection of a cost perspective, and may not include appropriate cost measures. For example, a comprehensive approach to estimating costs from the hospital perspective would explore the costs associated with foregone revenue when infected patients occupy beds for longer periods of time [3].

One of the main drivers of hospital costs attributable to HAI is the associated excess LOS of a patient in hospital. Quantifying excess hospital stay is essential for assessing how many bed-days might be gained from prevention [3,11]. If an HAI in a given patient is prevented, it is expected that the total cost for this patient will decrease through the elimination of variable costs associated with treating the infection and fixed costs associated with excess LOS resulting from the infection. However, the hospital may not realize actual economic savings. This is dependent on the distribution of total costs between fixed and variable costs. Expenditures associated with infection that can be avoided, resulting in actual 'cash' savings to the hospital, are generally referred to as 'variable', because they increase or decrease as patient volume increases and decreases. Examples of variable costs include drugs and consumables. However, many expenditures cannot be easily terminated when infections are avoided. These expenditures are generally referred to as 'fixed', and may include capital equipment, buildings, and staff who are employed on a long-term or permanent basis. When infection is avoided, these 'fixed' costs cannot quickly be eliminated. As the majority of hospital costs are fixed and not avoidable in the short term, these costs are the ones that are most relevant for economic analysis. Although these costs cannot be avoided to produce 'cash' savings, they do represent significant consumption of resources that could be targeted to other productive areas. Consequently, interpretation of cost savings resulting from the prevention of HAI should not be as cash savings, but instead as resources that are freed up for application to other revenue-generating activities. Only with this strict definition can the costs be viewed as those associated with infection. However, for the purposes of economic evaluation, a short-term perspective that examines the alternative uses of the fixed costs, and the corresponding gains and losses of these alternative uses, is more relevant. In particular, fixed costs made available through prevention of HAI (e.g. bed-days) can be re-allocated to the treatment of more patients, thereby generating additional benefits (revenue) for the hospital along with additional (variable) costs for each new case. The net benefit of these additional cases represents the opportunity costs of infection, and more closely reflects the short-term costs (or potential savings with successful intervention) that are

relevant for hospital administrator decision-making regarding investments in infection control [3].

Assessing Excess LOS Associated with HAI: Quality and Limitations of the Available Evidence

As outlined above, cost analyses of HAI pose an important concern for accuracy. This is partly but crucially explained by the assessment of excess LOS associated with HAI, which represents an important and underestimated methodological challenge [12–16]. Inaccurate estimations may arise from two major sources of bias. First, the time-dependent nature of HAI implies that infection can impact on LOS and costs only after the infection has started. Time-fixed studies that include time-varying exposures as artificially fixed in time generate a type of bias called 'time-dependent', which overstates the prolonging effect of the exposure on LOS [17]. Second, factors other than infection may affect patients' LOS and healthcare utilization. These factors may themselves increase the risk of infection, and may vary with time [16]. Omission of these confounders, such as patient's comorbidities or daily severity of illness, in the estimation of extra LOS has the potential to produce misleading results [13,16].

Matching design, linear regression models and instrumental variables

When assessing the impact of HAI on outcomes such as extra LOS and costs, the first challenge is to tease out the independent effect of infection on the outcome by making allowances for all observable confounders. Comparative cohort studies, using either a matching design in which patients with HAI are matched to one or more control patients who did not experience the infection [18–22], or multivariable statistical regression analyses, which may avoid the selection bias induced by the matching process and may allow for the control of a larger number of confounders [13,23,24], are commonly preferred to overcome this bias. Although the use of these statistical techniques is a significant step forwards, there remains the potential for bias through the omission of variables, especially given the paucity of well-designed studies that can shed light on all potential confounders of healthcare utilization. As a result, the number of independent explanatory variables should be significantly expanded to reduce the risk of confounding and increase the accuracy of the estimate. In an extreme example, Graves *et al.* [13] included up to 123 possible confounding variables in an analysis of the effect of nosocomial infec-

tions on LOS, minimizing bias resulting from omitted variables.

More recent techniques for the use of regression models have raised the potential for endogeneity bias. This source of bias arises from the reverse causality between risk of HAI and LOS in hospital. In fact, the direction of causality between HAI and LOS is not one-way. This bias results from the interaction between time in hospital and risk of HAI, as a key driver of costs is the additional LOS associated with the infection, but the risk of developing an infection is increased every day that a patient stays longer in the hospital [25–27]. For instance, the longer the patient is hospitalized, the greater the opportunity for the patient to experience the use of invasive medical devices that may cause HAI, and the higher the cumulative probability of occurrence of a nosocomial infection.

A two-stage instrumental variable strategy has been proposed for controlling bias from endogenous variables. Instrumental variables are 'variables which are strongly correlated with the endogenous variable, but uncorrelated with the main outcome variable, once other covariates have been controlled for. Instrumental variables act as a kind of randomizing device, identifying a portion of the endogenous variable that is beyond the control of the individual' [28]. In other words, this approach relies on the identification of an instrumental variable that is correlated with the exposure term (HAI) in the model but is not endogenous, or an independent predictor of LOS. Generally, the stronger the relationship between the instrument and the exposure, the more precise will be the estimate of the outcome [29]. The appropriate modelling of endogenous predictor variables is a critical challenge with this analytical method. Using data previously collected by Plowman *et al.* [30] on 899 patients from a district general hospital in the UK, Graves *et al.* [31] used a two-stage instrumental variable estimation strategy to overcome the bias from endogenous variables to estimate the costs associated with lower respiratory tract infections. On the basis of the results of the regression analysis, the authors tested the presence of nasogastric tube and oxygen therapy as instruments, because of the evidence that both were risk factors for the development of HAI, but neither of them was a determinant of LOS. The model predicted that for every 10% decrease in the probability of acquiring a lower respiratory tract infection, the expected costs will fall by £693 [31].

Matched-cohort studies remain the most commonly used method for estimating LOS and costs associated with HAI, and produce heterogeneous results [32]. Such studies 'match' controls to account for factors unrelated to HAI that may influence hospital utilization and resource use. Thus, infected and uninfected patients are usually matched for

patient demographic data, indicators of disease severity, and factors relating to hospital admission, as well as additional variables that may have contributed to excess morbidity and LOS [33,34]. However, the matching factors used in various studies have varied, as have the types of infection investigated, suggesting that the identification of appropriate matching factors for specific HAIs may not be straightforward. Vrijens *et al.* [22] recently used a matched-cohort study to estimate the effect of hospital-acquired bloodstream infection on LOS and costs in 1839 patients from 19 acute hospitals in Belgium, and investigated the influence of the choice of different matching factors on the estimates. Authors showed that the more matching variables included, the smaller the increase in LOS and cost. The most critical factor influencing the final estimate was the time preceding the infection. After inclusion of this matching factor, the estimation of additional LOS dropped from 21 to 7 days. Nevertheless, the matching process may suffer from important sources of bias. A key issue is the selection bias arising from the number of matching variables used to control for confounding [32]. For instance, the most accurate estimate in the matched study by Vrijens *et al.* [22] relied upon only a selected sample (50%) of patients initially included in the analysis.

Longitudinal and multistate models

Analytical techniques that account for variation in time at risk are particularly valuable when exposures change over time. In outcome studies in which the aim is to estimate the effect of HAI on endpoints such as LOS or costs, HAI is a time-varying exposure. Infected patients are deemed to be exposed after onset of infection, and the interval from start of follow-up to onset of HAI differs from patient to patient. Prior to this, patients are unexposed, as are patients who never experience an infection.

When the time at risk varies substantially from individual to individual, the incidence rate, denominated by person-time experience, is the appropriate measure of disease frequency. This concept is widely understood in infection control, and forms the basis for measures of disease frequency such as number of catheter-related infections per 1000 catheter-days [35]. However, the implications of variation in time at risk for the choice of an analytical method are less often recognized. The incidence rate is a hazard estimator, assuming the hazard to be time-constant. However, investigation of LOS also requires consideration of other hazards, such as the daily probability of discharge, either with prior infection or without prior infection. Generally, if there is a need for adjustment on time at risk, the target parameter of an epidemiological analysis should be person-time based, usually the incidence rate ratio or hazard ratio (HR) [36]. Analyses of

data from case-control or cohort studies by logistic regression often neglect this issue. Sometimes in such analyses, the time at risk is treated as a conventional risk factor. Although this approach may be less biased than not accounting for time at risk at all, it neglects the distinction between time at risk and other types of confounding [5].

One source of bias occurs when infected and uninfected patients are compared with regard to total hospital costs or total hospital LOS. For infected patients, only those days and costs incurred after the occurrence of the infection are possibly secondary to infection. The association between pre-infection outcome and infection is entirely non-causal from the perspective of measuring the excess burden of HAI. Therefore, combining pre-infection outcomes with post-infection outcomes dramatically amplifies confounding, and overestimates the economic impact of infection [5]. Modifying the analysis such that average post-infection LOS in infected patients is compared with average total LOS in non-infected patients does not completely remove confounding by time. Bias persists even in matched-cohort studies in which non-infected patients are selected to have an LOS at least as long as the interval to infection in the corresponding infected patients, irrespective of differences in severity of illness [37,38]. The reason for this bias is that conditioning on the presence or absence of HAI induces an association between the time to infection and time to discharge. In other words, the matching procedure labels patients as 'infected' or 'uninfected' before the events 'HAI' or 'discharge without HAI' occur. In doing this, matching induces a bias regardless of the matching variables.

Thus, these study designs have several limitations because of the time-varying nature of the exposure. They do not take into account the time-dependent nature of nosocomial infections, but treat HAIs as time-fixed events. These time-independent (or time-fixed) studies, i.e. outcome analyses that do not account for the time prior to the occurrence of nosocomial infection, lead to biased effect estimation, in the direction of an overestimation of the time to reach the endpoint [12,14,15,17,39–41]. Beyersmann *et al.* [40], when studying the effect of nosocomial pneumonia (NP) on LOS, documented this distortion, showing a difference of end of LOS HR of 0.65 when NP status was included as a time-dependent covariate and 0.38 if NP status was treated as time-fixed, which means that, in both analyses, NP status prolonged LOS, but in the time-fixed analysis the effect was overestimated. The biased effect is shown by displaying the daily end of LOS HRs with and without NP (Fig. 1).

Multistate modelling represents a suitable method to avoid time-dependent bias, offering a more precise estimation of extra LOS attributable to HAIs, as well as many other

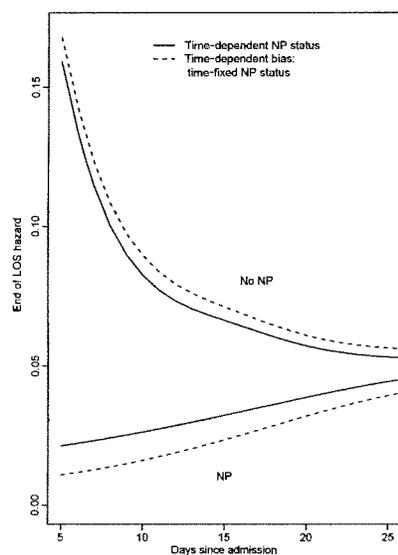


FIG. 1. Illustration of the effect of nosocomial pneumonia (NP) status on end of length of stay (LOS) hazard ratios. End of LOS hazard ratios with and without NP; the x-axis starts with day 5, the first end of LOS day of patients with NP. Solid lines: the unbiased analysis. Dashed lines: the biased analysis. Both analyses find that LOS is prolonged after NP, but the effect is overestimated in the biased analysis.

cost-consuming in-hospital adverse events [12]. Multistate models describe several possible events and the transition between events in a cohort of individuals. Future exposure status (such as the occurrence of HAI) is considered to be time-dependent; therefore, individuals move into states at the times when the events occur, and the composition of the infected and uninfected groups is subject to change at any time. The structure of a multistate model can be viewed as unexposed individuals moving into the exposure state only when the exposure occurs and into the final state when the study endpoint is observed. In a multistate model assessing the excess LOS associated with HAI, the occurrence of HAI would be the time-dependent exposure status, and discharge and deaths would be the study endpoint (Fig. 2). In addition, discharge and death can be handled as separate outcomes [42].

The standard technique used to adjust for confounders is Cox regression analysis between the transition hazards in

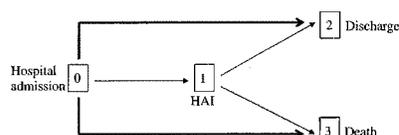


FIG. 2. Multistate model describing time-dependent exposure. Patients are entered into the model on the day of admission to hospital. Patients move into the following states on the day when the healthcare-associated infection (HAI) and/or discharge and/or death are detected. Thus, infected patients move from 'admission' (state 0) into 'HAI' (state 1), and into 'discharge' (state 2) or 'death' (state 3); uninfected patients move from 'admission' (state 0) into 'discharge' (state 2) or 'death' (state 3).

the multistate model. The overall excess LOS, adjusted for confounders, may then be computed by first computing the 'individual' excess LOS, i.e. the excess LOS in a population with identical confounder values, based on the results from the Cox models. Next, these numbers are averaged over the study population. This approach is analogous to adjusted Kaplan–Meier curve estimation [43].

Multistate models also have some limitations. First, because a multistate model is a representation of events as they occur over time, individual patient-level data need to be collected on a daily basis. This might be costly in terms of labour. Second, multistate models rely on two restricting assumptions. The first assumption is that the probability of transition into the next state depends only on the current state. In other words, the future course of a patient (such as to be discharged or to die) is assumed to depend on the current HAI status, but not on the time of HAI diagnosis. The first restriction may be relaxed by including the time since HAI diagnosis in a regression model for the multiple states. The second assumption concerns the issue that multistate models assume that the exact time of the appearance of HAI is known. The second restriction might be more relevant in clinical trials with periodic follow-up visits of patients (e.g. every 3 or 6 months) than in a hospital setting, where daily data records are currently available. Finally, the statistical analysis might require some sophisticated statistical expertise and programming.

Typically, survival analysis and multistate models consider time as a continuous phenomenon, but there are also approaches that work in a discrete time setting. Recently, Barnett et al. [16] used a time-discrete multistate model to quantify the additional LOS spent in an intensive-care unit associated with MRSA infection. The authors found that MRSA infection decreased the risk of discharge by 20% with respect to patients without MRSA infection. They also found

that the assumption underlying the commonly employed incidence rate, i.e. assuming time-constant daily event probabilities, was not fulfilled.

In practice, multistate modelling typically requires daily individual patient data, as collected in a prospective cohort study. Key data are the timing of HAI, because LOS before HAI must not be attributed to HAI, and vital status at the end of LOS (or at the end of a predefined time period after hospital stay). Censored data of patients still in hospital by the end of the study should be also reported properly. The first step is describing the possible state transitions of the model. This obviously depends on the research question. Fig. 2, for example, shows the classic model used to analyse change in LOS attributable to HAI, or in general, an intermediate event. The available data, including hospital admission, HAI and discharge (or death), can be entered in a one-row-per-subject format (patient-oriented dataset) or in a transition-oriented format (where each row represents a transition), using a 'clock forward' approach as time-scale; that is, the times of intermediate (HAI) and final (discharge and death) events refer to the time since the patients entered the initial state. Describing the statistical analysis of multistate models is beyond the scope of this review. On the other hand, some headway has been made in making these analyses generally available, and statistical packages to compute excess LOS are freely available online in the open-source environment R for statistical computing [44,45]. An excellent introduction to multistate models, including a section on the practical steps, has also been provided by Andersen *et al.* [46].

Conclusion

HAIs unquestionably have substantial effects on morbidity and mortality. However, quantifying the exact economic burden attributable to HAIs still remains a challenging issue. The matched-cohort study design produces bias in the estimation of the effects of HAI on LOS and costs. Cost effects or excess LOS are likely to be overestimated if the interval to onset of HAI is not properly accounted for in the study design or analysis. The most frequent mistake in previously published evidence is the introduction of time-dependent covariates as time-fixed, on the assumption that the impact of such exposure on the outcome remains constant. Longitudinal and multistate models avoid the time-dependent bias and address the time-dependent complexity of the data. Appropriate statistical methods are important in the analysis of excess costs associated with HAI, because informed decisions and policy developments may depend on them.

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Transparency Declaration

No conflict of interest is declared in relation to the topic of this article.

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THE DIRECT MEDICAL COSTS OF Healthcare-Associated Infections in U.S. Hospitals and the Benefits of Prevention



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SUMMARY

This report uses results from the published medical and economic literature to provide a range of estimates for the annual direct hospital cost of treating healthcare-associated infections (HAIs) in the United States. Applying two different Consumer Price Index (CPI) adjustments to account for the rate of inflation in hospital resource prices, the overall annual direct medical costs of HAI to U.S. hospitals ranges from \$28.4 to \$33.8 billion (after adjusting to 2007 dollars using the CPI for all urban consumers) and \$35.7 billion to \$45 billion (after adjusting to 2007 dollars using the CPI for inpatient hospital services). After adjusting for the range of effectiveness of possible infection control interventions, the benefits of prevention range from a low of \$5.7 to \$6.8 billion (20 percent of infections preventable, CPI for all urban consumers) to a high of \$25.0 to \$31.5 billion (70 percent of infections preventable, CPI for inpatient hospital services).

I. INTRODUCTION

Healthcare-associated infections (HAIs) in hospitals impose significant economic consequences on the nation's healthcare system. The most comprehensive national estimate of the annual direct medical costs due to HAIs (published in 1992) was based on the results from the Study on the Efficacy of Nosocomial Infection Control (SENIC) that was conducted in the mid-1970s. [1] With an incidence of approximately 4.5 HAIs for every 100 hospital admissions, the annual direct costs on the healthcare system were estimated to be \$4.5 billion in 1992 dollars.[1] Adjusting for the rate of inflation using the CPI for all urban consumers, this estimate is approximately \$6.65 billion in 2007 dollars. However, more recent published evidence indicates that the underlying epidemiology of HAIs in hospitals has changed substantially since the SENIC study, along with the costs of treating HAI. [2, 3] The purpose of this report is to update the annual national direct medical costs of HAIs based on published studies selected for this analysis. As there has not been another national study since the SENIC project, national estimates must be inferred from studies based on more limited study settings. Therefore, only ranges of costs will be provided to reflect the uncertainty that results from using published cost estimates from studies with more limited scope.

While this report itself is not a meta-analysis or a systematic review, there were three criteria used to identify the most appropriate cost estimates for use in this analysis. First, the study investigators must have conducted their economic analysis from the cost perspective of the hospital. Second, the estimate must be from either a multi-center study, a systematic review, or a single-center study that estimated the cost of an HAI for most, if not all, of a hospital population (as opposed to a specific setting such as an intensive care unit). Finally,

the investigators must have used either actual costs (micro-costing methods) or hospital charges that were adjusted using a cost-to-charge ratio to represent the actual opportunity cost of the hospital resources used.

The next section of this report begins with the justification for the three criteria used to select the published evidence to develop cost estimates. In the third section, the annual national cost estimates for five different infection sites will be developed, including surgical site infections (SSIs), central line associated bloodstream infections (CLABSIs), ventilator-associated pneumonias (VAPs), catheter-associated urinary-tract infections (CAUTIs), and Clostridium difficile-associated disease (CDI). Cost estimates for each of the various infection sites are inferred from published studies and combined with annual HAI incidence estimates from the National Nosocomial Infection Surveillance System (NNIS). The fourth section develops an estimate of the annual national direct medical costs of all HAIs to U.S. hospitals. Given the different epidemiologic methods (retrospective cohort, prospective observational) and costing methods (actual expenditures, charges, cost-to-charge ratios) used in studies of HAIs, it should be acknowledged that the cost estimates from the separate infection site studies do not lend themselves to simple addition for the purposes of creating an aggregate cost estimate for all HAIs. To estimate the overall national direct medical cost of all HAIs, this analysis used results from two studies employing different study methodologies: a systematic review of economic studies and an economic model of hospital-wide patient costs from a single hospital. A sensitivity analysis is also conducted that takes into account the uncertainty associated with the effectiveness of infection control programs and the proportion of HAIs that are preventable in order to assess the potential opportunity costs that HAIs impose on hospitals.

II. Justification of Study Criteria

The hospital perspective on the Cost of HAI

Three broad components of cost comprise the socio-economic costs of HAI: direct medical costs, the indirect costs related to productivity and non-medical costs, and intangible costs related to diminished quality of life (Table 1). The vast majority of economic and cost analyses of HAI focus primarily on direct medical costs as these costs directly impact hospital finances. Given the current Diagnosis Related Group classification system does not have specific codes for HAIs, hospitals may not be able to recover the extra patient costs to treat HAIs from third party payers.¹ Most researchers perform their analysis from the hospital perspective only to provide evidence that hospitals can see economic benefits through investment in infection control programs. However, there are other analytical perspectives that incorporate broader interpretations of the costs of HAIs, particularly in terms of the economic impacts resulting from diminished worker productivity (resulting from additional morbidity due to an HAI) or the loss of life. While such impacts affect patients, third party payers and society as a whole, there is little empirical evidence on the costs associated with these long term outcomes. Additionally, these impacts probably do not affect hospital administration and decision making. For the purposes of this report, only studies that provide evidence on the direct hospital costs associated with treating HAIs are considered.

Study Designs

The most common analytical approach for measuring the cost of HAIs by infection site usually employs some type of observational epidemiologic study in which a group of patients not infected with a specific microorganism is compared to a group of

infected (or exposed) patients.[5,6] However, study populations and methods vary and include differing economic evaluation methods (cost analysis, cost-effectiveness analysis, or cost-benefit analysis), observational study designs (prospective versus retrospective, concurrent versus comparative design, matched versus unmatched analysis, selection and number of confounders used), patient populations and settings (e.g. ICU, specific disease), and cost information used (charges, adjusted charges, or micro-cost data).[6] A recent systematic review of the economic analyses of HAIs conducted by Stone and colleagues noted that, given the differences in study methods, the published literature on the cost of HAI shows considerable variation in the cost estimates for the various sites of infection.[3] As the purpose of this report is to provide representative cost estimates for the entire population of infected patients with any HAI, the analysis reported here considered only cost estimates from systematic reviews or studies that were based on larger, hospital-wide study populations that captured more of the potential variation in hospital costs in patients with an HAI.

Cost Information

An important consideration for any economic evaluation of resource use in hospitals is distinguishing between actual micro-costs (the expenditures the hospital makes for goods and services) and charges (what the hospital charges the patient). [7,8] Micro-costing provides more precise estimates of the economic value of the resources used in hospital care. However, the prospective payment system currently used by the CMS and other third party payers to set reimbursement rates for hospitals for their services can lead to distortions in patient costs referred to as cost shifting. Here, hospitals will raise charges above the amount that

¹Under the Prospective Payment System used by the Centers for Medicare and Medicaid Services (CMS), the level of reimbursement to hospitals for patient care is set according to the Diagnosis Related Group (DRG) classification system. This system classifies hospital patients into groups of patients expected to consume the same level of hospital resources based on a number of different patient characteristics including gender, age, diagnosis, types of procedures, and any co-morbidities present on admission.[4] This same classification system is also used by other third party payers to set their reimbursement rates.

would accurately reflect actual patient costs to payers with more generous reimbursement schedules which, in effect, subsidizes less generous payers as well as patients who cannot pay for their own care. Thus, the use of hospital charges to reflect the costs of patient care can overestimate the actual costs of resources consumed. [9,10] Similarly, cost shifting can occur within the hospital when some services are reimbursed at a higher rate than others. Because micro-costing provides cost information that more accurately reflects the opportunity costs of resources used to treat infected patients, only cost estimates based on micro-cost data, or alternatively, cost estimates based on charges that have been adjusted to more accurately reflect actual hospital expenditures on patient care are used for this report. Such adjustments include using published cost-to-charge ratios provided by CMS, or a hospital's own internal cost-to-charge ratios based on their own reimbursement agreements with third party payers.

III. Estimates of the annual direct medical costs for five HAI sites

Estimates of the direct medical costs associated with five major sites of HAIs will be calculated by taking estimates of the number of infections and then multiplying these estimates with both a low and a high average patient cost estimate from the published literature. The patient cost estimates are adjusted for the rate of infection using two different inflation indexes: the CPI for all urban consumers (CPI-U) and the CPI for inpatient hospital services with all cost estimates adjusted to 2007 dollars. As the various studies used in this report were conducted at different points in time, the cost estimates must be adjusted to 2007 dollars in order to make them comparable. As both indexes measure price changes for broadly defined

expenditure groups, there is no research to date on which measure would be most appropriate to use to accurately adjust for inflation in the prices of the hospital resources used to treat HAIs. Given the potential to mismeasure the rate of inflation on these resources prices, all cost estimates will be adjusted using both indexes. A description of the construction and composition of each consumer price index and the potential limitations of each index to adjust cost estimates of HAI follows below.

Consumer Price Indexes

The CPI-U is constructed by the U.S. Bureau of Labor Statistics (BLS) and is a measure of the average change over time in the prices paid by all urban consumers (defined as all urban households in Metropolitan Statistical Areas and in urban places of 2,500 inhabitants or more) for a market basket of consumer goods and services purchased for day-to-day living. The all urban consumer group includes almost all residents of urban or metropolitan areas, including professionals, the self-employed, the poor, the unemployed, and retired people, as well as urban wage earners and clerical workers and represents about 87 percent of the total U.S. population.[11] The goods and services that are included in the CPI market basket have been determined from an annual BLS survey on consumer expenditures which provides detailed information on consumer spending habits. Combining the consumer expenditure data with other survey data on prices from retail outlets, the CPI-U is updated on a monthly basis. The various goods and services that consumers purchase are classified into over 200 categories that fall into eight major classification groups including food and beverages, housing, apparel, transportation, medical care, recreation, educational and communication, and a final group representing other goods and services. As an estimate of the percent change in

prices between any two price periods, the CPI-U is the most widely used measure of inflation and is used by federal and state governments to adjust government income payments or to make cost-of-living adjustments to wages.

The inpatient hospital services index is a subcategory of the expenditure items found under the medical care major expenditure group (Table 2). The medical care expenditure group is divided into subcategories that include two intermediate groups: medical care commodities and medical care services. The medical care services intermediate group is composed of two expenditure classes that include professional services and hospital services. The CPI for hospital inpatient services is a one of two item strata (or subsets) that comprises the hospital services expenditure group (the other item being outpatient hospital services). This inpatient hospital services index is derived from a survey of price changes for goods and services that hospitals (also in urban areas) consume while treating a patient during a hospital visit. A hospital visit consists of a bundle of goods and services that are used to achieve a desired outcome, regardless of the length of the hospital stay, and is based on the contents of a "live" hospital bill that is submitted to a payer that reflects actual hospital service delivery patterns.[12] As the CPI is used to measure out-of-pocket expenditures by the consumer, only payments made by either a private insurer and/or the patient are considered (payments by employer provided insurers, along with payments by Medicare and Medicaid are excluded). [12] The goods and services in this index include a mixture of itemized services (such as lab tests, emergency room visits), diagnosis related group (DRG) based services, daily room charges etc., but treats them as a bundle of complementary services provided by hospitals during a hospital visit (as opposed to pricing each item consumed separately) whose value is determined by surveying

payer reimbursements or other set fee schedules. Table 2 presents the annual percentage change in prices for the years 2001-2007 for the CPI-U, the medical care expenditure group, and other subcategories related to hospital services including the inpatient hospital services index. The increase in prices (or the level of inflation) as measured by CPI-U has been lower compared to the price increases measured by the various indexes for the medical care and hospital services, reflecting the higher level of inflation as measured in these more narrowly defined indexes. For 2007, the CPI-U increased 2.8 percent from 2006 while the CPI for hospital related services and CPI for inpatient hospital services increased 6.6 percent and 6.3 percent respectively.

In this report, both the CPI-U index and the CPI for inpatient hospital services are used to adjust the various cost estimates to 2007 dollars. Given that the CPI-U is a broad measure of price changes for a market basket of goods comprised of a number of different expenditure groups, the use of CPI-U index might understate the rate of inflation on the prices of the hospital resources used to treat HAIs given that inflation in medical services has been higher than the CPI-U. While the CPI for hospital inpatient services is a more narrowly defined expenditure subcategory for hospital resources, it is possible this index might over inflate price increases that results from the adoption of new medical technology (i.e. new diagnostic tools, drugs, procedures, etc.). Without adjusting for the improvement in patient outcomes due to new technology, the CPI for hospital inpatient services can overstate price changes.[13] As both indexes may misrepresent the actual impact of inflation on the resources used to treat HAI, both are used to adjust the range of HAI cost estimates from the published studies used in this report.

Estimates for the number of HAIs

The estimates for the number of infections, except for CDI, are based on estimates from Klevens et al. [14]. As the estimates from the Klevens et al. incorporate both device and non-device related infections, these numbers are adjusted to provide estimates of the number of device-related infections by each site (Table 3) to be consistent with the cost information from the literature which has focused on device-related infections. The proportions used to make the adjustments to the total number of BSIs (37 percent device-related) and pneumonia (21 percent device-related) are based on a study by Weber et al., while the proportion for urinary tract infections (80 percent device-related) is based on a study by Saint et al. [15, 16]. The estimate for the number of CDIs cases comes from a study by McDonald et al. (2003). [17]

Two recent systematic reviews of the published literature on the costs associated with various HAIs in hospitals are available. Updating a previous review from 2002, Stone et al. derived the following attributable cost estimates: \$25,546 for SSI, \$36,441 for BSI, \$9,969 for VAP and \$1,006 for CAUTI.[3] These authors did note that there was considerable variation in the cost methodology used by the studies incorporated in their review which included results from vaccination studies as well as studies on community-acquired infections. Anderson et al. [18] also developed estimates of the cost of HAIs from published studies but used a more stringent inclusion criterion by including only studies that estimated the attributable costs of getting an HAI. Anderson et al. weighted the various cost results by giving higher weight to estimates from larger studies. The resulting attributable costs of various HAIs included: \$10,443 for SSI, \$23,242 for BSI, \$25,072 for VAP, and \$758 for CAUTI.

The results from both systematic studies have limitations and must be used with caution. As an example, the nine studies used by Stone et al. to estimate the mean cost attributable to BSI included five studies from outside the U.S., while three of the four U.S. studies used charges (as opposed to actual costs). Likewise, the five studies used by Anderson et al. to estimate the cost of BSI included three non-U.S. studies, while the two U.S. studies were based on ICU populations only. Given the lack of consistency between locations, populations and cost information from the studies in these systematic reviews, this report also used cost estimates from other single hospital studies that incorporated both hospital-wide study settings and micro-cost data in their analysis. The studies selected for their direct medical cost estimates for each infection site are described below.

SSI

Starting with SSIs, the studies used for the average attributable cost of SSIs include Anderson et al. [18] for a low estimate (\$10,443 per infection in 2005 dollars) and Stone et al. [3] for a high estimate (\$25,546 per infection in 2002 dollars).

CLABSI

The cost estimates for CLABSIs were taken from a cost-effectiveness analysis to measure the impact of using maximal sterile barriers to prevent CLABSIs conducted by Hu et al. [19]. In evaluating the literature, the study authors developed a range of estimates for the attributable cost of CLABSI (\$5,734 to \$22,939 in 2003 dollars) that would be representative of all hospitalized patients.

VAP

The studies used for the estimates on VAP include a low estimate from Warren et al. [20] and a high estimate from Anderson et al. [18]. The Warren study

examined the cost of VAP in intensive care patients, but the setting involved a nonteaching, suburban medical center rather than an urban or university tertiary care and teaching center where a majority of cost studies are usually performed. From this study, the average attributable patient cost of VAP is \$11,897 (in 1999 dollars). The estimate of the cost of VAP from Anderson et al is \$25,072 (in 2005 dollars).

CAUTI

For costs associated with CAUTI, the Anderson et al. [18] study provides an estimate of \$758 per infection. The second estimate of \$589 (in 1998 dollars) comes from Tambyah et al. [21]. While the Tambyah et al. study is a single-center study, it was a hospital-wide prospective study. Because of the differing CPI adjustments, the higher estimate using the CPI for all urban consumers comes from the Anderson study, while the higher estimate using the CPI for inpatient hospital services comes from the Tambyah study.

CDI

Few studies have estimated the cost of hospital-associated CDI. The estimate used here comes from a study by Dubberke et al. [22]. This is a single-center, retrospective cohort study; however, two different methods were used to estimate costs and the analytic time horizon was 180 days (from the index hospital admission) to capture any potential readmissions resulting from CDI. The lower bound estimate of \$5,042 was determined using linear regression analysis while the higher estimate of \$7,179 was determined using propensity-score matched-pairs analysis. These estimates are conservative as they did not include any patients that had any operating room costs associated with their hospital stay. Both estimates were in 2003 dollars.

Range of cost estimates by infection site

The estimates developed for each infection site and their CPI-adjusted values are displayed in Tables 4 and 5. Starting with a low and a high cost estimate from selected studies in Table 4, these estimates are then adjusted to 2007 dollars using the CPI-U and the CPI for inpatient hospital services. Using the results from Table 4, Table 5 presents the estimated ranges of the total annual costs associated with specific sites of HAI infection in U.S. hospitals adjusted by the two CPI indexes. The infection site with the largest range of annual costs is SSI (\$3.2 billion to \$8.6 billion using the CPI-U and \$3.5 billion to \$10 billion using the CPI for inpatient hospital services) while the site with the smallest annual cost is CAUTI (\$340 million to \$370 million using the CPI-U and \$390 million to \$450 million using the CPI for inpatient hospital services). The costs associated with the remaining infection sites are also significant with the direct medical cost of CLABSI, VAP, and CDI ranging from \$590 million (adjusted by CPI-U) to \$2.68 billion (adjusted by CPI for inpatient hospital services), \$780 million (adjusted by CPI-U) to \$1.5 billion (adjusted by CPI for inpatient hospital services), and \$1.01 billion to \$1.62 (adjusted by CPI for inpatient hospital services), respectively.

IV. Estimates of the cost of all HAIs in general

Studies Used

While published studies on the cost of HAIs tend to focus on a single device-related infection site (thus requiring adjustments to the counts of each separate infection site as done in the previous section), there are two published cost estimates available that are appropriate for assessing the overall direct patient costs of all HAIs (both device-related and non-device-related infections) using the estimated annual total number of HAIs (1,737,125 from the Kleven's study) for 2002. An earlier systematic review of the economic costs of HAI conducted by Stone et al. included an estimate of the average attributable patient costs of HAIs in general.[23] The inclusion criteria for this review included papers published (in English) between 1990 and 2000 that contained abstracts and original cost estimates. The collected cost data were converted into U.S. dollars (for studies conducted outside the U.S.) and all dollar values were adjusted to 2001 dollars. The resulting mean estimate of \$13,973 (with a standard deviation of \$17,998) was based on nine selected studies. The large standard deviation associated with the mean estimate is probably due to the variety of study locations (inside and outside the U.S.) and costing methods (actual costs and hospital charges) employed by the study investigators.

The Roberts et al. study was a single-center study that measured the attributable costs associated with HAI in a hospital-wide random sample of adult medical patients.[24] The study used unit costs that were derived from the hospital expenditure report. The study excluded certain patient subpopulations who acquired an HAI in hospital service departments (pediatric, surgical, trauma, obstetrical wards) where the cost structures are significantly different from other hospital service

wards. Exclusion of these locations from the analysis introduces a downward bias in the estimate of overall HAI cost. A multivariate regression model was analyzed using total patient costs as a dependent variable with APACHE III score, ICU admission, surgery, and the presences of an HAI as independent variables. The mean attributable cost of HAI of \$15,275 (with a standard deviation of \$5,491), in 1998 dollars, from the model represents a conservative cost estimate of HAI.

The National Annual Direct Hospital Costs of HAI Tables 6 shows the CPI adjustments made for the range of estimates on the average attributable per patient costs for all HAIs from the selected studies. Table 7 presents the overall annual direct medical costs to U.S. hospitals of all HAIs among hospital patients. The direct cost ranges from \$28.4 to \$33.8 billion adjusting for the rate of inflation using CPI-U. Using the CPI for inpatient hospital services, the overall direct cost ranges from \$35.7 billion to \$45 billion.

While the cost estimates illustrate the magnitude of the potential savings of preventing all infections, these savings must be weighted against the effectiveness of the interventions to prevent them and the cost of the resources needed to invest in the interventions. In assessing the extent that HAIs are preventable, Harbarth et al. [25] concluded that the literature provides no clear answers. In conducting a systematic review of the published evidence on the preventable proportion of HAIs resulting from multi-modal interventions, the authors found considerable variability in impacts, ranging from a 10 percent reduction to 70 percent reduction in HAIs. Interventions focusing on reducing CLABSI had the greatest impact with observed reductions ranging from 38 percent to 71 percent. Pronovost et al. [26] observed a 66 percent decrease in CLABSIs from their multi-modal intervention for all ICU

units in hospitals located in Michigan. A similar decrease in CLABSIs has also been observed in ICU units in southwestern Pennsylvania after the implementation of a multi-faceted intervention that included targeted, evidence based insertion practices and an education program on prevention strategies. [27] However, the Harbarth study concluded that approximately 20 percent of all HAIs are probably preventable based on current medical practice and technology.

To reflect the uncertainty associated with the effectiveness of infection control prevention efforts, Table 8 presents the range of cost estimates after adjusting for prevention effectiveness levels of 20 percent, 50 percent and 70 percent. After these adjustments, the benefits of prevention range from a low of \$5.7 to \$6.8 billion (20 percent of infections preventable, 2007 CPI-U) to a high of \$25.0 to \$31.5 billion (70 percent of infections preventable, 2007 CPI for inpatient hospital services).

Discussion

While there is considerable variability in the costs of HAI, the low cost estimates of \$5.7 to \$6.8 billion annually are still substantial when compared to the cost of inpatient stays for other medical conditions. According to the Agency for Healthcare Research and Quality, the three principle diagnoses with the highest annual aggregate inpatient hospital costs (in 2006 dollars) include coronary artery disease (\$17.5 billion), heart attack (\$11.8 billion) and congestive heart failure (\$11.2). [27] Even if the effectiveness of HAI prevention is low, the direct medical cost of preventable HAIs are comparable to the costs of stroke (\$6.7 billion), diabetes mellitus with complications (\$4.5 billion), and chronic obstructive lung disease (\$4.2 billion). [28]

There are several important study limitations to consider when interpreting and using the cost estimates reported here. First, the national cost estimates have been inferred from studies with more limited study settings (regional or single hospital). To reflect the uncertainty associated with the representativeness of these studies, the national estimates have been presented as ranges. Second, it should be emphasized that this analysis is based on the estimated number of infections that occurred in 2002. As noted in the previous section above, the incidence of some types of infections (particularly CLABSIs) have been shown to be on the decline, whereas it is possible that the incidence of other HAIs may have changed (either increased or decreased) as well. Therefore, the estimated benefits of preventing HAIs for 2007, using 2002 infection data, is only an approximation of the actual benefits for 2007. Also, the published 2002 national estimates of the number of HAIs, in total and by site of infection, did not include information on the statistical uncertainty (or standard errors) associated with using NNIS hospitals as a sample for all hospitals in the United States. If this information were used in this analysis, the cost ranges presented here would be wider for they would now also reflect the variability in the estimated number of HAIs. Third, the proportions used to estimate the number of device-related infections from the total number of HAIs is based on a single study of HAI surveillance for a single hospital and may not be representative for all hospitals nationwide. Finally, this study did not attempt to provide any assessment of the cost associated with any interventions (outside the normal working conditions for established infection control programs) that would be used to curb HAIs. Such intervention costs will certainly reduce the magnitude of the direct medical cost savings (or benefits) and must be considered in any cost-effectiveness or cost-benefit analysis of infection control policies and programs.

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Table 1: The Social Costs of Hospital-Associated Infections

Categories of Cost*	
Direct Hospital Costs	Fixed Costs: Buildings Utilities Equipment/Technology Labor (laundry, environmental control, administration)
	Variable Cost: Medications Food Consultations Treatments Procedures Devices Testing (laboratory and radiographic) Supplies
Indirect Costs	Lost/Wages Diminished worker productivity on the job Short term and long term morbidity Mortality Income lost by family members Forgone leisure time Time spent by family/friends for hospital visits, travel costs, home care
Intangible Cost	Psychological Costs (i.e., anxiety, grief, disability, job loss) Pain and suffering Change in social functioning/daily activities

*Adapted from Haddix AC and Shaffer PA. Cost-effectiveness analysis. In Prevention Effectiveness: A Guide to Decision Analysis and Economic Evaluation. Oxford University Press, 1996.

Table 2: Consumer Price Index for Urban Consumers (CPI-U): U.S. city average by select expenditure category and commodity and service group*

Expenditure Category	Percentage change 12 months ended in December						
	2001	2002	2003	2004	2005	2006	2007
All items (CPI-U)	1.6	2.4	1.9	3.3	3.4	2.5	4.1
Medical Care	4.7	5.0	3.7	4.2	4.3	3.6	5.2
Medical Care Services	4.8	5.1	4.5	5.0	4.8	4.1	5.3
Hospital and Related Services	6.6	8.7	7.3	5.9	5.3	6.4	6.6
Hospital Services	6.6	9.0	7.4	6.0	5.3	6.5	6.7
Inpatient Hospital Services	6.3	8.4	6.8	5.7	5.7	7.0	6.3
Outpatient Hospital Services	6.6	10.2	9.1	5.4	4.7	5.9	7.4
Nursing Home and Adult Daycare	4.1	5.0	5.7	3.8	3.3	4.1	5.7

*Source: Bureau of Labor Statistics. Consumer Price Index Detailed Reports. [cited 2008, Nov. 13]. Available at www.bls.gov/cpi/cpi_dr.htm

Table 3: Estimated Number of HAIs by site of infection¹⁴

Major site of Infection	Estimated Number of Infections
Healthcare-Associated Infection (all HAI)	1,737,125
Surgical Site Infection (SSI)	290,485
Central Line Associated Bloodstream Infections (CLABSI)*	92,011
Ventilator-associated Pneumonia (VAP)**	52,543
Catheter associated Urinary tract Infection (CAUTI)***	449,334
Clostridium difficile-associated disease (CDI) ¹⁷	178,000

* Total BSI adjusted to estimate CLABSI (248,678 x 0.37%) = 92,011
 ** Total Pneumonia infections adjusted to estimate VAP (250,205 x 0.21%) = 52,543
 *** Total UTIs adjusted to estimate CAUTI (561,667 x 0.80%) = 449,334

Table 4: The average attributable per patient costs of HAI by selected sites of infection adjusted by 2007 CPIs for all urban consumers and inpatient hospital services

Infection site	Low Estimate of average attributable Costs (\$ base year)	High Estimate of average attributable Costs (\$ base year)	Low estimate adjusted to 2007 \$ using CPI-U	High estimate adjusted to 2007 \$ using CPI-U	Adjusted to 2007 \$ using CPI for Inpatient Hospital Services	Adjusted to 2007 \$ using CPI for Inpatient Hospital Services
SSI	\$10,443 ¹⁸ (2005)	\$25,546 ¹ (2002)	\$11,087	\$29,443	\$11,874	\$34,670
CLABSI	\$ 5,734 ¹⁹ (2003)	\$22,939 ¹⁹ (2003)	\$ 6,461	\$25,849	\$ 7,288	\$29,156
VAP	\$11,897 ²⁰ (1999)	\$25,072 ¹⁸ (2005)	\$14,806	\$27,520	\$19,633	\$28,508
CAUTI	\$ 589 ²¹ (1998)	\$ 758 ¹⁸ (2002)	\$ 749	\$ 832	\$ 862	\$ 1,007
CDI	\$ 5,042 ²² (2003)	\$ 7,179 ²² (2003)	\$ 5,682	\$ 8,090	\$ 6,408	\$ 9,124

Table 5: Aggregate attributable patient hospital costs by site of infection

Infection site	Estimated Number of Infections	Low Estimate of average attributable Costs (\$ base year)	High Estimate of average attributable Costs (\$ base year)	Low estimate adjusted to 2007 \$ using CPI-U	High estimate adjusted to 2007 \$ using CPI-U	Adjusted to 2007 \$ using CPI for Inpatient Hospital Services	Adjusted to 2007 \$ using CPI for Inpatient Hospital Services
SSI	290,485	\$10,443	\$25,546	\$11,087 - \$29,443	\$11,874 - \$34,670	\$11,874 - \$34,670	\$11,874 - \$34,670
CLABSI	92,011	\$ 5,734	\$22,939	\$ 6,461 - \$25,849	\$ 7,288 - \$29,156	\$ 7,288 - \$29,156	\$ 7,288 - \$29,156
VAP	52,543	\$11,897	\$25,072	\$14,806 - \$27,520	\$19,633 - \$28,508	\$19,633 - \$28,508	\$19,633 - \$28,508
CAUTI	449,334	\$ 589	\$ 758	\$ 749 - \$ 832	\$ 862 - \$ 1,007	\$ 862 - \$ 1,007	\$ 862 - \$ 1,007
CDI	178,000	\$ 5,042	\$ 7,179	\$ 5,682 - \$ 8,090	\$ 6,408 - \$ 9,124	\$ 6,408 - \$ 9,124	\$ 6,408 - \$ 9,124

*Example calculation for SSI: 2007 CPI for all urban consumers: Low 290,485 x \$11,087 = \$3.22 billion High 290,485 x \$29,443 = \$8.55 billion
 2007 CPI for hospital inpatient services: Low 290,485 x \$11,874 = \$ 3.45 billion High 290,485 x \$34,670 = \$10.07 billion

Table 6: The attributable per patient costs of all HAIs

	2007 CPI-U	2007 CPI	2007 CPI-U hospital inpatient services	2007 CPI hospital inpatient services	2007 CPI-U all hospital services	2007 CPI all hospital services
HAI (all)	\$13,979*	\$15,275*	\$18,359	\$19,430	\$20,549	\$21,668

Table 7: Annual aggregate direct medical hospital patient costs by site of infection

	2007 CPI-U	2007 CPI	2007 CPI-U hospital inpatient services	2007 CPI hospital inpatient services
All HAI	\$4,737.125	\$16,359 - \$19,430	\$20,549 - \$25,005	\$28.4 - \$33.8

Table 8: Range of estimated annual direct medical cost of all HAIs adjusted by the preventable proportion of infections

	Range of Estimates (billions \$)	20% of infections preventable (billions \$)	50% of infections preventable (billions \$)	70% of infections preventable (billions)
2007 CPI-U	\$28.4 - \$33.8	\$5.7 - \$6.8	\$14.2 - \$16.9	\$19.9 - \$23.7
2007 CPI hospital inpatient services	\$35.7 - \$45.0	\$7.1 - \$9.0	\$17.9 - \$22.5	\$25.0 - \$31.5

Estimating the Cost of Health Care–Associated Infections: Mind Your p’s and q’s

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Monetary valuations of the economic cost of health care–associated infections (HAIs) are important for decision making and should be estimated accurately. Erroneously high estimates of costs, designed to jolt decision makers into action, may do more harm than good in the struggle to attract funding for infection control. Expectations among policy makers might be raised, and then they are disappointed when the reduction in the number of HAIs does not yield the anticipated cost saving. For this article, we critically review the field and discuss 3 questions. Why measure the cost of an HAI? What outcome should be used to measure the cost of an HAI? What is the best method for making this measurement? The aim is to encourage researchers to collect and then disseminate information that accurately guides decisions about the economic value of expanding or changing current infection control activities.

Because health care resources are scarce, they should be allocated to programs that deliver quantifiable health benefits. A rule of thumb for decision making is that the more benefit gained per dollar spent, the better [1]. This applies to those working to reduce the number of health care–associated infections (HAIs). They should aim to allocate their budget across infection prevention strategies that deliver the largest possible health benefit [2–5]. To demonstrate the “biggest bang for your buck” argument, estimates of how health benefits (the bang) and costs (the buck) change with the adoption of novel infection control interventions are required [3, 6]. That increasing investment for infection control is economically justified is not questioned. HAI is a major problem that prolongs hospital stays, prevention is relatively cheap, and many prevention strategies are effective [7]. Whether the economic argument has always been made in the best way and whether optimal analytic methods have been used to estimate the primary economic parameters are worth discussion.

Many decisions about expanding infection control have been based on partial economic studies that show only the gross cost of an HAI [8, 9]. Costing studies may influence decision makers because the estimated gross cost per HAI has been found to be very high, and the conclusion that the cost saved from expanding infection control will exceed the cost incurred is assumed to be true without rigorous analysis. To evaluate completely a new infection control strategy requires accurate estimates of the extra cost of implementing the strategy, the cost savings from the predicted number of prevented cases of HAI, and the clinical effectiveness and health benefits. Simple costing studies that show the gross costs of an HAI are partial evaluations and provide none of this information [10]. Good decision making about infection control should emerge from cost-effectiveness research [11, 12]. Those working for infection control are publishing complete economic appraisals at a rate faster than before [13–16], and this is positive. This research often makes use of modeling studies with various pieces of information harvested from the literature. A key piece of information is the cost per case of HAI, which informs, albeit indirectly, the expected cost saving from extra infection control [17].

Data are now emerging that seriously question the validity of previously applied methods used to determine the cost of an HAI [18–25]. The main cost of an HAI is the extra stay in the hospital. Estimates of extra length of stay based on sounder statistical methods tend to show a shorter estimated extra stay,

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which means that the cost of an HAI may have previously been overestimated [18]. Also problematic is the method used to attach monetary value to lost bed-days, which is often based on cost accounting practices and not economic principles—yet these 2 disciplines have quite different objectives. There may be serious problems with how the economic costs of an HAI have been estimated. Given the importance of estimates of the cost of an HAI for decision making, we are motivated to discuss the approaches used. Three important questions are considered; our aim is to stimulate research that accurately guides decision making about the economics of changing current infection control activities.

WHY MEASURE THE COST OF AN HAI?

The primary reason to understand the cost of an HAI is to inform decisions about how to reduce the problem [2–5]. Because health care resources are scarce, HAIs should be reduced by allocating resources only to efficient infection control programs. One approach is to maximize the amount of health gained from a defined pot of resources. This is called an extrawelfarist view of economics [26] and is used widely in health services decision making [27]. Other approaches to solving resource allocation problems are available [28], and their merits have been debated elsewhere [26, 29–31].

The extrawelfarist approach uses a conceptually simple rule to guide decision making. The change to cost from a decision to adopt a new health intervention (such as a novel infection control intervention) should be adequately compensated by the change to health benefit. Changes to cost are summarized in monetary terms, and changes to health benefit are normally described by means of quality-adjusted life-years (QALYs), which combine information on the quantity and quality of years of life gained [28, 32]. The number of QALYs gained from infection control demonstrate improved quality of care, because lives are saved and events that reduce the quality of life for hospital patients are avoided.

The extrawelfarist decision rule can be written as

$$\Delta C/\Delta E < \lambda,$$

where ΔC is the total dollar costs under a new intervention less the total dollar costs under an appropriate comparator (usually the existing practice), ΔE is the change in health outcomes that arises from a decision to invest in a new health intervention (the total number of QALYs under a new intervention less the total number of QALYs under an appropriate comparator), and λ is the decision maker's maximum willingness to pay for each QALY. Challenges exist for the analyst who quantifies the change to QALYs (health benefits) from infection control, and a critique of these is beyond the scope of this article. When the decision rule is met, those working under an extrawel-

farist economics framework might adopt the new intervention on the grounds that it promotes efficiency. If $\Delta C = 100$, $\Delta E = 5$, and $\lambda = 30$, the rule is met and the intervention should be adopted. Finding an appropriate value for λ is not straightforward [33]. The value varies in practice, often to accommodate other important objectives, such as equity and fairness [28]. The use of the extrawelfarist decision rule for infection control has been discussed in detail elsewhere [3].

For infection control decisions, the change in cost statistic (ΔC) arises from 2 opposing forces. The first is that costs always increase with a decision to implement extra infection control strategies. The second is that cost savings arise from avoided cases of HAI. Because the cost of a case of HAI affects the value of ΔC , it is important to estimate costs with accuracy. Otherwise, the ΔC statistic will be incorrect, and bad decisions may result.

WHAT OUTCOME SHOULD BE USED TO MEASURE THE COST OF AN HAI?

The number of bed-days lost to a case of HAI is an appropriate outcome to describe a large proportion of the cost, and this number can be represented by the letter q . The marginal number of bed-days released by reducing the rate of HAIs may well have a positive economic value or price, which can be elicited from the appropriate source and represented by the letter p . A large part of the cost of an HAI is, therefore, the quantity of bed-days saved (q) multiplied by their economic value or price (p)—or pq . The remainder of the costs of an HAI arise from consumable items used to treat the infection and from physician fees that are billed separately. The consumables saved can result in substantial cost savings, such as when a bloodstream infection leads to septic shock. Very expensive drugs might be required and a high volume of other consumable items used. More modestly, a treatment protocol for respiratory infection due to methicillin-resistant *Staphylococcus aureus* may account for less costly consumables. It will be hard to identify exactly the extra physician fees that arise from treating an HAI, but concurrent attribution methods may be useful for this task [34].

We propose that counting the number of bed-days saved first (q) and valuing them in dollar terms second (p) is a powerful method for describing much of the economic cost of an HAI. Our reasons emerge from considering the different objectives of the hospital-based cost accountant and the public policy economist. The rest of this section is about finding a value for p , and the next section is about the methods used for estimating q .

A public policy economist would take a different approach than a cost accountant to valuing p . The economist would investigate the value of the bed-days in the next best alternative use and so seek the economic opportunity cost incurred from using it to treat an HAI. The accountant would estimate the cash expenditures made to supply the average bed-day. These

2 values for p are likely to be different, because health care is an unusual commodity in economic terms [35]. Yet the value for p is critical for decision making about investments for infection control. Those who make the argument for extra investment in infection control are making an economic argument. They wish to reallocate scarce resources toward infection control and thus away from the supply of some other health-producing activity. They must therefore consider the opportunity cost of the marginal bed-day. Using data collected by hospital accountants to find p may lead to erroneous decisions about new infection control strategies. We explain the reasons for the divergent valuations of p by considering the objectives of the hospital accountant and then the economist.

The hospital accountant strives to keep the organization financially viable for current and future annual budgeting cycles; the objective is to maintain a going concern [36]. In this task, hospital accountants face a high proportion of fixed costs, up to 85% [37, 38]. Examples of fixed costs are power, information and finance systems, and the salaries of many staff. They must recover all the fixed and variable costs of supplying hospital care. Variable costs are those not fixed and can be assigned to individual patients on the basis of use. For example, the number of antibiotics or bags of saline used can be counted and the cash expenditures added to a patient's bill. Fixed costs are likely to be used jointly by many patients over an annual budgeting cycle. Hospital accountants will allocate fixed costs by surrogate measures of activity—such as bed-days, tests ordered, or units of staff time—and then count the units of each measure assigned to patients. The majority of hospital costs are allocated by length of stay [39–41]. If rates of HAIs fall, fewer bed-days, tests, or units of staff time are used, but the cash expended on fixed costs will not change. The result is spare capacity in the hospital, and, unless it is redeployed for new patients, the average fixed cost recovered for every unit of activity (eg, a bed-day) will rise. Cost estimates that emerge from accounting departments are managerial costs designed to recover total expenditures for an annual budgeting cycle. They are a convenient way to keep the hospital financially viable and arise from measures of patient throughput. Accounting costs are not designed to represent the economic value of the marginal health care resources released from a reduction in the number of HAIs [42].

The economist will focus on the marginal number of bed-days and other resources released and on the cash from saved variable costs. Economists will ignore the expenditures made for fixed costs that correctly occupy accountants. These are irrelevant to any decision about allocating scarce resources for new infection control strategies, because they will not change with lower rates of HAIs. The marginal number of bed-days released by infection control may, however, take a positive economic value in some other use. They can be used to increase productivity and treat more patients. Their opportunity cost is

the value that someone is willing to pay to access the marginal bed-day. As long as the effective demand exceeds the supply for hospital-based services, then marginal bed-days will be valuable items in economic terms.

In a decentralized system (such as in the United States), the next patient or his or her insurance company may be willing to pay a certain price (p) to access the bed-days released by the positive effect of extra infection control. In a centrally managed health care system (such as the UK National Health Service) that is owned by the public sector, politicians and bureaucrats can be asked their willingness to pay for hospital bed-days given other demands on public sector spending. One scenario is that there is zero demand for newly released bed-days, so their opportunity cost is zero (ie, $p = 0$). This is unlikely when we consider the long waiting lists and large pool of unmet health needs in almost every jurisdiction. If opportunity costs are positive, then the value is likely to vary. Local demand conditions may play a role. If patients face long waiting lists for elective admission, there are demands for higher throughput by hospitals, and no new building programs are planned to increase supply, then marginal bed-days may be valued higher than in a jurisdiction with less severe constraints. The perspective of the person making the valuation may also play a role. If an election is looming and a politician has promised to improve health care services by treating more patients in hospitals and reducing waiting lists, he or she will put a high value on extra bed-days. If, however, the chief executive of the hospital believes that adequate compensation for any extra patients admitted will not be provided, he or she may see only an increased workload and level of stress for the hospital's staff and so attach a lower economic value to bed-days released. This view will, of course, be tempered by a desire to provide high-quality services, and this improvement in quality is described by the gain in health benefits (QALYs) used in cost-effectiveness research.

WHAT IS THE BEST METHOD FOR MAKING THIS MEASUREMENT?

Because costs are strongly dependent on length of stay, we need to accurately measure the extra length of stay caused by a case of HAI (q). Any method used should account for the fact that HAIs arise at different times during a hospital stay in different patients and that other factors influence length of stay, such as primary diagnosis and comorbidity. A seminal article on methodology [34] compared physician assessment with matched cohort studies, where infected patients are matched with uninfected control subjects on variables thought likely to cause an excess stay. Physician assessments provide the ideal measure but are time-consuming; matched cohort studies are easier to conduct but suffer from 2 sources of bias. The first bias arises because some patients are predisposed to a long hospital stay regardless

of HAI status, and matching on confounding variables is not able to control all the bias. The second bias arises from increasing the number of matching variables in an attempt to control the first bias, as this often causes infected individuals to be selected out of the study because the pool of uninfected control subjects is exhausted. In matched cohort studies, one can only find the best tradeoff between these 2 biases; they cannot be simultaneously eliminated [6].

The time-varying nature of infection also discombobulates a matched cohort study [19]. Exposure to an HAI can occur at any point during a hospital stay, but matched cohort studies tend to compare infected and uninfected patients by their total hospital stay. Infected patients can start generating costs due to an HAI only after the infection has begun. If the timing of events is ignored, costs that manifest before the HAI are included. Combining preinfection outcomes with postinfection outcomes can dramatically amplify confounding [19]. This bias is often called *time-dependent bias*, and it has been shown mathematically to always overstate the prolonging effect of an HAI on length of stay [21]. Another closely related problem is a feedback effect between an HAI and length of stay. Methods that fail to account for this issue will produce biased estimates of extra length of stay (q). Despite these severe limitations, matched cohort studies remain the most commonly used method for estimating cost and produce heterogeneous results [6].

Methods that are less labor intensive than physician assessment and that are methodologically superior to matched cohort studies can be used; however, they are technically complex. Most promising are statistical models that control for differences between patients at the analysis stage rather than at the design stage. A statistical model can be built to describe the relationship between a cost outcome, such as length of stay in the hospital, and predictors of that outcome [43]. An advantage is that multiple predictors can be included without selecting out cases of HAI [24]. Statistical models, such as event history analysis or survival analysis, can be used to account for the time-varying nature of infection. They model the hazards or rates between hospital admission, potential onset of HAI, discharge alive from the hospital, and death in the hospital. Additional time-dependent information, such as daily intubation status, may also be included. Methods for both discrete and continuous time are available [18, 44] and have their merits, which we will not discuss here. These methods have been applied and show extra lengths of stay that are substantially lower than those from methods that do not account for the timing of events and important covariates [18, 45–47].

CONCLUSION

The “HAI costs a lot” approach to influencing decision making has served the infection control community well. Important articles have stated that very large costs arise from HAIs [38,

48–50]; all have been cited frequently and used to attract resources toward infection control programs. The time has arrived, however, for the methodological advances that have been achieved in this area to be implemented by researchers. Complete economic evaluations that include changes to all costs and health benefits should be performed. The information used to update these studies should be of high quality and bias free. Those working in other areas of disease are using state-of-the-art research methods to successfully make economic arguments for increased spending. Examples include cost-effectiveness analyses of different screening methods for colon cancer [51], of interventions that improve physical activity [52], and of screening for osteoporosis and treatment with hormone-replacement therapy [53].

Inexorable growth in health care costs is forcing decision makers to respond to scarcity and work toward extracting greater value from health care resources. The United States, Switzerland, France, Germany, Belgium, Portugal, Austria, and Canada all devote >10% of their gross domestic product to health spending [54]. The time when reliable economic arguments will be paramount for obtaining extra resources—and even retaining existing ones—is close. Those working toward reducing the number of HAIs should craft valid economic arguments on the basis of sound methods and use them to build strong and cost-effective infection control programs.

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Review

Variations in analytical methodology for estimating costs of hospital-acquired infections: a systematic review

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SUMMARY

Quantifying the additional costs of hospital-acquired infections (COHAI) is essential for developing cost-effective infection control measures. The methodological approaches to estimate these costs include case reviews, matched comparisons and regression analyses. The choice of cost estimation methodologies can affect the accuracy of the resulting estimates, however, with regression analyses generally able to avoid the bias pitfalls of the other methods. The objective of this study was to elucidate the distributions and trends in cost estimation methodologies in published studies that have produced COHAI estimates. We conducted systematic searches of peer-reviewed publications that produced cost estimates attributable to hospital-acquired infection in MEDLINE from 1980 to 2006. Shifts in methodologies at 10-year intervals were analysed using Fisher's exact test. The most frequent method of COHAI estimation methodology was multiple matched comparisons (59.6%), followed by regression models (25.8%), and case reviews (7.9%). There were significant increases in studies that used regression models and decreases in matched comparisons through the 1980s, 1990s and post-2000 ($P=0.033$). Whereas regression analyses have become more frequently used for COHAI estimations in recent years, matched comparisons are still used in more than half of COHAI estimation studies. Researchers need to be more discerning in the selection of methodologies for their analyses, and comparative analyses are needed to identify more accurate estimation methods. This review provides a resource for analysts to overview the distribution, trends, advantages and pitfalls of the various existing COHAI estimation methodologies.

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Introduction

In 2008, the Centers for Medicare & Medicaid Services adopted a 'no pay for errors' policy in the USA in which hospitals would no longer be reimbursed for preventable adverse events. As an indication of the recognition of their effects, these adverse events included several hospital-acquired infections (HAIs).¹ Accurate estimations of the additional costs associated with HAIs (COHAI) support the decision-making process for infection control measures by making possible the accurate assessments of these measures.

Most studies in the existing literature that produce COHAI estimates have used case reviews, matched comparison analyses or regression analyses as their estimation methodologies. In case reviews, researchers are able to accurately distinguish between resources used in the treatment of the primary diagnosis of patients, and the additional resources used for HAIs. Recent development of methods such as appropriateness evaluation protocols (AEP) have allowed for more rigorous evaluations.² The accuracy of the case review approach is dependent on the quality of information recorded in patient charts, and hampered by the associated labour intensiveness.

The main advantage of the matched comparisons method is its relative simplicity, which eschews the need for overly complicated statistical knowledge on the part of analysts. However, variations in patient attributes make it extremely difficult to find a corresponding uninfected patient for every infected case. Selection bias may consequently arise due to the exclusion of unmatched cases and controls.

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The regression analysis approach enables the inclusion of almost all infected and uninfected patients in analysis, and therefore provides a means to avoid selection bias. Though vulnerable to the influence of endogenous variables, methods such as instrumental variable models have been developed in order to minimise the effects.³

Other biases may arise from the failure to account for the influence of confounding factors such as disease severity or patient time at risk.^{3–5} The occurrence of an HAI generally extends the hospital length of stay (LOS) of a patient, and therefore contributes to increased healthcare costs.⁶ Longer LOS prior to infection may also represent a risk factor for infections, and this presents a potential endogeneity problem in COHAI estimates.^{3,7,8}

Graves *et al.* have recently highlighted the importance of accurate HAI cost estimations, and the need for more stringent measurement methodologies.⁹ Over the years, pioneering researchers have developed new strategies to minimise the aforementioned issues and produce more accurate COHAI estimates for downstream use.^{3,10} There has been an increase in the number of published studies that have conducted COHAI estimates, and it is entirely plausible that these estimates have been used in downstream research such as the assessments of infection control measures. However, the trends and distribution of methodologies that have been used in COHAI estimation studies remain unknown. Furthermore, researchers who intend to conduct COHAI estimates, as well as third parties who use the published estimates may benefit from a review of the trends, advantages and pitfalls of the various methodologies. Therefore, the first objective of this study was to conduct a systematic review of the analytic methodologies used in published studies that produced COHAI estimates, and observe the distribution of approaches employed to deal with the issues as described above. The second objective was to observe changes in trends, if any, of methodologies over time.

Methods

Data sources and search strategies

This systematic review was conducted according to the general principles of the Cochrane Collaboration framework.¹¹ We conducted a systematic review of studies published in the English language from 1980 to 2006 that had produced original COHAI estimates. Candidate studies were identified using a MEDLINE search using the following keywords: 'economics'[Subheading] OR 'Hospital Costs'[MeSH] AND ('Cross Infection'[MeSH] OR 'Surgical Wound Infection'[MeSH] OR 'Bacteremia'[MeSH] OR 'Bacterial Infections'[MeSH] OR 'Sepsis'[MeSH] OR 'Staphylococcal Infections'[MeSH] OR 'Pseudomonas Infections'[MeSH] OR 'Pneumonia'[MeSH] OR 'Urinary Tract Infections'[MeSH]).

Study selection

Studies that corresponded to the abovementioned search keywords were subjected to a two-step review process consisting of an abstract review and a full literature review. The abstract review was conducted in order to identify studies that had produced original cost estimates for the treatment of HAIs and excluded (1) studies that had utilised existing cost estimates obtained from other published studies, (2) studies that had included community-acquired infections in their sample, and (3) studies that had included infected patients in the reference comparison group. The subsequent full literature review stage included studies identified as having produced original COHAI estimates, and studies that could not be fully evaluated from the abstract review stage. In the full literature review stage we confirmed the suitability of the studies for inclusion

in analysis, and through the use of data collection forms we evaluated the analytic methodologies used for COHAI estimation.

Additionally, we conducted a hand-search of the references cited in the studies obtained in the MEDLINE search, and identified other publications that had also produced original COHAI estimates using the same two-step review method as outlined above.

All reviews were conducted independently by two evaluators (H.F. and J.L.), and non-congruent evaluations were discussed before decisions were made.¹¹

Analytic methodologies

There are three major analytic approaches used in COHAI estimation research: (1) case reviews, (2) matched comparisons, and (3) regression analysis.^{2,4,5} We evaluated the distribution of analytic methodologies categorised by infection type, and analysed the matching variables in matched comparisons and independent variables used in regression analysis. COHAI estimates were also reported for reference purposes.

Trends in methodology

Several treatises regarding novel methodologies have been published, and these studies may have influenced shifts in trends in COHAI estimation approaches: of particular importance are those developed by McGowan in 1981, Haley in 1991, and Howard *et al.* in 2001.^{3–5} Taking into account the year of publication of these studies, we analysed the methodology of COHAI estimates by categorising the papers according to whether they were published in the 1980s, 1990s or post 2000. Statistical analysis of the shifts in trends over the years was conducted using Fisher's exact test.

Results

Of the 3069 studies that matched our search terms on MEDLINE, we identified 79 studies that produced estimates on incremental COHAI using the abstract review and full literature review. The subsequent hand-search identified a further 110 non-duplicate candidate publications from the references in the original 79 studies, 10 of which were evaluated as suitable for our analysis. Therefore, the final analysis consisted of 89 studies.^{A1–A89}

Analytic methodologies

The characteristics of the studies used in our analysis are presented in Table 1. Of the 89 studies, 28 studies produced estimates on surgical site infections (SSI), 20 bloodstream infection (BSI) studies, 12 pneumonia/ventilator-associated pneumonia (VAP) studies, 10 urinary tract infection (UTI) studies, 5 respiratory tract infection (RTI) studies, and 40 studies with unspecified infections. There was an observed increase in studies producing COHAI estimates over the years, with 10 of the studies published in the 1980s, 21 in the 1990s, and 58 from 2000 to 2006. With regard to the distribution of analytical approaches used in producing COHAI estimates, the most frequent method used was multiple matched comparisons (53 studies, 59.6%), followed by regression models (23 studies, 25.8%), case reviews (7 studies, 7.9%), unmatched comparisons (3 studies, 3.4%) and unspecified methods (3 studies, 3.4%).

Forty of the studies that used matched comparisons employed a 1:1 matching method in which each case (infected) patient was matched to a single reference patient. An approximately equal number of studies assumed a normal distribution for regression models (10 studies), or used a logarithm transformation for the dependent variable of healthcare costs (9 studies). While there

Table I
Characteristics of published studies that had produced estimates of additional healthcare costs due to hospital-acquired infections ($N = 89$)

Study characteristics	No. (%) of studies
Type of infection	
Surgical	28 (31.5%)
Bloodstream	20 (22.5%)
Pneumonia/ventilator-associated pneumonia	12 (13.5%)
Urinary tract	10 (11.2%)
Respiratory tract	5 (5.6%)
General	40 (44.9%)
Country/region	
USA	41 (46.1%)
Europe	26 (29.2%)
Asia	13 (14.6%)
Other	9 (10.1%)
Year of publication	
1980–1984	7 (7.9%)
1985–1989	3 (3.4%)
1990–1994	9 (10.1%)
1995–1999	12 (13.5%)
2000–2004	35 (39.3%)
2005–2006	23 (25.8%)
Methods for estimating cost of hospital-acquired infection	
Case review	7
Standardised case review (AEP)	3 (3.4%)
Standardised case review	1 (1.1%)
Case review	3 (3.4%)
Unmatched comparison (1:x)	3 (3.4%)
Matched comparison	53
Multiple matched comparison (1:1)	40 (44.9%)
Multiple matched comparison (1:x)	8 (9.0%)
Multiple matched comparison (1:2)	4 (4.5%)
Multiple matched comparison (1:all)	1 (1.1%)
Regression analysis	23
Multiple linear regression (normal distribution)	10 (11.2%)
Multiple linear regression (logarithmic transformation)	9 (10.1%)
Multiple linear regression (gamma model)	1 (1.1%)
Generalised estimating equation	1 (1.1%)
Heckman's two-stage model	1 (1.1%)
Multiple regression (unknown)	1 (1.1%)
Unknown	3 (3.4%)

AEP, appropriateness evaluation protocol.

Europe includes UK (5), France (5), Belgium (4), Germany (3), Spain (3), Netherlands (2), Ireland (1), Italy (1), Scotland (1), and Switzerland (1). Asia includes Turkey (6), Taiwan (4), India (1), Thailand (1), and China (1). Others include Canada (2), Argentina (2), Mexico (1), Trinidad and Tobago (1), Australia (1), New Zealand (1), and multi-country study (1).

were no studies that addressed the endogeneity problem by employing an instrumental variables model, there was one publication that used Heckman's two-stage model in order to reduce bias. There was also one study that used matched comparisons as the primary approach with regression analysis as the secondary approach, and five studies that used regression analysis as the primary approach with matched comparisons as the secondary approach.

The details of the studies used in analysis, including year of publication, country of origin, types of healthcare institution, patient sample, analytic methodologies, COHAI estimates and matching variables or independent variables are presented in Table II.

We observed that 18 of the 53 publications that used matched comparison analyses, and 8 out of the 23 publications that used regression analyses, had included time at risk in the estimation of COHAI. In matched comparisons, the selection of control reference patients with an LOS of at least the same duration as infected cases was the most frequently used method of taking into account time at risk. However, none of the studies had used the methods proposed by Schulgen.⁷ In studies that employed regression analysis, time at risk was taken into account by the inclusion of LOS before surgery, ventilator duration, or intensive care unit duration in the independent variables.

Trends in methodology

Table III shows the changes in methodologies by publication year. Regression analyses had not been used for COHAI estimations in the 1980s. In the 1990s, there were three studies that had used regression analyses, and this number rose to 20 (34.5%) in studies published after 2000. While matched comparisons accounted for the majority of studies in our sample in the 1980s and the 1990s, this method was less popular in studies published post 2000. Also, the proportion of studies using case reviews has also decreased greatly in recent years. These changes in COHAI estimation methodologies were found to be statistically significant ($P = 0.033$).

There was a transition in the number of studies that accounted for LOS relating to both HAI rates and resource use for patients: in the 1980s, there were no studies that had included LOS as a variable, but this has increased in recent years. These studies have accounted for about one-third of all COHAI estimate publications since 2000, showing a marginally statistically significant change over the years ($P = 0.058$).

Discussion

Quantifying the additional costs associated with HAIs supports the decision-making process in infection control measures, and is therefore essential to healthcare policy development and hospital management. There are many potential biases that can affect the validity of these estimates, and methods have been developed to minimise their effect. In this study, we have conducted a systematic review of the methodologies used in studies that produced COHAI estimates published from 1980 to 2006. It was found that studies that had used measures to minimise biases and deal with confounding factors were in the minority, and there is a strong possibility that many of the published COHAI estimates are biased to varying extents. Furthermore, we observed a gradual shift from matched comparisons to regression analyses in recent years. This is a desirable trend as regression analyses are generally preferable to the matched comparisons method in order to obtain estimates with reduced bias. Within regression analyses, it has also been suggested that instrumental variable models can address the issues of endogenous variables.^{3,8}

Haley *et al.* analysed the differences in COHAI estimates produced by clinicians' assessments, unmatched comparisons and matched comparisons. It was found that the lowest estimate arose from the clinicians' assessments, followed by matched comparisons and unmatched comparisons.¹² In the case of clinicians' assessments, the distinction between healthcare costs for the primary diagnosis at admission and the additional treatment costs for HAIs are based on subjective opinions, and therefore vulnerable to the effects of bias.^{2,4,5} Another study has conducted a comparative analysis of the additional LOS due to surgical site infections (SSI) as calculated by two different methodological approaches. In the case of general SSIs, the standardised case reviews method produced shorter LOS extensions, but with no statistically significant difference.¹³ To the best of our knowledge there are no reports of comparisons between standardised case reviews and regression analyses. Furthermore, standardised case reviews have the disadvantage of requiring high labour intensiveness. The current evidence therefore provides little incentive to conduct standardised case reviews for the purpose of COHAI estimates.

By contrast, there have been several studies comparing matched comparisons and regression analyses, with results ranging from no significant difference between the two methods, higher estimates in regression analysis, and higher estimates in matched comparisons.^{14–17} Warren *et al.* found that a matched comparison using a propensity score produced COHAI estimates more than twice

Table II
Analytical methodology, estimates of additional costs of hospital-acquired infections, matching variables and regression analysis covariates used in the studies cited in the systematic review

First author	Year	Country	Type of setting	Type of patients	Analytical methodology	Additional cost to HAQ II stated [infected vs uninfected]	Matching variables or regression analysis covariates
Surgical site infection							
Herwaldt ¹	2006	USA	Mixed: 2 hospitals	Surgical	Linear regression (log)	<Non-fatal> + US\$1,574 [3,473 vs 1,694] (P < 0.001) <Fatal> + US\$2,005 [3,904 vs 1,891] (P < 0.001)	(1) Knausky score; (2) NNIS risk index* (3) No. of comorbid illnesses; (4) Obesity; (5) Preoperative length of stay (6) Type of surgery and the McCabe and Jackson classification Not specified
Vogel ²	2006	USA	University hospital	Surgical	Regression	-0.0594,331 [284,778 vs 170,447] (P < 0.001) -€3,816	NA
Gawald ³	2006	Spain	Teaching hospital	Mixed	Standardized case review (AEP); mean	+€4,018 [7,718 vs 3,700]	Not specified
Wilson ⁴	2006	UK	University hospital	Surgical	Unknown; mean	Mean: +1943,658 [7,544 vs 3,861] (P < 0.001)	
Kasapbal ⁵	2005	Thailand	University hospital	Surgical	Matched comparison (1:1); mean & median	Mean: +€3,040 [50,951 vs 24,568] (P < 0.001)	
Sheng ⁶	2005	Taiwan	University hospital	Admissions	Matched comparison (1:1); median	+T\$17,802 [357,013 vs 126,519] (P < 0.001)	(1) Surgical operation; (2) Diagnosis; (3) ASA
Coskun ⁷	2005	Turkey	University hospital	Surgical	Matched comparison (1:1); mean	<Deep sternal> + US\$6,851	(1) Age; (2) Sex; (3) Underlying medical illness; (4) Types of surgery; (5) Diagnosis at admission; (6) Admission date;
McGarry ⁸	2004	USA	Mixed: 2 hospitals	Surgical	Linear regression (log)	<Superficial sternal> + US\$3,741 +US\$41,117 (P < 0.001)	(7) Types of wards and disease severity (1) Operation year; (2) Sex; (3) Age
Hollenbeak ⁹	2003	USA	Mixed: 3 hospitals	Surgical (children)	Linear regression (normal)	+US\$132,907 (P < 0.05)	(1) Diabetes; (2) Renal disease; (3) ASA score; (4) Duration of surgery (5) Age at admission; (6) Klinefelter disorder; (7) Malnutrition; (8) History
Engemann ¹⁰	2003	USA	Mixed: 2 hospitals	Surgical	Matched comparison (1:2); median	<MESA> + US\$21,316 [52,791 vs 29,453] (P < 0.001) <MISA> + US\$62,908 [92,385 vs 29,453] (P < 0.001) +US\$12,477	(1) Base* (2) Ventilator support; (3) Age; (4) Packed red blood cells; (5) Cold ischaemia time; (6) HLA-A and -B mismatches; (7) Sex (1) Type of surgical procedure; (2) Calendar years of surgery
Apisarntharak ¹¹	2003	USA	Community hospital	Surgical	Matched comparison (1:2); mean		(1) Surgery; (2) Time period
Whitehouse ¹²	2002	USA	University hospital	Surgical	Matched comparison (1:1); median	+US\$27,969 [38,640 vs 10,671] (P < 0.001)	(1) Operative procedure; (2) NNIS risk index; (3) Age; (4) Date of surgery within the same year; (5) Surgeon [Matched comparison] (1) Age; (2) Sex; (3) Diabetes; (4) Renal insufficiency; (5) Length of surgical procedure
Hollenbeak ¹³	2002	USA	Community hospital	Surgical	1. Linear regression (normal) 2. Heckman's two-stage method 3. Matched comparison (1:1); mean 4. Unmatched comparison: mean	US\$20,163 (P < 0.001) <Heckman's two-stage> + US\$14,211 (P = 0.0553) <Matched> + US\$19,579 (P = 0.0001) <Unmatched> + US\$20,012 (P = 0.0001)	[Linear regression] (1) Intra-aortic balloon pump* (2) Diabetes [Heckman's two-stage] (1) Intra-aortic balloon pump* (2) Diabetes; (3) Hazard function (1. Obesity; 2. Renal insufficiency; 3. Connective tissue disease; 4. Antibiotic prophylaxis > 60 min; 5. OR duration > 240 min; 6. Re-exploration for bleeding; 7. Diabetes)
Jenny ¹⁴	2001	Australia	Tertiary hospital	Surgical	Matched comparison (1:1); mean	+A\$12,419 [20,888 vs 6,468]	(1) Sex; (2) Age; (3) NNIS risk index scores; (4) No. of comorbidities
Hollenbeak ¹⁵	2001	USA	Mixed: 3 hospitals	Surgical	Linear regression (normal)	+US\$13,276 (P < 0.001)	(1) Knausky score; (2) Packed red blood cells* (3) Cold ischaemia time; (4) HLA-A and -B mismatches; (5) Oedema* (6) Sex; (7) Race (1) Age; (2) Sex; (3) Diagnosis; (4) No. of comorbidities; (5) Admission specialty; (6) Admission type NA
Plowman ¹⁶	2001	UK	General hospital	Mixed	Linear regression (gamma)	+£1,694 (P < 0.05)	
Reilly ¹⁷	2001	UK	Not stated	Surgical	Unmatched comparison (1:2); mean	+£1,743	

Hallenbeck ^{A18}	2000	USA	Community hospital	Surgical	Linear regression (normal)	+US\$18,938 (P < 0.001)	(1) Intra-aortic balloon pump*, (2) Age*, (3) Emergic LOS, (4) COPD, (5) Renal insufficiency, (6) Shock, (7) Preoperative LOS, (8) Re-exploration for bleeding, (9) Clamp duration, (10) Surgery duration, (11) CHF, (12) Diabetes
Kirkland ^{A19}	1999	USA	Community hospital	Surgical	Matched comparison (1:1); median	-US\$3,089 [7,486 vs 3,842] (P < 0.05)	(1) Age, (2) Sex, (3) Type of operation, (4) Surgeon
Zitman ^{A20}	1998	Canada	University hospital	Surgical	Standardized case review (487); mean	Mean: -CA\$3,937 Median: -CA\$1,373	(1) Procedure code, (2) NNIS risk index, (3) Age, (4) Date of surgery, (5) Surgeon
VandenBerghe ^{A21}	1996	Netherlands	University hospital	Surgical	Unknown; median	< Postoperative ^a , + US\$8,320 [1,456 vs 5,240] (P < 0.001)	Not specified
Cuello ^{A22}	1993	UK	General hospital	Surgical	Matched comparison (1:1); mean	+£1,456	(1) Sex, (2) Age, (3) Surgical service, (4) Underlying condition or complication
Vegas ^{A23}	1993	Spain	Tertiary hospital	Surgical	Matched comparison (1:1); mean	+US\$4,449 (P < 0.01)	(1) Primary diagnosis, (2) Operative procedure, (3) No intervention if the infected patient was not operated on, (4) Age, (5) Sex, (6) Postoperative LOS, (7) Infection and emergency procedures, (8) Duration at risk (LOS)
Lynch ^{A24}	1992	Scotland	Teaching hospital	Surgical	Matched comparison (1:1); mean	+£1,072 [2,680 vs 1,607]	(1) Age, (2) Sex, (3) Type of operation, (4) Surgeon
Boyer ^{A25}	1990	USA	University hospital	Surgical	Matched comparison (1:1); mean	-US\$13,162 [25,957 vs 12,795] (P = 0.0002)	(1) DRG, (2) Age, (3) Sex, (4) Urgency of surgery, (5) Type of cardiac surgery, (6) No. of vessels bypassed, (7) Internal mammary artery graft, (8) Type of valve
Mugford ^{A26}	1989	Several countries	Mixed: several hospitals	Surgical	Unmatched comparison (1:2); mean	+£716 [1,435 vs 719]	NA
Fabry ^{A27}	1982	France	Teaching hospital	Surgical	Matched comparison (1:1); mean	+FF4,258	(1) Age, (2) Surgical procedure, (3) Level of medical risk (infection at entry, heavier surgery, and associated chronic conditions)
Scheckler ^{A28}	1980	USA	Teaching hospital	Admissions	Case review; mean	-US\$1,329	NA
Bloodstream infection							
Herwaldt ^{A1}	2006	USA	Mixed: 2 hospitals	Surgical	Linear regression (log)	<UTI & RTI & O&I> <Non-fatal> + US\$6,535 [8,435 vs 1,899] (P < 0.001) <Fatal> + US\$3,249 [5,148 vs 1,899] (P < 0.001)	(1) Karmali score*, (2) NNIS risk index*, (3) No. of comorbid illnesses*, (4) Obesity, (5) Preoperative LOS*, (6) Age*, (7) Interaction of type of surgery and the McCabe and Jackson classification*
Vogel ^{A2}	2006	USA	University hospital	Surgical	Regression	[5,148 vs 1,899] (P < 0.001) [24,244 vs 60,940] (P < 0.001)	Not specified
Warren ^{A29}	2006	USA	Suburban hospital	Patients with CVC – ICU	Linear regression (log) & matched comparison by propensity score; median	<CABS: Regression> + US\$11,971 [29,256 vs 17,285] (P < 0.05) <CABS: Matched comparison> US\$26,241 [54,242 vs 26,001] (P: unknown)	[Matched comparison]
Laupland ^{A30}	2006	Canada	Mixed: 3 hospitals	Intensive care	Matched comparison (1:1); median & mean	Median: -CA\$12,321 Mean: -CA\$16,887 [103,987 vs 87,120] (P: unknown)	(1) Duration at risk (LOS), (2) CHF, (3) Age, (4) APACHE II, (5) Mechanical ventilation (Regression analysis) (1) APACHE II*, (2) CHF, (3) Hemodialysis*, (4) Ventilator days*, (5) Age, (6) Sex, (7) Chronic obstructive pulmonary disease, (8) Cancer, (9) Diabetes, (10) Sepsis, (11) Surgical procedure, (12) Renal failure (1) Regional ICU location, (2) Surgical/medical diagnosis, (3) Chronic renal dialysis dependence, (4) Duration at risk (LOS), (5) Age, (6) Sex, (7) APACHE II, (8) Hospital LOS

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Table II (continued)

First author	Year	Country	Type of setting	Type of patients	Analytical methodology	Additional cost to HAIs if stated (infected vs uninfected)	Matching variables or regression analysis covariates
Bierl ³⁷	2005	Belgium	University hospital	Intensive care	Linear regression (normal) & matched comparison (1:2 or 1:1); median	<CABSI: Regression> + €16,814 (P < 0.001) <CVC: Matched comparison> + €13,365 (51,495 vs 37,826) (P < 0.001)	[Matched comparison] (1) APACHE II, (2) Diagnostic category, (3) Duration at risk (ICU LOS), (4) CVC
Sheng ⁴⁶	2005	Taiwan	University hospital	Admissions	Matched comparison (1:1); median	-€11,104, 536 (323,479 vs 193,365) (P < 0.001)	(1) LOS*, (2) Age, (3) APACHE II*, (4) Surgical or medical admission diagnosis, (5) Need for mechanical ventilation, (6) Need for renal replacement therapy*, (7) Need for vasopressors, (8) Need for inotropic treatments
Elward ^{43a}	2005	USA	Tertiary hospital	Admissions – PICU	Linear regression (log)	-US\$59,219 (45,615 vs 6,296) (P < 0.001)	(4) Type of admission, (5) Admission date, (7) Types of wounds and disease severity
Payne ^{43b}	2004	USA	Mixed: 17 hospitals	Inborn and outborn infants	Generalised estimating equations (log)	-US\$5,875 (248,987 vs 123,612) (P = 0.141) – +US\$12,480 [94,080 vs 81,580] (P = 0.008)	(1) PRISM III*, (2) Ventilator days*, (3) CHF*, (4) Transplant*, (5) Underlying lung disease*, (6) Age
Wisplinghoff ⁴⁴	2003	Germany	University hospital	Patients with a haematological malignancy	Matched comparison (1:1); mean	+US\$31,170	(1) Birth weight, (2) Birth location, (3) Sex, (4) Race, (5) Prenatal care, (6) Antenatal steroids, (7) Multiple birth, (8) Apgar score, (9) Respiratory distress syndrome, (10) CDD, (11) Necrotizing enterocolitis, (12) Major surgery, (13) Other surgery, (14) Mechanical ventilation
Rosenthal ⁴⁵	2003	Argentina	Mixed: 3 hospitals	Patients with CVC – ICU	Matched comparison (1:1); mean	<CVC-associated BSIs> + US\$4,888 (7,972 vs 3,083) – €16,556	(1) Date of admission, (2) Duration at risk (LOS), (3) Age, (4) Sex, (5) Type and stage of underlying malignancy, (6) Radiation therapy, (7) Duration and severity of neutropenia prior to BSI
Ons ^{46a}	2002	Italy	University hospital	Admissions	Matched comparison (1:1); mean	-€16,556	(1) Hospital, (2) ICU type, (3) Year of admission, (4) LOS, (5) Sex, (6) No. of discharge diagnoses
Liu ⁴⁷	2002	Taiwan	Tertiary hospital	Surgical	Matched comparison (1:2); median	-€16,556	(1) Duration at risk (LOS), (2) Primary diagnosis, (3) Ward of admission, (4) Age, (5) Sex, (6) No. of comorbidities, (7) Age, (8) Sex, (9) Diagnosis, (10) Admission type
Flowerman ⁴⁸	2001	UK	General hospital	Mixed	Linear regression (gamma)	+€6,209 (P < 0.05)	(1) APACHE II*, (2) Age*, (3) Sex, (4) Univariate factors of significance, (5) PRISM III, (3) Primary diagnosis, (4) Admission date
Dimick ^{49a}	2001	USA	Tertiary hospital	Surgical – ICU	Linear regression (log)	<CABSI> + US\$65,167 (10,000 vs 111,000) (P < 0.001) -US\$38,344 (99,177 vs -6,038) (P < 0.001)	(1) Age, (2) Underlying disease, (3) Age, (4) Duration at risk (LOS)
Shunji ^{49b}	2001	USA	Children's hospital	Admissions – PICU	Matched comparison (1:1); mean	-US\$38,344 (99,177 vs -6,038) (P < 0.001)	(1) Level of severity, (2) Underlying disease, (3) Age, (4) Duration at risk (LOS)
Relia ^{49c}	2000	Spain	Tertiary hospital	Admissions – ICU	Matched comparison (1:1); mean	+€3,124 (10,052 vs 6,914)	(1) Predicted mortality, (2) Sex, (3) Age, (4) Race, (5) LOS, (6) Admission during the study period, (7) Admitting diagnosis, (8) Chronic health conditions, (9) No. of secondary diagnosis, (3) Age, (4) Sex, (5) Hospital ward
Digiovine ^{49d}	1999	USA	University hospital	Medical – ICU	Matched comparison (1:1); median	-US\$15,965 (60,650 vs 36,899) (P < 0.001)	(1) Primary diagnosis for admission, (2) Date of admission, (6) No. of discharge diagnoses
Abramson ⁴²	1999	USA	University hospital	Admissions	Matched comparison (1:1); median	-US\$54 – US\$9,661 (P = 0.03)	(1) APACHE II*, (2) Age*, (3) Sex, (4) Admission date
Plitt ^{49e}	1994	USA	University hospital	Surgical intensive care	Matched comparison (1:1); mean	+US\$33,268 (91,241 vs 57,973) (P < 0.01)	(1) Age, (2) PRISM III, (3) Primary diagnosis, (4) Admission date
Pneumonia/VAP							
Vogel ⁵⁰	2006	USA	University hospital	Surgical	Regression	<VAP> + US\$69,187 (232,080 vs 142,893) (P < 0.001) <Pneumonia & KTI> + €358	Not specified
Cavallide ⁴⁰	2006	Spain	Teaching hospital	Mixed	Standardised case review (4AP); mean	<Pneumonia> – US\$28,161 (P < 0.05)	NA
Thompson ^{44a}	2006	USA	Mixed: 994 hospitals	Surgical	Linear regression (normal)	<VAP> + US\$57,198 (82,196 vs 25,097) (P < 0.05)	(1) Surgical procedure, (2) Age, (3) Sex, (4) Race
Cocour ^{45a}	2005	USA	Tertiary hospital	Ventilated patients – ICU	Matched comparison (1:1); mean	25,097 (P < 0.05)	(1) Age, (2) Injury severity score
Rosenthal ^{45b}	2005	Argentina	Mixed: 3 hospitals	Intensive care	Matched comparison (1:1); mean	<Pneumonia> + US\$2,253 (4,946 vs 2,594) (P < 0.001)	(1) Hospital, (2) ICU type, (3) Admission year, (4) LOS, (5) Sex, (6) Age, (7) ASIS at admission
Huguenet ⁴⁷	2004	Switzerland	University hospital	Ventilated patients – ICU	Matched comparison (1:1); mean	<VAP> + US\$10,860 [24,727 vs 17,496] (P < 0.05)	(1) No. of discharge diagnoses, (2) Duration at risk (ventilation), (3) Age, (4) Diagnosis at admission, (5) Sex, (6) Study period

Author	Year	Country	Study Design	Setting	Population	Intervention	Comparison	Outcome	Statistical Analysis	Notes
van Nieuwenhoven ^{A48}	2004	Netherlands	University hospital	Intensive care	Non-ventilated patients	None	None	Unknown: mean	<VAP> + US\$15,623 [29,260 vs 13,737]	None specified
Warren ^{A49}	2003	USA	Tertiary hospital	Ventilated patients – ICU	None	None	Linear regression (log)	Linear regression (log)	<VAP> + US\$11,897 [27,033 vs 15,136] (P < 0.05)	(1) CHF; (2) Corticosteroid use; (3) APACHE II; (4) Tracheostomy; (5) No. of CVC; (6) Bacteremia; (7) H2-histamine antagonist use
Dietrich ^{A50}	2002	Germany	University hospital	Admissions	None	None	Matched comparison (1:1): mean	Matched comparison (1:1): mean	<Pneumonia> + DM29,610	(1) Severity of disease; (2) Age; (3) Primary ward; (4) Status of ventilation; (5) Immunosuppression; (6) Sex; (7) Duration at risk (LOS)
Merciani ^{A51}	1998	India	Teaching hospital	Admissions	None	None	Unmatched comparison (1:x): mean	Unmatched comparison (1:x): mean	<Pneumonia> + US\$486	None
Kappstein ^{A52}	1992	Germany	University hospital	Ventilated patients – ICU	None	None	Matched comparison (1:x): mean	Matched comparison (1:x): mean	<VAP> + DM14,253 (US\$8,800)	(1) Underlying condition; (2) Age; (3) Duration at risk (ventilation); (4) Time that control patients were subjected to the risk of acquiring nosocomial infections
Scheckel ^{A53}	1980	USA	Teaching hospital	Admissions	None	None	Case review: mean	Case review: mean	<Pneumonia> + US\$878	NA
Urinary tract infection										
Herwaldt ^{A1}	2006	USA	Mixed: 2 hospitals	Surgical	None	None	Linear regression (log)	Linear regression (log)	<UTI & RTI & BSI> + US\$6,536 [8,435 vs 1,899] (P < 0.001)	(1) Karnofsky score; (2) NNIS risk index; (3) No. of comorbid illnesses; (4) Obesity; (5) Preoperative LOS; (6) Age
Gavaldà ^{A3}	2006	Spain	Teaching hospital	Mixed	None	None	Standardised case review (AEP): mean	Standardised case review (AEP): mean	[5,148 vs 1,899] (P < 0.001)	Jackson classification*
Sheng ^{A6}	2005	Taiwan	University hospital	Admissions	None	None	Matched comparison (1:1): median	Matched comparison (1:1): median	+US\$1,792	NA
Lai ^{A33}	2002	USA	University hospital	Admissions	None	None	Case review: mean & median	Case review: mean & median	+US\$14,682 [34,678 vs 1,99,953] (P < 0.001)	(1) Age; (2) Sex; (3) Underlying medical illness; (4) Types of surgery; (5) Diagnosis at admission; (6) Admission date; (7) Types of wards and disease severity
Tambayak ^{A44}	2002	USA	University hospital	Admissions	None	None	Case review: mean	Case review: mean	<CAUTI>: Mean: –US\$1,214	NA
Plozman ^{A16}	2001	UK	General hospital	Mixed	None	None	Linear regression (log)	Linear regression (log)	<CAUTI>: Median: +US\$614	(1) Age; (2) Sex; (3) Diagnosis; (4) No. of comorbidities; (5) Underlying condition or complication
Coello ^{A22}	1993	UK	General hospital	Surgical	None	None	Matched comparison (1:1): mean	Matched comparison (1:1): mean	+£467	(1) Sex; (2) Age; (3) Surgical service; (4) Underlying condition
Fabry ^{A27}	1982	France	Teaching hospital	Surgical	None	None	Matched comparison (1:x): mean	Matched comparison (1:x): mean	+FFZ,726	(1) Age; (2) Surgical procedure; (3) Level of medical risk (infection at entry, heavier surgery, and associated chronic conditions)
Givens ^{A55}	1980	USA	Teaching hospital	Surgical	None	None	Matched comparison (1:x): mean	Matched comparison (1:x): mean	<CAUTI> + US\$558	NA
Scheckel ^{A58}	1980	USA	Teaching hospital	Admissions	None	None	Case review: mean	Case review: mean	+US\$146	NA
Respiratory tract infection										
Herwaldt ^{A1}	2006	USA	Mixed: 2 hospitals	Surgical	None	None	Linear regression (log)	Linear regression (log)	<UTI & RTI & BSI> + US\$6,536 [8,435 vs 1,899] (P < 0.001)	(1) Karnofsky score; (2) NNIS risk index; (3) No. of comorbid illnesses; (4) Obesity; (5) Preoperative LOS; (6) Age; (7) Interaction of type of surgery and the McCabe and Jackson classification
Gavaldà ^{A3}	2006	Spain	Teaching hospital	Mixed	None	None	Standardised case review (AEP): mean	Standardised case review (AEP): mean	[5,148 vs 1,899] (P < 0.001)	NA
Sheng ^{A6}	2005	Taiwan	University hospital	Admissions	None	None	Matched comparison (1:1): median	Matched comparison (1:1): median	<Pneumonia & RTI> +£358	(1) Age; (2) Sex; (3) Underlying medical illness; (4) Types of surgery; (5) Diagnosis at admission; (6) Admission date; (7) Types of wards and disease severity
Plozman ^{A16}	2001	UK	General hospital	Mixed	None	None	Linear regression (gamma)	Linear regression (gamma)	+£117,100 [366,435 vs 180,059] (P < 0.001)	(1) Age; (2) Sex; (3) Diagnosis; (4) No. of comorbidities; (5) Admission date; (6) Age
Fabry ^{A27}	1982	France	Teaching hospital	Surgical	None	None	Matched comparison (1:x): mean	Matched comparison (1:x): mean	+FFZ,060	(1) Age; (2) Surgical procedure; (3) Level of medical risk (infection at entry, heavier surgery, and associated chronic conditions)

(continued on next page)

Table II (continued)

First author	Year	Country	Type of setting	Type of patients	Analytical methodology	Additional cost to HA, if stated [infected vs uninfected]	Matching variables or regression analysis covariates
General							
Gavaldà ⁶³	2006	Spain	Teaching hospital	Mixed	Standardised case review	+€2,730	NA
Earoglu ⁶⁶	2006	Turkey	Clinics	Not stated	Matched comparison (1:1); mean	-US\$2,027 [3,507 vs 1,524] (P < 0.001)	(1) Age, (2) Sex, (3) Clinic, (4) Primary diagnosis
Sanchez-Velazquez ⁶⁵⁷	2006	Mexico	National hospital	Intensive care	Matched comparison (1:2); median	+US\$12,155	(1) Duration at risk (LOS), (2) Age, (3) APACHE II
Lazarus ⁶⁵⁸	2005	USA	Teaching hospital	Trauma admissions	Linear regression (log)	2.04 times	(1) Age, (2) Sex, (3) Injury Severity Score*
Noskin ⁶⁵⁹	2005	USA	Mixed: 986–994 hospitals	Admissions	Linear regression (log) & matched comparison (1:1); mean	Regression: -US\$32,858 (P < 0.001) Matched comparison: +US\$36,119 (P < 0.001)	[Matched comparison] (1) Hospital, (2) Age, (3) Sex, (4) Race, and (5) Comorbidity [Regression analysis] (1) Hospital (2) DRG, (3) Age, (4) Sex, (5) Race, (6) Payer, (7) Comorbidities
Sheng ⁶⁶	2005	Taiwan	University hospital	Admissions	Matched comparison (1:1); median	-TS127,354 [363,425 vs 165,985] (P < 0.001)	(1) Age, (2) Sex, (3) Underlying medical illness, (4) Types of surgery, (5) Diagnosis at admission, (6) Admission date, (7) Types of wards and disease severity
Chen ⁶⁶⁰	2005	Taiwan	Tertiary hospital	Intensive care	Linear regression (log)	+US\$3,306 (P < 0.05)	(1) APACHE II, (5) Pulmonary artery catheter*, (8) Mechanical ventilator*, (9) Urinary catheter*
Upoon ⁶⁶¹	2005	NZ	Specialised hospital	Surgical	Matched comparison (1:1); mean	+NZ\$45,577 [76,104 vs 30,527] (P < 0.001)	(1) Sex, (2) Age, (3) Surgical procedure, (4) Month of procedure, (5) Diabetes mellitus
Sheng ⁶⁶²	2005	Taiwan	Mixed: 3 hospitals	Admissions	Matched comparison (1:1); mean	<Hospital 1> + US\$5,335 [13,476 vs 8,092] (P < 0.001) <Hospital 2> + US\$5,058 [8,014 vs 2,955] (P < 0.001)	(1) Age, (2) Sex, (3) Underlying medical illness and surgical operation, (4) Diagnosis at admission, (5) Admission date, (6) Ward, (7) Disease severity
Pison ⁶⁶³	2005	Belgium	General hospital	Admissions	Matched comparison (1:1); mean	+€12,852 [18,288 vs 5,440] (P < 0.001)	(1) DRG
Writers ⁶⁶⁴	2004	Ireland	Tertiary hospital	Surgical	Matched comparison (1:1); mean	+€1,395 [1,795 vs 2,840]	(1) Procedure
Pedricci ⁶⁶⁵	2003	France	University hospital	Child admissions	Matched comparison (1:1); mean	+€1,930 [3,097 vs 1,167]	(1) Primary diagnosis for admission, (2) Admission to the infant ward during the same period, (3) Age, (4) Sex, (5) Duration at risk (LOS), (6) No. of discharge diagnoses
Roberts ⁶⁶⁶	2003	USA	Teaching hospital	Admissions	Linear regression (normal)	+US\$15,275 (P < 0.001)	(1) APACHE III*, (2) ICU case*
Song ⁶⁶⁷	2003	USA	University hospital	Admissions	Matched comparison (1:1); median	+US\$81,208	(1) Age, (2) Year of admission, (3) Duration at risk (LOS), (4) Principal diagnosis at admission, (5) Primary procedure, (6) All patient refined – DRG [Matched comparison]
Zhan ⁶⁶⁸	2003	USA	Mixed: 994 hospitals	Not stated	Matched comparison (1:2); mean & linear regression (mixed-effect model)	<Postoperative sepsis> Mean: -US\$57,727 (P < 0.001) <Selected infection due to MRSA> Mean: -US\$18,656 (P < 0.001) +US\$502 [579 vs 77] (P = 0.001)	(1) Hospitals, (2) DRG, (3) Sex, (4) Race, (5) Age, (6) Comorbidity [Regression analysis] Not specified
Oncul ⁶⁶⁹	2002	Turkey	Teaching hospital	Burned admissions	Matched comparison (1:1); mean	+US\$452 [963 vs 511] (P < 0.001)	(1) Age, (2) Sex, (3) Primary illness
Oney ⁶⁷⁰	2002	Turkey	Surgery clinic	Child admissions	Matched comparison (1:1); mean	+€11,750 [24,722 vs 12,972] (P < 0.001)	(1) Gestational age, (2) Patent ductus arteriosus, (3) Surgery, (4) Ventilator support
Mahieu ⁶⁷¹	2001	Belgium	University hospital	Neonates in NICU	Matched comparison (1:1); mean	+€2,917 (P < 0.05)	(1) Age, (2) Sex, (3) Diagnosis, (4) No. comorbidities, (5) Admission specialty, (6) Admission type
Plowman ⁶⁷²	2001	UK	General hospital	Mixed	Linear regression (gamma)	+US\$442 [2,419 vs 1,977] (P = value: NS)	(1) Age, (2) Sex, (3) ICU location, (4) Principal diagnosis
Khan ⁶⁷²	2001	Turkey	Tertiary hospital	Admissions	Matched comparison (1:1); mean		(1) Age, (2) Sex, (3) Medical and surgical setting, (4) Total burn surface area

Author	Year	Country	Study Design	Setting	Comparison	Statistical Method	Results	Notes
Dominguez ^{a73}	2001	USA	Tertiary children's hospital	Admissions – PICU	Linear regression (normal) & matched comparison (1:1); mean	Regression: $-US\$50,362$ ($P < 0.001$) Matched comparison: $+US\$32,040$ [63,971 vs 32,291]	Matched comparison (1) Duration at risk (LOS), (2) Duration at risk (LOS), (3) PMSM Regression analysis (1) Age, (2) Severity of illness, (3) Organ system failure, (4) Diagnosis, (5) Chronic disease, (6) Ventilator use, (7) Vascular catheter use, (8) Referral source, (9) Sex, (10) Complication categories (1) RSV season, (2) Principal discharge diagnosis, (3) No. of secondary diagnoses, (4) Approximate age (1) Medical admission, (2) Medical admission, (3) Modified acute physiology score, (4) No. of organ system failures at ICU admission, (5) Duration at risk (ICU LOS)	
MacIntyre ^{a74}	2000	USA	Children's hospital	Child admissions	Matched comparison (1:1); mean	$-US\$45,335$	(1) Age, (2) Sex, (3) Operative procedures, (4) Services, (5) Discharge diagnoses	
Chalk ^{a75}	1999	France	University hospital	Medical – ICU	Matched comparison (1:1); median & mean	Mean: $-US\$9,275$ [30,225 vs 20,950] ($P = 0.004$) Median: $+US\$5,895$ [24,525 vs 17,105] ($P = 0.003$)	(1) Age, (2) Sex, (3) Medical and surgical setting, (4) Underlying disease, (5) Birth weight, (6) Gestational age, (3) Admission route, (4) Previous stay in an ICU, (5) CVC (1) Ward, (2) Date of admission, (3) Sex	
Orrett ^{a76}	1998	Trinidad and Tobago	Tertiary hospital	Admissions	Matched comparison (1:1); mean	$-US\$1,582$ [2,280 vs 698]	(1) Birth weight, (2) Score for Neonatal Acute Physiology, (3) Retrotransport	
Yalcin ^{a77}	1997	Turkey	University hospital	Not stated	Matched comparison (1:1); mean	$-US\$1,582$ [2,280 vs 698]	(1) Primary diagnosis, (2) Operative procedure, (4) Age, (5) No intervention if the infected patient was not operated on, (6) Presence of neoplastic or endocrine disease, (7) Elective and emergency procedures, (8) Duration at risk (LOS)	
Lercy ^{a78}	1997	France	Paediatric hospital	Neonates	Matched comparison (1:1); mean	Mean: $-US\$1,582$ [2,280 vs 698]	(1) Sex, (2) Underlying disease, (3) Surgical procedure, (4) Age, (5) Preoperative stay, (6) Duration at risk (LOS)	
Wilcox ^{a79}	1996	UK	Teaching hospital	Admissions	Matched comparison (1:1); mean	Mean: $-US\$1,582$ [2,280 vs 698]	(1) Complication, (2) Respiratory failure, (3) Left ventricular failure, (4) Death	
Gray ^{a80}	1995	USA	Mixed: *2 hospitals	Admissions – NICU	Linear regression (normal)	$+US\$25,090$	(1) Sex, (2) Underlying disease, (3) Surgical procedure, (4) Age, (5) Preoperative stay, (6) Duration at risk (LOS)	
Vegas ^{a81}	1993	Spain	Tertiary hospital	Surgical	Matched comparison (1:1); mean	$-US\$2,850$ ($P < 0.01$)	(1) Type of operation, (2) Age, (3) Sex, (4) Date of operation, (5) Non-invasive procedure (1) Hospital unit, (2) Birth weight, (3) Duration of pregnancy, (4) Diagnosis (1) Sex, (2) Age, (3) Operative procedure, (4) Diagnosis	
Shulkir ^{a81}	1993	USA	University hospital	Surgical	Linear regression (normal)	$+US\$12,542$ ($P < 0.01$)	NA	
L ^{a82}	1990	China	Specialised hospital	Surgical	Matched comparison (1:1); mean	$-US\$41,559$ ($P < 0.001$)	(1) Sex, (2) Underlying disease, (3) Surgical procedure, (4) Age, (5) Preoperative stay, (6) Duration at risk (LOS)	
Taylor ^{a83}	1990	USA	Teaching hospital	Surgical	Linear regression (normal)	$-US\$41,559$ ($P < 0.001$)	(1) Complication, (2) Respiratory failure, (3) Left ventricular failure, (4) Death	
Wakelield ^{a84}	1988	USA	University hospital	Admissions	Standardized case review (AEP); mean & median	Mean: $-US\$3,198$ Median: $-US\$1,058$	(1) Type of operation, (2) Age, (3) Sex, (4) Date of operation, (5) Non-invasive procedure (1) Hospital unit, (2) Birth weight, (3) Duration of pregnancy, (4) Diagnosis (1) Sex, (2) Age, (3) Operative procedure, (4) Diagnosis	
Nelson ^{a85}	1986	USA	Not stated	Surgical	Matched comparison (1:1); mean	$-US\$6,605$ [14,443 vs 7,838]	NA	
Girard ^{a86}	1983	France	University hospital	Neonates	Matched comparison (1:1); mean	$-US\$6,605$ [14,443 vs 7,838]	(1) Type of operation, (2) Age, (3) Sex, (4) Date of operation, (5) Non-invasive procedure (1) Hospital unit, (2) Birth weight, (3) Duration of pregnancy, (4) Diagnosis (1) Sex, (2) Age, (3) Operative procedure, (4) Diagnosis	
DeClercq ^{a87}	1983	Belgium	Not stated	Admissions – ICU	Matched comparison (1:1); mean	$-US\$6,605$ [14,443 vs 7,838]	NA	
Hailey ^{a88}	1981	USA	Mixed: 3 hospitals	Admissions	Standardized case review; mean	$-US\$6,605$ [14,443 vs 7,838]	NA	
Scherder ^{a88}	1980	USA	Teaching hospital	Admissions	Case review; mean	$-US\$6,605$ [14,443 vs 7,838]	NA	
Hailey ^{a88}	1980	USA	General hospital	Admissions	Matched comparison (1:1); mean	$-US\$6,605$ [14,443 vs 7,838]	(1) First discharge diagnosis, (2) Main procedure, (3) Second operative procedure, (4) Hospital service, (5) Sex, (6) Age	

US, United States; FF, French franc; DM, Deutsche Mark; BF, Belgian franc. PICU, paediatric ICU; RSV, respiratory syncytial virus. *Significant variables (if stated).

Table III
Changes in analytical methodologies for estimating additional healthcare cost of hospital-acquired infection (HAI) (N = 89)

	Year of publication			P-value
	1980–1989 (N = 10)	1990–1999 (N = 21)	2000–2006 (N = 58)	
Analytic approaches for estimating cost of HAI				0.033
Case review	3 (30%)	1 (4.8%)	3 (5.2%)	
Matched comparison	6 (60%)	15 (71.4%)	32 (55.2%)	
Regression analysis	0	3 (14.3%)	20 (34.5%)	
Unknown	0	1 (4.8%)	2 (3.4%)	
Unmatched comparison	1 (10%)	1 (4.8%)	1 (1.7%)	
Adjustment by length of stay				0.058
Adjusted by LOS	0 (0%)	6 (28.6%)	21 (36.2%)	
Not adjusted	10 (100%)	15 (71.4%)	37 (63.8%)	

LOS, length of stay.

Statistical analysis conducted using Fisher's exact test.

that of regression analysis.¹⁸ Due to this high degree of variation in the published literature, the degree of influence of methodological approach on estimates remains unclear.

In recent years, there has been an increase in analyses that use models that make it possible to adjust for endogenous variables and confounding factors in linear regression models.^{8,10,14} In a comparison of matched comparison analysis, linear regression analysis and Heckman's two-stage model, it was found that whereas the difference was not statistically significant, Heckman's two-stage model produced lower COHAI estimates than both of the other methods.¹⁴ The lack of statistical significance supported the conclusion that matching and linear regression analyses could be used as valid methodologies. Graves has stated with regard to instrumental variable models that 'the conventional wisdom has been that the endogeneity between length of stay and lower respiratory tract infection should bias the traditional estimates upwards, not downwards'.¹⁹

A major issue in the matched comparisons approach is the trade-off required in the quality of matching: if matching is conducted with the utmost stringency, the exclusion of unused cases and controls can lead to selection bias. However, reducing the stringency for matching criteria may increase the number of possible matched references, but also result in insufficient accounting for detailed patient characteristics such as disease severity. The use of stepwise fashion matching and a scoring system has been recommended to increase the quality of matching, but this technique was used by only seven studies in our analysis.²⁰ Furthermore, while patient factors such as age and sex are used in virtually all of the matching comparison analyses, patient disease severity factors were used in less than half of these studies.

In order to evaluate the possible effects of bias, the proportion of successful matches should be reported as part of the results in all studies, using a ratio of the final number of infected cases used in analysis to the number of all original infected cases. Of the 53 studies that used matched comparisons, only 28 (52.8%) had reported the proportion of successful matches. Given its simplicity, we advocate the reporting of this indicator in all matched comparison analyses. Furthermore, the use of propensity scores as summaries of covariate information has been recommended, and analysts should endeavor to use this method if employing the matched comparisons approach.^{18,21}

The shifts in analytic methodologies for COHAI estimates over the years have shown that analysts have started to lean towards regression analysis. More than half of the studies published post 2000 had used matched comparisons, and there was only a marginally significant difference between studies that had accounted for LOS and those that did not. LOS is a highly important factor to include in analysis, even in the matched comparisons method. In the 89 studies

in our sample, only 27 (30.3%) had included LOS as a factor in COHAI estimation. This highlights the fact that the inclusion of time at risk variables has yet to become sufficiently adopted among analysts.

Based on an analysis of the citation rates of the studies in our sample using the ISI Web of Science[®] database, we found that studies using the more stringent methodology of regression analysis were not cited with a significantly higher frequency than studies that had less stringent methodologies (data not shown). This indicates the possibility that COHAI estimates with biases have been used in downstream analyses, and may even have influenced decision-making by supporting inaccurate business cases.

The Society for Healthcare Epidemiology of America (SHEA) has produced guidelines that permit the extrapolation of estimates calculated from the published literature; we feel that this is a risky stance, as COHAI estimates have a high degree of uniqueness based on the particular conditions in which they were calculated.²² There is a large degree of variation in costing scopes, unit costs per item, clinical practice variations for HAI treatment, and costing methodologies (actual costs vs ratio of costs-to-charges (RCC) vs charges), and these factors have a direct and substantial influence on the resulting estimates (H. Fukuda, J. Lee, Y. Imanaka, unpublished data).

A limitation was that the dearth of detailed information concerning methodological approach might be due to space limitations set by the various journals. However, as these data are essential for editors, reviewers and readers to evaluate the quality of the methods used, the authors feel this information should be reported in all COHAI estimate studies.

Greater insight is needed on the characteristics and limitations of different COHAI estimation methodologies, as this would allow analysts to identify and select more accurate methods, as well as employ the correct tools for avoiding biases. More transparency in the reporting of methodologies and limitations would provide readers with the necessary information to evaluate the appropriateness of extrapolating published COHAI estimates in their own research. Accurate methodologies would produce COHAI estimates of better quality, and provide better support for the decision-making process in infection control.

Conflict of interest statement

None declared.

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Appendix. Studies used in systematic review

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Attributable Cost and Length of Stay for Patients With Central Venous Catheter–Associated Bloodstream Infection in Mexico City Intensive Care Units: A Prospective, Matched Analysis

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BACKGROUND. No information is available about the financial impact of central venous catheter (CVC)–associated bloodstream infection (BSI) in Mexico.

OBJECTIVE. To calculate the costs associated with BSI in intensive care units (ICUs) in Mexico City.

DESIGN. An 18-month (June 2002 through November 2003), prospective, nested case-control study of patients with and patients without BSI.

SETTING. Adult ICUs in 3 hospitals in Mexico City.

PATIENTS AND METHODS. A total of 55 patients with BSI (case patients) and 55 patients without BSI (control patients) were compared with respect to hospital, type of ICU, year of hospital admission, length of ICU stay, sex, age, and mean severity of illness score. Information about the length of ICU stay was obtained prospectively during daily rounds. The daily cost of ICU stay was provided by the finance department of each hospital. The cost of antibiotics prescribed for BSI was provided by the hospitals' pharmacy departments.

RESULTS. For case patients, the mean extra length of stay was 6.1 days, the mean extra cost of antibiotics was \$598, the mean extra hospital cost was \$11,591, and the attributable extra mortality was 20%.

CONCLUSIONS. In this study, the duration of ICU stay for patients with central venous catheter–associated BSI was significantly longer than that for control patients, resulting in increased healthcare costs and a higher attributable mortality. These conclusions support the need to implement preventive measures for hospitalized patients with central venous catheters in Mexico.

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Bloodstream infection (BSI) is a major cause of mortality among critically ill patients.^{1–10} The presence of a central venous catheter (CVC) is a major risk factor for the development of BSI.^{4,11–13} Several studies have demonstrated that CVC-associated BSIs are associated with an extended hospitalization duration and increased patient morbidity.^{5,14} One important means of reducing CVC-associated BSI in Latin America and elsewhere has been implementation of infection control programs that emphasize improved hand hygiene adherence,^{15,16} improved care of the catheter-insertion site,^{17–23} and use of antimicrobial agent–impregnated catheters.²⁴ We report the findings of a prospective, multicenter, nested, matched case-control study that assessed attributable extra length of stay (LOS), antibiotic use, costs, and mortality

among patients with CVC-associated BSI who were hospitalized in intensive care units (ICUs) in Mexico City.

METHODS

Setting

The study was conducted in 3 hospitals in Mexico City. Each center had an infection control team comprising an internal medicine physician with formal education in infectious diseases and an infection control nurse.²⁵

General Hospital (hospital A) is a public 1,100-bed hospital; Specialties Instituto Mexicano del Seguro Social (IMSS) Hospital (hospital B) and Gabriel Mancera IMSS Hospital (hospital C) are social-security hospitals of 600 beds and 400

From the General Hospital (F.H., G.F., J.R., P.D.), the Specialties Instituto Mexicano del Seguro Social Hospital (M.S.R.-F., J.C., N.T.), and the Gabriel Mancera IMSS Hospital (J.M.S.), Mexico City, Mexico; the Medical College of Buenos Aires, Buenos Aires, Argentina (V.D.R.); and the School of Public Health, Queensland University of Technology, Queensland, Australia (N.G.).

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TABLE 1. Baseline Characteristics of Intensive Care Unit (ICU) Patients in Mexico City With Central Venous Catheter-Associated Bloodstream Infection

Characteristic	Case patients (n = 55)	Control patients (n = 55)	P
Mean length of stay ≥ 5 d	55 (100)	55 (100)	>.99
Mean age, y	46.22	43.69	.43
Male sex	25 (45)	25 (45)	>.99
Admitted to medical or surgical ICU	55 (100)	55 (100)	>.99
Mean severity of illness score	3.98	3.49	.32
ICU type, hospital			
Medical-surgical, General Hospital	26	26	>.99
Neurosurgical, General Hospital	16	16	>.99
Medical-surgical, Specialties IMSS Hospital	10	10	>.99
Medical-surgical, Gabriel Mancera IMSS Hospital	3	3	>.99

NOTE. Data are no. (%) of patients, unless otherwise indicated. IMSS, Instituto Mexicano del Seguro Social.

beds, respectively. The ICUs of the hospitals treat patients who have had open heart surgery, neurosurgery, or orthopedic surgery performed and patients who have a complicated medical illness. The institutional review board at each center approved the study protocol.

Study Population and CVC Practices

We included all patients admitted to the study ICUs during the 18-month period from June 2002 through November 2003 who had had a CVC in place for at least 24 hours. Patients at hospital A were admitted from June 2002 through November 2003, patients at hospital B were admitted from November 2002 through November 2003, and patients at hospital C were admitted from April through November 2003. Nontunneled, non-antimicrobial-impregnated CVCs were inserted from the bedside by treating physicians after the skin was prepared with povidone-iodine.

At the beginning of the surveillance period, measures to improve healthcare worker compliance with hand washing, care of CVC sites, and care of intravenous administration sites were implemented. Measures comprised education, training, outcome surveillance, process surveillance, and performance feedback.²⁶

Nosocomial Infection Surveillance and Data Collection

All patients admitted to the hospital with a CVC-associated BSI detected by prospective nosocomial surveillance were enrolled and included as case patients. An infection control nurse at each study center collected data prospectively from patient medical records. The study coordinator (V.D.R.) trained the data collectors at each center before commencement of the study. For each study patient, age and sex, hospital, ICU type, mean severity of illness score, and LOS were recorded. In addition, antibiotic consumption was recorded. We followed the recommendations of a 1969 World Health

Organization European symposium on the consumption of drugs. We also used the Anatomical Therapeutic Chemical Classification system, which is a common classification system for drug use, and the defined daily dose (DDD) was used as the comparative unit of drug consumption.²⁷ Active surveillance for CVC-associated BSI was performed at each study center, starting in June 2002 and finishing in November 2003.

Definitions

Centers for Disease Control and Prevention definitions were used to define CVC-associated BSI as laboratory-confirmed BSI or clinical primary nosocomial sepsis.²⁸

Laboratory-confirmed BSI. To meet the criteria for laboratory-confirmed BSI, the first criterion was recovery of a recognized pathogen unrelated to infection at another body site from one or more cultures of percutaneous blood. Common skin commensals (eg, diphtheroids, *Bacillus* species, *Propionibacterium* species, coagulase-negative staphylococci, and micrococci) must have been recovered from 2 or more cultures of blood specimens drawn on separate occasions. The second criterion was the presence of at least 1 of the following signs or symptoms unrelated to infection at another body site: fever (temperature of greater than 38°C [greater than 100.4°F]), chills, and/or hypotension.

Clinical primary nosocomial sepsis. To meet the criteria for clinical primary nosocomial sepsis, the presence of at least 1 of the following clinical signs unrelated to another recognizable cause of infection was required: fever (temperature, $>38^{\circ}\text{C}$ [$>100.4^{\circ}\text{F}$]), hypotension (systolic blood pressure, <90 mm Hg), and/or oliguria (urine output, <20 mL/h). However, for these patients, blood cultures were either not performed or did not yield pathogens, and no infection was apparent at another body site. The physician recommended treatment for sepsis.

TABLE 2. Studies in Which Central Venous Catheter–Associated Bloodstream Infection Was Associated With Extra Costs

Study	Country	Extra cost, US\$
Liu et al. ³⁵	Taiwan	66,302
Orsi et al. ¹⁴	Italy	21,612
Pittet et al. ⁵	United States	29,000
Elward et al. ³⁶	United States	39,219
Payne et al. ³⁷	United States	5,875
Rosenthal et al. ¹⁰	Argentina	4,888

Culture Techniques

The patients' attending physicians independently decided whether to perform cultures of catheters and blood cultures. We used the semiquantitative culture method for identifying organisms from catheter culture,²⁹ and results were compared with organisms isolated from blood culture, when available. Specimens not immediately cultured were refrigerated at 4°C. All cultures were inoculated with specimens within 8 hours of catheter removal. Standard laboratory methods were used to identify microorganisms in blood and catheter cultures.²⁹⁻³¹

Selection and Matching of Case and Control Patients

To conduct the study, we analyzed patients with CVC-associated BSI (case patients) and patients without CVC-associated BSI (control patients) who were hospitalized for at least 5 days in the facility to which they were admitted. ICU type, year of admission to the ICU, LOS, sex, age, and mean severity of illness score were recorded.³² Each case patient was matched to one control patient.³³

Cost Estimation

The duration of ICU stay was obtained prospectively for each patient, and the number of ICU bed-days were used as a proxy for fixed costs of ICU stay. Current expenditures on fixed costs were used to convert the number of ICU bed-days into US dollars. DDDs³⁴ and their associated market prices were provided by the hospitals' pharmacy departments. The consumption of all other resources that reflect variable costs (ie, cash expenditures) were obtained from each study center's finance department, and the relevant market price was assumed to reflect opportunity costs. The extra cost attributable to BSI was defined as the median difference in variable costs (ie, cash expenditures) and LOS between case patients and their matched control patients. A monetary valuation of the opportunity costs of the ICU bed-days lost to BSI was also made.

Outcomes

The primary outcome effects evaluated in this study included additional days of hospitalization, extra costs, and attributable mortality of CVC-associated BSI.

Statistical Analysis

Epi Info statistical software, version 6.04b (Centers for Disease Control and Prevention), was used to perform the data analysis. The χ^2 analysis (for dichotomous variables) and the Student *t* test (for continuous variables) were used to analyze baseline differences between treatment groups. When appropriate, the Fisher exact test was used. Relative risk ratios, 95% confidence intervals, and *P* values were assessed for all primary and secondary outcomes.

RESULTS

During the study period (June 2002 through November 2003), 1,615 adult patients were admitted to the study ICUs; 172 (10.6%) of these patients developed a CVC-associated BSI (22 [40%] had laboratory-confirmed BSI, and 33 [60%] had clinical sepsis). Fifty-five (31.9%) of the 172 patients had a LOS of 5 days or more and were included in the study. Fifty-five control patients were matched with case patients on the basis of a LOS longer than 5 days, hospital, ICU type, sex, age, and mean severity of illness score. Baseline characteristics were not different between case and control patients (Table 1).

The cumulative number of ICU bed-days was 739 for case patients and 406 for control patients. The mean number of ICU-days was 13.4 for case patients and 7.34 days for control patients. The cumulative number of extra ICU bed-days for case patients was 333, with a mean excess LOS of 6.05 days per case patient (Table 2). Each ICU bed-day lost to BSI was assumed to be worth \$1,200, on the basis of data provided by the finance department of each hospital. This finding implies that the value of the 333 lost bed-days in terms of alternative use was \$579,133, or \$7,260 per BSI case (Table 2). The additional costs of antibiotics were \$32,912, or \$598 per case patient; the additional value of the remaining variable costs was \$146,622, or \$2,666 per BSI case. The total costs were \$1,593,149 for case patients and \$955,648 for control patients, for a difference of \$637,501, or \$11,591 per BSI case (Table 2). Case patients were much more likely to have received antimicrobial therapy, with a mean of 10.3 extra antibiotic DDDs (Table 2). Twenty-three case patients (41.8%) and 12 control patients (21.8%) died, for an attributable mortality due to CVC-associated BSI of 20.0% (relative risk, 1.92 [95% confidence interval, 0.95-3.85]; *P* = .06).

DISCUSSION

The presence of a CVC is a major risk factor for BSI.^{4,11-33} Critically ill patients often require extended use of CVCs and have a high risk of developing a BSI.^{38,39} Increases of 4%-37% in attributable mortality have been reported in several studies of CVC-associated BSI,^{3,5,8,40,41} although this association has not been a consistent finding.^{42,43}

In our study, we found that CVC-associated BSI was related

to a median excess costs of \$11,591 and an extra LOS of 6.1 days per episode. In contrast, almost all studies that evaluated the impact of CVC-associated BSI on patient outcomes have found significantly increased healthcare costs and excess LOS for patients who developed this type of nosocomial infection (Table 2). The excess healthcare costs reported from developed countries are significantly higher than costs found in our study^{2,7,14} and higher than costs reported from Argentina, where the extra costs were reported to be \$4,888.¹⁰

Our study may underestimate the true costs of CVC-associated BSI in other countries where expensive medical technologies not yet available in Mexico are routinely used. For example, the mean cost per day of hospitalization in most US centers is more than 5 times that in Mexico. Also, the real attributable mortality might be higher in Mexico, because patients whose care was prohibitively expensive might have died early during their hospital stay. Notwithstanding these possibilities, our data demonstrated that CVC-associated BSIs significantly increased the cost of treatment for these patients.

Studies of nosocomial infection have revealed that the use of antibiotics is increasing. Our study, for example, revealed a mean of 10 additional antibiotic DDDs for patients with CVC-associated BSI, which accounted for \$589 of the mean excess healthcare costs per episode. The excess use of antibiotics has important consequences for patients in the ICU setting, for whom the risk of acquiring drug-resistant nosocomial pathogens may be higher than that for patients hospitalized in other settings.⁴⁴ Thus, prevention of CVC-associated BSI may reduce healthcare costs through reducing LOS, antibiotic use, and the antibiotic pressure that is driving the selection of resistant microorganisms in hospitals.⁴⁵

Finally, our discoveries are concordant with those of other studies that have found an increased mortality among patients with CVC-associated BSI.^{3,5,9,40,41} It is possible that the 20% attributable mortality found in this and other studies is an artificial product of the measurement techniques used (ie, mean severity of illness score or other severity of illness scores calculated at ICU admission rather than at the moment of onset of CVC-associated BSI).⁴³ In our study, we were unable to find statistically significant differences in mortality between case and control patients. The main reason for this was probably our small sample size (55 case patients and 55 control patients).

This study has a number of limitations. In Mexico, laboratory resources are expensive and scarce, and frequently the only BSI criterion we can use is the presence of clinical sepsis. The number of matching variables used might not account for all of the variation in LOS and cost outcomes. A weakness of case-control studies is that it is only possible to match subjects on the basis of a relatively small number of variables before selection bias arises. The inability to measure severity of illness scores on a daily basis in our study hospitals was another limitation of our study. Future studies must use more-rigorous analytic methods, such as time series analysis,⁴⁶ to assess the true impact of CVC-associated BSI on mortality.

However, the preponderance of current evidence suggests that CVC-associated BSI is associated with excess patient mortality, and our data are consistent with this body of evidence.

Multifaceted programs developed for preventing CVC-associated BSI have proved to be useful. Examples of these measures are rigorous hand washing compliance, improved care of vascular catheter-insertion sites, judicious use of antimicrobial therapy, and use of antimicrobial-impregnated catheters. Our data suggest that successful implementation of such programs would not only significantly reduce patient mortality but also result in considerable cost savings and reduced LOS.

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Raising Standards While Watching the Bottom Line: Making a Business Case for Infection Control

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While society would benefit from a reduced incidence of nosocomial infections, there is currently no direct reimbursement to hospitals for the purpose of infection control, which forces healthcare institutions to make economic decisions about funding infection control activities. Demonstrating value to administrators is an increasingly important function of the hospital epidemiologist because healthcare executives are faced with many demands and shrinking budgets. Aware of the difficulties that face local infection control programs, the Society for Healthcare Epidemiology of America (SHEA) Board of Directors appointed a task force to draft this evidence-based guideline to assist hospital epidemiologists in justifying and expanding their programs. In Part 1, we describe the basic steps needed to complete a business-case analysis for an individual institution. A case study based on a representative infection control intervention is provided. In Part 2, we review important basic economic concepts and describe approaches that can be used to assess the financial impact of infection prevention, surveillance, and control interventions, as well as the attributable costs of specific healthcare-associated infections. Both parts of the guideline aim to provide the hospital epidemiologist, infection control professional, administrator, and researcher with the tools necessary to complete a thorough business-case analysis and to undertake an outcome study of a nosocomial infection or an infection control intervention.

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Despite the fact that nosocomial infections pose a significant risk to patient safety, resources targeted to prevent these infections are limited. Although society would benefit from a reduced incidence of nosocomial infections, there is currently no direct reimbursement to hospitals for the purpose of infection control, which forces healthcare institutions to make economic decisions about funding infection control activities. Unfortunately, one current perception is that investments to improve quality might actually financially penalize the hospitals that make these improvements.¹ Because infection control programs are often seen as cost centers and not as revenue generators, they are often identified as potential areas for budget cuts.² In fact, many infection control programs have faced downsizing in recent years.^{3,4} Demonstrating value to administrators is increasingly important as healthcare executives are faced with the need to support many initiatives with limited resources.⁵ A recent survey of Society for Healthcare Epidemiology of America (SHEA) members showed that hospital epidemiologists already provide expertise in a wide variety of areas beyond traditional infection control (eg, an-

timicrobial stewardship, patient safety, employee health, and emergency preparedness), but compensation for these services occurs in less than 25% of cases.⁶ Increasingly, directors, managers, and infection control professionals (ICPs) must develop a business case to initiate a new intervention, justify continuing a program during budget negotiations, or fend off downsizing.

Because US national health expenditures were estimated to be \$2.08 trillion in 2006, or 16% of the gross domestic product,⁷ there is no inherent reason that infection control interventions must save society money. Ideally, society should be willing to spend money to prevent either a myocardial infarction or a surgical site infection. To make a policy case for additional investment in infection control interventions or changes in reimbursement practices, many more quality cost-effectiveness analyses must be completed and published.⁸ Thus, a business case for infection control requires both the use of existing literature to make optimal decisions at an individual institutional level and support for the completion

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of additional cost-effectiveness analyses to guide future societal decisions and improve public health.

In part 1 of this article, we describe the basic steps needed to complete a business-case analysis for an individual institution. A case study using a representative infection control intervention is provided. In part 2, we detail important basic economic concepts, including types of economic analyses and their strengths, as well as the different perspectives of various analyses (eg, hospital vs societal). We also describe approaches used to assess the financial impact of infection prevention, surveillance, and control interventions, and approaches used to measure the attributable costs of specific healthcare-associated infections. All of these additional considerations provide the hospital epidemiologist, ICP, or administrator with the tools necessary for a thorough and accurate business-case analysis. This article outlines important considerations regarding the economic measurement of healthcare-associated infection and related interventions, although more detailed texts about the design and analysis of healthcare economic research are available.⁹⁻¹¹ Infection control has been at the forefront of improving patient safety. The aim of this article is to assist infection control specialists and hospital epidemiologists in their understanding and use of economic analyses to help justify the need for and benefits of effective infection control interventions and programs.

PART 1: BUSINESS-CASE ANALYSIS

A business-case analysis is a type of cost analysis performed from a business's perspective, in this instance, that of the hospital. Broadly defined for use in an intervention to improve health care, a business case "exists if the entity that invests in the intervention realizes a financial return on its investment in a reasonable time frame."^{12(p18)} The reasonable return can occur through profit, reduction in losses, or cost avoidance. In this case, the purpose is to look purely at the dollar costs and benefits of an infection control intervention or an entire infection control program to justify its existence to hospital administrators. In the business case, patient outcomes such as infection-associated morbidity and mortality are not considered unless they impact the hospital economically, either positively or negatively.

The difficulty in making a business case cannot be overlooked, because many infection control programs often lack the economic expertise necessary to complete such an analysis on their own. Anyone considering a business-case analysis should contact their local institution's finance administrators for assistance in using the available local cost data. Importantly, most (90%) of published studies of studies that claim to be cost-effectiveness analyses of infection control interventions actually adopt the hospital perspective and are more correctly called business-case analyses, with only 3% of the studies adopting a societal perspective.^{13,14}

Often, an infection control intervention program has existed for several years and has kept infection rates low. If

hospital-acquired infections are now rare and no longer perceived as a problem, administrators might want to cut a program focused on controlling the infections, not realizing that the program is highly effective and even cost saving. The same difficulty arises when trying to initiate a new intervention program, because it is easy to quantify the extra costs of a new program but often difficult to estimate the incremental benefits, particularly when there are very few clinical trials available to convince administrators and likely even fewer resources available to complete studies at an individual institution.

One partial, although usually suboptimal, solution to facilitate saving an existing program is to examine areas where the intervention is not in place and compare infection rates there with rates in areas where the intervention is used. An example would be comparing central venous catheter-associated bacteremia rates in a medical intensive care unit (ICU) where a prevention program exists to rates in a surgical ICU that does not have a prevention program. Alternatively, if cost reductions force the elimination of a specific program, it would be helpful to stagger the elimination, so that as infection rates rise in certain units where an intervention is eliminated, this evidence could be used to support reinstatement of the program.

When an identified problem, new mandate, or new technology leads to the desire to introduce a new infection control intervention, it is important to remember that this is the time to collect outcome, cost, and implementation data. Careful review of these data will help justify the intervention in the future if it faces elimination when the institutional will supporting it dissipates. To that end, it is often helpful from an analysis perspective, and more importantly, from an implementation perspective, to roll out a new intervention in a stepwise or randomized fashion.¹⁵ This allows comparison of the intervention's effects with results in control populations (eg, wards or ICUs where the intervention has not yet been implemented) by use of a higher-level quasi-experimental design.¹⁶ Importantly, when completing a business-case analysis, it is important to make an honest assessment of the situation. Most hospital epidemiologists or infection control specialists want to increase the resources available for infection control activities, but it is important to avoid overestimating benefits or underestimating staff and time costs. Overestimation in an initial analysis may improve the situation in the short term, but it will hinder efforts and necessary trust in the long term after actual resource audits are performed.

Business-case analyses conducted from a hospital perspective are important to local decisions; however, these types of analyses are not useful at the level of public health decision making because they typically do not include the health impact of infection-associated morbidity and mortality. It has become increasingly important to justify the importance of funding infection control activities at a broader level through the completion of cost-effectiveness analyses conducted from the societal perspective.

TABLE 1. Representative Reports of Attributable Costs and Excess Length of Stay (LOS) Associated With Various Hospital-Acquired Infections

Infection type	Attributable costs, mean (range), 2005 US\$	Excess LOS, mean (range), days	Reports
VAP	22,875 (9,986-54,503)	9.6 (7.4-11.5)	[19-23]
Catheter-related BSI	18,432 (3,592-34,410)	12 (4.5-19.6)	[24-26]
CABG-associated SSI	17,944 (7,874-26,668)	25.7 (20-35)	[27-30]
Catheter-associated UTI	1,257 (804-1,710)	...	[31, 32]

NOTE. BSI, bloodstream infection; CABG, coronary artery bypass graft surgery; SSI, surgical site infection; UTI, urinary tract infection; VAP, ventilator-associated pneumonia.

In the following paragraphs, we describe an example of a business-case analysis for expansion of an infection control program. The process of completing a business-case analysis can be broken down into several steps.

Step 1: Frame the Problem and Develop a Hypothesis About Potential Solutions

For example, you may wish to implement an intervention to reduce the incidence of surgical site infection (SSI) following coronary artery bypass graft (CABG) surgery in your hospital. To implement an intervention to reduce these infections, it might be necessary to hire additional staff for your infection control department. Thus, you are faced with the task of convincing your hospital administration that the cost of an additional full-time employee (FTE) will be offset by the cost savings created by a reduced rate of infections, including SSIs.

Step 2: Meet With Key Administrators

Prior to the start of the analysis, schedule a meeting with the key administrators (eg, vice president of quality improvement, chief medical officer, and/or chief operating officer) who oversee hospital epidemiology and other groups who will be involved in the program or intervention. The purpose of this meeting is threefold. First, it is important to obtain agreement that the issue that you are addressing is of institutional concern and has the support of hospital leadership. Second, the administrators can help to identify critical individuals and departments who may be affected by your proposal and whose needs should be included in the business-case analysis. Third, the administrators can help identify the critical costs and factors that should be included in the analysis, including administrative data.

Even for interventions that estimates suggest would be cost saving, initiation is often difficult in hospitals. One of the reasons it is difficult to initiate interventions is that it is not always clear who should pay for an intervention, because the cost center that benefits (eg, patient care or surgical care) is not always where the cost of the intervention arises (eg, infection control or microbiologic analysis). In this example, should the cardiothoracic surgery service contribute to hiring a new ICP because it will see the benefits of the added staff through lower reported infection rates and lower costs? The cost-shifting issues can become even more problematic when

interventions are effective but not cost saving. It is often the case that strong institutional support and understanding of cost-sharing is needed to initiate effective interventions, even when they are cost saving.

Step 3: Determine the Annual Cost

In the current example, the cost is the salary of an FTE plus the price of benefits for that individual. This information is available from many sources, including your own institutional budgets or surveys available online.¹⁷ As an example, a full-time ICP might earn \$60,000, and benefits may cost the institution 28% of that total, which brings the hospital's cost for the FTE to \$76,800. Other interventions may involve more wide-ranging costs. For example, an intervention that uses surveillance cultures will include the costs associated with nurses on the floor obtaining the culture samples and the costs associated with culture processing by the microbiology laboratory; similarly, an intervention that requires increased gown use will include additional costs for waste disposal.

Step 4: Determine What Costs Can Be Avoided Through Reduced Infection Rates

Optimally, the up-front cost of hiring a new ICP can be recouped over a reasonable period, usually the current fiscal year. Ideally, you might have data from your own institution that can be analyzed to determine whether CABG-associated SSIs decreased after hiring an ICP. Alternatively, the medical literature may be reviewed to see whether others have published data regarding a similar issue (Table 1). For example, if 500 CABG operations are completed at your institution annually and the current SSI rate is 5%, then 25 CABG-related SSI occur per year. Your experience or a literature review might suggest that hiring an ICP would be expected to reduce SSI by over 35% through targeted interventions, including improved prospective surveillance, increased reporting of rates to surgeons, and improved timing of perioperative antibiotics.¹⁸ Thus, if 25 CABG-related SSIs occur annually in your hospital, an effective ICP could prevent 9 of these SSIs.

Step 5: Determine the Costs Associated With the Infection of Interest at Your Hospital

If hospital administrative data are readily available, the attributable cost of an SSI could be calculated as described

below. Alternatively, if they are not available, a literature review might be performed, which, in this case, reveals that the mean CABG-associated SSI costs approximately \$18,000 (Table 1).

At this point, it might be tempting to multiply the number of SSIs expected to be prevented by the estimated cost per SSI and state that hiring an ICP will save \$162,000 (ie, $9 \times \$18,000$) in CABG-related SSI costs alone. If calculated in this way (\$162,000 in savings minus \$76,800 for the new ICP), the resulting figure suggests that the hospital will save \$85,200 overall. However, from the hospital's financial perspective, a certain percentage of these costs are currently reimbursed by third-party payers. Therefore, the emphasis in a business-case analysis should be on the *attributable costs* (and attributable complications) of excess complications, infectious or otherwise. An attributable cost or complication is one that would not have occurred during a hospital stay that is *identical* to the one being analyzed except for the absence of the complication or infection of interest. For example, a recent study found that profits on surgical cases fell from \$3,288 when there were no complications to \$755 when complications, such as infections, occurred.³³ Assuming that the individuals in whom complications occurred were *identical* to those without complications, except for the presence of the complication, one would say that the approximately \$2,500 in hospital revenues that were not received during the treatment of individuals with complicated stays constituted the attributable cost of this particular complication. As a result of preventing 9 SSIs, then, the hospital revenues would be \$22,797 (ie, $9 \times \$2,533$) higher. In our example, if only 50% of costs are reimbursed, the cost savings from preventing 9 SSIs would be estimated at \$81,000 instead of \$162,000. After subtracting the cost of the ICP (ie, \$76,800), the overall savings would be \$4,200 annually.

An additional problem with the use of hospital administrative data or literature estimates of infection costs in an analysis is that most hospital costs are fixed costs.³⁴ Fixed costs include buildings, equipment, and salaried labor, which are difficult to eliminate in the short term. It has been estimated that as much as 84% of hospital costs are fixed.³⁵ Thus, if only 16% of the costs attributable to infections are variable costs (eg, medication, supplies, or tests), our estimate of costs might be \$25,920 instead of \$162,000. In this case, after adding the cost of the ICP, the annual cost of the new employee is estimated to be \$50,880.

An alternative method for calculating the attributable cost of a nosocomial infection is to multiply the mean increase in length of stay by the mean daily cost for a hospital stay. This cost can be determined specifically for your own institution or taken from the literature. Literature estimates are available at the Centers for Medicare and Medicaid Services.³⁶ From the information provided by the references in Table 1, we estimate that the mean attributable length of stay for a CABG-associated SSI is approximately 26 days. Preventing 9 SSIs reduces the overall length of stay by a total of 234 days,

at a mean cost of approximately \$1,200 per day, for a cost savings of \$281,000. Perhaps one-half of this is reimbursed, so the total savings would be estimated to be \$63,700 after the cost of the ICP is considered.

A newer method suggested by Ward and colleagues³⁴ focuses on optimizing the investment in fixed costs instead of focusing on cost savings when justifying a new program. In infection prevention, the greatest opportunity to improve hospital profits comes from reducing excess length of stay. Thus, instead of focusing on how much an additional hospital-day costs, as above, one could estimate the additional revenue gained by filling the additional bed-days available, because patients who do not develop infections are discharged sooner. In the example, the question becomes how many new patients could be admitted to the hospital without additional investment in new buildings and equipment, given that we estimate SSI prevention will reduce overall length of stay by 234 days? If the mean length of stay in the hospital is 4 days, then 59 new patients could be admitted, and the associated profits from these admissions could offset the investment in the new ICP.

Step 6: Calculate the Financial Impact

To complete the business-case analysis, we must take the estimated cost savings or additional profits and subtract the costs of the up-front outlay, in this case the salary and benefits for an ICP. In this example, the total economic impact at the hospital for CABG-related infections as a result of hiring an additional ICP is estimated to range from an annual cost of \$50,880 to an annual savings of \$63,700. Although this is quite a range, by thinking through all the possible permutations and assumptions and presenting the different scenarios, the administrator is able to make a thoughtful decision. Furthermore, all of these estimates assume that the ICP's activities are focused only on preventing CABG-associated SSI, which is highly unlikely.

Step 7: Include the Additional Financial or Health Benefits

Many infection control interventions have multiple benefits. For instance, a contact isolation program developed in response to an outbreak of *Acinetobacter baumannii* infections would also be expected to reduce the rate of methicillin-resistant *Staphylococcus aureus* (MRSA) infections and vancomycin-resistant *Enterococcus* (VRE) infections.³⁷ In this example, the efforts of the new ICP could also be expected to reduce the incidence of catheter-related bloodstream infection, prevent other SSIs, and improve compliance with hand hygiene. All of these factors need to be included in a proper business-case analysis. To further make the business case for an additional ICP, one must include the reduced costs expected to be associated with these other types of preventable infections. After these are included, it would be expected that hiring an additional ICP would save the hospital money.

TABLE 2. Evaluation of Outcomes in Various Types of Economic Analysis

Analysis	Benefit measurement unit	Formulation of final reported outcome
Cost-effectiveness	Most natural unit of comparison*	Cost per unit
Cost-utility	QALYs	Cost per QALY saved
Cost-benefit	Monetary units	Net financial benefit (or loss)
Business-case	Monetary units	Net financial benefit (or loss)

NOTE. QALY, quality-adjusted life-year.

* For example, infections prevented or life-years saved; final outcome is then reported in terms of that unit (eg, cost per infection prevented or cost per life year saved).

Even though business-case analyses do not typically include the adverse consequences of nosocomial infections, such as patient mortality, hospital administrators do respond to these important issues as well. Thus, some calculation of the patient safety improvement associated with the intervention should be included. If mortality associated with CABG-related SSI is 20%, then preventing 9 of these infections would be estimated to prevent approximately 2 deaths. In this example, these 2 deaths could be prevented with an estimated maximum cost of \$50,880 per year. Additionally, preventing complications, such as SSI, might be associated with reduced legal costs.³⁸ Furthermore, with the increased call for regulations requiring mandatory reporting of healthcare-associated infections, there may be other benefits to the hospital that have not yet been considered (eg, pay-for-performance or an enhanced reputation for the institution).^{39,40} These benefits must be included in a proper business-case analysis and may be used to influence hospital administrators with respect to the importance of infection control programs. Thus, a hospital's risk management group should be involved early on in any business-case analysis for a quality improvement program.

Because of the transmissible nature of communicable diseases, it is possible that an intervention used in one group of patients (eg, identification and isolation of ICU patients who are colonized with VRE) benefits another group to whom the intervention is not directly applied (eg, patients on a general medical floor who reside with VRE-colonized patients after they are transferred to that floor). Clearly, an ideal business-case analysis would capture such additional benefits (and potential cost savings). In reality, it may be difficult to identify such indirect effects (or "externalities," as they are sometimes called) with infection control data. More sophisticated analyses may attempt to identify externalities through the use of mathematical modeling.⁴¹

Step 8: Make the Case for Your Business Case

The completed analytical portion of a business case must be complemented by effective communication of its findings and your recommendations to critical stakeholders at your institution. Once a business-case analysis has been completed, the first instinct may be to immediately schedule an executive-level group meeting to present your findings and recommendations. That may work in certain instances, but it may

be best to meet again with key stakeholders individually (eg, the chief medical officer, chief operating officer, and/or nurse-managers on affected units). These discussions can serve several purposes, including the presentation of initial findings, the development of an implementation plan, and the determination of current support for the initiative. Additionally, when the results are formally presented at a committee meeting, the key administrators will have had most of their questions answered already and will, more often than not, provide critical support during the final discussion before approval of the initiative.

Often, more attention is given to the formulation of an initiative than to its actual implementation.⁴² After the individual discussions, it is likely that the key findings of the analysis will need to be presented at an executive-level meeting. Importantly, successful implementation requires consensus building, which leads to higher levels of commitment even if it slows implementation speed.⁴³ Much has been written about the successful implementation of initiatives in healthcare settings, including developing action plans, setting budgets, and measuring performance improvement.⁴²

Step 9: Prospectively Collect Cost and Outcome Data Once the Program Is in Effect

If an infection control intervention program has been in existence for several years and has kept infection rates low, administrators might be tempted to eliminate or reduce the program even though associated costs would have been higher in its absence. Therefore, it is imperative that intervention-specific outcome data and costs be collected after the intervention is implemented. It is important to show stable outcome rates or continued improvement associated with the intervention, to maintain consensus support and organizational momentum.

PART 2: BASIC ECONOMIC CONCEPTS

Types of Economic Analyses

In addition to the business-case analysis, there are 3 basic types of economic analysis used in healthcare decision making: cost-effectiveness analysis, cost-utility analysis, and cost-benefit analysis (Table 2). Experts have noted that the distinctions between these various forms of analysis are often

blurred, yet it is important to consider what is included in and excluded from each specific analysis so that informed decisions can be made.⁹ A recent review of the infection control literature found that of 30 publications that claimed to be economic analyses, only 8 were cost-effectiveness or cost-consequences analyses.¹³

Cost-effectiveness analysis. Cost-effectiveness analysis compares interventions or products that have different costs and different levels of effectiveness. If a new intervention costs more and is less effective than an existing intervention, or if the new intervention costs less and is more effective than an existing intervention, then the choice is easy. However, if a new intervention delivers more benefit at an increased cost, which occurs frequently in the setting of rapid technological innovation, then the choice is often difficult. In cost-effectiveness analysis, the benefits of an intervention are measured in the most natural unit of comparison, such as the number of lives saved or infections prevented.⁹ Programs are then compared in terms of cost per unit (eg, dollars per life-year gained or dollars per infection prevented).

Cost-utility analysis. Cost-utility analysis is very similar to cost-effectiveness analysis, except that benefits of a specific intervention are adjusted by health preference scores or are utility weighted.⁹ In this type of analysis, programs are compared in terms of quality-adjusted life-years (QALYs) gained. The rationale behind this approach is that it not only values life, but it also allows the analysis to take account of disability or morbidity associated with the condition being treated or with adverse effects from the treatment. For instance, a year spent in an ICU would be valued differently by a patient, compared with a year spent at home with their family. Perhaps 4 years spent in an ICU would be equal in value to 1 year spent healthy, so 4 years spent in an ICU would equal only 1 healthy year, or rather, 1 QALY. A good example of a cost-utility analysis (and a cost-effectiveness analysis) in the infection control literature studied the use of vancomycin in perioperative prophylaxis during coronary-artery bypass surgery.⁴⁴

Cost-benefit analysis. A cost-benefit analysis is one in which all aspects of the analysis, including the consequences of the intervention, are valued in monetary or dollar terms. If an intervention's benefits measured in dollars exceed its costs, then this analysis considers it worthwhile.¹⁰ The major impediment to the use of cost-benefit analysis in healthcare decision making is the requirement to set a monetary value on human life or health benefits, such as setting a human life-year equal in value to \$250,000. Of note, most economic analyses of infection control interventions that claim to be cost-benefit analyses are mislabeled, because they do not include a dollar value for the important outcomes of interest (eg, they do not place a dollar value on a human life or quality of life and they do not include dollars saved as a result of saving a life or improving quality of life in the analysis.)

Which type of analysis is preferred? Over the past 10 years, cost-effectiveness analysis and the closely related cost-utility analysis have emerged as the preferred methods for economic

evaluation in health care.^{10,45} Importantly, it is recommended that researchers compare new interventions to a reference case whenever possible, using standard units such as cost per lives saved or per QALYs saved.¹⁰ If an agency wanted to choose between funding a hand-hygiene promotion initiative and a cancer screening program, it would be difficult to compare the cost per infection prevented with the cost per cancer detected. However, if the comparison was cost per life-year saved or cost per QALY saved for each program, then an informed decision could be made.

What is considered cost-effective? A standard threshold for calling a program cost-effective stipulates that the intervention should cost less than \$50,000 per QALY saved; however, some suggest the threshold has increased to \$100,000 per QALY saved.⁴⁶ The World Health Organization recommends that the threshold for calling an intervention cost-effective should be 3 times a country's gross domestic product per capita, and this threshold is \$94,431 in the United States.¹⁷ Frequently, but incorrectly, researchers will only state that an infection control intervention is cost-effective or cost-beneficial if it is cost saving from a hospital perspective. Most healthcare interventions are not cost saving. A review of all cost-effectiveness analyses published between 1976 and 2002 found that only 130 (9%) of 1,433 cost-effectiveness ratios reflected cost saving, in which the interventions saved lives and money at the same time.⁴⁸

Perspective

The economic impact of nosocomial infections and infection control interventions can be assessed from various perspectives: that of society, that of the hospital, that of a third-party payer (eg, a health maintenance organization or the Centers for Medicare and Medicaid Services), that of a government agency (eg, the Veterans Health Administration), or that of the patient. Studies that examine a nonsocietal perspective can underestimate the full economic effect of an infection or intervention. Thus, it is important to recognize the perspective of a study to interpret its results appropriately. In addition, it is important to design the study so that it evaluates the issue from the perspective of interest (Table 3). For instance, outpatient physician visits to treat an SSI would be important to include in an analysis for the Centers for Medicare and Medicaid Services but would not be included in a typical acute care hospital business-case cost analysis.

The societal perspective incorporates all costs and all health outcomes, regardless of who incurs the costs or who receives the benefits.¹⁰ The US Panel on Cost-Effectiveness in Health and Medicine states that even when an analysis from a nonsocietal perspective is requested, a complete societal perspective analysis should also be completed.¹⁰ Importantly, an analysis from the societal perspective will inform broader comparisons of programs and could lead to more equitable distribution of resources to improve public health. It is possible that the current lack of cost-effectiveness analyses of

TABLE 3. Costs and Outcomes That May Be Included When Examining the Economic Impact of an Infection Control Intervention From Various Perspectives

Cost or outcome	Perspective		
	Societal	Payer	Hospital
Hospitalization costs			
Antibiotics	X	X	X
Excess length of stay	X	X	X
Intensive care stay	X	X	X
Intervention costs			
Test Costs	X		X
Gown and glove	X		X
Nurse and physician time	X		X
Isolation room	X		X
Outpatient costs			
Physician visits	X	X	
Antibiotics	X	X	
Home health visits	X	X	
Rehabilitation center stay	X	X	
Patient costs and outcomes			
Mortality	X		
Morbidity	X		
Infections	X		
Lost wages	X		
Travel expenses	X		

infection control interventions from the societal perspective has facilitated the current underfunding of infection control programs and the continued incidence of preventable health-care-associated infections.

Stating Monetary Values in Constant Dollar Terms

Adjusting for inflation: using published cost estimates from prior years. When the cost estimates used in an economic analysis come from different years, the data should be converted to current-year values. For instance, if you wanted to include the cost of a CABG-associated SSI in a business-case analysis for your hospital and you only had access to an estimate of the costs associated with such an SSI in 2002, then you would need to inflate that amount to reflect costs incurred in the current year. The typical method for handling these adjustments is to inflate the dollar amounts by use of a standard price index, such as the medical care services component of the Consumer Price Index.^{10,49} Alternatively, a simpler method for use in a business-case analysis is to use the Bureau of Labor Statistics Consumer Price Index calculator.⁵⁰ This calculator allows a researcher to enter a value and select the year of the study, and the calculator then accurately inflates the value to that of the current year. Although this method is easy to use, it will likely underestimate costs because the rate of inflation in medicine is far higher than standard inflation rates. Therefore, it should be used only for convenience.⁵¹

Discounting: incorporating future benefits and costs in a cost analysis. It is widely accepted that in economic analysis, all future costs and future health consequences should be stated

in terms of their present value.^{9,10} The process of converting both future dollars and health outcomes to their present value is called discounting. The US Panel on Cost-Effectiveness in Health and Medicine recommends using a discount rate of both 5% and 3%.¹⁰ For example, if you assume that you will save \$10,000 for preventing an MRSA infection next year if you decolonize a patient with intranasal MRSA colonization this year, then, by use of a 3% discount rate, the discounted savings would be $\$10,000/(1 + 0.03)^n$, or \$9,709, where n is the number of years in the future the benefit is accrued. Although counterintuitive to some, it is often recommended that the future health benefits of disease control programs (such as life-years gained) also be discounted to the present value at the same rate as costs. Failure to do so may result in the misleading impression that the most attractive strategy is simply to defer the initiation of the program indefinitely.⁵²

Measuring the Attributable Cost of Nosocomial Infections

Obtaining data on the incidence and attributable cost of a nosocomial infection allows an individual institution to understand the financial burden created by the infection. Many studies have been published that aim to define the attributable cost of nosocomial infections. Generally, these studies involve a set of patients who develop the infection of interest and a reference group who do not develop the infection. Outcomes such as attributable mortality, length of hospitalization, and costs are then compared between the 2 groups. These studies are, by definition, cohort studies because the outcomes of interest (eg, morbidity, mortality, and/or cost) occur after the exposure of interest (ie, nosocomial infection). Examples of these studies include examinations of the mortality and costs associated with catheter-associated bloodstream infection and SSI.^{24,53}

Studies that aim to assess the impact of infection with a specific antibiotic-resistant organism may have 2 reference groups, one with infection due to the susceptible form of the same organism and another without infection. For example, the outcomes for patients with SSI caused by MRSA can be compared with the outcomes for patients with SSI caused by methicillin-susceptible *S. aureus* to determine the incremental cost associated with methicillin resistance; the outcomes for patients with MRSA SSI can also be compared with the outcomes for patients without infection to determine the cost associated with MRSA SSI.^{53,54} The latter comparison results in a much higher estimate of costs attributable to resistance.

Important concepts to consider when determining the attributable costs and outcomes of nosocomial infection are adjustment for prior length of stay, severity of illness, and underlying comorbid conditions. Failure to consider and adjust for these factors can result in biased estimates of attributable cost. These concepts are discussed below.

Adjustment for length of hospitalization prior to onset of infection. When comparing costs and outcomes for patients who developed nosocomial infection with outcomes for those

who did not, it is important to control for length of stay prior to the onset of infection for the patients who developed infections and to control for total length of hospital stay for the comparator group who did not develop infection. Studies that make no adjustment for the time at risk of development of nosocomial infection have been shown to overestimate the length of hospitalization and the costs that are attributable to nosocomial infection by up to 2-fold because prolonged length of stay may itself be an important risk factor for nosocomial infection.⁵⁵

Several methods have been proposed for accurately estimating the extra days spent in the hospital as a result of nosocomial infections and the associated increased costs. At a minimum, the hospital stays of the patients in the reference group who did not develop infection should be least as long as the time that the patients who developed infection were hospitalized before developing infection. This can be accomplished by matching case and reference patients on the basis of length of stay before infection or by performing more complicated statistical analyses.⁵⁵

Adjustment for underlying severity of illness and comorbidities. Patients who develop nosocomial infection typically have greater severity of acute illness and more substantial histories of past chronic medical illnesses, compared with patients who do not develop infection. Because severity of illness and past medical illnesses are also independent predictors of resource use (eg, length of stay), it is important to control for illness severity and comorbidities present prior to infection because these variables may distort or confound the relationship between infection, costs, and outcomes.

Various methods have been proposed and employed to grade severity of illness, including subjective scores (eg, the McCabe and Jackson scores), ICU-data driven measures (eg, the Acute Physiology, Age, and Chronic Health Evaluation score⁶⁰), and administrative severity scores (eg, the Medical Illness Severity Grouping System admission severity group score and the All Patient Refined Diagnosis Related Groups classification system). However, there is currently no well-validated aggregate illness severity score for infectious disease outcomes, and each of the tools mentioned above has important limitations as well as strengths, particularly with respect to its applicability to infectious disease outcomes.⁵⁷

The timing of the assessment of underlying disease severity is important. Severity of illness may be a risk factor for infection, but severe illness can also be caused by the presence of infection, in which case it represents an intermediate variable in the chain of events between the exposure (ie, the infection) and the outcome of interest (eg, death or length of stay). Because adjustment for an intermediate variable usually causes an underestimation of the effect of the exposure of interest on the outcome, care must be taken to assess severity of illness prior to the first signs of infection (ie, more than 48 hours).⁵⁸ Results of studies that assign the illness severity score at the time of the infection should be interpreted with caution as they may underestimate the magnitude

of the effect that the nosocomial infection has on outcomes.^{59,60} Preexisting comorbidities may confound the association between infection and costs in a manner similar to that of the initial severity of illness. Aggregate comorbidity measures, such as the Charlson Comorbidity Index⁶¹ and the Chronic Disease Score,⁶² have been used to summarize patients' underlying comorbidities for the purpose of adjustment in studies examining the risk factors and outcomes of patients with nosocomial infections.⁶³⁻⁶⁷

Defining costs. It is critically important to decide which costs to measure. Potential approaches to evaluating the economic burden of nosocomial infections in an institution include the following measurements: hospital costs, hospital charges, resources used, and/or actual reimbursed charges.⁶⁸ Hospital costs include daily operating costs (sometimes called "fixed costs"), which do not vary based on patient volume, as well as the cost of drugs, tests, and other patient care-related activities (sometimes called "variable costs"), which are dependent on the number of patients admitted or their length of hospitalization.⁶⁹ Under the US system of healthcare financing, a hospital must ensure that all of its costs are reimbursed by third-party payers; therefore, it assigns fees to hospital resources, which appear on a patient's bill as charges. Insurance companies, Medicare, and Medicaid do not pay the amount stated on the bill because they receive discounts; therefore, for all patients the charge on the bill is greater than the actual hospital costs, to cover these losses.⁷⁰ Hospital costs can be a useful outcome measure for an individual hospital because they best reflect the actual economic burden of the hospital. Although some institutions have implemented complex cost accounting systems that track resources used and assign costs, in most institutions, actual or true costs are difficult to retrieve.⁷¹ In contrast, hospital charges are less indicative of actual cost but are usually easy to retrieve from administrative databases and are consistent from patient to patient in most settings. Because hospital charges typically overestimate actual cost by 25%-67%, adjustment can be performed by use of cost-to-charge ratios.^{71,72} Both hospital and departmental cost-to-charge ratios are determined annually on the basis of data submitted to the Centers for Medicare and Medicaid Services. Hospital cost-to-charge ratios may be a more accurate measure of costs for a cohort of patients in multiple diagnosis related groups, while departmental cost-to-charge ratios may be more accurate for a cohort of patients in the same diagnosis related groups.^{71,73,74} It is important to note that physician professional fees and costs to the patient in the form of lost work are not captured when assessing only hospital costs or charges.

Direct measurement of resource use, through the use of microcosting, assesses specifically what services or procedures are used by a patient. Such methods may be preferred in countries where hospital operating costs are financed directly by the state rather than through reimbursement for patient care by third-party payers (eg, Canada). When microcosting is used, the resources consumed must be identified, measured,

and valued to translate resource use into monetary units. For example, one might *identify* gowns as an important source of variable costs in a program to control the rate of VRE infection. The number of gowns used in an ICU in a year could be *measured* by counting, and the *value* of the gowns used could be determined by multiplying the number of gowns used by the cost of an individual gown.

A comparison of the ratio of the total costs or charges for patients with nosocomial infections and those for comparable patients without nosocomial infections in one institution over a relatively short period provides the most generalizable estimate of the magnitude of the attributable economic impact of nosocomial infections. In contrast, the absolute values of cost or charge cited in studies should be interpreted with more caution because they may not be applicable beyond the institution in which they were collected. It is important to note that some administrators may view business-case analyses with skepticism if the cost data used are not from the local institution. Multicenter studies must report measures that are standardized across institutions.

Using cost estimates in the existing literature to supplement institutional estimates. If the costs of nosocomial infections cannot be measured within an institution, it may be necessary to use literature sources to estimate the economic impact of specific infections prior to completing a business-case analysis for an intervention. A synthesis of the published literature regarding the cost of representative healthcare-associated infections was created by the authors with literature published during 1995-2006 (Table 1). All cost estimates were inflation adjusted to 2005 US dollars, using the medical care services component of the nonseasonally adjusted Consumer Price Index.^{16,49} Length of stay data means the total hospital stay, including ICU stay, if available, that was attributable to the specific infection. All amounts not in US dollars were converted to US dollars with the Economic Research Federal Reserve Bank of St. Louis's Federal Reserve Economic Database II,⁷⁵ by use of the rate from January 1 of the year the study data were collected. Most cost estimates from the studies shown in Table 1 represent hospital costs, although a few estimates included the total societal costs of the infection.

Measuring the Economic Impact of Interventions to Reduce Nosocomial Infections

Optimal decisions concerning infection control programs must incorporate the economic impact of specific interventions. Most of the utility of economic analyses in the area of infection control lies in their ability to help convince hospital administration or public health authorities to fund and support a specific intervention. Unfortunately, the current literature is lacking in high-quality studies, such as randomized controlled trials, that could be used to support the efficacy and cost-effectiveness of specific interventions.

Decision making about infection control interventions requires the availability of proper cost-effectiveness analyses.

Several important articles have outlined the optimal methodologies to use when measuring the economic impact of antimicrobial-resistant pathogens.^{68,71} However, a 2005 survey assessing all of the infection control intervention studies published found that 69% of the studies used a quasi-experimental design, and only 4% incorporated a cost analysis.⁷⁶ From January 2001 through June 2004, of the 30 studies published that claimed to be economic analyses of infection control interventions, only 5 were proper cost-effectiveness analyses.¹³ Because so few studies have been published that assess the cost-effectiveness of interventions, there is a glaring need for proper economic evaluation of most infection control interventions. Importantly, even among the few studies completed, many have inherent methodological weaknesses that create bias against reporting an infection control intervention as cost-effective. Below, we describe the strengths and weakness of the basic study designs, which should be considered when assessing the efficacy and cost-effectiveness of infection control interventions.

Randomized controlled trials and cluster-randomized control trials. Infection control interventions can be broken down into 2 basic categories. In the first, the patient who undergoes the intervention is the same patient who directly benefits from the intervention. An example of this type of intervention is optimal timing of antibiotic prophylaxis to reduce the risk of a SSI.⁷⁷ Here, the person who receives the antibiotics at the correct time would be at reduced risk of developing a SSI, and no other patients in the hospital would directly benefit from this intervention. Therefore, if we were trying to measure the benefit of appropriately timed antibiotic use, it can be said that for this type of intervention the unit of analysis is the individual patient. In this case, the "gold standard" study design to evaluate efficacy and safety is the randomized controlled trial. Even though observational trials, such as cohort studies, can yield results similar to those of randomized controlled trials, a randomized controlled trial is considered the "gold standard" for evaluating the efficacy of interventions.⁷⁸⁻⁸⁰

The second category of infection control interventions includes those interventions in which the specific infection control program is directed at either individual patients or a specific population of patients, and a different group of patients benefits from the program. An example of this type of intervention is the collection of surveillance culture samples to detect MRSA colonization on ICU admission and the isolation of colonized patients in a medical ICU. To study these types of programs, a cluster-randomized trial is necessary to adjust for the clustering effect that is inherent in control programs that involve transmissible infectious diseases.^{81,82} Patients who are impacted by these types of infection control programs represent a cluster (eg, an ICU) exposed to a common environment, common care practices, and other patients who are colonized with MRSA. Studies that fail to control for the nonindependence of patient outcomes may overestimate the effectiveness of the intervention. Thus, if we were

trying to measure the benefit of active surveillance in reducing MRSA colonization and infection, the unit of analysis in this case is the entire ICU. Instead of randomizing individual patients, individual ICUs need to be randomized; this requires that multiple hospitals be involved, which requires a substantial investment of both money and time. These types of trials are called cluster-randomized trials or group randomized trials, and they are increasingly used by public health officials to study group interventions and also to study individual interventions that have group-level effects.⁸³ Numerous articles have been written about the specific methodological and ethical issues involved in cluster-randomized trials.⁸⁷⁻⁹⁶

Quasi-experimental studies. Situations in which randomized trials cannot be completed ethically and/or economically are common in hospital epidemiology; consider, for example, a trial to evaluate the cost and effectiveness of an intervention to stop an active outbreak.^{87,88} Quasi-experimental studies, also known as pre-post intervention studies, can be used when it is not feasible to perform randomized controlled trials or cluster-randomized control trials. Quasi-experimental studies differ from randomized trials in that patients are put into the intervention group and the control group without randomization. As a result, these studies have a potentially lower internal validity because multiple confounders and biases can affect their quality.⁸⁹ Even with these limitations, the quasi-experimental study design has been used with increased frequency in infection control research; a 2004 review of published studies that assessed interventions to reduce healthcare-associated infections found that 69% used a quasi-experimental design and 23% used a randomized trial design.⁷⁶ A recent systematic review of infection control and antibiotic stewardship articles published during 2002 and 2003 found that 39 (53%) of 73 studies used the most basic quasi-experimental study design, which involved single measurements taken before and after the intervention and no control group.⁹⁰ Importantly, studies that assess the cost-effectiveness of specific infection control interventions by use of the basic quasi-experimental design should be interpreted with caution, particularly when completed during an outbreak. Detailed options for improving and interpreting quasi-experimental studies can be found elsewhere.^{16,89-91}

Decision-analytic models and mathematical models. Mathematical models are useful tools for evaluating interventions prior to implementing them in human populations.^{41,92-96} Models allow researchers to use existing knowledge and data in a rigorous, efficient, and testable manner towards the goal of making medical decisions for the assessed population's greatest benefit. Importantly, clinical trials are expensive, are labor intensive, and do not necessarily provide adequate data to make decisions for populations with all possible baseline characteristics. Therefore, models can be an ideal way to determine which interventions would be most cost effective and where an intervention would be most cost effective in pre-

venting the spread of transmissible pathogens, including MRSA and VRE.^{41,95,97}

As an example, active surveillance and isolation of patients have been available for years as tools to control the spread of antimicrobial-resistant organisms in hospitals, but these strategies are only implemented in a minority of hospital ICUs because of their perceived costs and a lack of definitive clinical trial data.⁹⁸ Many factors or variables that are related to the population (eg, ICU size and discharge rate), to individual patients (eg, comorbidities and age), or to the infectious organism being evaluated (eg, duration of colonization and likelihood of infection) can be individually evaluated with modeling strategies to assess their individual and combined importance in causing the observed outcome. This type of evaluation is called "sensitivity analysis," and it is used in most mathematical and decision models.^{41,99} Thus, mathematical models can focus future clinical trials, greatly benefit patients, and optimize expenditures within the limited budgets of microbiology and infection control departments. Importantly, given the number and great variety of hospitals and other healthcare institutions that exist, it would be close to impossible to perform clinical trials to test the cost-effectiveness of all potential infection control interventions.

In conclusion, demonstrating the value of infection control programs is increasingly important in the context of limited budgets and no direct reimbursement for infection control activities. Hospital epidemiologists and infection control specialists must be able to complete accurate and timely business-case analyses to justify existing or planned quality improvement initiatives. Currently, the availability of accurate published estimates measuring the economic impact of healthcare-associated infections and related interventions is limited. In the future, accurate estimates of the attributable costs of hospital-acquired infections and the relative value of specific interventions will be required to inform clinical decisions, develop guidelines, and direct societal resource allocation optimally.

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Research

Original Investigation

Health Care–Associated Infections A Meta-analysis of Costs and Financial Impact on the US Health Care System

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IMPORTANCE Health care–associated infections (HAIs) account for a large proportion of the harms caused by health care and are associated with high costs. Better evaluation of the costs of these infections could help providers and payers to justify investing in prevention.

OBJECTIVE To estimate costs associated with the most significant and targetable HAIs.

DATA SOURCES For estimation of attributable costs, we conducted a systematic review of the literature using PubMed for the years 1986 through April 2013. For HAI incidence estimates, we used the National Healthcare Safety Network of the Centers for Disease Control and Prevention (CDC).

STUDY SELECTION Studies performed outside the United States were excluded. Inclusion criteria included a robust method of comparison using a matched control group or an appropriate regression strategy, generalizable populations typical of inpatient wards and critical care units, methodologic consistency with CDC definitions, and soundness of handling economic outcomes.

DATA EXTRACTION AND SYNTHESIS Three review cycles were completed, with the final iteration carried out from July 2011 to April 2013. Selected publications underwent a secondary review by the research team.

MAIN OUTCOMES AND MEASURES Costs, inflated to 2012 US dollars.

RESULTS Using Monte Carlo simulation, we generated point estimates and 95% CIs for attributable costs and length of hospital stay. On a per-case basis, central line–associated bloodstream infections were found to be the most costly HAIs at \$45 814 (95% CI, \$30 919–\$65 245), followed by ventilator-associated pneumonia at \$40 144 (95% CI, \$36 286–\$44 220), surgical site infections at \$20 785 (95% CI, \$18 902–\$22 667), *Clostridium difficile* infection at \$11 285 (95% CI, \$9118–\$13 574), and catheter-associated urinary tract infections at \$896 (95% CI, \$603–\$1189). The total annual costs for the 5 major infections were \$9.8 billion (95% CI, \$8.3–\$11.5 billion), with surgical site infections contributing the most to overall costs (33.7% of the total), followed by ventilator-associated pneumonia (31.6%), central line–associated bloodstream infections (18.9%), *C difficile* infections (15.4%), and catheter-associated urinary tract infections (<1%).

CONCLUSIONS AND RELEVANCE While quality improvement initiatives have decreased HAI incidence and costs, much more remains to be done. As hospitals realize savings from prevention of these complications under payment reforms, they may be more likely to invest in such strategies.

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As one of the most common sources of preventable harm, health care-associated infections (HAIs) represent a major threat to patient safety.^{1,2} Recent estimates of the national morbidity and mortality burden of HAIs have made it clear that HAIs represent a major public health problem.³ Furthermore, a robust body of evidence exists describing interventions that can substantially reduce the incidence of HAIs,⁴ and recent analyses indicate that at least 50% are preventable.^{5,6} Standard-setting organizations such as the National Quality Forum have identified HAIs as a key area of focus for patient safety with the development of a number evidence-based, HAI-specific safe practices.⁷ As a target for those seeking to improve care in the United States, HAIs represent a key opportunity to save lives and reduce costs.^{1,2,8,9}

However, despite the availability of solutions, the strong ethical case for improvement, and the intuitive argument that saving lives ought to save money, large-scale progress against HAIs has been slow. Only recently have health care organizations begun to achieve successes and overcome doubts about the scalability of pilot studies and vanguard institutions. Along with leadership of patient safety professionals, an important driver of progress is the move by payers to deny reimbursement for health care related to preventable harm.^{10,11} By placing the costs of HAIs with hospitals, this shift has accentuated the fiscal case for prevention.

We believe that better evaluation of the costs of HAIs could help providers and payers justify investing in this area. In addition, for policymakers, sound estimates of the potential systemwide cost savings could mobilize the resources needed to catalyze progress in the cause of improving care and restraining rising health care costs. The purpose of this study was to generate estimates of the costs associated with the most significant and targetable HAIs. To do this, we compiled examinations of the costs of HAIs into robust, precise, broadly applicable estimates of each HAI and also estimated the aggregate annual costs of infections in adults acquired in the inpatient setting.

Methods

To estimate the impact of HAIs on the US health care system, we performed 3 steps. First, we estimated epidemiologic and economic parameters for each main infection type (namely, incidence rates, attributable costs, and added length of hospital stay). Second, we modeled the variation of these outcomes within a large population of patients. And third, we used simulation to extrapolate totals for the US health care system. Because key data were not available for all HAIs, we focused on the 5 with the highest impact on the health care system, that is, the most common, costly, preventable, and well-tracked infections in hospitalized patients. On this basis, surgical site infection (SSI), central line-associated bloodstream infection (CLABSI), catheter-associated urinary tract infection (CAUTI), ventilator-associated pneumonia (VAP), and *Clostridium difficile* infection (CDI) were chosen. Methicillin-resistant *Staphylococcus aureus* (MRSA) is presented as a subcategory where applicable.

Estimation of HAI Incidence

We opted to rely on a single source for HAI incidence estimates: the National Healthcare Safety Network (NHSN) of the Centers for Disease Control and Prevention (CDC), formerly called the National Nosocomial Infections Surveillance (NNIS). The NHSN regularly collects data on the major device-associated and procedure-associated HAIs across a network of 1700 reporting sites (www.cdc.gov/nhsn/about.html). Compared with stand-alone investigations, the NHSN offers superior robustness to regional variation, more current figures amidst epidemiologic fluctuations, and greater methodologic consistency. Using 2009 NHSN data (chosen for concordance with hospital care data described herein), incidence rates for CLABSI, CAUTI, and VAP were estimated as the number of infections per total patient-days and stratified between critical care units and inpatient wards. For SSI and MRSA incidence calculations, 2008 NHSN data were used, which were the most current available. Since NHSN does not yet provide reporting data for CDI, these were estimated from high-quality studies obtained through systematic review. The body of literature used to estimate HAI impacts was found to draw almost entirely on adult populations, and it was believed that results could not be generalized further, and so for all incidence calculations, pediatric and neonatal units were excluded. Long-term acute care settings, whose patients were believed to differ significantly from hospital inpatients by demographics, health status, payer mix, and type of care received, were similarly excluded.

Literature Review for Estimation of Attributable Resource Utilization

To obtain the best available estimates of the key HAI parameters, a systematic review of the literature was conducted, following previously published methods.^{1,4,6,12} Searches were conducted through PubMed using medical subject headings (MeSH). For specific search strategies, see eTable 1 in the Supplement. The first pass was limited to listings published in English between 1986 and April 2013 with abstracts for review. Abstracts were next eliminated if the study was conducted outside of the United States, since epidemiology, medical practice, and health care economics vary widely internationally, or if they indicated no relevance to the research question. Full-text reviews were performed on the remaining articles. Inclusion was determined on the basis of criteria believed to indicate highly informative sources, specifically (1) robust comparison using either a matched control group or an appropriate regression strategy; (2) generalizable populations typical of inpatient wards and critical care units; (3) methodologic consistency with CDC definitions; and (4) soundness of handling economic outcomes. Review article bibliographies were scanned for potentially useful primary references. Three review cycles were completed, with the last iteration carried out from July 2011 to April 2013.

The research team then undertook a secondary review of selected publications to determine whether articles on the borderlines fit the inclusion criteria. This process eliminated a large proportion of articles, typically because economic outcomes were considered only secondarily. Even among included ar-

ticles, some variation in methods or definitions could not be avoided. However, all included articles followed similar methodology in which the attributable cost was generated from a comparison of patients with index infection and without index infection. In cases where charges, rather than costs, were reported, costs were estimated by a cost-to-charge ratio of 0.50, a conservative and commonly used value.^{9,13} All cost estimates were inflated to 2012 dollars using the annual producer price index¹⁴ (PPI) for general medical and surgical hospitals, and if a base dollar year was not reported, it was assumed to be the year of article publication.

Sensitivity Analysis of Costs and Resource Utilization

The literature review resulted in a point estimate of incremental cost savings and length of stay (LOS). Each measure was calculated as a weighted average of the point estimate from each study selected for inclusion; each study was weighted by its relative sample size.¹⁵ We then conducted a Monte Carlo simulation to develop confidence intervals (CIs) around each point estimate.¹⁶ We chose the Monte Carlo simulation to estimate CIs for its ability to provide relatively realistic estimates of uncertainty.^{15,17} This was important owing to the variety of sources and measures used in the studies included in the analysis.

For the Monte Carlo simulation, we used a variant of the approach described by Jha et al⁹ to develop CIs for such measures. For each acceptable study, we simulated a distribution then pooled the results, weighting by sample size. The approach described by Jha et al is essentially dependent on 3 observations: the point estimates for the 3 studies composing the best measure of central tendency and lower and upper bounds. This allows us to include as many studies as we determine are appropriate for inclusion. There was 1 exception to our weighting method: in the case of SSI, a single very large database study would have obviated the findings of others if pooled only by size. Therefore, we separately pooled the smaller studies by sample size and weighted the small sample size pool equally with the result of the large study.

For each parameter of interest for each HAI (ie, cost of SSI; LOS for SSI) we first fit a triangular distribution for each of the relevant published studies based on the reported measures of central tendency and dispersion. In general, we used the 95% CI, if it was either reported in the article or could be calculated from the article, to set the end points for the distribution so that 2.5% of the distribution fell below the lower value and above the upper value. We then set the most likely value of the triangular distribution equal to the published central tendency measure and checked to determine if the modeled triangular distribution reasonably matched the study results. In some cases, we found that the distribution was heavily skewed because the mean value of the triangular distribution differed from the study mean by more than 10%. In these cases, we adjusted for the skewness by fitting a general distribution in which the distribution was piecewise adjusted to shift the density of the probability function to account for the underlying asymmetry.

Finally, for each HAI, we simulated 100 000 sample draws from the modeled distribution for each relevant study simultaneously. At each iteration, we calculated the weighted av-

erage of the included studies. We reported the mean and 95% CI from the resulting distribution of those 100 000 weighted averages for each HAI. This approach eliminated the need to rely on normally distributed data and facilitated inclusion of studies that would otherwise be difficult to combine (eg, those reporting means and others reporting medians).¹⁵

Monte Carlo simulations were conducted using the Monte Carlo simulation software @RISK, version 5.5 (Palisade Corp).

Estimation of National Impact

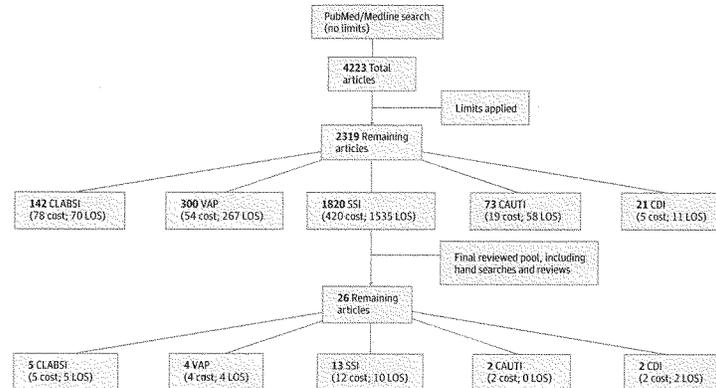
To determine the financial impact of HAIs on the US health care system, the 2009 National Inpatient Sample (NIS) of the Health Care Utilization Project (HCUP) was used to estimate population exposure (ie, total patient-days or total procedures). The NIS 2009 is the largest publicly available all-payer inpatient database in the United States, holding data on 7.8 million stays from 1050 hospitals in 44 states where 96% of the US population resides. The data set approximates a 20% stratified sample of US community hospitals, allowing calculation of national estimates.^{18,19} Since the NIS reports incidence rates for both intensive care units (ICUs) and inpatient wards, to calculate national estimates, we used an overall ratio of 1 to 7 for critical care to inpatient ward days, as used previously.²⁰ The total incidence of SSI was calculated from total numbers of ICD-9-coded procedures (*International Classification of Diseases, Ninth Revision*) involving surgical sites. To avoid double counting of separately billed procedures comprising a single actual operation, we counted multiple procedures within a record that are commonly associated with a single surgical site (eg, colectomy and appendectomy, as determined by a physician reviewer) as one if they occurred on the same calendar day. From total patient-days and patient-procedures, using the above described incidence rates and estimates of attributable cost and LOS for each HAI, we generated point and interval estimates for impacts at the national level.

Results

We identified 26 studies providing reasonably robust estimates of attributable costs and/or LOS for the 6 HAIs of interest (Figure). For more detail on studies included, see eTable 2 in the Supplement. For SSIs, we identified 12 studies based on our search strategy²¹⁻³² and 1 more that dealt specifically with MRSA SSIs.³³ For CLABSI, we identified 4 studies³⁴⁻³⁷ and another study specifically dealing with MRSA bloodstream infections.³⁸ We identified 4 studies for VAP,³⁹⁻⁴² while for CDI, 2 were identified.^{43,44} For CAUTI, 2 studies were found for estimating cost,^{45,46} but we were unable to find any studies that met our criteria for estimating the attributable LOS. For CLABSI and VAP, estimates were available for LOS specific to both the ICU and for the total hospital stay. For other studies, we were not able to provide separate estimations for both ICU stay and non-ICU stay. We estimated the incidence rate for CDIs based on 3 studies identified through our literature review.⁴⁷⁻⁴⁹

Using Monte Carlo simulation techniques, we generated point estimates and 95% CIs for both costs and LOS (Table 1). On a per-case basis, CLABSI was found to be the most costly

Figure. Search Results for Major Procedure-Associated or Device-Associated Health Care-Associated Infection



The first set of limiting criteria were publication in the last 25 years; study design either randomized clinical trial, clinical trial, or meta-analysis; and English language publication. For complete search strategy and limit strategy, see Table 1 in the Supplement. CAUTI indicates catheter-associated urinary tract

infection; CDI, *Clostridium difficile* infections; CLABSI, central line-associated bloodstream infections; LOS, length of stay; SSI, surgical site infections; VAP, ventilator-associated pneumonia.

HAI, at \$45 814 (95% CI, \$30 919-\$65 245). CLABSI cases caused by MRSA resulted in even higher associated costs to hospitals (\$58 614 [95% CI, \$16 760-\$174 755]). Similarly, both CLABSI and SSI cases caused by MRSA resulted in the highest attributable excess LOS (15.7 and 23.0 days, respectively).

In 2009, approximately 34.7 million adults received inpatient care in America's hospitals, totaling 165.1 million patient-days. These patients were treated with invasive medical devices during 96.2 million days of care and underwent approximately 8 million operations, all of which placed them at risk for HAIs. The estimated hospitalized adult populations at risk per HAI are reported in Table 2. On an annual basis, SSI (n = 158 639) and CDI (n = 133 657) were estimated to be the most frequent HAIs nationwide (36.0% and 30.3%, respectively) (Table 2). In decreasing frequency were CAUTI (17.4%), CLABSI (9.2%), and VAP (7.1%). From the per-case costs, the aggregate incidence rates, and the population at risk, the cumulative annual costs to the health care system were determined (Table 3). In total, annual costs for the 5 major HAIs was \$9.8 billion (95% CI, \$8.3-\$11.5 billion), with SSIs contributing the most to overall costs (33.7% of the total). Notably, CAUTIs accounted for only 0.3% of the total costs. VAP accounted for 31.7%; CLABSI, 18.9%; and CDI, 15.4%.

Discussion

More than a decade since the landmark report *To Err Is Human*¹ brought patient safety to the fore, US hospitals remain less safe

Table 1. Estimates of Costs and LOS Attributed to the 5 Major Health Care-Associated Infections for the US Adult Inpatient Population at Acute Care Hospitals^a

Health-Care-Associated Infection Type	Cost, 2012 \$US	LOS (as Total, ICU), d
Surgical site infections	20 785 (18 902-22 667) ^b	11.2 (10.5-11.9) ^b
MRSA	42 300 (4005-82 670) ^b	23.0 (14.3-31.7) ^b
Central line-associated bloodstream infections	45 814 (30 919-65 245) ^{b,c}	10.4, 6.9 (6.9-15.2, 3.5-9.6) ^{b,c}
MRSA	58 614 (16 760-174 755) ^c	15.7 (7.9-36.5) ^c
Catheter-associated urinary tract infections	896 (603-1189) ^b	NR
Ventilator-associated pneumonia	40 144 (36 286-44 220) ^{b,c}	13.1, 8.4 (11.9-14.3, 7.8-9.0) ^{b,c}
<i>Clostridium difficile</i> infections	11 285 (9118-13 574) ^b	3.3 (2.7-3.8) ^b

Abbreviations: ICU, intensive care unit; LOS, length of hospital stay; MRSA, methicillin-resistant *Staphylococcus aureus*; NR, not reported.

^a Data are reported as mean (95% CI) values.

^b Estimates obtained from literature and 100 000-trial Monte Carlo simulations using triangular distribution.

^c Estimates obtained from literature and 100 000-trial Monte Carlo simulations, using general distribution.

than they should be. Hospital-acquired infections account for a large proportion of the harms caused by health care and high rates of morbidity, mortality, and costs. We estimated that there

Table 2. Epidemiology of Health Care–Associated Infections Among US Adult Inpatients (Including ICUs) at Acute Care Hospitals, 2009^a

Health Care–Associated Infection Type	Incidence Rate	Population at Risk	Cumulative Incidence
Surgical site infections	1.98 ^b	8 020 658	158 639
MRSA	0.29 ^b	8 020 658	23 417
Central line–associated bloodstream infections	1.27 ^c	31 695 922	40 411
MRSA	0.21 ^c	31 695 922	6638
Catheter-associated urinary tract infections	1.87 ^d	41 115 000	77 079
Ventilator-associated pneumonia	1.33 ^e	23 392 785	31 130
<i>Clostridium difficile</i> infections	3.85 ^f	34 716 079	133 657
Total health care–associated infections	NA	NA	440 916

Abbreviations: ICU, intensive care unit; MRSA, methicillin-resistant *Staphylococcus aureus*; NA, not applicable.

^a Estimates based on data from National Healthcare Safety Network (2009) and National Inpatient Sample (2009). Incidence rate for *Clostridium difficile* infections based on systematic review of literature.

^b Incidence rate in cases per 100 patient procedures; population at risk in total

patient procedures.

^c Incidence rate in cases per 1000 device-days; population at risk in total device-days.

^d Incidence rate in cases per 1000 patient-days; population at risk in total patient-days.

Table 3. Total Attributable Financial Impacts of Health Care–Associated Infections in US Adult Inpatients at Acute Care Hospitals, 2009^a

Health Care–Associated Infection Type	Costs		
	Total	Lower Bound	Upper Bound
Surgical site infections	3 297 285 451	2 998 570 584	3 595 841 680
MRSA	990 539 052	93 785 080	1 935 883 296
Central line–associated bloodstream infections	1 851 384 347	1 249 464 195	2 636 608 279
MRSA	389 081 519	111 253 391	1 160 029 019
Catheter-associated urinary tract infections	27 884 193	18 765 813	37 002 574
Ventilator-associated pneumonia	3 094 270 016	2 796 898 212	3 408 445 101
<i>Clostridium difficile</i> infections	1 508 347 070	1 218 707 008	1 814 293 587
Total	9 779 171 077	8 282 405 811	11 492 191 220

Abbreviation: MRSA, methicillin-resistant *Staphylococcus aureus*.

^a All cost estimates reported in 2012 \$US rounded to the dollar.

are approximately 440 000 of these infections annually among US adult inpatients and that their annual costs are \$9.8 billion. Over a third of these costs are attributable to SSIs, with a quarter due to VAPs, CAUTIs.

These figures are in many cases lower than previous estimates, which have placed the yearly number of HAIs around 1.7 million and the costs at between \$20 billion and \$40 billion.^{2,50} These discrepancies arise from both methodologic differences and differences in epidemiology. Methodologically, whereas the prior studies sought to examine all HAIs, our focus was on the 5 most important ones with the highest presumed targetable impact. Our focus on adult inpatients only also contributes to the difference. While Klevens et al³ included pediatric inpatients in estimating incidences, we excluded this group for 2 reasons. First, we found the evidence on HAI costs in pediatric populations to be insufficient for robust cost modeling. Second, we believe that the data from adult populations could not be generalized to children, particularly to the approximately 3 million generally healthy newborns. A large part of the differences in estimates is also due to the lower incidences of infections, in turn, likely due to the success of widespread quality-improvement efforts. While CLABSI is most notable, where infection rates appear to have decreased more than 50%,^{5,6} similar trends have also been observed for other HAIs.⁵¹

Reported evidence over the last decade shows that major progress has been made in preventing specific types of HAIs, which at one time were viewed as a largely unavoidable risk of care. In a recent systematic review, the authors estimated that as many as 65% to 70% of CLABSIs and CAUTIs and 55% of cases of VAP and SSI are preventable with current evidence-based interventions.⁸ In a retrospective medical chart review study performed at 10 hospitals, Landrigan et al⁵² estimated that more than 75% of HAIs identified were preventable. Applying these rates to our national cost estimates translates into potential cost savings of \$5.0 billion to \$5.5 billion annually, which hospitals could still tap into. Thus, implementation of readily available strategies has the potential to produce significant bottom-line savings to hospitals.

For financial incentives to drive improvement in quality and safety of care, hospitals will want to know how much of these potential cost savings would actually contribute to bottom-line savings. Under fee-for-service payment systems and Medicare's traditional diagnosis-related groups (DRGs) system that allow reclassifying to a higher DRG when complications occur, hospitals formerly had little financial incentive to prevent infections. However, Medicare's nonpayment policy for treatment of largely preventable in-hospital conditions, launched in 2006 and amended in 2008, sought to change that. This policy currently translates prevention of CLABSI, CAUTI,

and certain SSIs into cost savings for hospitals treating Medicare and Medicaid patients.⁵³ Even this has been criticized as not going far enough to drive either patient safety or substantial cost savings.⁵⁴ Indeed, under a new Centers for Medicare & Medicaid Services (CMS) rule that authorizes states to identify other provider-preventable conditions for which Medicaid payment will be prohibited,¹¹ and with emerging payment reforms, hospitals should see financial benefits from preventing HAIs.

Since SSIs constitute the largest portion of HAI-related costs nationally, and since less progress has been made in preventing these infections than in other areas of care, research and quality improvement efforts are clearly needed in this area. In addition, policy efforts must also target SSIs. This might be achieved by increasing federal support to evaluate effectiveness of HAI prevention approaches, encouraging innovation to expand the list of effective interventions, or enhancing surveillance programs to include post discharge tracking of SSIs. While enhancing our ability to prevent SSIs, CMS could expand the list of procedures for which it will not reimburse for a higher-charge DRG due to SSIs and encourage private payers to implement nonpayment strategies. However, it should be noted that the consequences of such policies have not been fully evaluated, and there is a need to assess whether these initiatives might have substantial unintended effects.

Our study has several limitations. First, we based our cost estimates on published studies that used heterogeneous methods to assess attributable costs, sometimes using older data. Though a stringent review process sought to mitigate this limitation, some heterogeneity was inevitable. Indeed, for some HAIs, we had to exclude all available sources. Additionally, we used Monte Carlo simulation as an attempt to account for the heterogeneity and uncertainty in our probabilistic analysis. The paucity of high-quality studies that would assess the costs and excess LOS associated with CAUTI and CDI suggest a clear need for further research.

It is also likely that our results contain some underestimations. One such underestimation might result from the tradeoff between consistency and sensitivity in our decision to rely on NHSN data only. SSIs provide a clear example of this in that many become evident after discharge and are thus not captured within the NHSN surveillance programs. Still, the NHSN program provides the largest data source for real-life HAI rates and has clear benefits over relying on more vigilant published reports from single institutions. Another source of potential underestimation is related to the patient population in this study. Our report is limited to HAIs in the adult inpatient population, excluding not only neonatal and pediatric patients but also patients in non-acute-care facilities such as long-term care and dialysis centers. Total incidence and national HAI-attributable cost estimations for the entire health care system are likely much higher, and if this is the case, a recommendation to increase quality improvement initiatives would be even more applicable.

Finally, we acknowledge that there is a variety of factors, such as comorbidity and other acute conditions, that may contribute to infections. Although comorbidities and primary diagnosis were accounted for in the included studies, it is obvious that this was not a complete list.

In summary, our study provides updated, robust, and applicable estimates for resources attributable to the major HAIs that continue to plague modern health care systems and create considerable harm to patients. While widespread quality improvement initiatives have resulted in a decrease in HAIs incidence, much more remains to be done. These estimates may be used for business case development to support investment in HAI reduction efforts. Investment in leadership, practices, and technologies will continue to drive patient safety and allow hospitals to realize cost savings attributed to prevention of HAIs. Ongoing payment reforms such as value-based purchasing coupled with incentives to reduce the frequency of these events should drive local, state, and federal efforts and bring about substantial reduction in patient harm.

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Costs Attributable to Healthcare-Acquired Infection in Hospitalized Adults and a Comparison of Economic Methods

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Background: Hospitals will increasingly bear the costs for healthcare-acquired conditions such as infection. Our goals were to estimate the costs attributable to healthcare-acquired infection (HAI) and conduct a sensitivity analysis comparing analytic methods.

Methods: A random sample of high-risk adults hospitalized in the year 2000 was selected. Measurements included total and variable medical costs, length of stay (LOS), HAI site, APACHE III score, antimicrobial resistance, and mortality. Medical costs were measured from the hospital perspective. Analytic methods included ordinary least squares linear regression and median quantile regression, Winsorizing, propensity score case matching, attributable LOS multiplied by mean daily cost, semi-log transformation, and generalized linear modeling. Three-state proportional hazards modeling was also used for LOS estimation. Attributable mortality was estimated using logistic regression.

Results: Among 1253 patients, 159 (12.7%) developed HAI. Using different methods, attributable total costs ranged between \$9310 to \$21,013, variable costs were \$1581 to \$6824, LOS was 5.9 to 9.6 days, and attributable mortality was 6.1%. The semi-log transformation regression indicated that HAI doubles hospital cost. The

totals for 159 patients were \$1.48 to \$3.34 million in medical cost and \$5.27 million for premature death. Excess LOS totaled 844 to 1373 hospital days.

Conclusions: Costs for HAI were considerable from hospital and societal perspectives. This suggests that HAI prevention expenditures would be balanced by savings in medical costs, lives saved and available hospital days that could be used by overcrowded hospitals to enhance available services. Our results obtained by applying different economic methods to a single detailed dataset may inform future cost analyses.

Key Words: healthcare-acquired infection, economic methods, cost analysis

(*Med Care* 2010;48: 1026–1035)

Over 1.7 million patients suffer a healthcare-acquired infection (HAI) annually and one-third or more are believed to be preventable.^{1–4} HAI prevention is an example where the goals of improving quality and decreasing cost may be synergistic.^{5–7} HAIs are now the subject of mandatory reporting and the Centers for Medicare and Medicaid Services have revised reimbursement rules to reduce payment for a variety of hospital-acquired conditions, including selected infections.^{3,8–11} HAI prevention may also reduce the spread of antimicrobial resistant infection (ARI).^{3,12,13} We recently reported the costs attributable to ARI for our facility.¹⁴ Hospitals have been urged to make an economic or business case for enhanced infection control.⁷ The elements include program costs, program effectiveness, and potential cost-savings due to prevented infection.⁷

An important consideration in economics is time frame. Variable costs of healthcare are those that could be saved over the short-term. Examples include costs for consumables that increase with each additional treatment, such as medication or blood products.^{7,15,16} In overcrowded hospitals, employee overtime or part-time agency staff might also be reducible over the short-term. Additionally, the total cost of healthcare includes fixed costs such as buildings and capital equipment; costs that would not be saved immediately if an infection was prevented.¹⁵ However, opportunity cost for a resource is defined as the benefit that could be gained from the next best use of that same

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resource. Hospitals are often overcrowded, so if a facility with enhanced infection control is able to offer healthcare to more patients because of reduced infection and length of stay (LOS), then fixed costs are also a true societal cost of HAI.¹² Economic perspective refers to the fact that costs are defined differently, depending on who is paying. The costs of HAI are different when comparing the perspectives of the hospital, third-party payor, or the affected patient.¹⁵ Poor outcomes such as loss of life and productivity, or reduced quality of life represent additional economic costs of HAI.

Many HAI studies have focused on single infection sites, specific emerging resistant pathogens or treatment settings such as the intensive care unit (ICU). Study designs and analytic methods vary. Synthesis of results from diverse patient subgroups in different settings makes it difficult to estimate savings from prevention programs that are ideally implemented hospital-wide. The problem is predicting what patients with HAI would have cost had they not developed infection. In addition, health cost data are usually skewed to the right and heteroscedastic—meaning that the variance is not constant over the data range.^{17–20} The goal of this project was to examine the cost of HAI in a sample of high-risk hospital patients, including ICU, non-ICU, medical and surgical patients, all infection sites, and infecting organisms. Multiple cost definitions and analytic methods are reported. The medical cost was measured from the hospital perspective and included total and variable costs. A second total hospital cost was measured for each patient, excluding physician salary and surgical procedure costs, because those fees are often billed separately. Societal costs were estimated using excess hospital LOS and mortality. This project is an expansion of earlier work.^{14–16,21,22} We have now added specific infection sites, surgical patients, treatment setting subgroup analysis, and adjustment for ARI.

METHODS

Patient Sample Selection and Study Setting

This study was conducted at a large, acute care, urban, public teaching hospital. A random sample of 1500 patients admitted in the year 2000 was selected from those aged 18 years or older. To ensure sufficient numbers with HAI, patients were selected from a higher risk pool; those discharged with greater than 5 International Classification of Diseases; 9th revision, Clinical Modification (ICD-9-CM) diagnostic codes.¹⁶ Patients hospitalized for trauma, burn, or obstetrical care were excluded as their small numbers and unique infections could lessen the generalizability of our findings.^{4,23–25} The research was deemed exempt from review by the Institutional Review Boards of our hospital and the Centers for Disease Control and Prevention.

Measurements

Patients were classified as “Suspected HAI” or “Confirmed HAI” using criteria from the Centers for Disease Control and Prevention National Nosocomial Infection Surveillance definitions, with minor modifications for a retrospective study.^{16,26} Prior work demonstrated that severity of illness, surgery, and ICU treatment predicted increased hos-

pital cost.^{14,16} To control for confounding due to severity of illness, the highest Acute Physiology and Chronic Health Evaluation III (APACHE III) score during the first 24 hours of hospitalization was measured and patients were categorized as having received surgery or ICU treatment.²⁷

The random sample was selected using the electronic medical record database developed for the Chicago Antimicrobial Resistance Project.²⁸ Patient data abstracted from the electronic records included LOS in all locations of care, number and type of laboratory and radiologic tests received, inpatient and outpatient pharmaceuticals prescribed, and laboratory results needed for APACHE III scoring. Additional data needed to complete the eligibility assessment, measurement of APACHE III score, patient resource use, and development of HAI were obtained on review of the entire written medical record by trained physician and nurse abstractors using preprinted forms. Abstracted data included comorbidities, vital signs, urine output, blood product transfusions, procedures such as bronchoscopy, minutes of operating room time for surgery, and review of clinical notes for signs of infection. All abstracted data were quality reviewed to ensure completeness and accuracy.

Medical costs were measured from the hospital economic perspective.^{10,15,16,22} Unit costs for each resource were calculated using the annual hospital expenditure report for the year 2000. The total hospital cost included building costs, plus all annual operating expenses for both service and support departments. To calculate the total cost for each resource, the multiple distribution method was used to allocate support costs to the departments that provide directly measurable patient services.²⁹ Variable costs for consumables for each service were added. The resulting service department totals were divided by annual work outputs to calculate the total unit cost for each resource. To maintain internal validity, the same data sources used for annual work outputs were used for individual patient resource counts. Physician costs included the salaries for faculty, residents, part-time providers, and overtime. Physician support department costs, such as credentialing, were allocated based on the number of full-time faculty in each department. All clinic hours, hospital inpatient days, specialty consultation and procedure times were estimated using clinic schedules, hospital administrative and operating room data, and effort-reporting. All costs were actual hospital expenditures.

To illustrate potential savings for different hospital circumstances, variable costs for each hospital resource were sequentially added. Variable Cost 1 consisted only of consumable materials such as medications, medical supplies, laboratory reagents, and food. These are costs that any hospital could save immediately with HAI prevention. Variable Cost 2 added nursing overtime and part-time agency costs that represent additional savings for overcrowded hospitals. Variable Cost 3 added physician salary costs, for hospital inpatient care, consultations and bedside procedures that represent additional savings for hospitals that pay staff physician salaries. Physician support was not included in the variable cost. Physicians at our teaching hospital are salaried whereas many US physicians bill separate service and surgery fees. Therefore, an alternate total hospital cost was calculated exclusive of physician

salary and operating room procedure costs. For all cost measures, the total for each patient was calculated by summing the unit costs of all resources used.

Analysis Plan

In the initial approach, ordinary least squares (OLS) linear regression models were used to estimate costs attributable to HAI. The following confounders were included in all models: APACHE III score, surgery, and ICU care. ARI was subsequently added as a confounder to further isolate the cost of HAI, especially because the prevalence of ARI has varied among hospitals and over time.^{13,30–33} (See Appendix A for ARI definitions). The total medical cost for “Any HAI” was calculated using 1 economic model, while a second model included each specific infection site. The patient was the unit of analysis, so a new variable was created for patients with multiple infections.

This study is unusual in that medical, surgical, ICU, and non-ICU patients, different infection sites and any infecting organism were combined in a single analysis to reflect hospital-wide impact; so, a sensitivity analysis was performed. We calculated ratios to compare unadjusted mean costs of patients with and without HAI for each of the hospital service and treatment settings. OLS linear regression analyses, including the same confounders, were performed using the total cost minus physician and surgery costs, and each of the 3 sequential variable cost measures. Medical cost was also calculated by multiplying the attributable LOS by the mean cost per day. We expected that both LOS and cost per day would be additional independent cost confounders.^{34–39} Each additional day in the hospital provides more opportunities to acquire infection, and some excess daily costs may be related to procedures or severity of illness that caused rather than resulted from HAI.⁴⁰ To correct the potential problem with LOS endogeneity bias, we used a 3-state proportional hazards model to estimate change in LOS due to HAI.^{37–39} The sensitivity analysis included 3 different mean cost per day measures; HAI patients, non-HAI patients, and all sample patients. Propensity scores derived from comorbidities, APACHE III scores, surgery, and ICU were calculated for all patients with HAI and used to select matched cases without HAI from the rest of the cohort. Two matched samples were compared; 1 with and 1 without matching for ARI. The mean cost differences for these matched groups were compared using paired T-tests.^{41,42}

Hospital cost data are often skewed with heteroscedastic variance.^{17–20,43,44} To address these problems, heteroscedasticity consistent standard errors were provided for the OLS models and quantile regression using the 0.5 or median quantile was conducted.^{44,45} To address the effect of outliers, Winsorizing was done, where the costs for the highest 2% and 5% of patients were replaced with the sequential next cost in the series.^{46,47} To reduce the effects of skewed data, the total costs were transformed to log-cost.⁴⁴ After regression, the exponentiated parameter estimate for HAI minus 1 can be interpreted as the proportional change in baseline cost attributable to HAI.⁴⁸ Finally, to further reduce the effect of skewed cost data, total medical costs were estimated using a generalized linear model (GLM) with log as link function and a gamma distributed disturbance term, then

converting the results back to dollars.^{17–19} Retransformation to dollars was done individually for each unique patient subgroup. There were 16 possible combinations based on surgery, ICU, ARI, and HAI classification. The APACHE III scores were included in the equations, as they do predict cost, but they were not included in the predicted cost calculation because that would overestimate the cost of HAI. The mean predicted cost for non-HAI patients was subtracted from the mean predicted cost for HAI patients with the same subgroup classification. These differences were multiplied by the number of HAI cases in each subgroup, summed, and then divided by 159 for an HAI average. The same procedure was followed for those with and without ARI.

In summary, the sensitivity analysis started with OLS linear regression to measure the total and variable hospital costs and LOS attributable to HAI, with and without adjusting for concurrent ARI. Heteroscedasticity consistent standard errors were used. Attributable LOS was also derived using a 3-state proportional hazards model. Alternate total costs were calculated by multiplying attributable LOS measures by the mean total and variable costs per day. Cost comparisons were also performed using case-matching based on propensity scores. Finally, median quantile regression, Winsorizing, semi-log cost transformation, and GLM were used to dampen the effects of skewed cost distribution and outliers (Statistical Appendix, Supplemental Digital Content, online only, available at: <http://links.lww.com/MLR/A103>).

Excess deaths attributable to HAI were estimated using logistic regression to measure the mortality predicted by APACHE III score, ARI, and HAI. The resultant parameter estimates predicting death were used to calculate the adjusted mortality odds-ratio and excess number of deaths attributable to HAI alone. Long-term societal costs for excess deaths were calculated using productivity loss tables. The 3% discounted rate used for life lost was \$585,903. This is the estimated total future earnings and household productivity for men and women aged 55 years who died in the year 2000.⁴⁹ That cost was multiplied by the excess attributable deaths. To calculate the short-term societal productivity loss caused by extended hospital stay, the attributable LOS was multiplied by the actual (not attributable) number of HAI patients who did not die by the national daily average for productivity in 2000 (\$165).⁴⁹ Cost calculations and analyses included all outliers and were completed using SAS (version 9.2, SAS Institute, Inc., Cary, NC) Microsoft Excel (version 2002, Microsoft Corporation, Redmond, WA) and R-Project; changeLOS package (available at: www.R-project.org, Vienna, Austria). The *a priori* 2-tailed alpha used for statistical significance was 0.05.

RESULTS

A total of 23,904 patients were hospitalized in the year 2000 and 4944 (20.7%) met our eligibility requirements. Among the 1500 selected, 67 had incomplete medical records and an additional 180 were excluded because on chart review it was clear they were hospitalized for pediatric, obstetrical, trauma, or burn care, which was missed by the electronic database extraction process. The 1253 patients available for analysis comprised 25.3% of the eligible pool (Table 1). Of

TABLE 1. Patients Characteristics Stratified by Presence of Healthcare-Acquired Infection

Patient Characteristics	All Patients	Patients Without HAI	Patients With HAI
All patients; number (%)	1253	1094 (87.3)	159 (12.7)
Age; mean (SD)	54.4 (14.3)	54.6 (14.1)	53.1 (15.8)
Male; number (%)	721 (57.5)	625 (57.1)	96 (60.4)
Apache III score; mean (SD)	40.4 (17.6)	39.4 (17.3)	47.1 (18.0)*
Antimicrobial resistant infection; number (%)	50 (4.0)	16 (1.5)	34 (21.4)*
Comorbidities			
Diabetes mellitus	422 (33.7)	373 (34.1)	49 (30.8)
Congestive heart failure	290 (23.1)	269 (24.6)	21 (13.2) [†]
Renal disease	221 (17.6)	175 (16.0)	46 (28.9)*
Hepatic disease	200 (16.0)	164 (15.0)	36 (22.6) [‡]
Cancer	192 (15.3)	152 (13.9)	40 (25.2)*
AIDS	180 (14.4)	157 (14.4)	23 (14.5)
COPD	114 (9.1)	106 (9.7)	8 (5.0)
Stroke	98 (7.8)	75 (6.9)	23 (14.5) [†]
Peripheral vascular disease	66 (5.3)	54 (4.9)	12 (7.6)
Dementia	39 (3.1)	33 (3.0)	6 (3.8)
Unadjusted outcomes			
LOS; mean (SD)	8.8 (9.6)	7.0 (5.8)	21.2 (17.7)*
Cost per day; mean US\$ (SD)	1634 (738)	1578 (701)	2015 (870) [†]
Variable cost 1 per day; mean US\$ (SD)	290 (527)	268 (539)	439 (404)*
Died; number (%)	44 (3.5)	28 (2.6)	16 (10.1)*

Patients who developed HAI had significantly higher APACHE III scores, LOS, total and variable costs per day, and rates of antimicrobial resistant infection, comorbidities and mortality ($P < 0.001$). Outcomes are unadjusted means and include all outliers.

* $P < 0.001$.

[†] $P < 0.01$.

[‡] $P < 0.05$.

For all others $P =$ not significant.

HAI indicates healthcare-acquired infection; LOS, length of stay, measured in days; SD, standard deviation; AIDS, acquired immunodeficiency syndrome; COPD, chronic obstructive pulmonary disease.

these, 159 developed HAI (12.7%; 95% confidence interval [CI]: 10.6–14.8), and 16 died (10.1%; 95% CI: 8.1–12.0). Among HAI patients, 34 (21.4%; 95% CI: 14.0–28.8) had concurrent ARI. Urinary tract infections and patients with multiple infection sites were most common, while only 5 isolated surgical-site infections occurred (Table 2). Overall, patients with HAI had significantly higher APACHE III scores, rates of surgery, ICU care, comorbidities, resistant infection, LOS, total cost, cost per day, and mortality. However, in the surgery subgroup, HAI patients did not have significantly higher APACHE III scores or comorbidity rates. Multiple HAI infections occurred in 40 patients (25.2%; 95% CI: 17.4–33.0) and were most common in surgery and ICU settings. Among those with only 1 HAI, 88 (74%) met criteria for confirmed and 31 (26%) for suspected. The mean unadjusted costs for confirmed and suspected were \$38,016 (standard deviation: 31,418) and \$34,979 (standard deviation: 26,250), respectively. As this difference was not significant, they were combined in all further analyses.

Attributable total hospital cost using OLS regression was \$19,917 for any HAI, when adjusted for APACHE III score,

surgery, and ICU care (Table 3). The total was \$16,527 when further adjusted for ARI. The variation in the attributable total cost for different infection sites ranged from \$5385 for urinary tract to \$37,658 for multiple-site. The hospital total minus physician and surgery costs were \$18,615 before and \$15,447 after adjusting for ARI. The attributable variable costs 1, 2 and 3 were \$5222, \$5907, and \$6824, respectively. When adjusted for base intercept, APACHE III score, surgery, ICU care, and ARI, the total costs attributable to HAI in the treatment setting subgroups were as follows: medical, \$15,257 (standard error [SE]: 1372); surgical, \$18,988 (SE: 5366); non-ICU, \$8906 (SE: 911); ICU, \$27,344 (SE: 4934) (data not shown).

Using OLS regression, the excess LOS for Any HAI was 9.6 days, without adjusting for ARI and 8.1 days with ARI adjustment (Table 4). Using 3-state proportional hazard modeling, the attributable LOS was 5.9 days. Multiplying the highest attributable LOS by the highest mean cost per day (HAI patients) resulted in a calculated total of \$19,344. Using the lowest LOS estimate and mean cost per day (non-HAI patients) resulted in a total of \$9310. Propensity score matching resulted in 146 HAI patient pairs matched for comorbidities, surgery, and ICU care, and 136 patients when ARI was added. The mean difference between those with and without HAI was \$19,251 without ARI matching and \$17,869 with ($P < 0.001$). The median quantile regression resulted in attributable costs of \$11,662 before, and \$10,207 after adjusting for ARI. When costs were Winsorized at 98%, the OLS regression results for HAI were \$15,203 and \$14,089 before and after adjusting for ARI. When Winsorized at 95% the attributable costs were \$11,299 and \$10,536. The average cost was \$13,907 per infection when the results of GLM were retransformed to dollars. The GLM costs for patients with and without ARI were \$20,888 and \$12,008, respectively. The HAI, ICU, surgery, attributable cost, and mortality distribution decomposed by APACHE III severity groups and the predicted mortality for HAI and Non-HAI patients are shown in Figure 1. Adding the attributable cost for each site-specific infection resulted in a total for the sample of \$2,777,946, and an average of \$17,471 per patient. Depending on the economic method used, total attributable medical costs for the entire cohort were between \$1,480,290 to 3,321,192. The semi-log transformation regression indicated that HAI increased cost by 100.9% when not adjusting for ARI and 88.9% with ARI adjustment.

We estimate that the entire cohort lost 844 to 1373 productive days because of extended LOS in those who survived. The short-term productivity cost because of excess LOS was \$974 to \$1584 per HAI patient. The adjusted odds ratio resulted in attributable mortality of 6.1% with 9 excess deaths resulting in a long-term societal cost of \$5.27 million.

DISCUSSION

The excess medical costs attributable to HAI were high in all subgroups, including those with lower severity of illness and 46.5% of infections occurred in non-ICU settings. Using economic models, the total hospital cost estimates per patient were between \$11,299 and \$21,013 before factoring out the effect of ARI, and between \$10,207 and \$17,869 after.

TABLE 2. Healthcare-Acquired Infection Frequency, Unadjusted Mean Cost, and Cost Ratios for All Patients and Treatment Subgroups

	All Patients	Hospital Service		Treatment Setting	
		Medical	Surgical	Non-ICU	ICU
Total in each group, frequency, number (%)	1253	1087 (86.8)	166 (13.2)	1041 (83.1)	212 (16.9)
Any HAI	159 (12.7)	99 (9.1)	60 (36.1)*	74 (7.1)	85 (40.1)*
Specific HAI sites					
Pulmonary	31 (19.5)	18 (18.2)	13 (21.7)	13 (17.6)	18 (21.2)
Bloodstream	26 (16.4)	18 (18.2)	8 (13.3)	10 (13.5)	16 (18.8)
Urinary	41 (25.8)	25 (25.3)	16 (26.7)	27 (36.5)	14 (16.5)
Surgical site	5 (3.1)	—	5 (8.3)	2 (2.7)	3 (3.5)
Other	16 (10.1)	15 (15.2)	1 (1.7)	12 (16.2)	4 (4.7)
Multiple site	40 (25.2)	23 (23.2)	17 (28.3)	10 (13.5)	30 (35.3)
HAI status; mean unadjusted total cost; US\$ (SD)					
Any HAI	44,637 (45,268)	34,496 (35,644)	61,369 (54038)	22,453 (15,060)	63,950 (53,351)
No HAI	10,898 (10,544)	9372 (8555)	25,126 (15,592)	9023 (7459)	25,174 (17,479)
Cost ratio (HAI/no HAI)	4.1*	3.7*	2.4*	2.5*	2.5*

The frequency of HAI is shown for the overall sample and each subgroup.

The classifications for specific healthcare-acquired infection sites are mutually exclusive; patients with more than one site of infection were categorized as multiple site. Single site infections that were not pulmonary, bloodstream, urinary or surgical site were all categorized as other.

*P < 0.001 for all cost differences between those with and without HAI and for the differences in HAI frequency in medical versus surgical patients and non-ICU versus ICU patients.

HAI indicates healthcare-acquired infection; ICU, intensive care unit; SD, standard deviation.

The estimates obtained by multiplying the attributable LOS and cost per day were \$9310 to \$19,344. The short-term variable cost estimates of \$1581 to \$6824 per infection represent savings available immediately with each infection prevented. The range of results, which we obtained by applying different economic methods to a single detailed dataset, may inform and facilitate interpretation of future cost studies.

Among all patients who died, 36.4% had an HAI and attributable mortality was more than doubled, even after adjusting for severity of illness, ICU care and ARI. Only 5 isolated surgical site infections occurred and HAI in surgery patients was not significantly associated with APACHE III score or comorbidities. This highlights the remarkable proportion of infections (61.7%) among surgical patients, which were pulmonary, bloodstream, or urinary and may be explained by the need for mechanical ventilation, central vascular and urethral catheters during surgery. Otherwise, high severity of illness, surgery, ICU care, and comorbidities were associated with HAI. If risk factors for HAI increase at the same time that enhanced infection control programs are implemented, a contradictory effect or apparent ineffectiveness may occur—even for successful interventions.⁵⁰

We were conservative in extrapolating national estimates because this sample was selected from a subset with higher risk of HAI and so, their attributable costs might also be higher. The eligible pool represented 20.7% of our hospital population in the year 2000, so we will infer to only 20.7% of the 33.1 million US community hospital admissions in that same year.⁵¹ The HAI rate will be set at 5% because these are older data, HAI rates have declined, and our chart review

permitted broader definitions of infection, whereas many surveillance programs include only device-related infections. This calculation resulted in 347,435 HAIs; only 20% of recent national estimates.^{1,4} This is surprisingly similar to the proportion eligible in the study sample. Applying our lowest and highest total medical cost estimates, the national total was between \$3.2 and \$7.3 billion. Excess hospital LOS totals were 1.5 to 2.5 million days and costs for premature loss of life were \$12.4 billion. If one-third of these infections were prevented, the minimum national savings would be \$1.1 billion for total medical cost, 511 million days of lost productivity and 7065 premature deaths. The total savings for medical and societal costs would be \$5.3 to \$6.7 billion in US 2000 dollars. Using the Consumer Price Index to inflate those costs to 2009 US dollars, the lowest and highest predicted savings for prevention of one-third would be \$6.6 and \$8.4 billion. To put this in perspective, payments for medical malpractice claims were believed to add \$3.6 billion to the total cost of health care in 2008.⁵² Short-term variable cost savings would be \$228 to \$753 million in 2009 US dollars. In the sensitivity analysis, our lowest attributable LOS, costs, and mortality are very likely underestimates. The analytic procedures used were intended to correct for the effect of outliers. We argue that patients who develop HAI are outliers. In addition, the 3-state proportional hazard model was only able to calculate the excess LOS attributable to the first HAI, while 25% of our sample developed multiple infections. Applying underestimates for HAI frequency, medical and societal costs still resulted in enormous national cost estimates, or a proof-by-contradiction.⁵³

TABLE 3. Total and Variable Hospital Costs Attributable To Healthcare-Acquired Infection

Cost Measure and Infection Site	Not Adjusted for ARI			Adjusted for ARI		
	P.Est. US\$	HscSE	R2	P.Est. US\$	HscSE	R2
Total cost						
Any HAI	19,917	2567	0.46	16,527	1957	0.49
Specific HAI sites			0.49			0.52
Pulmonary	21,571	4456		19,414	4934	
Bloodstream	21,960	7435		16,918	6893	
Urinary	5385	2010		2786	2206*	
Surgical site	12,845	5266		10,356	5209	
Other	16,490	4798		14,473	5384	
Multisite	37,658	9454		33,467	7975	
Total cost minus MD and surgery costs						
Any HAI	18,615	2432	0.41	15,447	1848	0.44
Specific HAI sites			0.44			0.47
Pulmonary	20,620	4387		18,605	4830	
Bloodstream	20,580	7128		15,870	6635	
Urinary	5420	1892		2992	2075*	
Surgical site	5934	4012*		3609	5306*	
Other	15,052	4375		13,167	4924	
Multisite	35,161	8966		31,246	7568	
Variable cost 1 (consumables alone)						
Any HAI	5222	820	0.30	4379	738	0.32
Specific HAI sites			0.33			0.35
Pulmonary	7244	2795		6701	2896	
Bloodstream	5343	2004		4074	1853	
Urinary	1170	553		516	602*	
Surgical site	1110	1023*		484	1464*	
Other	3923	1148		3415	1269	
Multisite	9606	2571		8552	2181	
Variable cost 2 (consumables and short-term labor)						
Any HAI	5907	891	0.32	4951	782	0.34
Specific HAI sites			0.35			0.37
Pulmonary	7953	2840		7338	2954	
Bloodstream	6073	2271		4635	2103	
Urinary	1403	617		662	672*	
Surgical site	1400	1224*		690	1716*	
Other	4517	1326		3942	1470	
Multisite	10,891	2888		9696	2448	
Variable cost 3 (consumables, short-term labor and physician salary)						
Any HAI	6824	979	0.34	5720	839	0.36
Specific HAI sites			0.37			0.39
Pulmonary	8840	2894		8129	3026	
Bloodstream	7005	2544		5345	2361	
Urinary	1799	704		943	760*	
Surgical site	1868	1433*		1049	1954*	
Other	5392	1585		4728	1754	
Multisite	12,540	3264		11,160	2763	

The attributable costs for any HAI and for specific infection sites were estimated using ordinary least squares linear regression. All models included the cost confounders: base intercept, APACHE III score, Surgery, and ICU care.

A second model for each cost further adjusted for the confounding due to infection with antimicrobial resistant organisms.

The standard errors were calculated assuming heteroscedastic variance. Diagnostics for detecting multicollinearity were performed on all OLS models. The variance inflation factors associated with each independent variable across all models were below the value of 10 while the condition number associated with each model was approximately 10, indicating that multicollinearity was not a significant problem in the models. All economic models were significant; $P < 0.001$. All standard errors were significant at $P < 0.05$ or less except where indicated.

The cost measures for each patient used included: (a) Total cost; (b) Total minus surgical procedures and physician salary cost; (c) Variable cost 1 (consumable costs only); (d) Variable cost 2 (consumables plus nursing overtime and agency costs); (e) Variable cost 3 (consumables, nursing overtime and agency, plus physician salaries).

* $P = NS$.

HAI indicates healthcare-acquired infection; ARI, antimicrobial resistant infection; P.Est., parameter estimate from ordinary least squares regression model; HscSE, heteroscedasticity consistent standard error; MD, physician or medical doctor.

TABLE 4. Sensitivity Analysis and Extrapolation for Length of Stay and Cost

	Not ARI Adjusted; Days (HscSE)	R ²	ARI Adjusted; Days (HscSE)	R ²
Attributable length of stay—Ordinary least square regression; d (SE)				
Any HAI	9.6 (1.1)	0.37	8.1 (1.0)	0.40
Specific sites				
Pulmonary	9.0 (1.8)	0.39	8.0 (2.0)	0.42
Bloodstream	9.5 (2.7)		7.2 (2.6)	
Urinary	4.6 (1.2)		3.4 (1.1)	
Surgical site	5.3 (2.3)		4.2 (2.3)	
Other	9.6 (3.1)		8.6 (3.4)	
Multiple site	16.9 (3.9)		15.0 (3.3)	
	% Cost Increase	R²	% Cost Increase	R²
Semi-log transformation; attributable percent cost increase over baseline				
Any HAI	100.9	0.59	88.9	0.59
Specific sites				
Pulmonary	117.4	0.59	109.0	0.59
Bloodstream	116.3		96.7	
Urinary	60.6		53.0	
Surgical site	54.4		47.4	
Other	127.3		118.8	
Multiple site	126.5		109.2	
		Calculated Cost US\$		Extrapolated Cost US\$ (Millions) Eligible Hospital Pool
Extrapolation to Eligible Hospital Population Analysis Method	Per Patient	Per Infection	Entire Sample	
Total cost: not adjusted for ARI				
Generalized linear model	2651	20,888	3,321,192	13.1
OLS linear regression	2527	19,917	3,166,803	12.5
OLS linear regression: total cost minus MD and procedures	2362	18,615	2,959,785	11.7
Propensity score matched comparison (number 146 in each group)	2443	19,251	3,060,909	12.1
LOS multiplied by mean HAI cost/d	2455	19,344	3,075,696	12.1
OLS linear regression; 98% Winsorized	1929	15,203	2,417,277	9.5
LOS multiplied by mean non-HAI cost/d	1922	15,149	2,408,691	9.5
3S-PHM LOS multiplied by mean HAI cost/d	1509	11,889	1,890,351	7.5
Quantile linear regression	1480	11,662	1,854,258	7.3
OLS linear regression; 95% Winsorized	1434	11,299	1,796,541	7.1
3S-PHM LOS multiplied by mean non-HAI cost/d	1181	9310	1,480,290	5.8
Total cost: adjusted for ARI				
OLS linear regression	2097	16,527	2,627,793	10.4
OLS linear regression: total cost minus MD and procedures	1960	15,447	2,456,073	9.7
Propensity score matched comparison (number 136 in each group)	2267	17,869	2,841,171	11.2
LOS multiplied by mean HAI cost/d	2071	16,322	2,595,198	10.2
OLS linear regression; 98% Winsorized	1788	14,089	2,240,151	8.8
LOS multiplied by mean non-HAI cost/d	1622	12,782	2,032,338	8.0
Generalized linear model	1524	12,008	1,909,272	7.5
OLS linear regression; 95% Winsorized	1337	10,536	1,675,224	6.6
Quantile linear regression	1295	10,207	1,622,913	6.4
Variable cost 1				
OLS linear regression; not adjusted for ARI	663	5222	830,298	3.3
OLS linear regression; adjusted for ARI	556	4379	696,261	2.7
3-S PHM LOS multiplied by mean variable cost 1	201	1581	251,379	0.99

(Continued)

TABLE 4. (Continued)

	Total Days		Total Days	
Length of stay				
OLS linear regression; not adjusted for ARI	1.1	9.6	1373	5417
OLS linear regression; adjusted for ARI	0.9	8.1	1158	4570
3-S PHM	0.7	5.9	844	3329

The attributable length of stay for any HAI and for specific infection sites were estimated before and after adjusting for concurrent ARI using OLS linear regression. The percent increase in hospital cost attributable to HAI was estimated by regression after semi-log transformation of the cost for each patient. All of the economic analyses described in the methods are shown in the extrapolation section. In the generalized linear model, the variables used were intercept, APACHE III Score, surgery, and ICU care, with and without ARI. The mean predicted cost for each subgroup was calculated using retransformed parameter estimates. The mean for non-HAI patients was subtracted from the HAI patient mean in each subgroup. These differences were each multiplied by the number of HAI patients in that group for the sample total.

In the OLS linear regression, all models included base intercept, surgery, and ICU care. A second model also included ARI. In the Propensity score method, each HAI patient was matched to a non-HAI control using propensity scores. The matching was based on comorbidities, surgery and ICU care, and then with and without ARI matching. Only comorbidities with significant association with HAI ($P < 0.05$) were included in the scores; $P < 0.001$ for cost differences using propensity scores. In the 98% and 95% Winsorized analysis, the top 2% and 5% cost outliers were Winsorized to the cost of the patient just preceding them in the cost distribution. Costs for HAI were also calculated by multiplying the attributable LOS by mean cost per day. Quantile regression using the 0.5 quantile (median) was performed. Finally, attributable LOS estimated using 3-State Proportional Hazard Model was multiplied by the lowest mean cost per day (non-HAI patients).

For the extrapolation, the result per infection was multiplied by 159 to determine the sample total. The sample total was divided by the total sample (1253 patients) to calculate the total per patient. Those per-patient totals were multiplied by total eligible patients (4944) for the hospital total. To avoid double counting societal excess costs, the attributable LOS per infection was multiplied only by the 143 HAI patients who did not die.

ARI indicates antimicrobial resistant infection; HAI, healthcare acquired infection; HsESE, heteroscedasticity consistent standard error; R2, coefficient of determination; SE, standard error; OLS, ordinary least squares; LOS, length of stay; 3-S PHM, 3-state proportional hazard model.

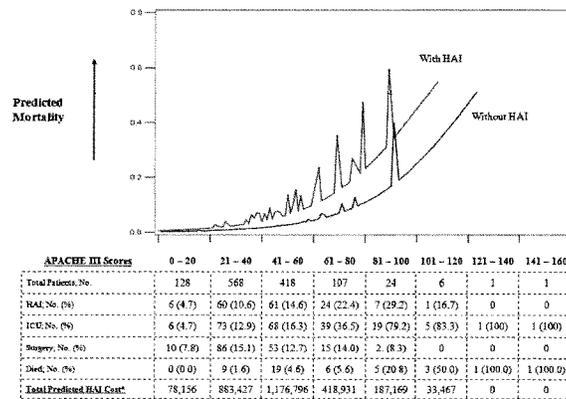


FIGURE 1. Outcomes for all patients by APACHE III score subgroup. The predicted mortality was calculated for each patient using parameter estimates from logistic regression models. The mortality predictors were APACHE III score, ARI, and development of HAI. This mean predicted mortality was plotted for patients in each APACHE III severity group. The table contiguous with the graph shows additional measured findings associated with each APACHE III subgroup: frequency and rates for HAI, ICU care, surgery, death, and attributable cost for HAI. *HAI cost: To calculate the total excess cost attributable to HAI for each APACHE III subgroup, the attributable cost for each specific infection that occurred among patients in that subgroup were summed. The HAI costs used were infection-site specific and adjusted using OLS regression for base intercept, APACHE III Score, Surgery, ICU care, and ARI. The total attributable medical cost using this cost method was \$2,777,946. HAI indicates healthcare-acquired infection; ICU, intensive care unit; ARI, antimicrobial resistant infection.

If overcrowded hospitals prevent infection, savings could be realized from both hospital cost accounting and societal economic standpoints. This is especially important now that Centers for Medicare and Medicaid Services have revised their rules to avoid extra payments for selected

HAIs.^{3,8-11} HAI significantly increases LOS. Hospitals that can effectively prevent HAI, will avoid providing excess hospital days that they will not get reimbursed for. Instead, they could offer earlier cancer treatment or semi-elective surgery that could potentially save life-years or improve

quality of life. They can also seek reimbursement for those services.

Limitations: Independent analysis is warranted to measure the impact of our excluded subgroups: pediatric, obstetric, trauma, and burn patients.^{4,23-25} Excluding patients with less than 6 ICD-9-CM codes means our findings may not be applicable to those less ill. However, many studies have similar limitations because eligibility is often restricted to ICUs, specific pathogens or infection sites.^{50,54-56} Another limitation was our inability to detect infections that arose after hospital discharge.⁵⁷ The HAI rates and infection sites also reflect a random sample from a single hospital in 1 year and the data are older. It is not clear how our sample patients compare with hospitalized patients elsewhere and this limited our ability to make national extrapolations. Even so, our costs are not far from the findings of others.^{6,35,36,54,56,58,59} We have also provided a comparison of different analytic techniques using the same dataset to help in the interpretation of future studies. Individual hospitals may apply geographic price indices and inflation rates to our total costs, or multiply their current cost per day by our attributable LOS, or use the semi-log proportional increases to make estimates that more closely match their own experience. As digital medical record technology advances, use of electronic data to complete multisite analyses will allow more timely evaluations and may make real-time cost-benefit studies feasible.^{58,60}

Hospital populations and new infection control interventions rapidly evolve. Different facilities may experience changing rates of HAI, ARI, and infection sites.^{5,13,31,50,61} Our intensive cost methods offered the opportunity to evaluate different cost perspectives and analysis methods for multiple infections in various hospital settings. We hope this report will assist decision makers in predicting potential savings from both enhanced general infection control⁶² and new technologies targeting specific infections, such as the 66% reduction in catheter-related bloodstream infections reported in Michigan ICUs.⁵⁵

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APPENDIX A

Definitions of Antimicrobial Resistant Organisms

Staphylococcus aureus

Methicillin resistant;
Vancomycin intermediate/resistant susceptibility.

Enterococcus (faecium, faecalis, Other)

Vancomycin intermediate susceptibility or resistant.

Escherichia coli

Fluoroquinolone intermediate/resistant susceptibility;
Cephalosporin third generation intermediate/resistant susceptibility.

Klebsiella pneumoniae

Cephalosporin third generation intermediate/resistant susceptibility.

Enterobacteriaceae; (Citrobacter, Enterobacter, Klebsiella, Proteus, E. coli, Morganella, Serratia)

Imipenem intermediate susceptibility or resistant;
Amikacin intermediate susceptibility or resistant.

Pseudomonas aeruginosa

Imipenem intermediate susceptibility or resistant;
Amikacin intermediate susceptibility or resistant.

Acinetobacter species

Imipenem intermediate susceptibility or resistant;
Amikacin intermediate susceptibility or resistant.



The NEW ENGLAND JOURNAL of MEDICINE

Perspective

The Savings Illusion — Why Clinical Quality Improvement Fails to Deliver Bottom-Line Results

Stephen S. Rauh, M.B.A., C.F.A., Eric B. Wadsworth, Ph.D., C.P.A., William B. Weeks, M.D., M.B.A., and James N. Weinstein, D.O.

It has become a core belief in U.S. health care that improving clinical quality will reduce health care costs. It seems intuitive that reducing readmissions, shortening lengths of stay, and building efficiency

into clinical processes will reduce resource utilization and thereby lower costs. Certainly, evidence suggests that there is no association between high quality and high costs.¹ Yet true bottom-line savings from improved clinical quality rarely materialize, and costs continue to climb. Manufacturing and service companies around the world have demonstrated the cost benefits of improving product quality and production efficiency. So why haven't nearly two decades of work on improving health care quality had a measurable effect on health care costs?

The explanation lies in the cost

structure of the typical health care setting. Its management and organization create a rigid cost structure that is relatively insensitive to small changes in patient volume, resource use, or the severity of patients' health conditions. This fixed-cost dilemma leaves most health care costs insensitive to changes in volume and utilization, so clinical quality improvements typically create additional capacity rather than bottom-line savings.² An examination of the different cost layers highlights the distinction between variable costs, such as supplies and medications, where reduced use produces true savings, and

fixed costs, such as facilities and ancillary services, where the costs persist despite reduced use.

To better understand the cost structure of health care delivery, it can be useful to consider how different costs behave depending on the degree to which they are sensitive to changes in resource utilization. The four cost layers we have identified are defined in the table.

Clinical improvements that reduce layer 1 costs, such as those of supplies and medications, will generally create bottom-line savings, since these are the only truly variable clinical costs in a hospital. To generate savings by reducing use of the resources that account for layer 2 costs, the need for the resource must be reduced enough to allow elimination of a payable unit. For instance, a single nursing unit might have to

Behavior of the Various Cost Layers in the Health Care System		
Cost Layer	Effects of Reduction in Use	Examples
Layer 1: truly variable costs of patient care	The item is not consumed, does not need to be replaced, and is available for later use.	Supplies, medications
Layer 2: semivariable costs of patient care	The item is not consumed, but the ability to repurpose the item is limited by time. Costs of providing the service may be reduced with sufficient reduction in volume.	Direct hourly nursing, respiratory therapists, physical therapists
Layer 3: semifixed costs of patient care	The item is not consumed, but the obligation to continue to pay for the item does not change.	Equipment, operating-room time, physician salaries, ancillary services
Layer 4: fixed costs not associated with patient care	Resource consumption is not altered in the short run but may be altered in the next operating cycle.	Billing, organizational overhead, finance

discharge multiple patients before any savings in hourly nursing labor costs could be captured by allowing an hourly employee to go home early. Reducing layer 3 resources — those for equipment, operating-room time, or physicians' salaries, for example — almost always produces additional capacity without bottom-line savings. If an intervention reduces operating-room time by 15 minutes, the costs of the equipment and salaried staff required to run the operating room do not change. Nonclinical layer 4 costs are primarily fixed in the short run, but reducing administrative labor costs by achieving administrative efficiency will produce true savings in future operating cycles.

Because of these cost behaviors, quality-improvement efforts that reduce lengths of stay or readmissions or increase radiology throughput do not create substantive bottom-line savings. They generally create capacity to treat additional patients. Similarly, efforts to expand the access of disadvantaged populations to primary care under the assumption that such access will be paid for through avoiding use of high-cost care sites — such as emergency departments — do not generate cost savings. The cost of

staffing and equipping an emergency department does not change if there are small reductions in utilization. Indeed, improved access will increase health care costs if new physicians and staff are hired to serve new patients in primary care practices.

Although capacity creation does not generate bottom-line savings, it does create an opportunity to admit another patient and collect additional revenue. Because health care costs are relatively fixed and do not change much at the margin, the cost of admitting a new patient is remarkably low, making volume growth a highly profitable strategy. Volume growth also can give the appearance of reducing costs, since the cost per case decreases when the high fixed costs are spread over a larger number of patients, although total costs will probably continue to rise. Growing volume and increasing revenue, rather than creating true bottom-line savings, are typically at the core of the business case for high-quality care.³

Because of the rigid cost structures, incremental reductions in resource use are unlikely to generate cost savings for either a health care setting or the health care system. The most meaningful way to achieve savings is to

focus on overall reductions in utilization rates for health care services and to eliminate the associated unnecessary capacity.

In a recent article, Kaplan and Porter argue that most health care costs are not fixed.⁴ Postulating that personnel costs can be adjusted and space reallocated on the basis of demand and patient mix, they suggest that cost behaviors are not responsible for the inability to generate cost savings, but “management inattention” is. Although we do not dispute this logic, its practical application is dependent on both procedure volume and the time horizon required for aligning resources with demand. High-volume procedures and treatments for which resource use can be standardized across the cycle of care and for which capacity can be readily adjusted to accommodate appropriate volume appear to be best suited to the aggressive cost management advocated by Kaplan and Porter. Presumably, lower-volume treatments and procedures would have to be consolidated regionally to be more amenable to effective cost management. Until that happens, the fixed-cost dilemma will remain an obstacle. Cost layering provides management with a framework for targeting chang-

es that will generate the most immediate savings.

Whereas quality improvement is producing significant benefits for patients, quality initiatives will continue to produce disappointing bottom-line savings as long as the capacity created is used to support growth in patient volume. As the U.S. health care system begins shifting its focus from volume to value, hospitals

will need to adapt their cost structures and capacity to accommodate lower per capita utilization rates as well as reductions in the per-episode intensity of care.

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Research

Original Investigation

Financial Impact of Surgical Site Infections on Hospitals The Hospital Management Perspective

John Shepard, MBA; William Ward, MBA; Aaron Milstone, MD, MHS; Taylor Carlson, BS; John Frederick, BS; Eric Hadhazy, MS; Trish Perl, MD, MSC

IMPORTANCE Surgical site infections (SSIs) may increase health care costs, but few studies have conducted an analysis from the perspective of hospital administrators.

OBJECTIVE To determine the change in hospital profit due to SSIs.

DESIGN Retrospective study of data from January 1, 2007, to December 31, 2010.

SETTING The study was performed at 4 of The Johns Hopkins Health System acute care hospitals in Maryland: Johns Hopkins Bayview (560 beds); Howard County General Hospital (238 beds); The Johns Hopkins Hospital (946 beds); and Suburban Hospital (229 beds).

PARTICIPANTS Eligible patients for the study included those patients admitted to the 4 hospitals between January 1, 2007, and December 31, 2010, with complete data and the correct *International Classification of Diseases, Ninth Revision* code, as determined by the infection preventionist. Infection preventionists performed complete medical record review using National Healthcare Safety Network definitions to identify SSIs. Patients were stratified using the All Patient Refined Diagnosis Related Groups to estimate the change in hospital profit due to SSIs.

EXPOSURE Surgical site infections.

MAIN OUTCOMES AND MEASURES The outcomes of the study were the difference in daily total charges, length of stay (LOS), 30-day readmission rate, and profit for patients with an SSI when compared with patients without an SSI. The hypothesis, formulated prior to data collection, that patients with an SSI have higher daily total costs, a longer LOS, and higher 30-day readmission rates than patients without an SSI, was tested using a nonpaired Mann-Whitney *U* test, an analysis of covariance, and a Pearson χ^2 test. Hospital charges were used as a proxy for hospital cost.

RESULTS The daily total charges, mean LOS, and 30-day readmission rate for patients with an SSI compared with patients without an SSI were \$7493 vs \$7924 ($P = .99$); 10.56 days vs 5.64 days ($P < .001$); and 51.94 vs 8.19 readmissions per 100 procedures ($P < .001$). The change in profit due to SSIs was \$2 268 589.

CONCLUSIONS AND RELEVANCE The data suggest that hospitals have a financial incentive to reduce SSIs, but hospitals should expect to see an increase in both cost and revenue when SSIs are reduced.

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E1

The US Health and Human Services Agency for Health-care Research and Quality states that health care-associated infections were the most common serious complication of hospital care in the United States in 2008.¹ The Centers for Disease Control and Prevention estimates that there are 45 million inpatient surgical procedures performed annually in the United States.² Approximately 20% of the estimated 2 million nosocomial infections in the United States each year are surgical site infections (SSIs)³ that have associated costs,⁴⁻²⁶ morbidity, and mortality.^{10,13,18-20,24-27} While most agree about the negative clinical outcomes associated with SSIs, there is little consensus on the financial ramifications to the hospital.^{24,27,28} The objective of this study was to estimate the change in hospital profit due to SSIs.

Methods

The study was authorized by The Johns Hopkins Hospital internal review board with a waiver of informed consent.

Definitions

We defined hospital cost as the financial amount a hospital spends to provide services. Hospital revenue is the financial amount earned through business operations. Hospital charges are the amount issued to the payers and patients. Real charges and costs are charges and costs adjusted for inflation. The admission All Patient Refined Diagnosis Related Group (APR-DRG) and complexity score are calculated based on the patient's present-on-admission diagnoses and other relevant characteristics.²⁸ The APR-DRG is a system used to stratify patients by resource use and has been used to classify patients for reimbursement purposes.²⁸ See eAppendix 1 in Supplement for supplemental definitions.

Outcome Variable

The primary outcomes of the study were the difference in daily hospital charges, intensive care unit (ICU) length of stay (LOS), floor LOS, 30-day readmission rate, and hospital profit for patients with an SSI when compared with patients without an SSI. Hospital charges were assumed to be a proxy for hospital cost; the terms will be used interchangeably. The daily charges were analyzed as a total and in 8 subcategories: room and board charges; operating room charges; pharmacy charges; radiology charges; laboratory charges; supply charges; therapy charges; and other charges. Using the Producer Price Index for hospitals from the US Bureau of Labor Statistics, all financial values referenced are measured in real dollars as of December 2010.²⁹

Patient Population

A retrospective study was performed at 4 of The Johns Hopkins Health System acute care hospitals in Maryland: Johns Hopkins Bayview, a 560-bed academic tertiary care center; Howard County General Hospital, a 238-bed tertiary care center; The Johns Hopkins Hospital, a 946-bed academic tertiary care center; and Suburban Hospital, a 229-bed tertiary care center. Billing, laboratory, and medical record data were compiled for pa-

tients admitted to the hospitals or having a surgical procedure, according to *International Classification of Diseases, Ninth Revision* procedure codes, between January 1, 2007, and December 31, 2010. Suburban Hospital's data were compiled for January 1, 2008, to December 31, 2010, only. The surgical procedures were identified using electronic health records.

Complete medical record review was performed by trained infection preventionists using National Healthcare Safety Network surveillance definitions to identify SSIs, as previously described.³⁰⁻³² Follow-up contact with the surgeon was used to increase the detection rate for SSIs at all the hospitals except The Johns Hopkins Hospital. Patients undergoing the following inpatient surgical procedures were included in the study³⁰:

- Nonpediatric coronary artery bypass graft chest and/or leg incision.
- Cesarean section.
- Colon surgery.
- Nonpediatric craniotomy.
- Hip prosthesis.
- Knee prosthesis.
- Nonpediatric laminectomy.
- Spinal fusion and refusion.

Eligible patients for the study included those patients with complete data and the correct *International Classification of Diseases, Ninth Revision* code, as determined by the infection preventionists. The data were stored in a Microsoft Access database.

Hypothesis Testing

The ICU LOS; floor LOS; daily total charges; daily room and board charges; daily operating room charges; daily pharmacy charges; daily radiology charges; daily laboratory charges; daily supply charges; daily therapy charges; and daily other charges were compiled for all patients. The daily hospital charges were calculated for each encounter by dividing the hospital charges by the patient's LOS. These continuous variables were used to test the hypothesis that the case patients, patients with an SSI, will have higher daily hospital costs, a longer LOS, and higher 30-day readmission rates than the control patients, patients undergoing the same procedure who did not contract an SSI.

For the procedures with a sample size of 25 or more, normality was tested using an Anderson-Darling test. If normally distributed, a nonpaired single-tailed Welch *t* test was used to test the hypothesis; otherwise, a single-tailed Mann-Whitney *U* test was used. For procedures with a sample size less than 25, a single-tailed Mann-Whitney *U* test was used to test the hypothesis. An analysis of covariance was also used to test the hypothesis while controlling for surgical procedure, admission APR-DRG, and admission complexity score. A Pearson χ^2 test was used to test the hypothesis that patients with an SSI will have a higher 30-day readmission rate. An α level of .05 was used. The statistical analysis was conducted using Minitab 16 Statistical Software (Minitab Inc) and SPSS (IBM).

Financial Analysis

For the financial analysis, a second control group was formed. This second control group comprised all patients admitted to

the health system during the study period who did not contract an SSI. The control group patients were grouped by their admission APR-DRG and complexity score. Eligible patients for the financial analysis were those patients with all required data available in their electronic health record; admission APR-DRG and complexity score were available only for patients admitted after June 1, 2007.

After being grouped by their admission APR-DRG and complexity score, the mean floor LOS, ICU LOS, and daily total hospital charges were calculated for each admission APR-DRG and complexity score present in the control group. The difference between the floor LOS, ICU LOS, and daily total hospital charges was taken between the case patients (patients with an SSI) and the average of the control patients (patients without an SSI who had the same admission APR-DRG and complexity score as the case patient).

The differences in floor and ICU LOS found in the previous step for all patients with an SSI were multiplied by the mean charge for a floor day and ICU day from the patient's respective hospital. Concurrently, the difference in daily total hospital charges found in the previous step was multiplied by the total LOS for all patients with an SSI. These results were used to provide an estimate of the change in revenue and cost, respectively, for the health system due to SSIs. The change in revenue minus the change in cost was calculated to estimate the change in health system profit due to SSIs.

Results

Over the study period, there were 399 627 inpatient admissions, 25 849 surgical procedures of interest, and 618 SSIs identified, resulting in an SSI rate of 2.76 per 100 surgical procedures. Twenty-two thousand three hundred seventy-eight procedures and 618 SSIs were eligible for the hypothesis testing while 348 445 inpatient admissions, 17 392 procedures, and 547 SSIs were eligible for the covariance and financial analysis. Fifty-one thousand one hundred eighty-two admissions, 4896 procedures, and 71 SSIs were not eligible for the covariance and financial analysis since their record did not contain the admission APR-DRG and complexity score (Table 1).

The daily total charges for patients with an SSI were \$7493 (95% CI, \$7101 to \$7884) vs \$7924 (95% CI, \$7788 to \$8060) for patients without an SSI ($P = .99$). The patients with an SSI had a mean LOS of 10.56 days (95% CI, 9.50 to 11.62) vs 5.64 days (95% CI, 5.34 to 5.95) for patients without an SSI ($P < .001$). After adjusting for surgical procedure, admission APR-DRG, and admission complexity score, there remained an increased LOS and lower daily total charges in patients with an SSI compared with those without SSIs (eAppendix 2 in Supplement). The 30-day readmission rate for patients with an SSI vs patients without an SSI was 51.94 vs 8.19 readmissions per 100 procedures (odds ratio, 12.12; 95% CI, 10.27 to 14.29) ($P < .001$). Among patients with an SSI, there were 321 patients with at least 1 thirty-day readmission and 402 thirty-day readmissions in total. Among patients without an SSI, there were 1782 patients with at least 1 thirty-day readmission and 2139 thirty-

Table 1. Number of Procedures Reviewed and SSIs Identified: 2007-2010^a

NHSN-Defined Surgical Procedure	No. of Procedures (% of Total)	No. of SSIs (% of Total)
Adult CABG	1985 (9)	66 (11)
Adult craniotomy	3829 (17)	99 (16)
Adult laminectomy	2553 (11)	45 (7)
Adult spinal fusion	4404 (20)	179 (29)
Adult spinal resection	542 (2)	12 (2)
Cesarean section	2607 (12)	110 (18)
Colon surgery	319 (1)	6 (1)
Hip prosthesis	2204 (10)	37 (6)
Knee prosthesis	3190 (14)	27 (4)
Pediatric spinal fusion or resection	743 (3)	37 (6)
Total	22 378 (100)	618 (100)

Abbreviations: CABG, coronary artery bypass graft; NHSN, National Healthcare Safety Network; SSI, surgical site infection.

^a Johns Hopkins Bayview, Howard County General Hospital, The Johns Hopkins Hospital, and Suburban Hospital.

day readmissions in total. The 547 patients with an SSI and eligible for the financial analysis had 2081 more hospital days (693 ICU days and 1389 non-ICU days) but lower daily total hospital charges of -\$132 (95% CI, -\$476 to \$212) ($P = .45$) when compared with patients without an SSI and the case patients' same admission APR-DRG and complexity score (Table 2).

If all 547 SSIs were eliminated, the data suggest that The Johns Hopkins Health System would experience a cost increase of \$9 124 029 (\$2 606 865.43 annually) and a billable capacity increase of 362 admissions (103 annually), equating to a revenue increase of \$11 392 618 (\$3 255 034 annually). Additionally, if it is assumed that payers refuse to reimburse for 30-day readmissions^b related to SSIs, then the elimination of SSIs would provide The Johns Hopkins Health System an increase in revenue of approximately \$21 288 486 (\$6 082 425 annually) over the study period by increasing their available billable capacity by 922 admissions (264 annually). The data suggest that the total change in profit over the period for the health system, if they eliminated all SSIs, would be \$2 268 589, \$12 164 457 if it is assumed 30-day readmissions would not be reimbursed (Table 3).

Discussion

While the topic of financial impact of SSIs may seem trivial, it is not. These infections can be a source of readmissions and a driver of hospital performance. Hence, hospitals have a mandate to improve patient care and safety, which requires infrastructure that can support interventions focused on decreasing adverse events such as SSIs. To support these interests, hospitals and their administrators need data to help balance budgets and support infection prevention and other groups focused on improving performance. Unfortunately, hospitals are failing to see the major reduction in their cost by reducing

Table 2. Metrics for Patients With or Without an SSI: 2007-2010*

Metric	Mean (95% CI)		P Value
	Patients With SSI	Control Patients	
LOS, d	10.56 (9.50-11.62)	5.64 (5.34-5.95)	<.001
ICU LOS, d	2.84 (2.28-3.41)	1.27 (1.21-1.33)	<.001
Non-ICU LOS, d	7.72 (7.01-8.43)	4.38 (4.32-4.44)	<.001
Total charges, \$	58 822 (43 352-74 292)	35 827 (36 348-35 305)	<.001
Daily total charges, \$	7493 (7101-7884)	7924 (7788-8060)	.99
Daily room and board charges, \$	1664 (1597-1730)	1639 (1627-1650)	.23
Daily operating room charges, \$	1271 (1169-1373)	1618 (1595-1641)	>.99
Daily pharmacy charges, \$	255 (206-304)	229 (217-240)	.15
Daily radiology charges, \$	293 (261-325)	320 (313-328)	.95
Daily laboratory charges, \$	334 (311-358)	307 (301-313)	.01
Daily supply charges, \$	2872 (2577-3167)	2739 (2690-2787)	.19
Daily therapy charges, \$	217 (202-231)	243 (239-246)	>.99
Daily other charges, \$	636 (573-700)	650 (635-664)	.69
30-d inpatient readmission rate per 100 procedures	51.94 (47.92-55.94)	8.19 (7.83-8.56)	<.001
No. of patients with at least one 30-d inpatient readmission	321	1782	NA
No. of 30-d inpatient readmissions	402	2139	NA

Abbreviations: ICU, intensive care unit; LOS, length of stay; NA, not applicable; SSI, surgical site infection.
* Mean real daily charges shown but Mann-Whitney nonparametric test used.

Table 3. Financial Impact of SSIs at The Johns Hopkins Health System: June 1, 2007, to December 31, 2010*

The Johns Hopkins Health System	\$			
	Change in Health System Cost if SSIs Are Eliminated	Change in Health System Revenue if SSIs Are Eliminated	Change in Health System Profit if SSIs Are Eliminated	Change in Health System Profit if SSIs Are Eliminated and 30-d Readmissions Not Reimbursed
Adult CABG	1 642 780	3 395 583	1 752 803	3 190 164
Adult craniotomy	1 746 906	2 423 582	676 676	2 362 416
Adult laminectomy	579 743	719 592	139 849	1 090 285
Adult spinal fusion	4 154 204	3 621 380	(532 824)	3 321 434
Adult spinal refusion	285 609	134 741	(150 868)	173 549
Cesarean section	(59 952)	740 045	799 997	950 064
Colon surgery	117 849	153 153	35 304	53 365
Hip prosthesis	228 855	39 693	(189 162)	636 957
Knee prosthesis	12 754	(3388)	(16 142)	350 419
Pediatric spinal fusion or refusion	415 281	168 236	(247 045)	35 803
Health system totals	9 124 029	11 392 618	2 268 589	12 164 457
Health system annual figures	2 606 865.43	3 255 034	648 168	3 475 559

Abbreviations: CABG, coronary artery bypass graft; SSI, surgical site infection.
* Admission All Patient Refined Diagnosis Related Group and complexity score available for patients admitted after June 1, 2007.

SSIs.¹² We attempted to rethink the approach to the financial calculations of SSIs and help demonstrate the financial ramifications associated with SSIs.

A number of previous publications have cited that the change in incidence of health care-associated infections is directly related to the change in hospital cost.^{3,11,19,26} This paradigm is the status quo and what much of the infection control and quality improvement community are basing their return on investment calculations on. The current method of calculating the change in hospital cost due to SSIs that we have observed most frequently is as follows. Assume patients with an SSI have costs of approximately \$79 134, and the average patient without an SSI had total hospital costs of approximately \$44 727. Taking the difference (\$79 134 - \$44 727), we derive

the cost savings of preventing an SSI as \$34 407. However, recent publications have challenged this paradigm.^{12,33} A recent article claims that quality improvement leads to improvements in profit for hospitals by creating additional capacity to treat patients, but quality improvement will not drastically alter the "typically rigid" hospital costs.³³ This is further supported by a publication citing that hospitals have high fixed costs, up to 84%.³⁴

The interpretation of cost often leads administrators and clinicians to confusion. The "lost opportunity to house new patients or increase capacity" will often be referenced appropriately by economists as a cost, an opportunity cost, but from a hospital administrator's or manager's perspective, this lost opportunity is not a cost, as previously defined, but rather a

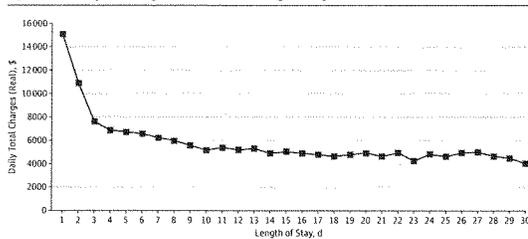
Table 4. Example to Demonstrate the Change in Hospital Cost, Revenue, and Profit With Respect to the Change in Prevalence of SSIs

SSI Rate, %	Assumed		Assumed Revenue per Admission, \$	Total Revenue, \$ ^a	Assumed Total Cost, \$	Total Profit, \$ ^c
	Mean LOS, d	Maximum No. of Admissions ^b				
0	5	500	30 000	15 000 000	12 500 000	2 500 000
25	6.25	400	30 000	12 000 000	12 500 000	(500 000)
50	7.5	333	30 000	9 990 000	12 500 000	(2 510 000)

Abbreviations: LOS, length of stay; SSI, surgical site infection.

^aMaximum No. of Admissions × Revenue Per Admission = Total Revenue.^b(25 Beds × 100 d)/Mean LOS = Maximum No. of Admissions.^cTotal Revenue – Total Cost = Total Profit.

Figure 1. Mean Daily Total Charges for a Patient vs the Length of Stay for the Patient



loss of potential revenue. This concept is illustrated in the following example.

For ease of calculation, assume a 25-bed unit has to plan a 100-calendar day budget with these factors:

- The 25-bed unit will have a 100% occupancy rate.
- The total cost for a bed day is fixed at \$5000 per bed, yielding the total cost for the unit of \$12 500 000 (\$5000 per bed × 25 beds × 100 days).
- All patients admitted have the same APR-DRG with reimbursement fixed at \$30 000 per admission.
- Patients with an SSI have a mean LOS of 10 days and patients without an SSI have a mean LOS of 5 days.

For a unit where 50% of the patients contract an SSI, the mean LOS will be 7.5 days, the maximum number of admissions will be 333, total revenue will be \$9 900 000, and total profit will be (\$2 510 000). However, if the SSI rate is 0%, the mean LOS will be 5 days, the maximum number of admissions will be 500, total revenue will be \$15 000 000, and total profit will be \$2 500 000 (Table 4).

Clarifying the semantics and concepts will provide administrators and clinicians the opportunity to understand their financial calculations. The method used under the current paradigm, as previously described, will provide the change in costs due to SSIs from the payer's perspective, not the hospital's perspective. For example, the data suggest a patient with an SSI will have an LOS of 10 days and total charges of approximately \$79 134. Assume that SSI was prevented. The data suggest that the LOS for the patient would decrease to 5 days and the patient would accrue a charge of \$44 727. The difference in charges, \$34 307, would be the amount that the payer, the

insurance company, or the patient would not have to expend. So, the payer would reduce their costs by \$34 307.

In the same situation where the SSI was prevented, the hospital would reduce their revenue by \$34 307 and would spend approximately \$34 307 less on the patient since they only cared for the patient for 5 days. However, the hospital has a bed that is now empty for 5 days. This bed cannot be instantly staffed or unstaffed, so there is a cost to keeping the bed. This leaves 2 possible scenarios: (1) the hospital closes the bed or (2) the hospital uses the 5 days of empty bed space and admits an additional patient, known as backfilling the bed.

In situation 1, the hospital can reduce their cost if they reduce SSIs. When an SSI is prevented, the hospital will not have a patient to backfill the bed, so the hospital can choose to lay off or repurpose the staff; sell the capital equipment; or eliminate all expenditure associated with the bed. The closing of the bed will lead to a reduction in hospital cost and increase hospital profit in the short term. In the long term, closing the bed will reduce the maximum possible revenue the hospital can receive since fewer beds will be available to patients.

In situation 2, the hospital may have the ability to backfill the bed if an SSI is prevented. Under a case-based payment system, the data suggest the hospital will receive additional revenue if an SSI is prevented, since the hospital could admit 2 patients at \$44 727 per case (\$89 454 total charges) instead of a single patient with an SSI at \$79 134 in charges. In this scenario, hospital revenue would increase when an SSI is prevented, but it is unclear how hospital cost is affected.

It was not surprising that patients with an SSI had higher total costs than patients without an SSI, but it was surprising

Figure 2. Equation to Determine Change in Profit Due to a Single Surgical Site Infection (SSI)

$$\left(\text{Change in Hospital Profit Due to 1 Preventable SSI} \right) = \sum_{i=1}^n \left\{ \begin{array}{l} \text{Change in Hospital Revenue} \\ \left(\frac{\text{Change in ICU LOS if 1 SSI Is Prevented}}{\text{ICU LOS}} \times \left(\frac{\text{Revenue per ICU Day}}{\text{Revenue per ICU Day}} \right) + \frac{\text{Change in Non-ICU LOS if 1 SSI Is Prevented}}{\text{Non-ICU LOS}} \times \left(\frac{\text{Revenue per Non-ICU Day}}{\text{Revenue per Non-ICU Day}} \right) \right) \\ - \left(\frac{\text{Change in Daily Hospital Cost if 1 SSI Is Prevented}}{\text{Daily Hospital Cost}} \times \left(\frac{\text{LOS for a Patient With an SSI}}{\text{LOS for a Patient With an SSI}} \right) - \frac{\text{Cost to Obtain Backfill Patients}}{\text{Cost to Obtain Backfill Patients}} - \frac{\text{Cost of Intervention That Prevented SSI}}{\text{No. of SSIs Prevented by Intervention}} \right) \\ \text{Change in Hospital Cost} \end{array} \right.$$

The equation is used for all *i* SSIs. The results must be summed for all *i* SSIs to derive the total change in profit for the health system or hospital due to SSI. ICU indicates intensive care unit and LOS, length of stay.

Figure 3. Equation to Determine Change in Profit Due to a Single Surgical Site Infection (SSI), Assuming That Payers Will Not Reimburse for Related 30-Day Readmissions

$$\left(\text{Change in Hospital Profit Due to 1 Preventable SSI} \right) = \sum_{i=1}^n \left\{ \begin{array}{l} \left(\frac{\text{Change in ICU LOS if 1 SSI Is Prevented}}{\text{ICU LOS}} \times \left(\frac{\text{Revenue per ICU Day}}{\text{Revenue per ICU Day}} \right) + \frac{\text{Change in Non-ICU LOS if 1 SSI Is Prevented}}{\text{Non-ICU LOS}} \times \left(\frac{\text{Revenue per Non-ICU Day}}{\text{Revenue per Non-ICU Day}} \right) \right) \\ - \left(\frac{\text{Change in Daily Hospital Cost if 1 SSI Is Prevented}}{\text{Daily Hospital Cost}} \times \left(\frac{\text{LOS for a Patient With an SSI}}{\text{LOS for a Patient With an SSI}} \right) - \frac{\text{Cost to Obtain Backfill Patients}}{\text{Cost to Obtain Backfill Patients}} - \frac{\text{Cost of Intervention That Prevented SSI}}{\text{No. of SSIs Prevented by Intervention}} \right) \\ + \left(\frac{\text{ICU LOS for 30-d Readmission Not Reimbursed}}{\text{ICU LOS}} \times \left(\frac{\text{Revenue per ICU Day}}{\text{Revenue per ICU Day}} \right) + \frac{\text{Non-ICU LOS for 30-d Readmission Not Reimbursed}}{\text{Non-ICU LOS}} \times \left(\frac{\text{Revenue per Non-ICU Day}}{\text{Revenue per Non-ICU Day}} \right) \right) \end{array} \right.$$

The equation is used for all *i* SSIs. The results must be summed for all *i* SSIs to derive the total change in profit for the health system or hospital due to SSI. ICU indicates intensive care unit and LOS, length of stay.

that patients with an SSI had lower daily costs (Figure 1). The data suggest that the reduction of SSIs will decrease the hospital's mean LOS, which could lead to an increase in daily total hospital cost and hence an increase in total hospital cost.

The Equation

We propose that the change in hospital profit due to the prevention of 1 SSI can be described in the equation in Figure 2. This equation can be summed across *i* patients with an SSI in the health system/hospital to determine the change in profit.

We calculate the change in hospital cost and revenue by stratifying by the admission APR-DRG and complexity score, as previously described. We then subtract the cost to obtain the backfill patients. This cost will vary widely because some hospitals have easy access to additional market share, making this cost low, where other hospitals will need to embark on a costly marketing campaign to attract additional customers. We then subtract the cost of the intervention that prevented the SSI. The cost of the intervention is divided by the number of SSIs prevented because the cost should be distributed equally across all the SSIs prevented. We then add the missed reimbursement if payers refused to reimburse for 30-day readmission related to SSIs (Figure 3).

Taking the difference between the change in hospital cost and hospital revenue due to preventing a single SSI, we sum across all *i* SSIs to derive the change in hospital profit due to SSIs. The data in this study suggest that the net loss in profits due to SSIs for The Johns Hopkins Health System was be-

tween \$4147 and \$22 239 per SSI, not accounting for the cost to backfill patients or the cost of the intervention to prevent the SSIs.

Limitations

This study had a couple of limitations. First, hospital charges were assumed to be an accurate proxy for hospital costs. This is not a suggested method, but the study was conducted in the state of Maryland, which was assumed to provide an accurate proxy given Maryland's all-payer reimbursement system. Second, a time-dependent bias, as described by Barnett et al,²⁵ can lead to overestimating the financial impact of SSIs. We adjusted for the time-dependent bias by selecting controls with the same admission APR-DRG and complexity score as the case patients for the financial analysis, but more accurate methods may be available.

Conclusions

Clinicians can spur hospital executives to invest in costly interventions or technology aimed at the reduction of SSIs by providing a cost-benefit analysis. When conducting such an analysis, the use of proper financial terminology is crucial. With the increasing need for additional infection prevention initiatives, which tend to require additional funding, clinicians must take care in presenting accurate financial figures to maintain the financial well-being of health care institutions and pro-

more the safety of patients. Infection control and quality improvement professionals can use the equation given in Figure 2 to develop interventions that they project are cost appropriate. Payers should look to withhold reimbursement for SSI-related readmissions, as this makes SSI prevention more cost-effective.

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Hospital-acquired, laboratory-confirmed bloodstream infections: linking national surveillance data to clinical and financial hospital data to estimate increased length of stay and healthcare costs

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SUMMARY

This matched cohort study estimates the effect of hospital-acquired bloodstream infection (HA-BSI) on length of stay (LOS) and costs during hospitalisation of 1839 patients (age range <1 to >80 years) gathered from 19 acute hospitals in Belgium. A second objective was to evaluate the impact of the choice of matching criteria. Data from national surveillance of HA-BSI were linked to hospital administrative discharge data, with respect for the patients' right to confidentiality of their health record. Controls were identified based on a set of matching factors: hospital, All-Patient Refined Diagnosis Related Groups, age, principal diagnosis, Charlson Comorbidity Index and time to infection. The results showed that, depending on the choice of matching factors, the estimation of additional LOS decreased from 26 to 10 days, with the most critical factor being the time to infection. The additional LOS attributable to HA-BSI was 9.9 days [95% confidence interval (CI): 7.8, 11.9]. The additional cost per infection was €4900 [95% CI: €4035, €5750]; 58% of those costs were due to LOS, 10% were due to antibiotics, 10% due to other pharmaceutical products and 15% were due to billed medical acts. The main conclusion is that laboratory-confirmed HA-BSIs increase the LOS by 10 days for patients surviving the infection, and that the time to infection plays a crucial role in this estimation.

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Introduction

One out of ten hospital-acquired infections (HAIs) is a bloodstream infection (BSI).¹ BSI, along with hospital-acquired pneumonia, is associated with high mortality and increased healthcare costs.^{1,2} This justifies specific BSI surveillance in high risk settings such as intensive care units in many European countries and in the USA, and hospital-wide (for all hospital wards) in some countries such as Belgium.^{3–5}

Numerous infection control measures exist to prevent BSI, but these measures have their associated costs.⁶ The first step to help decision-makers to choose and implement the most cost-effective strategies is to accurately quantify infection costs. The increase in

hospital length of stay (LOS) is frequently used as endpoint, because it is easily translated into monetary values in each country by applying the local cost of one day of hospitalisation (per-diem cost).^{7,8}

Matched cohort studies have been widely used to estimate the extra LOS and costs attributable to hospital-acquired bloodstream infections (HA-BSIs).^{7–13} Obviously, studies with different matching factors produce different results, and the more matching factors used, the smaller the effect of HAL.¹⁴ This hampers the comparison between studies. Also, most studies are conducted in a single centre, so it is difficult to assess whether the results can be generalised to other institutions.

These reasons motivated us to perform a study to estimate the attributable effect of HA-BSI on hospital LOS and on associated healthcare costs, in a large sample of hospitals participating in the Belgian national surveillance of those infections. Furthermore, we evaluated the influence of the choice of different matching factors on the estimate, including the time to infection, as used in some

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recent studies.^{7,8,10,11} In this study we linked the national surveillance data to the hospital clinical and administrative discharge data. To our knowledge this is one of the first studies of this kind in Europe.

Methods

Definitions of laboratory-confirmed HA-BSI

In Belgium, HA-BSIs are the subject of an ongoing specific surveillance in the National Surveillance of Infections in Hospitals program (NSIH).¹⁵ Data are gathered from all wards, including intensive care units (ICUs), in hospitals participating voluntarily in the NSIH surveillance programme. This study used data from the 19 hospitals which participated a full year (2003) in this programme. All age groups are included in this study (adults and children) in order to obtain a representative sample of the total population of patients infected by HA-BSI.

The NSIH programme definitions are based on international guidelines and are compatible with those used by the majority of HAI surveillance networks in Europe: all patients with a laboratory-confirmed BSI that was not present or incubating at the time of admission to the acute care setting should be reported.^{16,17} For most bacterial nosocomial infections, this means that the infection usually becomes evident 48 h (i.e. the typical incubation period) or more after admission. The definition takes into account the pathogenicity of the isolated micro-organism and the patient's clinical situation together with the nosocomial character of the infection. Laboratory-confirmed BSIs are defined as catheter-related if the patient had a central venous catheter in the 48 h preceding the infection and the same micro-organism was isolated from the catheter tip. A BSI is considered as primary if it cannot be traced back to any other site of infection, and includes the catheter-related BSI. Secondary BSI is defined as BSI due to a documented infection with the same organism present at a specific body site. The full methodology is described in the NSIH corresponding protocol.¹⁵

Hospital administrative discharge databases (clinical and financial data)

The Hospital Clinical Database (HCD) is an administrative database with data from all inpatient stays discharged from all Belgian hospitals. It contains demographic data, LOS, in addition to all diagnoses and procedures coded with the ICD-9 (International Classification of Diseases, 9th revision) and classified by All-Patient Refined Diagnosis Related Group (APR-DRG, version 15th grouper). The Hospital Financial Database (HFD) gathers the inpatient claims data provided by the hospitals to the health insurers. This database gives information on the reimbursed resources used during the stay (medical acts, medical supplies, pharmaceutical products). For each hospital stay, the HCD and HFD data are linked so that tracing the patients' medical history and the corresponding full cost of hospitalisation becomes possible, including the price of one hospitalisation day, which was on average €285 in 2003 in Belgian acute hospitals (per-diem price not counting treatment and drugs), as published by the National Institute for Health and Disability Insurance.

Coupling the infection data with administrative data

The infection control physician of each hospital sent the HCD identifier of the patients with HA-BSI to the central administration where the HCD was linked to the HFD. The linked data were provided to the authors after encryption of the patient's

identification by a trusted third party. The use and linking of these data were approved by the Belgian Privacy Commission.¹⁸

Study design and the choice of matching factors

The matching factors chosen in a matched cohort study should be real confounders: they should correlate both with the risk of HA-BSI (or in general the risk of HAI) and with the outcome (LOS). However, they should not be influenced by complications occurring during the stay, or by direct consequences of the infection. In our study, we selected control patients based on different sets of matching factors, always in a 1:1 ratio, and we assessed the variability of the different estimations.

Hospitals are considered as a confounding factor, as they tend to vary in infection rates and in LOS.¹⁹ Controls were thus selected from the same hospital as the cases.

The APR-DRG classification system was specifically designed to predict the costs, and was also shown to predict differences in HAI risks.¹⁴ Controls were selected in the same APR-DRG as cases.

Age does not per se predict costs, disease severity does. However, in the absence of information in administrative databases on disease severity and on patient's frailty, age is used as a proxy of many unobserved confounders. Sex was not used as a matching factor because there is no evidence that it predicts HA-BSI nor cost.²⁰

Principal diagnosis was used because of the wide variety of reasons for hospitalisation within the same APR-DRG. Controls were selected with the same principal diagnosis (reason for hospitalisation) as the case, coded with ICD-9 at the three-digit level.

The Charlson Comorbidity Index (CCI) is a validated score predicting one-year mortality, based on comorbidities available in HCD.²¹ The CCI is the sum of several predefined weights attributed to some specific conditions. The higher the CCI score, the higher the probability of one-year mortality. We defined four categories of CCI (0, 1–2, 3–4 and >4) and controls were selected from the same category as the cases. The CCI has been used previously to predict BSI mortality, and also to predict costs.^{22,23}

The time to infection is not a real matching factor, but is an important variable to define the pool of control patients. Controls were selected so that their LOS was at least equal to the time from admission to HA-BSI diagnosis of the cases (minus two days to allow for incubation time). This avoids the matching of cases infected after a long stay with controls staying hospitalised for a short period. Time to infection may thus be a proxy of the patient's frailty, the severity of the disease and the quality of care.^{24,25}

Statistical analyses

When available, one control patient was selected for each case (1:1 matching ratio). The difference in LOS and costs for each case–control pair was computed, and the additional LOS and costs were computed as the mean of these differences. To test whether the additional LOS attributable to HA-BSI was consistent across different baseline characteristics, subgroup analyses were performed. The interaction between the subgroup and the additional LOS was tested with an *F*-test in an ANOVA model.

Results

Description of patients with laboratory-confirmed HA-BSI

The 19 participating acute hospitals provided data on 1839 patients which were coupled with hospital clinical and financial

Table I
Characteristics of patients infected by a laboratory-confirmed, hospital-acquired bloodstream infection (N = 1839)

Age (years) [mean (median)]	66.9 (72.0)
Range	<1–101
Male [N (%)]	1070 (58.2)
Charlson Comorbidity Index [mean (median)]	3.1 (2.9)
Time to infection (days) [mean (median)]	18.9 (13.0)
Range	2–207
Length of stay [mean (median)]	42.6 (33.0)
In hospital mortality [N (%)]	585 (31.8)
Ward [N (%)]	
Intensive care unit	403 (21.9)
Internal medicine	278 (15.1)
Geriatric ward	233 (12.7)
Oncology	189 (10.3)
Other	736 (40.0)
Origin of infection [N (%)]	
Catheter-related	415 (22.6)
Secondary	826 (44.9)
Unknown	598 (32.5)

data (Table I). Patients' ages ranged from <1 to 101 years, with 51 patients (2.7%) aged <18 years. Half of the patients were aged ≥72 years. The median time to infection was 13 days, with 1332 patients (72.4%) infected within the first three weeks of their hospital admission. The most prevalent micro-organisms (prevalence >5%) were *Escherichia coli* (18.2%), *Staphylococcus aureus* (11.3%), *Pseudomonas aeruginosa* (5.3%) and *Candida albicans* (5.1%).

Selection of controls and the influence of matching factors on estimates of LOS attributable to HA-BSI

A total of 109 924 control patients were available for analysis. The impact of the matching criteria on the estimation of the additional LOS was huge as expected (Table II). If cases and controls were matched only for hospital and APR-DRG, HA-BSIs were estimated to increase the LOS by 26 days. When comorbidity measures and primary diagnosis were also taken into account this difference decreased to 21 days. The variable with the biggest impact on this

difference was the time to infection. If each control patient was chosen so that his/her LOS was at least as long as the time to the infection (minus 2 days to allow for incubation time) of the HA-BSI patient, the difference decreased to 6.7 days. It is important to note that the more matching criteria used, the lower was the percentage of patients included in the analysis (from 99.4% to 50.4%). In addition, the use of more matching factors also resulted in shorter LOS of cases included in the analysis (from 42.5 days with two matching factors to 32.2 days with six matching factors). When only surviving patients (cases and controls), were matched, the mean difference in LOS was 9.9 days (95% CI: 7.8, 11.9).

The prolongation of hospitalisation due to HA-BSI on the whole sample appeared to be consistent between the different age groups, the origin of the infection (primary, secondary) and the reporting service, as none of those *P*-values for subgroup by LOS interaction reached statistical significance (these results are available on request): age (*P* = 0.404), origin of infection (*P* = 0.823), and reporting service (*P* = 0.202). A larger effect of HA-BSI was observed for infections starting more than 3 weeks after hospitalisation (attributable LOS: 17.6 days; for time to infection effect: *P* = 0.040; Table II).

Costs attributable to HA-BSI

The average cost per hospital day (per-diem price) in acute Belgian hospitals was €285 in 2003. Each case of HA-BSI resulted in an additional €4893 (95% CI: €4035, €5750); 58% of this additional cost was due to the per-diem expenses (LOS), 20% was due to pharmaceutical products (half of which was due to antibiotics), 15% was due to medical acts, and 2.4% was due to in-vitro laboratory tests, taking into account the lump sums only (Table III).

Discussion

The effect of HA-BSI on LOS and cost is significantly reduced after correction for the many variables have an impact on the outcomes. This is confirmed by our results, based on a large sample of patients with a well-documented (laboratory-confirmed) HA-BSI, and an

Table II
Impact of matching criteria on estimation of additional length of stay, and subgroup analysis by time to infection

Matching criteria	% of cases matched	N	Length of stay (days)				
			Patients infected with HA-BSI (cases)		Patients not infected with HA-BSI (controls)		Mean difference
			Mean	(SD)	Mean	(SD)	
On patients' characteristics							
Hospital DRG	99.4	1828	42.5	(35.4)	16.8	(22.6)	25.8
Hospital DRG age	98.4	1810	42.5	(35.5)	17.0	(21.6)	25.5
Hospital DRG age PD	78.5	1444	39.4	(33.0)	15.7	(19.0)	23.7
Hospital DRG age PD CCI	62.4	1148	37.9	(33.0)	16.9	(21.5)	21.0
On patients' characteristics and time to infection (minus 2 days for incubation period)							
Hospital DRG age time	89.2	1640	39.6	(32.5)	30.5	(29.1)	9.1
Hospital DRG age PD time	65.1	1198	34.8	(28.7)	27.1	(27.1)	7.8
Hospital DRG age PD CCI time	50.4	926	32.2	(26.4)	25.5	(27.1)	6.7
Survivors only: on patients' characteristics and time to infection (minus 2 days for incubation period)							
Hospital DRG age PD CCI time	53.0*	665	32.6	(27.9)	22.8	(22.8)	9.9
Infection started							
during week 1	–	271	21.1	(18.1)	13.6	(14.4)	7.6
during week 2	–	219	31.0	(21.7)	21.4	(14.9)	9.6
during week 3	–	104	43.7	(30.1)	32.6	(31.1)	11.1
after week 3	–	71	65.5	(38.6)	48.0	(29.7)	17.6

HA-BSI, laboratory-confirmed hospital-acquired bloodstream infection; DRG, All-Patient Refined Drug Related Group; PD, principal diagnosis; CCI, Charlson Comorbidity Index.

* Percentage based on 1254 survivors.

Table III
Additional costs attributable to laboratory-confirmed hospital-acquired blood-stream infections (HA-BSIs)

	Costs (€)					
	Patients infected with HA-BSI (cases) N = 665		Patients not infected with HA-BSI (controls) N = 665		Mean difference	
	Mean	SD	Mean	SD	Mean	%
Total cost of stay	15 952.6	12 639.5	11 059.8	10 233.4	4892.8	100%
Cost per diem	9224.8	7896.6	6397.3	6087.3	2827.6	57.8%
Pharmaceuticals						
Antibiotics	904.2	1501.4	424.0	1494.7	480.2	9.8%
Other	1538.3	2297.0	1033.7	2215.6	504.6	10.3%
Billed medical acts	3132.1	3036.7	2389.8	2363.9	742.3	15.2%
In-vitro laboratory tests	268.7	283.6	151.3	191.3	117.4	2.4%
Other	884.3	1832.7	663.7	1473.2	220.6	4.5%

even larger pool of control patients, selected from the existing Belgian administrative databases. The more matching variables included, the smaller the increase in LOS and associated health insurance costs observed. The inclusion of the LOS preceding the HA-BSI was an important factor. After this correction, our final estimate of 10 extra days in hospital after HA-BSI is lower compared with the 21 days published by researchers on Belgian data, in a study which matched only for the APR-DRG.⁹ The estimation of 21 additional days due to HA-BSI is very similar to our initial estimate of 25 days using the same set of matching factors. Our final estimate of 10 days lies in the low range of all estimates found in previous studies, and is, to our knowledge, the first one on such a large sample.^{7–13}

The common limitation of matched cohort study applies here: the necessary trade-off that has to be found between internal validity (many matching factors on a small subset of patients) and external validity (a few matching factors on a large subset of patients). We tried to ensure that the more extensive matching efforts did not lead to the exclusion of too many cases and therefore guarded the external validity of the study. Still, we could only find appropriate controls for half of the patients infected. Other recent statistical methods avoid such a pitfall but require extensive daily measurements, which are seldom available in all hospital wards for a study of that size.^{26,27} Another limitation of the current study is that it is partially based on administrative databases, and hence it inherits their usual deficiencies: the lack of consistency and completeness of coding, the lack of some clinical parameters, inconsistencies in data that can be hardly validated (because of the labour intensity of verifying large multicentre retrospective data).

The use of an administrative database is nonetheless also one of the strengths of this study, as it allowed selecting good matches from a wide pool of control patients. Detailed cost data were also directly available for all controls (no additional data collection was needed). Moreover, the large sample of infected patients was identified directly from a surveillance programme, without using the administrative databases. All infections were thus laboratory-confirmed, and no selection bias was introduced by applying some detection algorithm on the administrative database. Important characteristics, such as the time and origin of infection, were also available, and were used to assess the consistency of the main results across different patients and infection characteristics.

In conclusion, this study, which is based on a large sample of hospitals and patients, shows that laboratory-confirmed HA-BSIs increase the hospitalisation LOS by 10 days for patients surviving the infection. It is also an example of an innovative linking of separate healthcare databases from different national

organisations, which can be performed while fully respecting the patient's right to confidentiality of his/her health record. Such privacy-controlled linking can create large amounts of enriched data in future research projects.

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Conflict of interest statement

None declared.

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