BRINGING INNOVATION TO PATIENT CARE WORLDWIDE

AdvaMed
Advanced Medical Technology Association

The Value of Diagnostics: The Impact of Hospital Antimicrobial Susceptibility Testing

MEDICAL TECHNOLOGY
PROGRESS YOU CAN SEE

The Value of Diagnostics: The Impact of Hospital Antimicrobial Susceptibility Testing

Author:
Frank R. Lichtenberg
Columbia University and
National Bureau of Economic Research
Columbia University
614 Uris Hall, 3022 Broadway
New York, NY 10027

Prepared for
The Advanced Medical Technology Association

March 2008

The Value of Diagnostics: The Impact of Hospital Antimicrobial Susceptibility Testing

Abstract

The number of U.S. hospital discharges in which there was a diagnosis of infection with drug-resistant microorganisms increased more than one hundred-fold between 1993 and 2005. Among the concerns over drug-resistant microorganisms is the rapid increase in the incidence of such infections acquired by patients within the hospital or healthcare setting. Infectious disease experts have argued that tests that reveal the susceptibility of the infecting agent (pathogen) to antimicrobial agents can allow physicians to administer more appropriate and effective treatments. Further, experts also suggest that such tests are essential in identifying healthcare-acquired infections and bringing them under control, with resulting positive patient outcomes, savings in costs, and improved quality.

In this paper, we perform an econometric analysis of the impact of antimicrobial susceptibility testing on the survival, length of stay, and treatment costs of inpatients with staphylococcal infections, based on a large sample of U.S. hospital admissions during 2004 – 2005. We test the hypotheses that patients infected with staphylococci in the hospital inpatient setting whose pathogens were isolated and tested for antimicrobial susceptibility had lower hospital mortality rates, length of stay, and overall treatment costs than patients whose isolates were not tested, controlling for a number of indicators of the nature and severity of illness.

The analysis is performed using data on two different patient populations:

1. Patients with a secondary diagnosis related to a Staphylococcal infection; and
2. Patients with any infectious & parasitic disease diagnosis (primary or secondary)

The analysis indicates that, within both populations, infected patients whose etiologic agent (pathogen) was tested for antimicrobial susceptibility had significantly lower inpatient mortality rates, lengths of stay, and overall treatment costs than infected patients whose pathogens were not tested, controlling for principal diagnosis, number of diagnoses, number of procedures, age, and sex.

- Among patients in the first group—patients with a secondary staphylococcal infection diagnosis – those who had isolates tested for antimicrobial susceptibility had 52% lower probability of death before discharge, 17% lower mean length of stay (-1.8 days), and 22% lower cost than those who did not. Antimicrobial testing in this group was associated with $6,978 lower cost per discharge. The potential aggregate cost reduction from antimicrobial susceptibility testing of isolates from all patients hospitalized with this diagnosis in 2005 was $8.3 billion.

- Among the patients in the second group—patients with any infectious & parasitic disease diagnosis—those who had isolates tested for antimicrobial susceptibility had 30% lower probability of death before discharge, 26% lower mean length of stay (-1.8 days), and

36% lower cost than those who did not. Antimicrobial susceptibility testing in this group is associated with $7,524 lower cost per discharge.

It is possible that the overall quality of care received by patients who had isolates tested for antimicrobial susceptibility was better than the overall quality of care received by patients who did not, and that part of the observed differences in mortality, length of stay, and cost are due to unobserved differences in treatment quality. But since the differences in outcomes and expenditure are so large relative to the cost of testing, administering antimicrobial susceptibility tests would be worthwhile even if it accounted for a very small fraction of the observed differences in mortality, length of stay, and cost.

Frank R. Lichtenberg, Ph.D.
Courtney C. Brown Professor of Business
Columbia University
614 Uris Hall
3022 Broadway
New York, NY 10027
Phone: (212) 854-4408
frank.lichtenberg@columbia.edu

INTRODUCTION

The incidence of multi-drug resistant infections has increased rapidly in the U.S. and other countries in recent years. Data from the Healthcare Cost and Utilization Project's Nationwide Inpatient Sample (http://hcupnet.ahrq.gov) indicate that the reported number of U.S. hospital discharges in which there was a diagnosis of infection with drug-resistant microorganisms (ICD9 code series V09) increased more than one hundred-fold between 1993 and 2005, from 3,000 to 394,000. (See Figure 1.) In 2005, just over one percent of patients discharged from hospitals had been diagnosed with infection with drug-resistant microorganisms.

Staphylococcus aureus, a highly virulent pathogen, is an example of an infectious agent in which drug resistance has become a serious problem. The widespread prevalence of methicillin resistant *S. aureus* (MRSA) in healthcare systems, the emergence of MRSA in community-acquired infections as well as the emergence of strains with reduced susceptibility to vancomycin have created a significant challenge for treatment of infected patients. The increasing incidence of resistant infections has raised concerns about both the short and long-term impact on health and health care costs. This has given new attention to the tools and technologies for identifying and addressing these infections.

A variety of medical tests identify infections caused by multi-drug resistant organisms, providing physicians with information they can use in selecting and administering appropriate treatment and interventions. One example is testing to identify multi-drug resistant organisms (MDROs) acquired within the hospital, thus enabling providers to take action to limit or stop their spread.

Infectious disease experts have asserted that such tests can improve care for patients and reduce costs--especially critical at a time when antibiotic resistance is becoming more serious in managing infectious disease and at a time in which controlling hospital-acquired infections has gained new urgency. When there is significant uncertainty about whether a patient's pathogen is resistant, rather than susceptible, to antimicrobial agents, tests that reveal the susceptibility of the pathogen can allow physicians to administer more appropriate and effective treatments. Moreover, the emergence of new, rapid and highly accurate diagnostic technologies has provided a potential opportunity for healthcare to move from the traditional approach of providing broad-

spectrum antibiotic therapy to patients with any infection, to a more focused, specific treatment based on a linkage between the actual characteristics of the targeted organism and the antibiotic drug that is most suitable to eliminate it.

Methicillin Resistant *S. aureus* (MRSA)

Of recent public health concern are patients who acquire a multi-drug resistant infection while they are in the hospital or other health care facility. Such infections are often referred to as healthcare-acquired infections (HAIs). Patients are typically exposed to these infections by transmission from contaminated healthcare workers' hands, clothing, or other devices, contaminated equipment, patient-to-patient contact, dirty bed linens, catheter insertion and maintenance practices, etc.

HAIs, including MRSA, are a major cause of death and medical complications around the world. In the U.S., infections contracted in hospitals are the fourth leading cause of death. According to the Centers for Disease Control and Prevention, an estimated 90,000 people die as a result of HAIs each year.

In addition to the toll on individuals and their families, HAIs result in a heavy financial burden on the U.S. health care system. These infections are estimated to add $30 billion to the nation's health care cost each year and are associated with significant increases in hospital stays and costs of additional treatment. Infections also affect worker productivity and increase employer disability and healthcare costs.

Of particular concern are infections caused by multi-drug resistant organisms (MDROs) such as MRSA, vancomycin-resistant enterococci (VRE) and certain gram-negative bacilli (GNB). People infected with MDROs are more likely to have longer and more expensive hospital stays (Hartemann-Heurtier et al (2004)), and may be more likely to die as a result of their infection. It is no surprise that MDROs, such as MRSA, have been featured prominently in the news media and their prevention and control is a national priority.

A variety of medical tests are used to detect and characterize infections in order to guide therapy and control measures. Results from these tests allow medical providers to take actions that isolate or limit spread of MDROs, as well as monitor the effectiveness of such efforts. Such actions are important across hospital populations. For patients who are infected with multi-drug

resistant organisms, these tests aid in treatment and management of infections. For patients who are colonized with such organisms, the tests provide information that will dictate decisions to decolonize and/or guide the choice of empiric antibiotics if the patient subsequently demonstrates signs or symptoms of infection. For other patients who have not yet been affected, such tests may be used to establish preventive, quarantine, and monitoring measures.

These infections are often identified using microbiological cultures. These are tests in which the etiology of the infection is determined by taking a specimen from the individual patient and then inoculating it into a variety of nutrient-rich materials in the laboratory. Culture-based tests typically require from 24 to 48 hours to isolate and identify the infecting agent (pathogen) and to determine drug resistance and susceptibility. Given this timeframe, antibiotic treatment often begins before the culture and susceptibility test results are available, and patients may need to be isolated until the test results are shown to be negative for MDROs.

There are also newer, rapid tests that utilize molecular-level methods to identify the presence of select, specific microorganisms, reducing detection time to a matter of a few hours.[1] This type of testing can provide results for select pathogens in real time, near patient entry to a facility, allowing treatment to be specifically tailored to the patient's particular infection. Rapid tests also create the potential to isolate only those patients who test positive (those who are either colonized or infected) for MDROs.[2]

As these newer tests largely were unavailable at the time the data for this study were generated, the results of this analysis do not reflect the newer technologies. However, it is important to note that any incremental value derived from the rapid technologies would function as a multiplier of values assessed for the traditional paradigm (the results of this analysis), and likewise, any incremental costs of new technologies above traditional technologies should be compared against such gains.

[1] See Cai et al (2007).

[2] It is important distinguish between isolation/identification of a pathogen and determination of antimicrobial drug susceptibility. Most rapid tests are geared toward identifying a pathogen (eg stain for *Legionella*, tests for rotavirus or RSV, molecular tests for influenza or Gr A streptococci). Only a very few are geared toward rapidly identifying the agent AND a specific resistance pattern (eg. test for MRSA)

METHODS

In this paper, we will present an econometric analysis of the impact of antimicrobial susceptibility testing on the survival, length of stay, and treatment cost of inpatients with staphylococcal infections, based on a very large sample of U.S. hospital admissions during 2004-2005. We will test the hypothesis that hospital inpatients infected with staphylococci whose pathogens were tested for antimicrobial susceptibility had lower hospital mortality rates, shorter lengths of stay, and lower overall treatment costs than patients whose pathogens were not tested, controlling for other factors including principal diagnosis (PDX), number of diagnoses (NDX), number of procedures (NPROC), age, and sex.

We will perform the analysis using data on two different patient populations: (1) patients with a secondary diagnosis related to a Staphylococcal infection; and (2) patients with any infectious & parasitic disease diagnosis.

- Patients in the first group include all admitted patients who had a secondary diagnosis of a staphylococcal infection, indicating that the staphylococal infection was not the primary reason for the admission; it may have manifested itself during the patient stay and may have been acquired in the facility. The use of antimicrobial testing in this group would be focused on identifying the infection promptly to keep it from spreading within the hospital and to aid in prompt and accurate treatment for the individual patient.
- The second group of patients includes all patients who had any sort of infection, encompassing both patients who had an infection upon hospital admission and those who acquired an infection while hospitalized. The first group is a subset of this group. A list of the top 25 infectious & parasitic disease diagnoses (ICD9 codes) of hospital inpatients in 2005 is shown in Appendix Table 1.

These hypotheses will be tested by estimating the following econometric models, using patient-level data on a large number of patents admitted to U.S. hospitals in 2004 and 2005:

$$MORT = \beta_1 AST + PDX\ dummies + NDX\ dummies + NPROC\ dummies + age * sex\ dummies + \varepsilon \quad (1)$$

$$DAYS = \beta_2 AST + PDX\ dummies + NDX\ dummies + NPROC\ dummies + age * sex\ dummies + \varepsilon \quad (2)$$

$$COST = \beta_3 AST + PDX\ dummies + NDX\ dummies + NPROC\ dummies + age * sex\ dummies + \varepsilon \quad (3)$$

where

MORT = 1 if the patient died prior to hospital discharge
= 0 if the patient was alive at time of hospital discharge

AST = 1 if the patient had isolates tested for antimicrobial susceptibility
= 0 if the patient did not have isolates tested for antimicrobial susceptibility

DAYS = number of overnight stays for a hospital admission

COST = total gross payment to all providers associated with the admission

ε = disturbance (error) term

β_1 is the difference in mortality rates between patients who had isolates tested for antimicrobial susceptibility and patients who did not, controlling for the other factors shown. β_2 is the difference in mean length of stay between patients who had isolates tested for antimicrobial susceptibility and patients who did not, controlling for the other factors shown. β_3 is the difference in mean overall treatment cost between patients who had isolates tested for antimicrobial susceptibility and patients who did not, controlling for the other factors shown. We hypothesize that $\beta 1$, $\beta 2$ and $\beta 3$ are negative.

We include the PDX, NDX, NPROC, and age-sex dummies to control for the nature and severity of illness, which are potentially correlated with the probability that the patient was tested for antimicrobial susceptibility. Patients with a large number of diagnoses and procedures are likely to be sicker than patients with relatively few diagnoses and procedures. Controlling for the number of procedures may also be appropriate because the larger the number of procedures recorded, the higher the probability that the patient will be identified as having a pathogen isolated and tested for antimicrobial susceptibility. These models will be estimated on two different samples of patients: (1) patients with secondary diagnosis of staphylococcal infection; and (2) patients with any infectious & parasitic disease diagnosis.

Data

The models will be estimated using data from the 2004 and 2005 Inpatient Admissions Tables from the MarketScan Commercial Claims and Encounters Database produced by Thomson Medstat (Ann Arbor, MI).[3] This database captures person-specific clinical utilization, expenditures, and enrollment across inpatient, outpatient, prescription drug, and carve-out services from approximately 45 large employers, health plans, and government and public organizations. The MarketScan Databases link paid claims and encounter data to detailed patient information across sites and types of providers, and over time. The annual medical databases include private sector health data from approximately 100 payers. Historically, more than 500 million claim records are available in the MarketScan Databases. The Commercial Claims and Encounters

Database contains data on active employees, early retirees, COBRA continues, and their dependents insured by employer-sponsored plans (i.e., non-Medicare eligibles).[4]
The Inpatient Admissions Table contains records that summarize information about a hospital admission. Medstat constructs this table after identifying all of the encounters or claims (service records) associated with an admission (e.g., hospital claims, physician claims, surgeon claims and claims from independent labs). Facility and professional payment information is then summarized for all services. The summarized information is stored in an admission record in the Inpatient Admissions Table.

The admission record also includes data that can only be identified after all claims for an admission have been identified. In addition to the principal procedure and diagnosis codes, the admission record includes all diagnoses and procedures (up to 14 each) found on the service records that make up the admission. These additional codes (Diagnosis 2 through Diagnosis 15 and Procedure 2 through Procedure 15) are assigned chronologically based on service dates and do not duplicate the principal code.

[3] The 2004 and 2005 Inpatient Admissions Tables contain data on 1.8 million discharges. According to the Healthcare Cost and Utilization Project (http://hcup-us.ahrq.gov/), there were 77.8 million U.S. hospital admissions during 2004-2005. The Marketscan database therefore covers 2.3% of all U.S. hospital admissions.
[4] I have access to these data because I am a Research Associate of the National Bureau of Economic Research (NBER), which has a site license to the MarketScan Commercial Claims and Encounters Database. NBER does not have access to the MarketScan Medicare Supplemental and COB Database, which covers Medicare-eligible retirees with employer-sponsored Medicare Supplemental plans.

To be considered an admission, the grouping of these service records must meet certain criteria (e.g., a room and board claim must be present). If these criteria are not met, the records are stored in the Outpatient Services Table and no admission record is created.

Identification of patients with pathogens isolated that were tested for antimicrobial susceptibility

In the MarketScan database, the vast majority of procedures are coded with CPT codes.[5] As shown in Table 1, just a few CPT codes are used for reimbursement of antimicrobial susceptibility tests. The two most frequently used CPT codes are 87186 (susceptibility studies, antimicrobial agent; microdilution or agar dilution (minimum inhibitory concentration (MIC) or breakpoint), each multi-antimicrobial, per plate) and 87184 (susceptibility studies, antimicrobial agent; disk method, per plate (12 or fewer agents)). Table 2 shows data on Medicare Part B allowed services and charges for these two procedures during 2003-2005. These procedures are very inexpensive: allowed charge per service is less than $12.[6]

If any of a patient's (up to 15) procedure codes were equal to 87184 or 87186, that patient will be considered to have had a pathogen isolated and tested for antimicrobial susceptibility (AST = 1). It is possible that there is incomplete recording of procedure codes in the Inpatient Admissions Tables, and therefore that our measure of antimicrobial susceptibility testing (AST) is subject to error. Random measurement errors are likely to result in conservative estimates of the effect of antimicrobial susceptibility testing on inpatient mortality and length of stay.

[5] CPT codes are not reported in other major hospital databases (the National Hospital Discharge Survey and the Healthcare Cost and Utilization Project). In these databases, procedures are coded using ICD9 procedure codes. It does not appear to be possible to identify patients whose isolates were tested for antimicrobial susceptibility from ICD9 procedure codes.

[6] As the following table shows, mean payments for these procedures for non-Medicare eligible, privately insured patients were similar:

CPT code	Year	Mean MEDSTAT payment	Allowed Medicare charge per service
87184	2004	$8.66	$9.49
87184	2005	$10.51	$9.48
87186	2004	$10.32	$11.85
87186	2005	$14.51	$11.84

Descriptive statistics are shown in Table 3. The top of the table shows statistics for patients with secondary staphylococcal infection (N = 15,695). The bottom of the table shows statistics for patients with any infectious & parasitic disease diagnosis (N = 114,092). Note that only 32.2% of patients with secondary staphylococcal infection, and 1.9% of patients with any infectious & parasitic disease diagnosis had infecting organisms that were tested for antimicrobial susceptibility. This finding will be discussed further below.

RESULTS

Ordinary least-squares (OLS) estimates of the parameters β_1, β_2 and β_3 from eqs. (1)-(3) for both patient populations are shown in Table 4.[7] All six of the coefficients are negative and statistically significantly different from zero (p-value < .02). This indicates that, within both populations, patients who had isolates tested for antimicrobial susceptibility had significantly lower inpatient mortality rates, length of stay, and overall treatment cost than patients who did not, controlling for principal diagnosis, number of diagnoses, number of procedures, age, and sex.

The β coefficients represent the *absolute* differences between patients who had isolates tested patients who did not, conditional on the covariates. One might also like to have a sense of the *relative* differences. We can do this as follows. Let

Y = grand (overall) mean Y

λ = fraction of patients who had isolates tested for antimicrobial susceptibility

Y_1 = mean Y of patients who had isolates tested for antimicrobial susceptibility

Y_0 = mean Y of patients who did not have isolates tested for antimicrobial susceptibility

$\Delta = (Y_1 - Y_0)$

where Y denotes one of the dependent variables (MORT, DAYS, or COST). Then

$$Y = \lambda Y_1 + (1 - \lambda) Y_0$$
$$= Y_0 + \lambda (Y_1 - Y_0)$$
$$= Y_0 + \lambda \Delta$$

[7] Estimation of eq. (1) using a probit procedure yielded results similar to the OLS estimates.

Hence

$$Y_0 = Y - \lambda \Delta$$

$$Y_1 = Y + (1 - \lambda) \Delta$$

Δ represents the *crude* difference in means, i.e. the difference *unadjusted* for the covariates. Instead of Y_0 and Y_1, we will calculate

$$Y_0' = Y - \lambda \beta$$

$$Y_1' = Y + (1 - \lambda) \beta$$

which are based on the difference in means *adjusted* for the covariates.
Values of Y_0' and Y_1' are displayed in Figure 2. $(Y_0' - Y_1') / (Y_0')$ may be considered the relative reduction in Y attributable to antimicrobial susceptibility testing. Absolute and relative reductions in inpatient mortality, length of stay, and cost attributable to antimicrobial susceptibility testing are shown Table 5.

Among patients with secondary staphylococcal infection, those who had isolates tested for antimicrobial susceptibility had 52% lower probability of death before discharge, 17% lower mean length of stay, and 22% lower cost than those who did not have isolates tested. Among patients with any infectious & parasitic disease diagnosis, those who had isolates tested for antimicrobial susceptibility had 30% lower probability of death before discharge, 26% lower mean length of stay, and 36% lower cost than those not tested.

According to HCUPnet, there were 1,189,258 hospital discharges of patients with secondary staphylococcal infection in 2005. In this group of patients, antimicrobial susceptibility testing is associated with $6978 lower cost per discharge. Therefore the potential aggregate cost reduction from antimicrobial susceptibility testing of all patients with secondary staphylococcal infection in 2005 was $8.3 billion (= 1,189,258 × $6978).

DISCUSSION

The number of U.S. hospital discharges in which there was a diagnosis of infection with drug-resistant microorganisms increased more than one hundred-fold between 1993 and 2005. Infectious disease experts have argued that tests that reveal the susceptibility of infection to antimicrobial agents can allow physicians to administer more appropriate and effective treatments.

We performed an econometric analysis of the impact of antimicrobial susceptibility testing on the survival, length of stay, and treatment costs of inpatients with infectious diseases, based on a very large sample of U.S. hospital admissions during 2004-2005. We tested the hypotheses that hospital inpatients who had isolates tested for antimicrobial susceptibility had lower hospital mortality rates, length of stay, and overall treatment costs than patients who did not have isolates tested, controlling for a number of indicators of the nature and severity of illness. The analysis was performed using data on two different patient populations: (1) patients with secondary staphylococcal infection, and (2) patients with any infectious & parasitic disease diagnosis.

The estimates indicated that, within both populations, patients who had isolates tested for antimicrobial susceptibility had significantly lower inpatient mortality rates, length of stay, and overall treatment cost than patients who did not have isolates tested, controlling for principal diagnosis, number of diagnoses, number of procedures, age, and sex. Among patients with secondary staphylococcal infection, those who had isolates tested had a 52% lower probability of death before discharge, 17% lower mean length of stay, and 22% lower cost than those who did not have isolates tested. Antimicrobial susceptibility testing was associated with $6984 lower cost per discharge. The potential aggregate cost reduction from antimicrobial susceptibility testing of all patients with secondary staphylococcal infection in 2005 was $8.3 billion.

It is possible that the overall quality of care received by patients who had isolates tested for antimicrobial susceptibility was better than the overall quality of care received by patients who did not have isolates tested, and that part of the observed differences in mortality, length of stay, and cost are due to unobserved differences in treatment quality. But since the differences in outcomes and expenditure are so large relative to the cost of testing, administering antimicrobial susceptibility tests would be worthwhile even if it accounted for a very small fraction of the observed differences in mortality, length of stay, and cost. This suggests that AST should be performed whenever an organism is isolated and AST is technologically feasible.

However in the sample of patients we examined, only 32.2% of patients with secondary staphylococcal infection had isolates tested for antimicrobial susceptibility. Other investigators have reported that recommended lab tests are infrequently used, even when the tests are convenient and inexpensive. For example, the Centers for Disease Control and Prevention has recommended that every emergency room patient ages 13 to 64 should be offered an H.I.V. test

(Brown (2007)). New tests requiring only a painless swab of the gums can reveal in 20 minutes if a person is infected. One year after these recommendations were made, almost no emergency rooms offered routine H.I.V. testing.

While the apparent failure to routinely perform antimicrobial susceptibility testing on hospital inpatients is costly and worsens health outcomes, it is unfortunately not surprising. The National Center for Quality Assessment (NCQA) has shown that the health care system remains plagued by enormous "quality gaps"—differences in performance between the top 10 percent of health plans and the national average—and that the majority of Americans still receive less than optimal care. For example, only 51% of adolescents are immunized for chicken pox, and only 48% of diabetics are monitored for nephropathy. NCQA estimates that the widespread, unexplained variation in quality results in thousands of unnecessary deaths, tens of thousands of avoidable hospitalizations and illnesses and billions of dollars in lost productivity.

In this study, we have examined the most recent available hospital data, for the years 2004-5. Since that time, newer, more rapid tests have reached the market. On December 21, 2006, the FDA granted 510(k) clearance for a test for the rapid detection of methicillin-resistant *Staphylococcus aureus* (MRSA).[8] In 2007 a new CPT code (87641) was established; this code refers to "infectious agent detection by nucleic acid (DNA or RNA); Staphylococcus aureus, methicillin resistant, amplified probe technique."[9] Once sufficient data become available, we will be able to investigate whether these newer, more rapid tests have even larger effects on the survival, length of stay, and treatment costs of inpatients with infectious diseases.

[8] http://www.medscape.com/viewarticle/568423

[9] The national limit for this procedure under CMS' 2008 Clinical Diagnostic Laboratory Fee Schedule is $49.04; the national limits for 87184 and 87186 are $9.63 and $12.08, respectively.

References

Brown, Jeremy (2007), "The Forgotten H.I.V. Test," *New York Times*, Sept. 22.

Cai, Fangping, et al (2007), "Detection of minor drug-resistant populations by parallel allele-specific sequencing," *Nature Methods* - 4, 123-5.

Center for Medicare and Medicaid Services, 2008 Clinical Diagnostic Laboratory Fee Schedule, http://www.cms.hhs.gov/apps/ama/license.asp?file=/ClinicalLabFeeSched/downloads/08clab.zip

Hartemann-Heurtier A, Robert J, Jacqueminet S, Ha Van G, Golmard JL, Jarlier V, Grimaldi A: Diabetic foot ulcer and multidrug-resistant organisms: risk factors and impact. *Diabet Med* 21:710–715, 2004

Healthcare Cost and Utilization Project, Nationwide Inpatient Sample, http://hcupnet.ahrq.gov

Moore, David A.J., et al (2006), "Microscopic-Observation Drug-Susceptibility Assay for the Diagnosis of TB," *New England Journal of Medicine* 355 (15), pp. 1539-1550, October 12.

National Committee for Quality Assurance, "The State of Health Care Quality 2004," Washington, D.C., http://web.ncqa.org/LinkClick.aspx?fileticket=JpipP%2fOqXoo%3d&tabid=447&mid=1642&forcedownload=true

Thomson Medstat, MarketScan Research Databases User Guide and Database Dictionary, (Ann Arbor, MI).

Figure 1
U.S. hospital discharges with diagnosis of infection with drug-resistant microorganisms (ICD9 code V09), 1993-2005

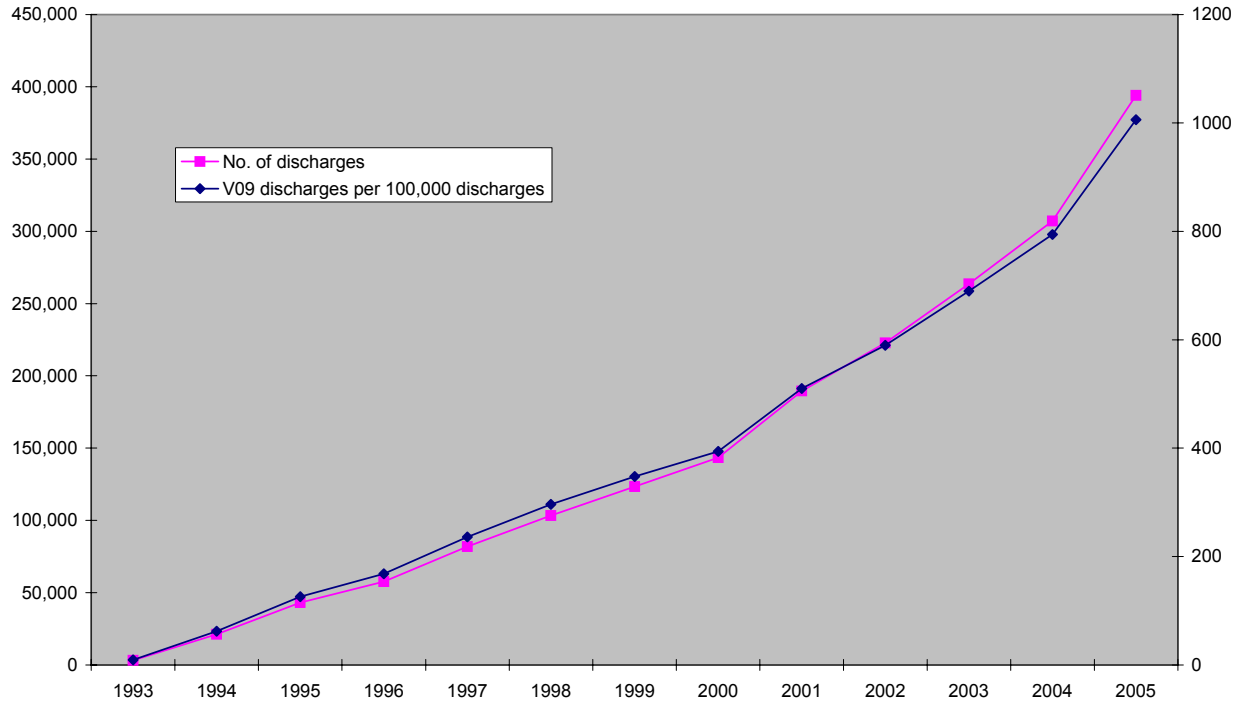


Table 1

Antimicrobial Susceptibility Tests

Test Name and Number	Methodology	CPT code
Antimicrobial Susceptibility Staphylococcus 0060707	Automated Broth Microdilution	87186
Antimicrobial Susceptibility - mecA Gene by PCR 0060211	Polymerase Chain Reaction	87641
Antimicrobial Susceptibility - D-Test (Macrolide, Lincosamide, Streptogramin Resistance) 0060059	Disk Diffusion	87184
Antimicrobial Susceptibility - Enterococcus 0060708	Automated Broth Microdilution	87186
Antimicrobial Susceptibility - Not Otherwise Specified 0060200	Broth Microdilution/Disk Diffusion/Gradient Diffusion	may vary based on method
Vancomycin-Resistant Enterococcus (VRE) Culture 0060363	Standard reference procedures for aerobic bacterial culture and identification	87081 presumptive identification. If definitive identification required, add 87077.
Antimicrobial Susceptibility - Yeast Susceptibility 0060235	Broth Microdilution	87186
Antimicrobial Susceptibility AFB/Mycobacteria 0060217	Varies with organism identification	87186
Antimicrobial Susceptibility - Extended Spectrum Beta Lactamase 0063999	Disk Diffusion	87184
Antimicrobial Susceptibility Streptococcus pneumoniae 0060221	Broth Microdilution	87186
Antimicrobial Susceptibility - Viridans Streptococcus 0060222	Broth Microdilution	87186
Antimicrobial Susceptibility - Nocardia 0060193	Broth Microdilution	87186
Antimicrobial Susceptibility - Anaerobe 0060202	Broth Microdilution	87186
Antimicrobial Susceptibility - MIC, Individual 0060201	Gradient Diffusion (E-Test) or Broth Microdilution	87181 Gradient dilution or 87186 Broth dilution
Antimicrobial Susceptibility Nonfermenter 0060216	Broth Microdilution	87186

http://www.arupconsult.com/Topics/InfectiousDz/Bacteria/AntimicrobSusceptibility.html#testsavailable

Table 2

Medicare Part B allowed services and charges for 2 antimicrobial test procedures, 2003-2005

Year	Allowed Services	Lab Procedure Rank	Allowed Charges	Allowed charge per service
CPT 87186: Susceptibility studies, antimicrobial agent; microdilution or agar dilution (minimum inhibitory concentration (MIC) or breakpoint), each multi-antimicrobial, per plate				
2003	1,353,285	48	$16,026,412	$11.84
2004	1,462,248	46	$17,321,143	$11.85
2005	1,619,541	46	$19,179,236	$11.84
CPT 87184: Susceptibility studies, antimicrobial agent; disk method, per plate (12 or fewer agents)				
2003	672,580	84	$6,370,242	$9.47
2004	739,173	79	$7,011,068	$9.49
2005	732,696	83	$6,943,650	$9.48

http://www.cms.hhs.gov/MedicareFeeforSvcPartsAB/04_MedicareUtilizationforPartB.asp

Note: Lab procedures ranked by number of allowed services.

Table 3

Descriptive Statistics

Variable	Mean	Std Dev	Minimum	Maximum
Patients with secondary staph infection (N = 15,695)				
AGE	42.9207	17.7872	0	64
MORT	0.023	0.1499	0	1
DAYS	10.1558	14.7092	1	366
COST	$29,931	$64,349	-$100	$1,433,987
NDX	8.30278	4.23437	1	14
NPROC	9.51535	4.15625	0	14
AST	0.32157	0.46709	0	1
Patients with any Infectious & Parasitic Disease diagnosis (N = 114,092).				
AGE	39.1779	20.3024	0	64
MORT	0.02839	0.16609	0	1
DAYS	7.09354	11.9152	1	370
COST	$21,025	$53,323	-$3,167	$2,445,475
NDX	8.06	4.17	1	15
NPROC	8.58	4.72	0	15
AST	0.01923	0.13732	0	1

Table 4

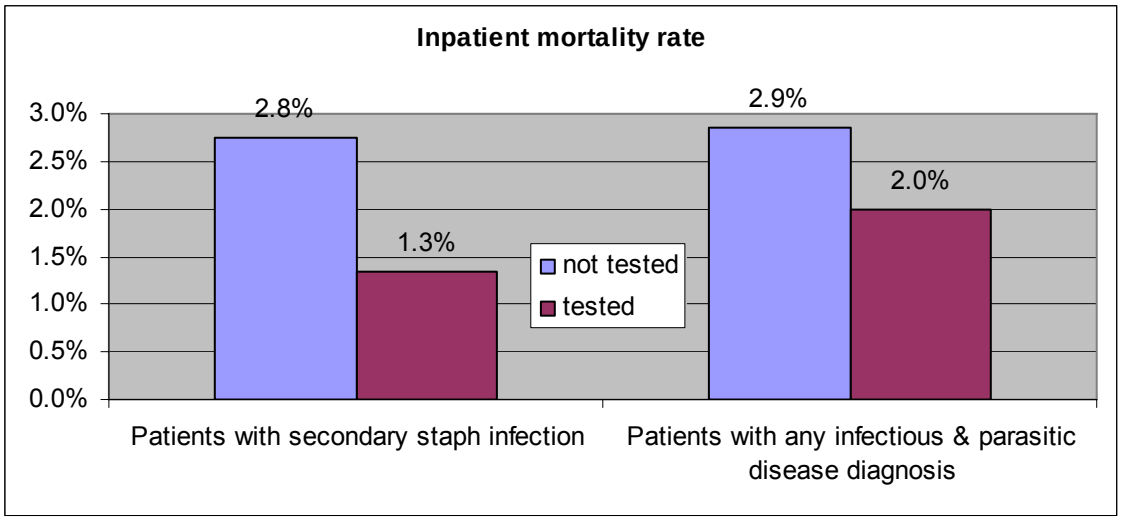
Estimates of AST coefficients in eqs. (1), (2), and (3)

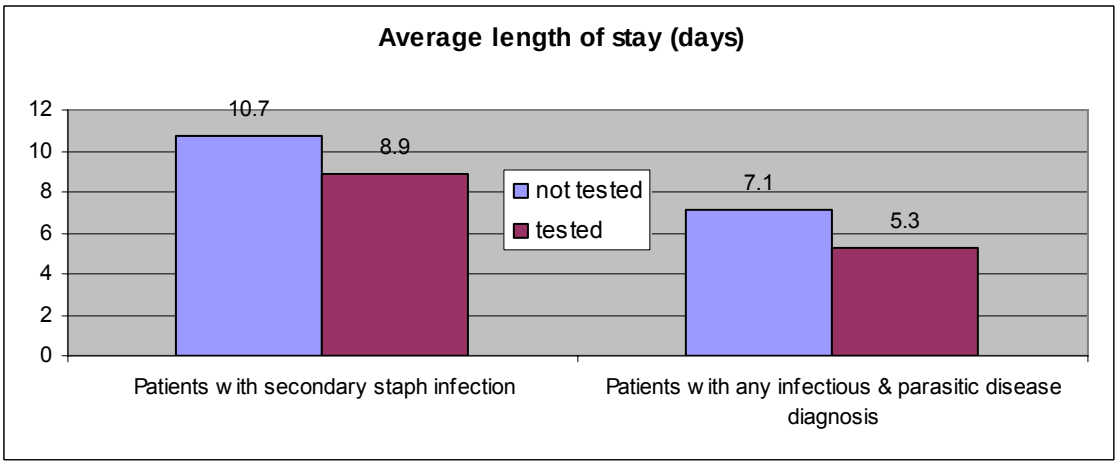
Sample	Patients with secondary staph infection (N = 15,695)	Patients with any Infectious & Parasitic Disease diagnosis (N = 114,092)
MORT		
β_1	-0.014	-0.009
std err	0.003	0.004
t stat	-5.320	-2.420
p value	<.0001	0.015
DAYS		
β_2	-1.837	-1.833
std err	0.217	0.219
t stat	-8.450	-8.360
p value	<.0001	<.0001
COST		
β_3	-6977.863	-7523.822
std err	986.733	1020.105
t stat	-7.070	-7.380
p value	<.0001	<0.0001

Patients with secondary staph infection have one or more of the following secondary diagnoses: V090, 48240, 48241, 48249, 03810, 03811, 03819, 04110, 04111, 04119.

Figure 2

Inpatient mortality rate, average length of stay, and average treatment cost of tested and untested patients





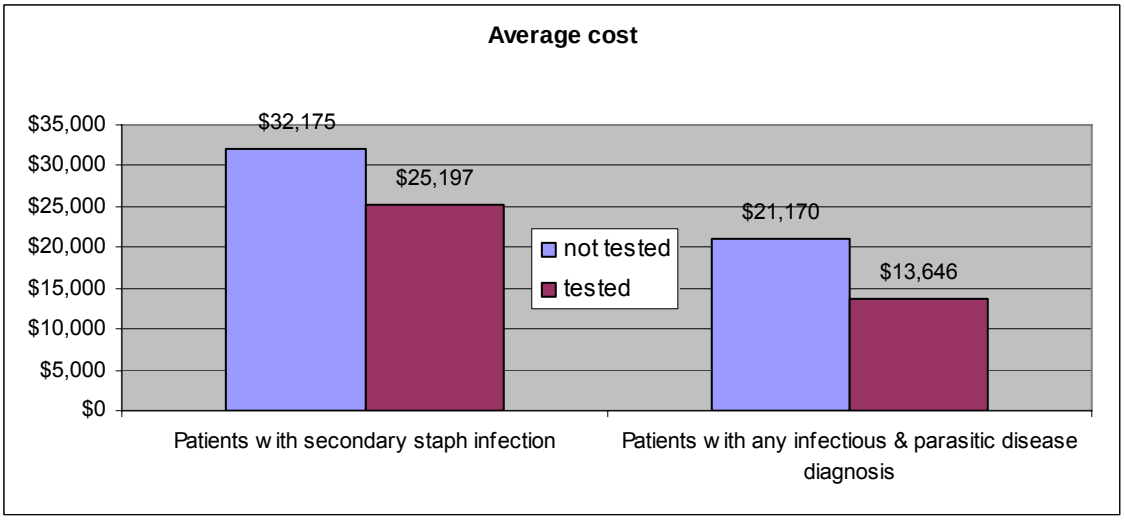


Table 5

Absolute and relative reductions in inpatient mortality, length of stay, and cost attributable to antimicrobial susceptibility testing

	Patients with secondary staph infection		Patients with any infectious & parasitic disease diagnosis	
	absolute reduction	relative reduction	absolute reduction	relative reduction
inpatient mortality rate	0.014	51.50%	0.009	30%
mean length of stay	1.84	17.10%	1.83	26%
mean cost	$6,978	21.70%	$7,524	36%

Appendix Table 1

Top 25 infectious & parasitic disease diagnoses: hospital inpatients in 2005

dx	COUNT	PERCENT	CUM PERCENT
0389 -Septicemia NOS	9900	12.4%	12.4%
04111-Staphylococcus Aureus	5522	6.9%	19.3%
07999-Viral Infection NOS	3984	5.0%	24.3%
0088 -Viral Enteritis NOS	3480	4.4%	28.6%
0414 -E. Coli Infect NOS	3242	4.1%	32.7%
00845-Int Inf Clstrdium Dfcile	2925	3.7%	36.3%
07054-Chrnc Hpt C wo Hpat Coma	2499	3.1%	39.5%
07070	2194	2.7%	42.2%
1120 -Thrush	2074	2.6%	44.8%
0479 -Viral Meningitis NOS	2010	2.5%	47.3%
042 -Human Immuno Virus Dis	1757	2.2%	49.5%
135 -Sarcoidosis	1678	2.1%	51.6%
03811-Staph Aureus Septicemia	1542	1.9%	53.6%
00861-Intes Infec Rotavirus	1516	1.9%	55.4%
0549 -Herpes Simplex NOS	1000	1.3%	56.7%
03842-E Coli Septicemia	995	1.2%	57.9%
0090 -Infectious Enteritis NOS	901	1.1%	59.1%
0417 -Pseudomonas Infect NOS	892	1.1%	60.2%
04102-Streptococcus Group B	864	1.1%	61.3%
0380 -Streptococcal Septicemia	849	1.1%	62.3%
04104-Enterococcus Group D	827	1.0%	63.4%
0340 -Strep Sore Throat	788	1.0%	64.4%
04119-Other Staphylococcus	786	1.0%	65.3%
04185-Oth Gram Negatv Bacteria	779	1.0%	66.3%
03849-Gram-Neg Septicemia NEC	747	0.9%	67.2%