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MRSA RATES AND TRENDS: A FOUNDATION FOR FUTURE ANALYSIS

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In December 2007, *Extending the Cure* (ETC) researchers Eili Klein, David Smith, and Ramanan Laxminarayan published the first analysis of recent trends in MRSA—methicillin-resistant *Staphylococcus aureus*—in the journal *Emerging Infectious Diseases*. An ETC policy brief (*Counting MRSA Cases*)[1] describes the results of this study and a recent study by researchers at the Centers for Disease Control and Prevention (CDC), detailing MRSA statistics from 2005.

By the time the ETC paper appeared, public consciousness about MRSA had already been raised by incidents that made news around the country. It probably came as no surprise that Klein and colleagues' analysis showed a steady rise in MRSA rates. The analysis was of primary value in establishing a benchmark of what rates have been in the recent past and how fast they have been increasing. The authors examined the data regionally and nationwide and found different patterns in both initial levels of infection and in rates of increase. Such benchmarks are a necessary prerequisite to tracking future trends.

But this type of analysis is not as straightforward as it might seem. Who had MRSA while in the hospital is not necessarily obvious, and determining who has died from it is even more challenging (*See Box)*.

Key questions for the future are:

1. How well is the relevant information represented in the databases used by Klein and colleagues?
2. Are there equally good or better data sources that should be investigated?
3. Might other analytic methods give different or more informative answers?

State Governments Respond

The importance of following MRSA trends and healthcare-associated infections (HAIs) is only going to increase, not just nationally or regionally, but specifically at the state level, because states are becoming more active in tracking infection rates and requiring intensified infection control in hospitals. Over the past five years or so, both the healthcare community and the public have recognized HAIs and MRSA as growing threats. Inevitably, state governors and legislatures have begun to act (see ETC Policy Brief, *The States Take Action*).[2]

The first wave of laws, now passed in more than half of the states, requires hospitals (and in some states, other healthcare facilities) to report HAI rates, usually to the State Health Department. MRSA itself has spawned what we see as the beginning of a second wave of laws that require action, not simply reporting. These state statutes require hospitals and other medical sites to either establish or step up efforts at active infection control. Some laws are prescriptive and state exactly what must be done, and are most often aimed directly at MRSA. Others allow more leeway for adapting measures to local conditions.

The intensified focus on HAIs, MRSA, and other antibiotic-resistant infections (smaller in scale, but nonetheless important) brings with it an interest in results: how do we know what effect the laws and subsequent interventions are having? Are some approaches better than others? As a nation, and at the state level, are things generally moving in the right direction?

ETC's Contribution

My colleagues, led again by Eili Klein, have begun an analysis similar to the one they presented in the recent MRSA paper, this time focusing on antibiotic-resistant gram negative organisms (see Table) among hospital

Table: Gram-positive and gram-negative organisms compared

	Organisms	Characteristics
Gram-positive	*Staphylococcus aureus* *Streptococcus pneumoniae* *Clostridium difficile* *Enterococcus spp.*	Thicker cell wall with no outer membrane, allowing bacteria to retain the purple stain in the Gram stain process. The cell wall is the target for many antibiotics, including penicillin.
Gram-negative	*Klebsiella pneumoniae* *Acinetobacter spp.* *Enterobacter spp.* *Pseudomonas aeruginosa* *Escherichia coli* (*E. coli*)	Thinner cell wall protected by an outer membrane. The outer membrane prevents the bacteria from retaining the purple stain during the Gram stain process, and it also renders many common antibiotics, including penicillin, ineffective.

patients. This new study will set another benchmark. The two papers also constitute the first steps of what we hope will be a lasting ETC contribution: to establish the most reliable methods and data sources for tracking trends in antibiotic-resistant infections.

Klein and his colleagues used two datasets for their work, adapting an innovative analytical method developed by Matthew Kuehnert and his colleagues at CDC. The datasets are 1) the National Hospital Discharge Survey (NHDS), a long-running, nationally representative survey conducted by the National Center for Health Statistics, and 2) The Surveillance Network (TSN) Database-USA (Focus Technologies, Inc., Herndon, VA), which comprises results from routine antimicrobial susceptibility tests conducted at laboratories around the country. Both the NHDS and TSN are reliable data sources and though they have limitations, a major strength for both is that they are likely to be available over the long term.

But these are not the only promising data sources. Over the next two years, we intend to systematically evaluate other major sources of data that could be used to analyze trends in HAIs and antibiotic resistance. We also intend to develop a deeper understanding of all the datasets that we consider so that we know their strengths, weaknesses, and biases (avoidable and not), and can better understand differences in results that stem from using different datasets.

Another ongoing national survey is the Healthcare Cost and Utilization Project (HCUP; sponsored by the Agency for Healthcare Research and Quality). One component, the Nationwide Inpatient Sample (NIS) contains data on 20 percent of all hospital stays every year. That is five to eight million patients per year (as of 2005), compared with about 270,000 in the NHDS. Both databases are large and both have been well characterized by their sponsoring organizations and other users, which increases their value. We have begun to explore the NIS and intend to compare it with the NHDS for the purpose of analyzing trends in antibiotic-resistant infections.

The reporting legislation passed by states during recent years, and more states expected to pass similar laws in coming years, means that hospitals (and other healthcare sites, as required) will be documenting their infection rates. The data onslaught from these laws has not yet materialized, but when it begins to appear later this year, we will evaluate its usefulness for tracking both HAIs and antibiotic-resistant infections. Some states will hold the data confidentially, but a number of others will be reporting to a CDC database, the National Healthcare Safety Network (NHSN), using a standardized format. HCUP also maintains State Inpatient Databases (SIDs). We intend to delve into all of these to determine how useful they are for analyzing trends in HAIs and in antibiotic-resistant infections. Our expectation is that different datasets and analyses will be complementary, illuminating different aspects of the problem.

We are in the process of identifying not only data sources, but also collaborators who can help us carry out analyses of current data and who would be in a position to conduct analyses in the future.

References

1. RFF (2007). “Counting MRSA Cases: An Evaluation of Recent Evidence.” http://www.extendingthecure.org/downloads/policy_briefs/Policy_Brief3_Dec07_MRSA_Trends.pdf (accessed January 23, 2008),
2. RFF (2007). “The States Take Action: Hospital Infection Reporting and Control.” http://www.extendingthecure.org/downloads/policy_briefs/Policy_Brief2_Nov07_State_Actions.pdf (accessed January 23, 2008).

BOX: The Challenge of Counting MRSA Infections and Deaths

While it would be useful to know precisely who gets infected with MRSA and where the infection was acquired, we never will. Those facts are not easy to determine, even at the individual patient level. Large databases that draw on hospital records make it possible to track trends over large segments of the population, but they are limited first to what is known and what has been recorded in the patient chart, and second by the limits of the database itself—not every piece of information in the patient record is likely to be captured by the database, and any piece left out may be of interest to a particular question. The concern about how well a database mirrors reality is one that any researcher relying on such information must confront, but MRSA poses special problems.

Clearly, information that either is 1) not known about a patient, 2) not recorded in patient files, or 3) not transferred to the database will not make it into an analysis. Judgments can be made about the importance of each of these, but they are not strictly quantifiable. For instance, hospitals are not required to test all incoming patients for MRSA and doctors do not have to test every bacterial infection for antibiotic sensitivity. Sensitivity testing is less likely, and logically so, when overall antibiotic resistance rates are low (why test when the outcome is almost certainly negative?). But, strikingly, sensitivity testing is also less likely also when rates are high. When a high proportion of staph infections in a hospital has been resistant to penicillin and related antibiotics, standard practice may be to use other antibiotics without routine testing. Without testing, a staph infection will not be identified as MRSA. And while the infection itself is a “primary” diagnosis that must be recorded, antibiotic susceptibility is not. The special secondary diagnostic code for antibiotic resistance may or may not appear. Finally, even if testing is carried out and recorded, it may not be picked up by the database. The NHDS (used by Klein and colleagues) takes only the first seven diagnoses in each medical chart, where there may be 15 or more. Codes for diagnoses after the initial seven are lost.

In terms of where an infection is acquired, a decade ago it may have been true that hospital patients who ended up with a staph infection (MRSA or not) checked in without it—they invariably were infected in the course of the hospital stay. Hospitals are still the most likely places to get serious cases of MRSA and drug-sensitive infections, but now more and more patients come in already infected (or carrying bacteria that may be harmless to a healthy person, but when passed on to a weakened patient in the hospital, may cause serious or even deadly infections). Many such patients got their infections from earlier hospital encounters or in other healthcare sites (especially nursing homes), and some became infected “in the community”—in schools, on sports teams, or in some less obvious way.

Determining how important MRSA infections are to mortality is even more difficult. We know that MRSA does not kill everyone who has it, and not everyone who has it when they die was killed by it. Most of those who die with MRSA are elderly and have serious medical problems—which is why they are in the hospital in the first place. The relevant question is “If this person hadn’t gotten MRSA in the hospital, would he or she have survived—infection free—to be released from the hospital and live another day?” In other words, did having MRSA contribute to the person’s death? Was it an “attributable” cause, perhaps one of several? These questions are usually impossible to answer precisely. The easier to come by and possibly more reliable—but substantially larger—number is of people who were infected with MRSA when they died.