DISCOVERY MEDICINE

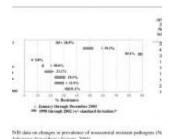
July 25, 2009

On the Importance of Incentives in Hospital Infection Control Spending

Ramanan Laxminarayan, Resources for the Future, Washington, DC 20036, USA David L Smith, Fogarty International Center, NIH, Bethesda, MD 20892, USA Leslie A Real, Department of Biology, Emory University, Atlanta, GA 30322, USA Simon A Levin, Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ 08544, USA

Abstract: Infections acquired in the hospital during visits and hospitalization have happened to 2 million patients and cause 90,000 deaths in the U.S a year -- a staggering number beyond comprehension or common sense. Due to the mobility and persistence of drug-resistant bacterial infections, one hospital's infection control effort, balancing both cost and benefit to that hospital, may not make a significant impact in a large population base, but it would if all hospitals act together.

Each year, nosocomial (acquired in hospital) infections affect nearly 2 million patients and cause over 90,000 deaths in the United States alone. According to the Centers for Disease Control and Prevention (CDC), seventy percent of all nosocomial pathogens are resistant to one or more classes of <u>antibiotics</u> (NNIS — National Nosocomial Infections Surveillance System, 2004). Antibiotic-resistant bacteria such as <u>vancomycin-resistant enterococci</u> (VRE) and methicillin-resistant <u>Staphylococcus</u> <u>aureus</u> (MRSA) are leading causes of hospital acquired infections, and they have proven difficult to eradicate and control (Figure 1).



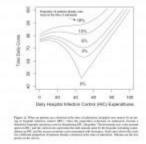
The spread of resistance is ultimately caused by the use and overuse of antibiotics. Antibiotics are effective medicines when used correctly — as is their purpose. The ability of VRE, <u>MRSA</u> and other antibiotic-resistant bacteria in hospitals to spread is affected by the percentage of people who use antibiotics in a population — the more that antibiotics are used, the quicker resistance to them appears and the faster the resistant strain can spread from person to person. Consequently, the more antibiotics that are used today, the greater the chance antibiotic therapy will fail in the future.

Unfortunately, antibiotics are often prescribed when they are not necessary because patients and doctors both have incentives to do so. Patients feel reassured when they take antibiotics (or any other drug for that matter), and doctors prescribe antibiotics to make their patients feel reassured. The potential side effects of taking the antibiotics, such as <u>diarrhea</u>, are usually minor, and patients can stop taking the drug if they experience these negative effects. Doctors also prescribe to protect

themselves — if a patient develops complications that an antibiotic might have prevented, the doctor who failed to prescribe faces legal risks. Even when there is only a small chance the antibiotic would help, the incentives encourage doctors to prescribe.

When antibiotics are deemed necessary, similar incentives may favor prescription of antibiotics that are effective against a *broad* spectrum of bacteria, although these can cause more collateral damage by affecting non-target bacteria. The bacterial species causing an infection is rarely known until a laboratory identifies it, and laboratory work takes time. Antibiotics work best when started early, so some doctors begin to treat patients using broad-spectrum antibiotics before laboratory tests are conclusive. If the broad-spectrum antibiotic works, experience and prudence mitigate against a switch to a narrow-spectrum antibiotic — one that would cause less collateral damage. Meanwhile, the decision to use antibiotics early often hastens the loss of effectiveness of the antibiotic within the population.

From a society's perspective, antibiotics are a resource to be used wisely in much the same way as the world's <u>fish</u> stocks or atmosphere. In fact, the efficacy of these drugs can be thought of as an "open access" resource where the actions of individuals, physicians, medical institutions and governments have consequences for their efficacy in the future. It would appear that the consequences of antibiotic overuse by patients and physicians or insufficient hospital infection control are partly borne by the individuals who use antibiotics or the hospitals where antibiotic resistant bacteria spread. For example, there appears to be evidence that individuals with a recent history of antibiotic use are at a greater risk for infection by a drug-resistant pathogen (Dowell and Schwartz 1997; Table 1).

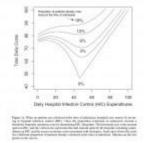


Similarly, hospitals are affected by the degree of nosocomial resistance in their wards and intensive care units (ICUs). Resistant pathogens result in longer hospital stays, and treatment can cost many times more than drug-sensitive pathogens. A portion of these costs is absorbed by the hospital. For instance, the cost of treating MRSA is between \$1,700 and \$5,100 per patient more than the cost of treating a methicillin-sensitive *S. aureus* infection, with total costs around \$42 million each year in the United States alone. Under the per-case prospective payment plan for Medicare patients, hospitals are reimbursed a lump sum, the amount of which is determined on the basis of diagnosis-related groups. Since Medicare pays only for the cost of a typical *S. aureus* infection, the hospitals must make up the difference.

Some of the costs associated with <u>antibiotic resistance</u> in nosocomial pathogens can be reduced by investing to improve hospital infection control (HIC), measures such as improving the frequency of hand washing, isolating patients who carry antibiotic-resistant bacteria from patients who do not, and making healthcare workers wear gloves and gowns. Unfortunately, there is little evidence that HIC has been increased in response to the resistance epidemic. Since hospitals bear a significant fraction of the burden of treating resistant infections, and since the cost of treating resistant infections is so high, the lack of a strong response by hospitals to the growing prevalence of antibiotic-resistant bacteria is perplexing.

One explanation is that HIC is also expensive, and it becomes more difficult and less effective when patients enter the hospital already carrying the resistant pathogens. Recent research on incentives that hospitals face in controlling antibiotic-resistant bacteria suggests that the large spillovers of antibiotic-resistant bacteria between medical care facilities may be one factor that explains the lack of response (Smith et al., 2005). When a number of institutions share patients, then a person colonized in one facility may be responsible for introducing or increasing the prevalence of drug-resistance in

another facility. As shown in Figure 2, when the proportion of patients that are admitted who have



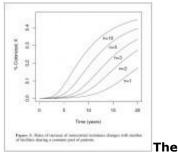
been colonized with a resistant pathogen

is low, there is some level of HIC that is optimal for the hospital to undertake. Because relatively few patients are colonized at the time of admission, it is relatively inexpensive to prevent resistant bacteria from spreading. However, when an increasing proportion of patients are admitted colonized, HIC becomes increasingly ineffective at controlling the prevalence of infection within the hospital. Also, the optimal level of HIC from the hospital's perspective shifts dramatically to spending nothing at all.

Since any single hospital (especially in the current era of cost-cutting and short term financial pressures) may ignore the benefits of their HIC programs outside their own walls. Hospitals may not benefit from decreasing the overall level of resistance in the population served by the hospital (the catchment population), when those patients are admitted later to other hospitals. Instead, hospitals may prefer to "free-ride" on the HIC investments of other hospitals. This results in an overall higher level of resistance.

In particular, the level of HIC that is in the interests of any hospital to undertake depends on the HIC efforts of other hospitals. Patients usually only spend a few days in the hospital at a time, but if they become carriers of resistance, they can spread it to others for years. From one hospital's perspective, the benefits of HIC are often passed on to other hospitals since the patient might choose a different hospital the next time. Thus, the money spent on HIC to prevent a patient from becoming a carrier ends up benefiting next hospital - in economic terms, the benefits of HIC are not internalized by hospitals.

Modeling shows that the selfishly "optimal" level of HIC that any hospital would undertake is lower when a greater number of hospitals share a catchment population. In fact, it is in the interests of the hospital to spend less and "free-ride" on the efforts of other hospitals. When everyone "free-rides," all hospitals will spend less on HIC, leading to epidemics that develop earlier and faster (Figure 3).



The Benefits of Coordination

It is useful to view these results in the light of two recent successes in controlling VRE and MRSA. Following years of aggressive infection control in the Netherlands, called "search-and-destroy," the frequency of MRSA infections was lowered to less than 0.5%, compared with 50% in some areas (Vriens et al., 2002). The 6 million Euros estimated as benefits of the campaign, in averted MRSA infections and reduced vancomycin-resistance in other bacteria (S. aureus and VRE). This far outweighed the cost (2.8 million Euros) of hospital infection control in the Netherlands during the same period.

An epidemic of VRE in the Siouxland Region of Iowa, Nebraska, and South Dakota was first detected in late 1996. Within a short time, VRE had quickly spread to nearly half of the health-care facilities in the region. In response, a VRE Task Force was created with representatives from all the acute and long-term-care facilities and public-health departments in the region (Ostrowsky, 2001). Following a comprehensive two-year intervention, (which included aggressive culturing of samples taken from patients to identify the VRE-colonized patients, isolation of those patients, improved antibiotic use, sterile device measures, and improved healthcare worker hand hygiene) VRE was eliminated from all acute-care facilities and significantly reduced in long-term-care facilities in the region.

In both examples, the infusion of massive investment in HIC was instrumental in controlling antibioticresistant bacteria epidemics. However, an important but overlooked fact is that the public health response was coordinated among institutions. From an economic perspective, the hospitals sought a cooperative optimum that would not have been in the interest of any single institution to seek on its own. In the absence of coordination, an intensive HIC effort by any single hospital may have resulted in other hospitals cutting back on their HIC expenditures, if they were behaving selfishly.

The incentive effect may explain why a higher prevalence of antibiotic-resistant bacteria is observed in urban hospitals where a number of facilities are located in the same geographical area and share a common pool of patients without identifying the carriers, compared to rural hospitals that are less likely to share patients with other facilities. Of course, there may be other reasons for a higher prevalence of antibiotic-resistant bacteria in urban areas. Larger population size, closer human contact and therefore greater scope for transmission of infections in the community, and lower socio-economic status may all be additional explanatory variables. It is also possible that antibiotic-resistant bacteria are introduced into city hospitals earlier because of patient sharing, and that prevalence is higher in urban hospitals because the epidemic is more advanced.

Public policy may be able to provide at least two remedies. The first is to shift state or federal efforts to promote infection-control standards at the hospital level to monitoring and responding to regional levels of antibiotic-resistant bacteria. Regional coordination of antibiotic-resistant bacteria could ensure that individual facilities do not "free-ride" on the infection-control efforts of other facilities in the region, and that cooperation between facilities is encouraged. The second is to ensure greater transparency in <u>nosocomial infection</u> data so that other hospitals and prospective patients can identify hospitals with the greatest risk of antibiotic-resistant bacteria infections.

Sharing information is especially helpful if the carrier status of individual patients is routinely included as a part of the patient's medical history, so that hospitals can implement control measures when a carrier is admitted. In the Siouxland Region, hospitals tracked VRE carriers. This improved the abilities of hospitals to prevent the spreading of VRE and also saved hospitals the additional cost of testing the admitted patients each time to identify the carriers. Dutch hospitals saved substantially on HIC because they knew that patients admitted from other Dutch hospitals were not likely to be carriers. A large fraction of the costs came from a few epidemics started by Dutch patients who had become MRSA carriers while hospitalized on vacation outside the Netherlands. If hospitals are required to report their nosocomial infection rates, they may increase spending on HIC to protect their reputation. Then patients and other institutions would stand to gain.

Improving hospital infection control is at least part of the solution to the epidemic of antibioticresistance in nosocomial pathogens. Nearly 30 states are considering or have passed legislation requiring hospitals to report how frequently patients contract infections while hospitalized. The threat of lower patient volumes in response to a greater risk of nosocomial antibiotic-resistant bacteria would play a powerful role in pushing hospitals towards greater infection control.

References and Further Readings

Dowell SF, Schwartz B. Resistant pneumococci: protecting patients through judicious use of antibiotics. *American Family Physician* 55(5):1647-1654, 1657-1658, 1997.

National Nosocomial Infections Surveillance System (NNIS). National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. http://www.cdc.gov/ncidod/hip/NNIS/2003nnisReport_AJIC.pdf, 2004.

Ostrowsky BE, Trick WE, Sohn AH, Quirk SB, Holt S, Carson LA, Hill BC, Arduino MJ, Kuehnert MJ, Jarvis WR. Control of vancomycin-resistant enterococcus in health care facilities in a region. *New England Journal of Medicine* 344(19):1427-1433, 2001.

Smith DL, Levin SA, Laxminarayan R. Strategic interactions in multi-institutional epidemics of antibiotic resistance. *Proceedings of the National Academy of Sciences USA* 102(8):3153-3158, 2005.

Vriens M, Blok H, Fluit A, Troelstra A, Van Der Werken C, Verhoef J. Costs associated with a strict policy to eradicate methicillin-resistant *Staphylococcus aureus* in a Dutch University Medical Center: a 10-year survey. *European Journal of Clinical Microbiology and <u>Infectious Diseases</u> 21(11):782-786, 2002.*

[Discovery Medicine, 5(27):303-308, 2005]