EXECUTIVE SUMMARY

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EXTENDING THE CURE

Policy responses to the growing threat of antibiotic resistance

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Extending the Cure: **Executive Summary**

Brandon Noble needs crutches to walk, and he has been relegated to spending much of his time at home on his sofa. When he's lying in bed at night and needs to move his left leg to get comfortable, he must lift it with his arms or nudge it with his right leg. He struggles to play with his children. But while Noble might have the typical limitations of a broken-down football player, the career of the Washington Redskins' defensive tackle isn't threatened by damaged ligaments or cracked bones. At 31, Noble has been sidelined by a staph infection, suffered after being injured, that in some cases is potentially fatal.

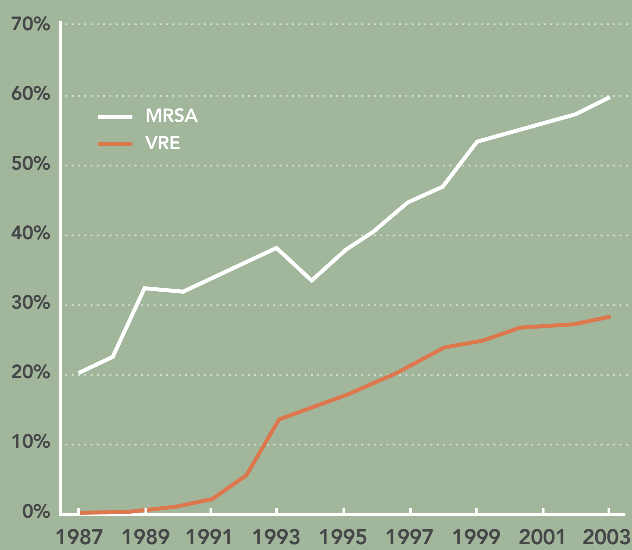
"It's been an incredible couple of years here," Noble said. "It's like I'm a modern-day Job." For the second time in a year, Noble is being treated for methicillin-resistant *Staphylococcus aureus*, or MRSA, a sometimes debilitating illness that is becoming increasingly common in the general population, according to national health experts. It is a growing concern for the NFL, which has experienced a recent increase in MRSA cases. —***The Washington Post***, January 27, 2006

Modern medicine depends on effective antibiotics to control bacterial infections. Since the first of these wonder drugs appeared a mere 65 years ago, they have transformed the practice of medicine and saved millions of lives. But today, at the start of the 21st century, the rapid rate of emergence and spread of bacterial pathogens resistant to antibiotics threatens to return us to an era when infections like Brandon Noble's were untreatable.

The growing problem of antibiotic-resistant *Staphylococcus aureus* (*S. aureus* or "staph"), the common bacterium infecting Brandon Noble, is illustrative (Figure ES.1). According to the Centers for Disease Control and Prevention (CDC), in 1974, 2 percent of patients infected with *S. aureus* failed to respond to methicillin, an inexpensive antibiotic that had been effective against these infections since the 1960s. By 2004, more than 50 percent of patients with *S. aureus* failed to respond to methicillin, with terrible consequences. Already a few cases of resistance to vancomycin, the drug often used to treat MRSA infections, have been reported.

FIGURE ES.1

The proportion of methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococcal infections is increasing (1987–2003)



Note: Data refer to infections in intensive care unit (ICU) patients only.

Sources: VRE and MRSA data, 1998–2000, 2002–2003 (CDC 1999; CDC 2000; CDC 2001; CDC 2003; CDC 2004); data for 2001 are the average of 2000 and 2002 data. MRSA data from 1987–1997 are estimated from (Lowy 1998). VRE data for 1989 and 1993 are from (CDC 1993). VRE data for 1990–1992 and 1994–1997 are interpolated based on geometric mean.

Streptococcus pneumoniae (*S. pneumoniae*), another common pathogen, causes bacterial meningitis and bacterial pneumonia, among other conditions. In 1987, only 2 of every 10,000 *S. pneumoniae* infections—0.02 percent—were resistant to penicillin, the antibiotic of choice. By 2004, this figure had risen to 1 in 5—20 percent—a 1,000-fold increase (CDC 2005).

According to the U.S. Food and Drug Administration (FDA), "Unless antibiotic resistance problems are detected as they emerge, and actions are taken to contain them, the world could be faced with previously treatable diseases that have again become untreatable, as in the days before antibiotics were developed." Major reports in recent years have called for steps to address this growing threat before it engulfs the medical system (ASM 1994; OTA 1995; Harrison and Lederberg 1998), yet policymakers have taken astonishingly little action.

Antibiotic effectiveness can be thought of as a natural resource, much like oil, fish, or forests (Laxminarayan and Brown 2001; Laxminarayan 2003): it is a resource accessible to anyone who can purchase it. All antibiotic use, appropriate or not, "uses up" some of the effectiveness of that antibiotic, diminishing our ability to use it in the future. Hastening the spread of resistance by overuse of antibiotics is like other shared resource problems, such as global warming or overfishing—a phenomenon referred to as "the tragedy of the commons" (Hardin 1968). Approaching antibiotic resistance as a resource problem is not just a convenient metaphor; it can help shape incentive-altering strategies to use antibiotics in ways that provide the greatest benefit to society, both today and in the future. Such incentives would encourage pharmaceutical companies to develop new antibiotics, and patients and health care providers to use existing antibiotics sustainably.

In this report, we examine the problem of antibiotic resistance from a natural resources perspective and propose solutions from an incentive-based perspective. Our purpose is to evaluate policy options that will enable society to make the best use of existing antibiotics, sensibly encourage the discovery of new antibiotics, and give drug companies a greater incentive to sell these new drugs responsibly. The policy changes considered here go beyond simply tinkering with the current system; instead, we address deep weaknesses in how we develop, regulate, and manage antibiotics.

The report is the result of a two-year study by researchers at Resources for the Future, the University of Chicago, the National Institutes of Health, and Emory University. It objectively evaluates

> The world could be faced with previously treatable diseases that have again become untreatable.
>
> — Interagency Task Force on Antimicrobial Resistance

a range of policy options for dealing with antibiotic resistance. The policy options presented here were debated at four consultations with medical and scientific experts who provided invaluable insights into the incentives behind choices concerning antibiotic use and development. The research focused on antibiotic use in medicine and did not explicitly address the problem of antibiotic overuse in agriculture for growth promotion, but clearly it is important to change incentives for how the drugs are used in that context as well.

A significant finding of this work is that we lack much of the information necessary to properly evaluate these policy options, prioritize them, or combine them in effective and efficient ways. It is important to distinguish policies, the subject of this report, from techniques—that is, the actual practices, such as multidrug treatment and infection control measures in hospitals—about which more is known. The policy options involve ensuring that these effective practices are followed. The full range of policy options considered in the study, with their pros and cons and the actors involved, is available on the project website, www.extendingthecure.org.

The second phase of the Extending the Cure project will expand the policy research and dialogue over the next few

years. Filling in these knowledge gaps should allow us to develop a comprehensive playbook of incentive-based policy options that government officials and other policymakers can use to make a real difference in the fight against antibiotic resistance.

ANTIBIOTIC RESISTANCE AND ITS SPREAD

Antibiotic-resistant bacteria are a natural consequence of antibiotic use, but development and spread of these pathogens can be hastened or slowed by the way antibiotics are used. Antibiotic-resistant bacteria arise as the natural result of mutation and natural selection within a population of organisms—say, an infection in a human host—faced with an agent that eliminates most of its members. Those that survive because of mutations that circumvent the effect of the antibiotic (through a variety of mechanisms) can multiply and give rise to larger numbers of antibiotic-resistant bacteria. In the absence of alternative antibiotics or other control mechanisms, these antibiotic-resistant bacteria can spread to other people just like any other bacterial infection (for example, through personal contact or inhalation of droplets from coughing). If they are robust enough, they can become widespread. Complicating matters, in many cases bacteria acquire resistance to antibiotics through the transfer of genetic material from other species of bacteria. In addition, resistance to one antibiotic may confer resistance to related antibiotics.

> More than 63,000 patients in the United States die every year from hospital-acquired (resistant) infections.

Antibiotic resistance cannot be prevented. Every time antibiotics are used, whether they save a life or are used to no effect (to treat viral rather than bacterial infections, for example), the effective lifespan of that antibiotic and perhaps related drugs is shortened. The tension between individual good and collective good is central to the issue. The average patient suffering from a cold or an ear infection wants immediate relief and sees a prescription for antibiotics as the ticket to recovery, and the physician may be only too happy to oblige if writing it benefits her practice. Neither may consider that antibiotic use by one patient eventually reduces the drug's effectiveness for everyone.

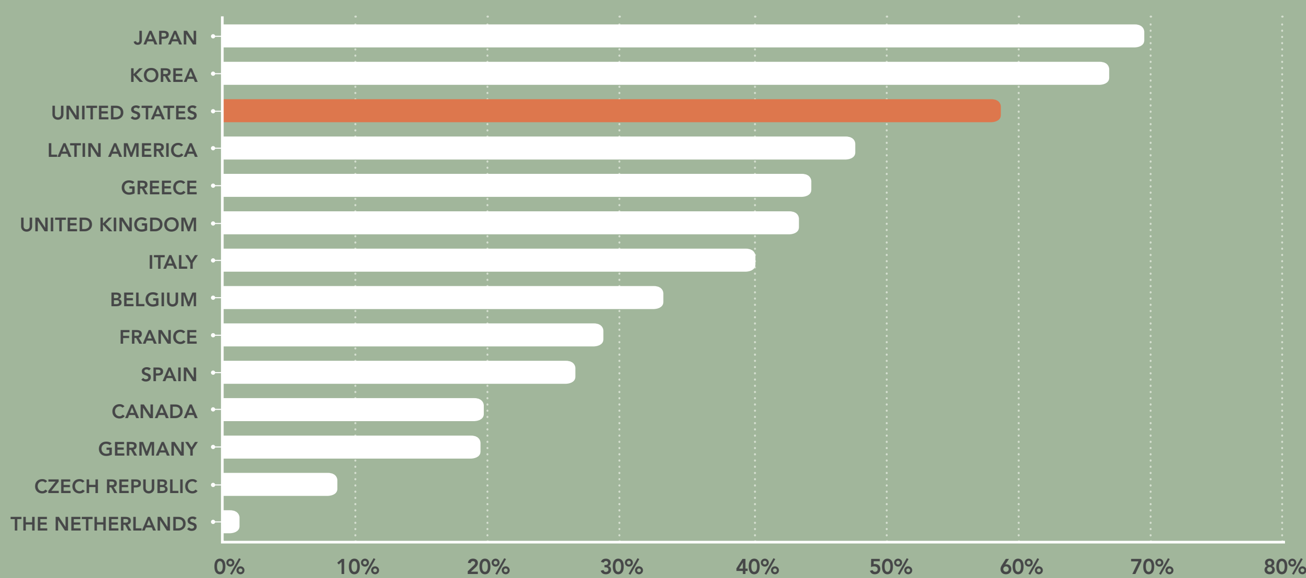
Hospitals, too, ignore the larger context of their response to infection, particularly hospital-acquired infection, by preferring treatment over prevention. Antibiotics are often less expensive than other forms of infection control, and hospitals can even pass off the costs of antibiotic treatment to managed-care providers. Compounding the problem, hospitals have no incentive to ensure that the patients they discharge are not carrying a resistant pathogen from their facilities to other health care institutions.

Although pharmaceutical companies, the makers of antibiotics, have a profit motive to consider the effect of resistance on the antibiotics they own, other firms may have drugs that work in similar ways. Just as many farmers drawing water from the same aquifer have no incentive to care about how fast the aquifer is being depleted, no one firm needs to care about resistance because the burden of resistance as it relates to the lifespan of salable antibiotics is borne by all firms.

The barriers to addressing the problem of antibiotic resistance all involve conflict between the interest of individual decisionmakers and the interest of society as a whole, now and in the future. Incentive-based policy solutions can help patients, physicians, hospitals, and pharmaceutical companies consider the impact of their decisions on others and give them the opportunity to help the solution evolve.

FIGURE ES.2

The proportion of MRSA infections in the United States is high compared with other high-income countries (2004)



Sources: United States (The Surveillance Network (TSN) Database-USA (Focus Diagnostics, Herndon, VA, USA)), Japan (Bell and Turnidge 2002), Korea (Lee, Kim et al. 2004), Latin America (Diekema, Pfaller et al. 2000), European countries (RIVM 2005).

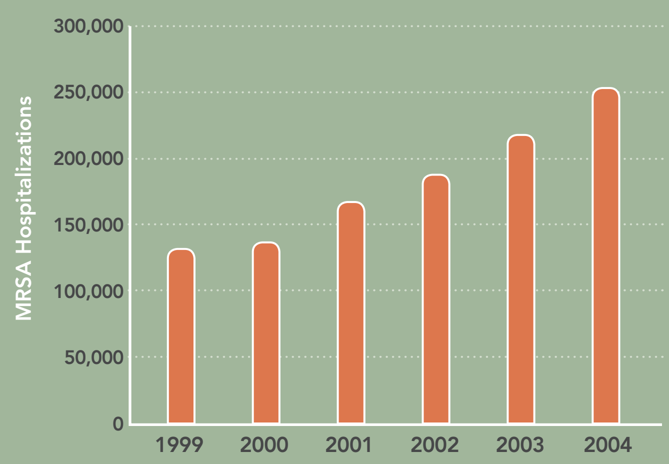
The phenomenon of antibiotic resistance has been anticipated since the introduction of penicillin. The search for new antibiotics was always aimed at more effective products, but also with the recognition that older drugs would be lost to resistance and new ones would be needed. Early on, the potential for new and better antibiotics might have seemed limitless. Today, the need for them is urgent. The challenge—the subject of this report—is how to change the incentives of all the actors and thereby maximize the useful lifespan of today's antibiotics and those still to be developed.

ANTIBIOTIC RESISTANCE IN THE UNITED STATES: STATUS AND IMPACT

More than 63,000 patients in the United States die every year from hospital-acquired bacterial infections that are resistant to at least one common antibiotic (Gerberding 2003)—more deaths than from AIDS, traffic accidents, or influenza. The number may actually be higher because many deaths attributed to other causes, particularly those of elderly patients suffering from multiple conditions, may in reality be due to antibiotic-resistant infections.

FIGURE ES.3

Growing resistance combined with the increasing number of *Staphylococcus aureus* infections has resulted in an increasing number of hospitalized patients who have MRSA infections



Source: The Surveillance Network (TSN) Database-USA (Focus Diagnostics, Herndon, VA, USA), and (Klein, Smith et al. 2007).

Comparison with other countries

Some of the most serious and widespread antibiotic-resistance problems worldwide are infections caused by MRSA and vancomycin-resistant enterococci (VRE). Data on the prevalence of these infections are available from many countries around the world, and the United States does not compare favorably.

About half of all patients treated in intensive care units for *S. aureus* in U.S. hospitals cannot be treated with methicillin or older antibiotics (CDC 2004), a much higher proportion than in most other high-income countries (Figure ES.2). Spreading resistance combined with an increasing number of *S. aureus* infections has resulted in a growing number of hospitalized patients who have MRSA infections (Figure ES.3).

U.S. hospitals also rank high in infections from species of the bacteria genus *Enterococcus* that are resistant to vancomycin—one of the most powerful antibiotics available. More than 12 percent of enteroccocal infections in U.S. hospitals are resistant to vancomycin, with even higher rates in intensive care units (McDonald 2006). In Europe, only Portugal reports a higher proportion of VRE infections.

Economic impact of antibiotic-resistant infections

In addition to their death toll, drug-resistant infections impose a significant financial cost on patients, health care systems, and society. The annual additional cost of treating hospital-acquired infections from just six species of antibiotic-resistant bacteria was estimated to be at least $1.3 billion in 1992 dollars ($1.87 billion in 2006 dollars)—more than annual spending on influenza (OTA 1995; AHRQ 2003). The Pennsylvania Health Care Cost Containment Commission estimated that during 2004, at least $20 billion was billed nationally to Medicare for hospital-acquired infections, many of which were resistant to one or more classes of antibiotics.

Many studies have documented longer hospital stays and increased costs for medication and care associated with resistant infections. The situation where an infection does not respond to any known antibiotic is becoming increasingly common. Since death or serious disabilities are likely outcomes, the future costs of multidrug-resistant strains are only going to increase.

Another significant cost of drug resistance comes from periodic switches to newer, more expensive antibiotics. As the risk of treatment failure increases, the entire system must shift to new drugs even if older drugs retain some effectiveness. Whereas penicillin costs pennies a dose, the newest antibiotics can run a few thousand dollars for a course of treatment. Even with modest levels of resistance to antibiotics, patients have to be dosed with two or more drugs to ensure successful treatment. As a result, for example, increased drug resistance has raised the annual national cost of treating ear infections by an estimated 20 percent, or $216 million (Howard and Rask 2002).

The expense of more powerful antibiotics affects the cost of not only treating infections but also preventing them. Modern medical practices—including all types of surgery, organ transplants, and cancer chemotherapy—involve using antibiotics to protect patients with other serious conditions, many of whom have temporarily or permanently impaired immune systems, from the added risks of serious infection. Because antibiotics are an important complement to other medical technologies, the higher cost (or diminished effectiveness) of antibiotics raises the price of other medical technologies and may imperil them if effective antibiotics are lost.

Measuring the costs of resistance

Quantifying the health and economic impacts of resistance is a significant research challenge, but it can be accomplished with the appropriate level of effort. To date, no reliable estimates of both the costs and the benefits of antibiotics in the hospital and community setting have been made. In hospitals, where antibiotic-resistant pathogens are often transmitted, one challenge is disentangling the effect of drug-resistant infections on the length of hospital stay: a hospital-acquired infection with a resistant pathogen increases the length of stay, and a longer stay increases the risk of acquiring such an infection. In community settings, the challenge is accurately estimating both the benefits and the costs of antibiotic use. Resistance-related costs alone are insufficient reasons to recommend that fewer antibiotics be used, since antibiotics have infection control benefits: they prevent the spread of susceptible pathogens.

OVERVIEW OF POLICY OPTIONS

The potential policy options presented in this report involve all possible participants and all incentive-based tools that might be brought to bear in a comprehensive strategy for the near- and long-term stewardship of antibiotics in health care. What is missing is the information needed to evaluate each option fully and hence the ability to rank them according to cost-effectiveness or economic efficiency. We therefore present them as starting points for discussion and as the basis of a future research agenda.

An overall strategy to maintain the effectiveness of existing antibiotics for as long as possible and to encourage the development of new antibiotics would have five components:

- discouraging inappropriate antibiotic use by changing how patients are reimbursed for antibiotic prescriptions and how physicians are paid for prescribing them;
- lessening the need for some uses of antibiotics by improving infection control and vaccinating against common infections;

- designing antibiotic use strategies, such as hospital formularies, combination therapies, and cycling, that delay the emergence of resistance;
- encouraging research and development into new antibiotics; and
- reducing incentives for pharmaceutical manufacturers to oversell their antibiotics.

Those five tactics, three that reduce demand and two that address supply, are not mutually exclusive. Partial solutions to the antibiotic resistance problem—those that focus only on supply or only on demand—are likely to be less effective in the long term than solutions that are mindful of their interrelatedness. Efforts to protect new antibiotics from bacterial resistance by keeping them on the sidelines, for example, potentially reduce incentives for new drug development by the pharmaceutical industry. Yet having a supply of new antibiotics that are fundamentally different from existing ones expands treatment options and lowers the likelihood that resistance to other drugs will evolve and spread.

DEMAND-SIDE SOLUTIONS: EXTENDING THE THERAPEUTIC LIFE OF EXISTING DRUGS

Few new antibiotics are in the development pipeline, so increasing the useful life of existing drugs must be an immediate priority. Several kinds of policies could help extend the useful therapeutic life of existing antibiotics.

- One set of policies focuses on reducing antibiotic prescribing by educating patients and physicians of the risks of greater antibiotic use and by changing incentives for health care providers and patients.
- Another set of policies reduces the need for antibiotics by lowering the burden of infections, using vaccinations in community settings and infection control in health care facilities.

- A third set of policies relies on a better understanding of strategies, such as cycling, combination therapies, and antibiotic heterogeneity, to delay the emergence and spread of resistance.

Reducing antibiotic prescribing

Lowering antibiotic use is critical to slowing the evolution of resistance. Rates of antibiotic prescribing in the United States are among the highest in the world (Figure ES.4). Reducing prescribing, however, involves a tension between what is good for the individual patient and what is good for the rest of society. Patient and physician education can decrease antibiotic use to some degree, but the long-term effectiveness of educational programs is unclear.

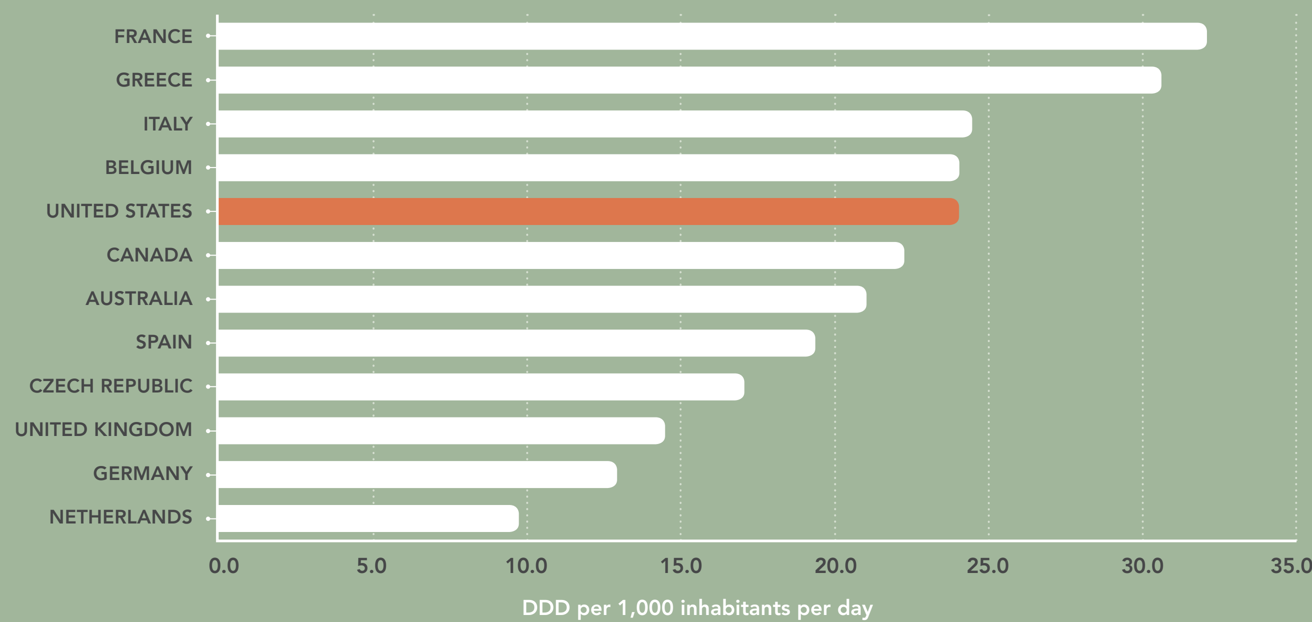
Reducing the need for antibiotics

Vaccination in the community. Vaccinations can lower the incidence of infections and thus the need for antibiotics, and this approach is immediately feasible. A policy of routinely vaccinating children against pneumococci, for instance, would reduce the number of infections. It is not currently mandatory, however, and it is relatively expensive. A national requirement for childhood pneumococcal vaccinations and a lower vaccine price could greatly reduce the need for antibiotics in children under the age of five, who consume a significant proportion of antibiotics used in the community. A vaccine to prevent MRSA infections could lower the need for antibiotics in health care facilities but is not yet available. Federal support of research on an MRSA vaccine may be useful in expediting vaccine development.

Infection control in hospitals. Containing bacterial infections in community settings will require significant time and resources, but relatively immediate infection control in health care facilities can be highly effective (and cost saving). Hospitals are focal points for the evolution of

FIGURE ES.4

The United States is among the most intensive users of antibiotics in the world



Sources: United States and Canada (McManus, Hammond et al. 1997), Australia (National Prescribing Service 2005), European countries (Goossens, Ferech et al. 2003)

DDD = defined daily doses, a standardized measure of antibiotic consumption

resistance because most hospital patients are administered antibiotics, and patients carrying a resistant strain are rapidly discharged—stays average just five days in U.S. hospitals (DeFrances, Hall et al. 2005) —and replaced with noncarriers. Infection control can therefore be very effective at reducing transmission within the hospital. Today, however, hospitals and long-term care facilities are reluctant to invest in practices that would reduce transmission—such as isolating incoming patients colonized with a resistant infection, encouraging hand washing and consistent use of caps and gowns, and changing staff cohorting (assigning nursing staff to a small number of patients to prevent wider contact)—because it is less expensive to use antibiotics.

Two other factors may affect hospitals' decisions to invest in infection control. One is financial: the costs of staff time and equipment purchased for infection control are borne by the hospital, whereas antibiotics are covered by health insurers. The other involves "free-riding:" because patients use more than one hospital, each institution has an incentive to take advantage of the infection control efforts of others while not making the investment itself, and consequently overall levels of infection with resistant strains remain high. Where infection control programs operate at a regional level—as in the Netherlands, for example—all hospitals share both the costs and the benefits of better infection control.

Using innovative treatment strategies

Ecological understanding can be applied to formulate antibiotic use strategies to lower the likelihood of resistance development. Strategies such as using drug combinations and cycling of antibiotics (similar to pesticide rotation in agriculture to delay the development of pesticide-resistant insects) have been proposed but have not been rigorously evaluated. A strategy of treating different patients who have the same type of infection with fundamentally different antibiotics has been proposed to slow the spread of resistance, but it remains to be tested widely.

SUPPLY-SIDE SOLUTIONS: ENCOURAGING DEVELOPMENT OF NEW ANTIBIOTICS

Even if we were to make the best use of existing drugs, resistance would arise. However, in recent decades the development of new antibiotics has not kept pace with resistance. Investment in antibiotics appears to be declining (Figure ES.5) and new antibiotic development has been limited mainly to addressing MRSA. While MRSA is a significant health risk, new antibiotics are needed to combat infections caused by Gram-negative organisms, where resistance is rising rapidly.

Encouraging new antibiotics

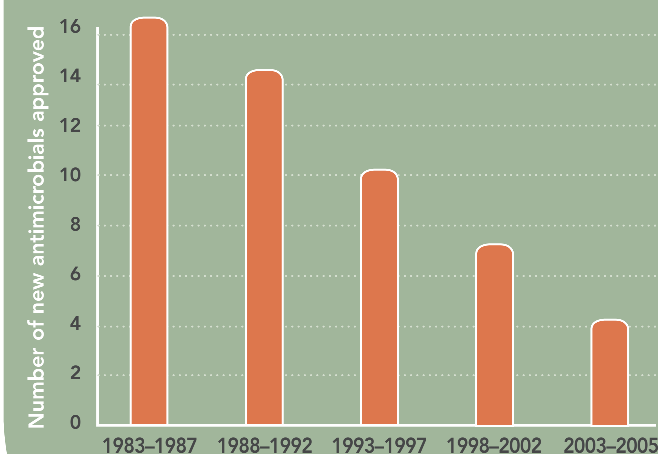
Policies to encourage development of new antibiotics that have been contemplated so far include tax incentives for research spending, patent extensions for other drugs in a pharmaceutical company's portfolio in exchange for developing a new antibiotic ("wild card" patent extensions), and liability protection from the adverse side effects of new antibiotics. They also include policies to reduce FDA approval times, thereby allowing manufacturers to obtain a return on their investments earlier, and tax breaks to defray the cost of the FDA approval process.

Reducing incentives to oversell existing drugs

Even if pharmaceutical companies invest in developing new antibiotics, a significant problem remains: one firm's antibiotic sales generate cross-resistance to related antibiotics produced by other firms. The cross-resistance problem applies not just to antibiotics already on the market but also to those yet to be developed. Resistance generated by the use of an antibiotic today could diminish the effectiveness of new drugs in the pipeline if they work in similar ways or are chemically related. For this reason, patents alone do not give pharmaceutical firms an incentive to care about resistance. Further, many antibiotics are off patent and manufactured by more than one company, each of which has an incentive to sell as much as possible.

FIGURE ES.5

Fewer new antibiotics are being brought to market as more firms leave the anti-infectives business



New antibacterial agents approved by FDA, 1983–2005

Sources: 1983–2002 (Spellberg, Powers et al. 2004), 2003–2005 (Bosso 2005).

Solving the problem of "who owns antibiotic effectiveness" is a significant challenge. Options include revisions of U.S. patent law to create a new, patent-like marketing right (similar in concept to market exclusivity under the Orphan Drug Act) and antitrust exemptions that would enable different antibiotic patent holders to work together to prevent the emergence of resistance.

FEDERAL STEWARDSHIP OF ANTIBIOTIC EFFECTIVENESS

Antibiotic effectiveness (in contrast to the antibiotics themselves) is a shared resource, like clean air or safe drinking water. Because it is not owned by any single entity, markets are unlikely to result in sustainable antibiotic use. Private markets may not be able to induce higher levels of infection control or appropriate antibiotic use, but government might.

A useful precedent for government intervention to protect against resistance is the successful effort by the Environmental Protection Agency (EPA) to prevent the emergence of pesticide-resistant agricultural pests. EPA currently regulates bioengineered crops, such as corn with transgenic *Bacillus thuringiensis* (*Bt*), and requires that farmers grow traditional crops in "refuges" that can harbor susceptible pests and thereby delay the emergence of resistance to the bioengineered variety. These policies have been in place since the mid-1990s, and thus far, no resistance to *Bt* crops has been detected.

Solving the problem of "who owns antibiotic effectiveness" is a significant challenge.

But for resistance to antibiotics, federal efforts to improve antibiotic management have been hindered by insufficient funding and attention. Since 1999, a U.S. Interagency Task Force on Antimicrobial Resistance, comprising representatives from the CDC, the FDA, the National Institutes of Health, and other agencies, has worked to bring greater attention to the resistance problem. Funding for the task force is lacking, however, and no lead agency is ultimately responsible for maintaining antibiotic effectiveness. Changing this would require congressional action recognizing a national interest in preserving antibiotic effectiveness and setting appropriations from the federal budget for a lead agency to coordinate the government's demand-side (antibiotic use) and supply-side (new antibiotic development) efforts. A congressional declaration that antibiotic effectiveness is a valuable societal resource could be a necessary step in resolving the "commons" problem inherent in antibiotic use, as it has for fisheries and waterways.

Summary of Findings

1. **Antibiotic resistance is a threat to public health. Its root causes lie in insufficient incentives for patients, physicians, hospitals, and pharmaceutical companies to act in ways that would conserve antibiotic effectiveness.**
   - Antibiotic use by one patient eventually reduces drug effectiveness for everyone, but individual patients and physicians have little reason to consider this when deciding whether to take or prescribe an antibiotic.
   - Antibiotics are an inexpensive substitute for infection control. Hospitals have little incentive to fully consider the adverse impact of poor infection control practices because they share patients and problems with other facilities.
   - Even pharmaceutical companies, which have a profit motive to consider the effect of resistance on their antibiotics, are not motivated to think about resistance except as a market opportunity for new antibiotics. Several companies may have patents on different drugs that generate cross-resistance, so one pharmaceutical company has little incentive to care about resistance as long as other firms sell related drugs.
   - Research is needed to identify incentive-altering policies that could lower inappropriate antibiotic prescribing, encourage hospital infection control, and limit overselling and overusing antibiotics.

2. **Reducing inappropriate antibiotic use is important but potentially problematic from an incentives perspective because what is good for the patient conflicts with what is good for society.**
   - Appropriate antibiotic use not only benefits the patient but also limits spread of his infection to the community. Even incentives that specifically target inappropriate prescribing will encounter resistance, however, because they involve a tension between what is perceived to be good for the patient and what is good for society as a whole.
   - Discouraging inappropriate antibiotic use is widely acknowledged as a priority, but there is less agreement on exactly what kinds of prescribing are inappropriate and how they affect resistance. Current educational efforts should continue, but more research is needed on how to redesign physician incentives so that antibiotics are not used to substitute for time spent with the patient or other more time-intensive approaches.
   - Research should focus on identifying strategies to selectively reduce inappropriate prescribing.

3. **Demand-side solutions that do not put patients at risk are most feasible now.**
   - Expanding vaccination against pneumococcal bacteria either by mandate or through a subsidy would reduce the need for antibiotics. The vaccine is not used widely, however, because it is expensive and voluntary.
   - Development and deployment of a vaccine for MRSA may be a worthwhile public investment.
   - Subsidizing infection control in hospitals could encourage such practices as staff cohorting (assigning nursing staff to a small number of patients to prevent wider contact) and isolation of incoming patients colonized with resistant bacteria. Hospitals currently lack sufficient incentives to do this on their own, and regulations requiring hospitals to report levels of resistance and hospital infections can be circumvented.

4. **Encouraging research and development into new antibiotics may be effective at replenishing the pipeline of new antibiotics. But incentives for new drug development are incomplete solutions unless linked to greater incentives for pharmaceutical companies to care about resistance.**
   - Tax credits and other subsidies for new antibiotic development may help in the short term, but they do not solve the basic problem of cross-resistance among antibiotics that work in similar ways.
   - Efforts to protect new antibiotics from drug resistance

by keeping them on the sidelines potentially reduce incentives for new drug development by the pharmaceutical industry.

- Supply-side policies must encourage truly novel antibiotics—drugs that do not inherit the resistance problems created by their predecessors. Unless new antibiotics are developed, we will be confronted with the possibility of untreatable bacterial pathogens.
- Demand-side policies, such as reserving antibiotics for life-threatening situations, should take into account their effect on R&D investment for new antibiotics.
- Research should focus on grouping antibiotics by the extent to which they promote bacterial resistance to other antibiotics. These groupings are essential to defining adequate patent rights or the allowable scope of patent pools under antitrust law. They will also identify the truly novel antibiotics that perhaps ought to be subsidized. Research should also attempt to quantify the extent to which, for example, extending the Orphan Drug Act to new antibiotics might encourage investment in developing these drugs.

5. **Comprehensive antibiotic effectiveness legislation may be needed to protect a long-term sustainable future for antibiotic use.**
   - Legislation recognizing the national interest in preserving antibiotic effectiveness would make the issue prominent. Explicitly recognizing the problem in the U.S. budget (with a budget line item, for example) and naming a lead agency would allow a coordinated government strategy to implement demand-side (antibiotic use) and supply-side (new antibiotic development) efforts.
   - Congressional action to declare antibiotics a valuable societal resource may be helpful in resolving the commons problem inherent in antibiotic use, as it has been for fisheries.
   - Policy research on natural resources legislation would assist in the design of comprehensive policies and legislation to extend antibiotic effectiveness.

Next Steps:

POLICY RESEARCH AND DIALOGUE

This report outlines various policy approaches to problems of antibiotic resistance, but assessing the approaches fully is challenged by gaps in the knowledge base. Our call for more data and research is not just a nod to the norm in such reports; we truly need more biological, medical, and economic analyses that can directly inform policy decisions. Although we have evaluated incentives and motivating factors from a theoretical perspective, policymakers will demand stronger evidence to act on policies like subsidizing infection control in hospitals. Pilot interventions are urgently needed, and the results of these experiments should be part of a national dialogue on what to do about antibiotic resistance.

At this time, death from drug-resistant pathogens, although increasing in frequency, is not yet a concern for most Americans. Many infections that are resistant to common antibiotics typically respond to other, more expensive drugs. However, running out of the cheapest antibiotics is somewhat like running out of oil. Just as oil is relatively cheap and convenient but not our only energy source, generic antibiotics are also inexpensive and available but may not be the only way to treat infectious diseases. Losing drugs that cost pennies a dose and moving to more expensive antibiotics, the newest of which can cost thousands of dollars per treatment, can have a profound impact on the health care system as a whole, and especially on the poor and uninsured, who are most likely to have to pay directly for their care.

Nevertheless, the time may come when even our most powerful antibiotics will fail. The proposals in this report are meant to offer a guide to policy and research to address this crisis now, rather than waiting until the pressure on policymakers to act—even in the absence of information—is unavoidable.

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ABOUT EXTENDING THE CURE

The Extending the Cure project is a research and consultative effort that frames the growing problem of antibiotic resistance as a challenge in managing a shared societal resource. The inaugural report of Extending the Cure provides an objective evaluation of a number of policies to encourage patients, health care providers, and managed care organizations to make better use of existing antibiotics and to give pharmaceutical firms greater incentives to both develop new antibiotics and care about resistance to existing drugs. The report has been widely debated at a series of consultations with representatives from the medical, insurance, pharmaceutical, government, and academic communities. It sets the stage for future action and continued research to prevent the impending health crisis of widespread antibiotic resistance.

The Extending the Cure project is funded in part by the Robert Wood Johnson Foundation through its Pioneer Portfolio, which supports innovative projects that may lead to breakthrough improvements in health and health care. Extending the Cure is advised by a distinguished panel of academics.

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The full report is available at www.extendingthecure.org

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