



Fighting Antibiotic Resistance: Can Economic Incentives Play a Role?

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Antibiotic resistance is on the rise, imposing enormous costs on society and spurring concerns about the treatment of infectious diseases. The problem can be traced to the widespread overuse of the readily available drugs. Policy-makers should consider creating economic incentives to encourage individuals and drug manufacturers to take into account the societal costs of using antibiotics.

Widespread reliance on antibiotics has spurred an alarming rise in resistant strains of bacteria, complicating the treatment of infectious diseases. Many blame the situation on doctors, patients, and livestock farmers who overuse, and sometimes even misuse antimicrobial agents. The challenge for policymakers is to promote the optimal use of antibiotics by creating economic incentives for individuals and drug manufacturers to consider the costs, as well as the benefits, of using these powerful drugs.

Resistance imposes enormous costs on society in the form of increased hospitalizations, higher mortality rates, and the diversion of resources from other medical needs into the development of new and more powerful antibiotics. Nevertheless, doctors understandably focus on the benefits to the patient, not the risks to society, when they prescribe an antibiotic. Similarly, livestock producers who use antibiotics in animal feed are motivated by the incentive of increased profits, and drug companies that encourage antibiotic use are motivated largely by objective to profit from the antibiotic before expiration of its patent life. Such economic incentives drive the evolution

of antibiotic resistance. As more antibiotics are used, bacterial resistance increases—a cycle that is exacerbated by the failure of antibiotic users to consider the full costs of their activities. Because resistance results from the selective use of drugs on sensitive strains of bacteria, it is likely to remain a pressing issue as long as we rely on antibiotics.

Although no one knows the exact costs that antibiotic resistance imposes on society, the most common estimates range from \$350 million to \$35 billion, depending on how long resistance persists in the bacterial population, and whether or not the cost of deaths is considered. Such assessments are incomplete, however, because they fail to take into account the biological dynamics of resistance and infection. Unfortunately, limited data exist on antibiotic use and bacterial resistance, making it difficult for economists to compare costs when trying to evaluate alternatives to antibiotics.

A number of studies and reports have proposed guidelines for limiting the use of antibiotics in order to reduce resistance. But neither such guidelines nor educational efforts have been successful. Short of directly monitoring clinical practice, which would be extremely

RESOURCES FOR THE FUTURE

expensive, public health policymakers can do little to enforce restrictions on antibiotic use. And any attempt to admonish doctors for overusing antibiotics is likely to spark strong opposition from the medical community.

If we are to use the drugs more judiciously, it may be necessary to create a system that stresses the economic value of preserving the effectiveness of the drugs. In the language of economists, antibiotic resistance is a negative “externality” associated with antibiotic use, much as pollution is an undesirable externality associated with the generation of power at a thermal power plant. There are no incentives for antibiotic users or power plants to take into account the negative impact of their actions on the rest of society. In the case of power plants, government agencies impose emissions restraints in the form of taxes and quotas to force them to take the cost of pollution into account when determining how much power to generate. Similarly, society should devise mechanisms by which the cost of antibiotic resistance is taken into account—or, in economic terms, “internalized”—in decisions regarding the use of the drugs.

However, the externalities associated with antibiotic use are not all negative. A positive externality associated with antibiotic use is that it may cure infections, thereby reducing the likelihood of the infection being transmitted to uninfected individuals. Therefore, we need to weigh the favorable and unfavorable effects against one another to determine the optimal antibiotic use policy.

Optimal Use

Antibiotic effectiveness may be thought of as an economic or natural resource that is of value to society because it enables doctors to both prevent and treat infections. The current debate over antibiotic resistance centers on whether the current rate of depletion of this resource is greater than optimal.

From an economic perspective, the optimal use of antibiotics depends on whether the drugs are a renewable or a nonrenewable resource. This distinction relies on a biological concept (known as “fitness cost”) that measures whether resistant strains of bacteria are placed at an evolutionary disadvantage when antibiotics are removed from the environment. If resistant bacteria were less likely to survive in the absence of antibiotics, one could conceive of temporarily removing an antibiotic from active use to enable it to recover its effectiveness. Antibiotic effectiveness would then be characterized as a renewable resource, much like a stock of fish that is harvested

periodically and allowed to regenerate between harvest seasons. On the other hand, if the resistant strain remained prevalent, then an antibiotic would fail to regain its effectiveness even if it were temporarily removed. Effectiveness would be treated as a nonrenewable or exhaustible resource, similar to a mineral deposit. The question of renewable versus nonrenewable is difficult to answer because scientists continue to debate whether resistant bacteria endure in an environment without antibiotics.

In hospitals, where the increased use of antibiotics has contributed to a growing number of infections, officials seek to achieve optimal use by altering the menu of antibiotics available to doctors. How the antibiotics should be used to limit resistance, however, is a difficult question. If two antibiotics are available, for example, should doctors prescribe one, both, or alternate between the two?

Scientists have used mathematical modeling to show that, in the case of two antibiotics that are identical except for their modes of antibacterial activity, the optimal strategy would be to use equal fractions of both on all patients simultaneously. But if the two drugs differ in price, initial effectiveness, or the rate at which resistance develops, the results change dramatically. For example, when the cost of two antibiotics is identical, the optimal approach is to use the more effective antibiotic until resistance increases to the point that the two antibiotics are equally effective, and then to use both drugs. Alternatively, if the two drugs are equally effective, but one costs more than the other, the recommended approach is to use the less costly antibiotic until, due to increased resistance, the cost-effectiveness of the two antibiotics becomes identical. Finally, if one drug produces resistance more slowly, that drug should be used to treat more of the patients.

Another issue for hospitals is the tradeoff between the costs of strengthening infection control measures and reducing antibiotic use. Infection control measures, such as sequestering nursing staff to a limited number of patients, can be effective in reducing the spread of infections in hospitals. One recent study has shown that these policies also can reduce microbial resistance in hospital settings. Further studies are required to develop the optimal mix of strategies to reduce resistance in an economically efficient manner.

Efforts to restrict antibiotic use in outpatient settings have been much less successful than in hospitals because no central agent (such as a hospital administrator or infection control committee) can enforce an antibiotic policy. Also, the high cost of malprac-

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tice lawsuits may induce doctors to err on the side of using stronger and broader spectrum antibiotics than may be called for. This tendency has the effect of increasing the level of resistance throughout the community, but the impact of each individual prescription is so small that the benefit perceived by the doctor of prescribing antibiotics often outweighs the small uncertain costs associated with increasing resistance. One solution would be to design guidelines that use community data to minimize the overall total cost of treatment and future resistance.

From a patient's perspective, the decision to request an antibiotic is based on two factors: the benefit of quickly recovering from an infection and the cost (minimized by insurance coverage) of

taking the medication. But patients may not be aware of studies that have demonstrated conclusively that prior use of antibiotics increases a person's risk of acquiring a resistant infection.

Patients who are educated about the risks of antibiotics may be more careful about demanding such medication from the doctor. In addition, policymakers may want to consider such economic instruments as taxes, subsidies, and redesigned prescription drug insurance programs to ensure that incentives faced by both doctors and patients are aligned with the interests of society.

Livestock producers, like doctors and patients, have few incentives to consider the risks of antibiotic use. But the practice of adding antibiotics to livestock feed in order to promote growth in cattle and poultry has spurred warnings that such drugs may increase the level of bacterial resistance to antibiotics used in humans. In 1997, the World Health Organization recommended that farmers refrain from using drugs that are prescribed for humans or that can increase resistance to human medications. Policymakers need to balance the social costs of using antibiotics in animal feed against the benefits (namely more efficient livestock operations) in order to arrive at a rational policy regarding such use of antibiotics.

The Role of Patents

Firms that manufacture antibiotics face conflicting incentives with respect to resistance. On the one hand, bacterial resistance to a product can reduce the demand for that product. On the other hand, the resistance makes old drugs obsolete and can therefore encourage investment in new antibiotics.

Pharmaceutical firms are driven to maximize profits during the course of the drug's effective patent life—the period of time between obtaining regulatory approval for the antibiotic and the expiration of product and process patents to manufacture the drug. Given the paucity of tools at the policymaker's disposal, the use of patents to influence antibiotic use may be worth considering. A longer effective patent life could increase incentives for a company to minimize resistance, since the company would

RESOURCES FOR THE FUTURE

enjoy a longer period of monopoly benefits from its antibiotic's effectiveness.

Patent breadth is another critical consideration. When resistance is significant, other things being equal, it may be prudent to assign broad patents that cover an entire class of antibiotics rather than a single antibiotic. In such a situation, the benefits of preserving effectiveness could outweigh the cost to society of greater monopoly power associated with broader patents. Broad patents may prevent many firms from competing inefficiently for the same pool of effectiveness embodied in a class of antibiotics, while providing an incentive to develop new antibiotics.

Patent policies must take into account the global reach of antibiotic resistance. The 1999 Agreement on Trade-related Aspects of Intellectual Property Rights, sponsored by the World Trade Organization, provides for stricter enforcement of patent rights worldwide, while creating a phase-in period for developing countries that lack certain patent protections. Once antibiotic patents are enforced worldwide, pharmaceutical firms will have more incentive to research new and more effective antibiotics. Such patent rights could also have the potential to reduce the inefficient use of antibiotics by providing incentives to a single agent to conserve antibiotic effectiveness.

Future Research

The importance of scientific research in providing a reliable

foundation for sound economic policy cannot be overstated. As we learn more about the relationship between antibiotic use and resistance, we can better quantify the social costs of overusing the drugs. Similarly, quantifying the relationship between antibiotic use in animal feed and resistance in humans will help us assess the economic tradeoffs involved in using the agents in livestock operations.

Further economic and scientific research could provide guidance for a number of policy issues. Such research could investigate the optimal antibiotic use in community settings, design incentives to promote the judicious use of antibiotics, and analyze the behavior of drug firms in investing in the development of new antibiotics. Finally, much research remains to be done to evaluate the costs of antibiotics in light of the biological dynamics of resistance. These efforts can help policy-

makers ensure that antibiotics remain a valuable resource for society.

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Ramanan Laxminarayan is a fellow in RFF's Energy and Natural Resources Division. This article is based on a longer, more technical paper he coauthored with Gardner M. Brown, "Economics of Antibiotic Resistance: A Theory of Optimal Use," which can be found on the RFF website, at www.rff.org/disc_papers/PDF_files/0036.pdf. RFF recently sponsored a conference on resistance economics, focusing on antimicrobial resistance and pest resistance in agriculture. Look in the next issue of *Resources* for coverage of the conference proceedings.