

Economic Responses to the Problem of Drug Resistance

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Economic Responses to the Problem of Drug Resistance

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The increasing resistance of bacteria to antibiotics is a consequence of selection pressure placed by the use of antibiotics on susceptible organisms to the benefit of resistant organisms. Addressed as a behavioral problem, resistance is, at least in part, a consequence of missing economic incentives. Resistant bacteria arise and proliferate at a rate faster than is socially desirable because individuals fail to recognize the cost imposed by their use or misuse of antibiotics on the rest of society. For this reason, economists are often asked what they bring to the table in terms of innovative responses to the problem of resistance. Broadly speaking, there are two fronts along which we can consider strategies to counter drug resistance, and economics can help on both. First, we can manage our existing arsenal of drugs and antibiotics carefully so as to maximize the value derived from their use by intervening on the demand side of the antibiotics market. Second, we can develop (or encourage the development of) new drugs and pesticides that could replace old products that resistance has rendered ineffective by intervening on the supply side¹.

On the demand side, measures to encourage more efficient antibiotic use include both price and non-price measures. Price measures involve increasing the cost of antibiotics for patients to discourage their use. Non-price measures include patient counseling on the societal effects of antibiotic use, physician education, and so forth. These could also include measures to encourage the use of an economically efficient variety of drugs.

On the supply side, measures to address the resistance problem would include incentives that not only encourage drug firms to develop new antibiotics, but also give them a greater incentive to care about the impact of drug resistance. We discuss each of these measures in turn.

* This paper is based on (Laxminarayan, 2002), where the interested reader will find a more complete discussion and references.

¹ These two strategies are linked in a very intricate way. Our efforts to better manage resistance to existing products could reduce the returns to investment in new products. So, paradoxically, the evolution of resistance may create a demand for new products, which in turn leads to greater investment in research and development. Conversely, the greater availability of new products may increase variety of products that we have available and this may help us make better use of existing products.

Intervening on the Demand Side

Price Measures

The most reliable axiom in economics is that as the price of any commodity goes up, the quantity of that commodity that people will consume declines, all else being equal. Therefore, if our objective is to reduce the use of antibiotics, then the most reliable way of doing so without second-guessing physicians' decision-making is by raising the cost of using antibiotics to the patient. One solution might be to impose a tax on antibiotics. However, a tax may be undesirable for two reasons. First, a tax may not discourage antibiotic use if insurance coverage shields many patients from drug costs and physicians are relatively insensitive to drug costs. Second, the burden of a tax may be disproportionately borne by poorer patients who are less likely to have health insurance to cover the cost of antibiotic prescriptions.

A logical alternative would be to mandate an increase in the extent of cost-sharing for antibiotics. This could be accomplished by increasing co-payments for antibiotic prescriptions for certain conditions where a regulatory or scientific body believes that antibiotics are overprescribed (such as for the treatment of ear infections)². Such a measure would not hurt the majority of economically disadvantaged patients who currently lack prescription drug coverage, but would effectively tax antibiotic use. Figure 1 shows how an increase in the cost-share borne by patients would decrease the quantity of antibiotics consumed from Q_1 to Q_2 .

² Some economists have proposed tradable permits for resistance that would work in much the same way as tradable permits for pollution. While these may be economically efficient, they may be difficult to implement in a largely private health care system such as the one in the United States.

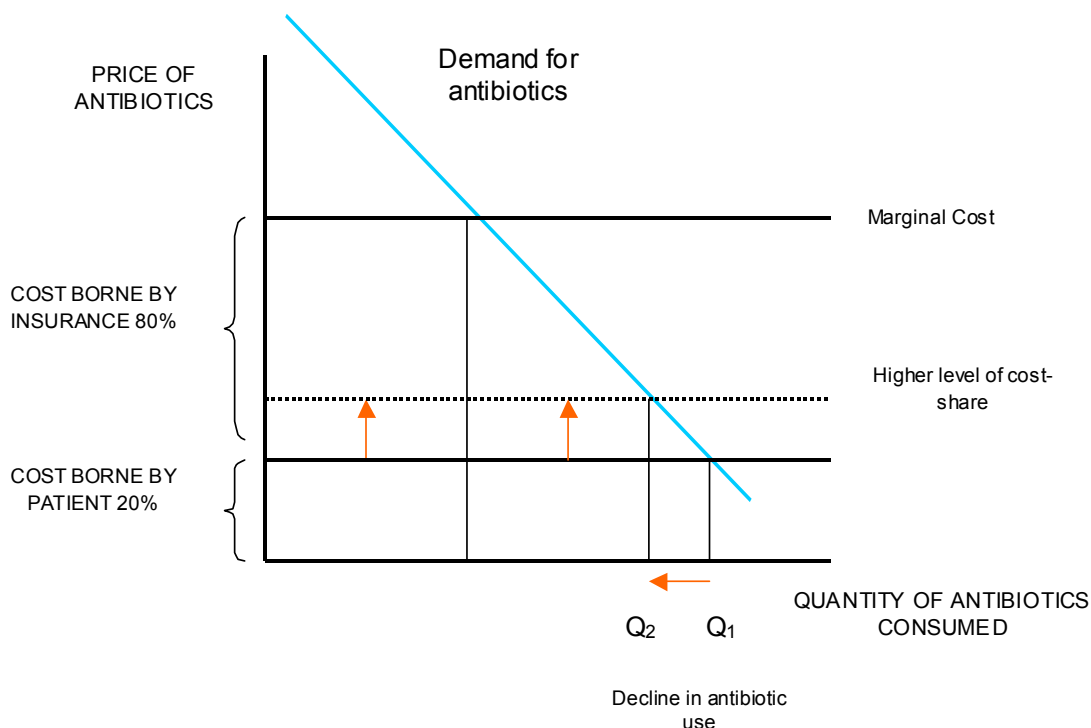


FIGURE 1 Increasing share of costs borne by patients decreases the quantity of antibiotics consumed from Q_1 to Q_2 .

Empirical evidence on the effect of cost-sharing on antibiotic use is limited but consistent. For instance, a large randomized study conducted in 1985 showed that people who received free medical care used 85% more antibiotics than those required to pay for at least some portion of their medical care (Foxman, Valdez et al., 1987). However, the same study found that cost-sharing was likely to equally reduce both appropriate as well as inappropriate antibiotic use.

To be sure, a price-based policy intervention is a blunt instrument, and may, in some instances, discourage the use of antibiotics even when their use is justified. However, targeted cost-sharing efforts aimed at certain diagnoses may be preferable to an across-the-board increase in mandatory cost-sharing for all antibiotics. Increased cost-sharing for antibiotics, or other methods of raising the cost of antibiotics to the patient may not be popular. However, short of direct case-by-case oversight of antibiotic prescriptions, there are few other alternative strategies that can effectively lower antibiotic use. Policy makers in the antibiotic resistance arena would

do well to learn from the use of tobacco taxes in the United States. The tremendous success of higher tobacco taxes on lowering smoking in this and other countries is self-evident.

Non-Price Measures

While price measures could be effective in lowering antibiotic use, their effectiveness may be enhanced when used in combination with non-price measures as part of an overall strategy to fight resistance. Increasing patient awareness of the drawbacks of antibiotic use and improving physician education could promote judicious antibiotic use; much has been written about these interventions and therefore these topics are not covered in this paper. Non-price measures could also include other innovative strategies, such as increasing treatment heterogeneity that have received relatively less attention from the public health and medical communities. Treatment heterogeneity refers to the policy option of treating different patients afflicted with the same disease with antibiotics that have unrelated modes of action.

The rationale for treatment heterogeneity follows from the notion that the likelihood that bacteria will develop resistance to any single antibiotic can be reduced by treating fewer patients with that antibiotic. This is achieved by using a larger variety of antibiotics (Laxminarayan and Weitzman, 2002). Variety reduces the selection pressure for resistance to evolve to any single drug class. However, one is struck by the degree of homogeneity in antibiotic treatment, a fact that is attributable to industry concentration, uniform treatment guidelines, and to some extent, emphasis on providing the safest, and most cost-effective treatment to all patients. For instance, in 1997, nearly 60% of all cases of acute otitis media in the United States were treated with amoxicillin (Laxminarayan et al., 1998)³. In fact, an earlier study found that in 1992, amoxicillin accounted for 39% of *all* antibiotics prescribed in the United States, and the five most commonly used antibiotics accounted for 80% of *all* antibiotics prescribed (McCaig and Hughes, 1995). The degree of treatment uniformity is even more striking in infectious disease treatment in the developing world. In most African countries, chloroquine has been the most commonly used drug to treat malaria for more than five decades.

³This level of market concentration is remarkable considering the \$240 million market for antibiotics for this condition alone.

To the extent that most patients in a region or country are treated with the same drug for a given infectious disease, the use of a single drug places excessively high selection pressure on organisms that are susceptible to that particular drug and increases the likelihood that a resistant strain will evolve and proliferate. As resistance to the recommended first-line drug builds up, that drug is replaced by an alternative that is used until resistance to this second drug also increases, and so on in succession. Therefore, the optimal solution may be to use not just a *single* drug throughout the population as first-line agent, but to prescribe a variety of drugs, randomized over patients, to ensure that inordinate selection pressure is not placed on any single drug, or class of drugs.

The notion that there is a single cost-effective treatment for an infectious disease fails to consider the effect of homogenous drug use on the evolution of resistance. Consequently, the standard cost effectiveness method may lead to flawed conclusions in the case of drugs such as antibiotics and anti-malarials since it has no way of capturing the notion that using the same drug on all patients may be undesirable from a societal perspective. Encouraging treatment heterogeneity may not require any specific policy beyond issuing treatment guidelines that recognize this aspect of infectious disease treatment. There may be sufficient heterogeneity in physicians' preferences and patients' willingness to pay that will bring about sufficient variation in drug choice. However, treatment heterogeneity necessarily requires the availability of a variety of drugs, and this may require regulatory intervention.

Supply Side

While increasing treatment heterogeneity and lowering the demand for unnecessary antibiotics through both price and non-price measures comprise one side of the solution, the other side deals with increasing incentives for pharmaceutical firms to increase research spending on new antibiotics as well as care about resistance to existing drugs.

The fundamental policy objective is not just to increase incentives for firms to develop and introduce *any* new antibiotics, but to specifically develop new products or classes of antibiotics that are significantly different from existing ones in their mechanisms of action. This minimizes the common property problem that arises when different firms make products with similar modes of action and consequently, no single firm has sufficient incentive to care about declining product effectiveness. If one were to use the analogy of thinking about product effectiveness as a resource, like oil for instance, then an optimal policy would encourage drug firms to search for new "wells" of effectiveness against bacteria, rather than to drill new "wells"

to extract existing reserves thereby competing with other producers. Given this latter criterion, standard policy solutions such as research investment tax credits, and longer patent length may not solve the problem of incentives.

One policy option that may address this problem is to extend patent breadth (or scope) for antibiotics as a way of encouraging innovation. To be sure, this is a more difficult policy to implement. While patent lengths can be easily extended by legislative action or administrative fiat, patent breadths are more difficult to change. Patent offices are reluctant to alter the rules that guide their decisions. However, one might argue that there are few, if any innovations, that are in need of such alterations to patent breadth. Under this proposed policy, the scope of antibiotics patents could be increased so they cover an entire class of compounds and pre-empt "me too" antibiotics that increase competition for the same mechanism of action. This may be a good idea for three reasons.

First, increasing patent scope gives firms an incentive to care about the evolution of resistance since the firm owning the patent would have nearly complete control over the stock of effectiveness. The common property problem arises with antibiotics because different firms sell similar antibiotics with similar modes of action, and no firm bears the full resistance cost of its production decisions. Indeed, the quantity of antibiotics sold is only one factor, albeit an important one, that influences the growth of resistance. For instance, the care that a drug firm might take in selecting the indications that an antibiotic will be marketed for can play an important role in influencing the growth in resistance. These and other strategies to reduce resistance are more likely to be employed by a firm if it has a broader patent on the antibiotic, and is likely to reap the benefits of sustained effectiveness to a greater extent.

Second, increasing breadth would dramatically increase the returns from investing in new compounds rather than just tinkering with existing compounds. The returns from new discoveries would dramatically increase since the innovator will have broad rights over the newly innovated class of antibiotics rather than just the narrow chemical entity. The third reason for increasing patent breadth is that we attain the basic objective of focusing new drug research on increasing the variety of modes of action of antibiotics. Variety has social value that is not fully compensated for in the current market for antibiotics, and increasing patent breadths would encourage variety (Ellison and Hellerstein, 1999).

There are drawbacks of broader patent scope for antibiotics that would need to be considered as well. First, increasing the allowable breadth of antibiotics patents increases the social welfare costs associated with greater imperfect competition. Second, broader patents may

discourage potentially valuable innovations such as new drugs that are closely related to existing antibiotics, but which are easier to administer and have fewer side-effects. These drawbacks should be addressed by other policies where possible, and balanced against the benefits of broader patents.

Recommendations

The problem of reducing inappropriate antibiotic use calls for a combination of price and non-price measures. The appropriate mix will have to be tailored to the particular cultural and medical context. Patient and physician education, better surveillance data, increasing antibiotic heterogeneity, providing warning labels on antibiotics are all part of the policy response mix. However, they are likely to be ineffective without a compelling economic incentive for patients and physicians to face the cost they impose on the rest of society in the form of resistance when they use or misuse antibiotics.

While lowering the demand for antibiotics is one part of the solution, further research should also look at incentives faced by pharmaceutical firms both with respect to research and development expenditure on new classes of antibiotics, as well as resistance to existing products.

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