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The Economics of Public Health in the Presence of Exploitation Strategies

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Abstract

Public health faces novel challenges because of rising bacterial resistance to antibiotics and the possible fatal spread of highly communicable viral infections. Multiple economic agents interact in the use and provision of anti-infective drugs, without accounting for their impact on others, and this gives rise to positive and negative externalities. Furthermore, anti-infective drugs may be linked on the supply side depending on the particular epidemiological context. A common example is that of antibiotic treatment effectiveness, which can be lost over time, affecting various antibiotics belonging to the same antibiotic family. This chapter describes how conflicting private objectives among economic agents may lead to exploitation strategies that lower the overall social welfare. Important open research questions are highlighted and various possible public policies addressed that can help address the problem of antimicrobial resistance.

Introduction

In developed countries, noncommunicable diseases associated with lifestyle change constitute a primary focus in public health. With the notable exception of HIV and avian influenza, communicable diseases receive less attention. This focus reflects the demographical and epidemiological change that has occurred in developed economies over the last decades, and has increased the demand for treatment of chronic diseases and conditions (e.g., high cholesterol, blood pressure, erectile dysfunction) as well as surgery interventions among the elderly (e.g., prostheses, heart stents). On the supply side, the pharmaceutical industry has kept pace with this evolution (for an empirical analysis, see Pammolli et al. 2011). The development of new drugs and treatments has ensured high, stable revenues while products are patented.

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The emphasis in research and development on chronic diseases, however, is about to change drastically. More importance will have to be allocated to the analysis of communicable diseases, even in developed economies, because of the rise of antimicrobial resistance coupled with the potential for new outbreaks of highly lethal viral infections—infections previously thought to have been eliminated by former vaccination programs, but which could reemerge to challenge public health in hospital and outpatient settings worldwide (WHO 2014).

Antibiotics are used intensively today to cure possibly fatal communicable bacterial infections among humans and to prevent infections during surgical interventions. Indeed, they have become a major component of modern human medicine and have contributed to the continuous increase in the welfare of humankind. Furthermore, antibiotics are used intensively to cure and prevent infections in animals (see, e.g., Singer et al. 2003). However, from an epidemiological point of view, it is well understood that intensive antibiotic *use* increases antibiotic *resistance*. Much effort is needed to draw a complete picture of the incentives that are driving economic agents (patients, physicians, pharmacists, hospitals, pharmaceutical firms, and health agencies) in their use of antibiotics.

Economic agents that use or supply drugs, such as antibiotics or vaccines, do not generally account for the potential benefits or costs to third parties. In economic jargon, these benefits and costs are termed "externalities," as the economic agent that causes them does not internalize their effect on others. On the demand side, the use of an antibiotic or vaccine lowers the prevalence of infection in the short and long term; this is an example of a positive externality that is beneficial to society. By contrast, the implied increase in bacterial resistance in relation with antibiotic use in the future implies a negative externality for the individual and society. On the supply side, efforts to preserve antibiotic effectiveness made by economic agents (e.g., a hospital, pharmaceutical producer, or country) may be obliterated by another supplier who does not engage in any preservation efforts, and hence causes important negative externalities.

The potential for free riding on another economic agent's investment—to preserve antibiotic effectiveness or to lower the prevalence of a viral infection via vaccination—is akin to the free riding and the tragedy of the commons (Hardin 1968) that can be observed in exploitation processes of more "classical" natural resources (e.g., open-access halieutic resources or oil fields). Laxminarayan and Brown (2001) were among the first to note the parallel between classical natural resources and those that can be defined in a public health context, such as antibiotic treatment effectiveness. Indeed, using an antibiotic may decrease the "level" of antibiotic effectiveness, such as a classical halieutic resource. When there is no possibility to prevent others from accessing such a resource pool, we can use the economic terminology of a common-pool resource. The particularity of resources related to public health, as described above, is that the free riding may affect both the demand and supply sides, while it only affects the supply side in relation to the more

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classical resources. Indeed, demand for oil (e.g., for transportation or heating), for instance, remains unaffected when oil resource pools are connected on the supply side, whereas the demand for an antibiotic should reflect the quality of the drug, which is intrinsically related to the level of antibiotic effectiveness available in the pool.

A further difference between the resources analyzed here and classical examples (e.g., halieutic resources and oil) resides in the subsequent development of backstop resources or techniques. As the stock of wild halieutic resources and oil fields diminish, the price of the natural resource should rise over time, allowing aquaculture and solar energy, for instance, to become eventually a competitive backstop technique. In the case of antibiotics, however, no new antibiotic class or technique seems to be able to substitute easily for the decreasing effectiveness of current antibiotic treatment, as was done in the past. New, alternative drugs may, in the future, be able to address genetically engineered or chemically induced bacterial strains that exploit the "social" interaction between bacteria to decrease bacterial fitness (see Brown, this volume). However, since these drugs are only at the beginning of development, their effectiveness remains highly uncertain.

As a consequence, preserving the antibiotic effectiveness of currently available drugs and reaching a sustainable antibiotic use is in the public interest. This could adversely lower the investment in research and development needed to identify new techniques and resources for the future. In this chapter, I argue that the externalities involved in using antibiotics, as described above (as well as antivirals and possibly vaccines), warrants public intervention, now as well as in the future, to correct the incentives of economic agents and to secure support for the research and development of new resources and techniques that will be needed in the future.

I concentrate mainly on the use of antibiotics and begin by presenting bioeconomic models that are used in the literature to address the socially optimal (normative) and market (positive) aspects of antibiotic use.[1] Thereafter I turn to the economic agents, providers, and users of antibiotics and identify possible strategic interactions among agents, and discuss how this may affect antibiotic resistance, in particular, and public health, in general. Open research questions are highlighted that merit future attention from the scientific community.

Bioeconomic Modeling: Normative and Positive Approaches

The network of economic agents involved in the provision and consumption of antibiotics and vaccines is relatively complex. It is particularly intricate in relation to the antibiotic consumption of an individual, which may occur

[1] Use of vaccines and antivirals implies similar positive and negative externalities as those present for antibiotic use.

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throughout any given year as well as over an individual's entire life span, as opposed to vaccination, which occurs at specific periods of time (e.g., before the flu season, at a particular age). Figure 8.1 illustrates the linkages between economic agents as well as the potential feedback effects from epidemiology related to antibiotic production, provision, and consumption. Economic agents (e.g., patients, physicians, pharmaceutical companies) are embedded in the epidemiological environment where the transmission of infection occurs, and which comprises various resource pools of antibiotic treatment effectiveness. Antibiotic use in animals may also affect this environment. The network is similar for antivirals and vaccines; however, hospitals play a lesser role.

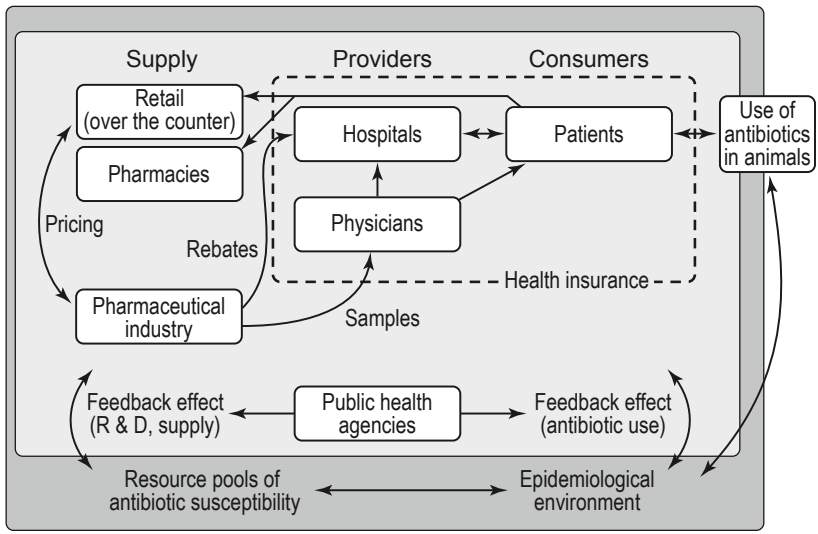

Figure 8.1 Schematic of interactions that occur in the epidemiological environment as a result of disease transmission, involving diverse economics agents. Anti-infective drugs can be characterized by treatment effectiveness, which vary as a function of antimicrobial use and in response to exogenous factors (e.g., microbial mutation). Eight groups of economic agents can be distinguished: on the supply side, the pharmaceutical industry sets the pricing strategy for anti-infective drugs, which impacts pharmacies and retail sales. On the demand side, patients, as the end users, interact with physicians in out- and inpatient (hospital) settings. This interaction is, in turn, affected by the coverage offered by health insurance companies. When necessary, antimicrobial drugs are prescribed by physicians. Public health agencies may regulate antimicrobial drug use. A complex relationship thus determines antimicrobial use, characterized by interactions between these diverse economic agents, the resultant pricing strategies, and availability (e.g., free samples, rebates, existing stock in hospital settings). This relationship impacts disease transmission and treatment effectiveness, which in turn affects both supply (research and development of new drugs) and demand (willingness to pay). As a final note, meat consumption of animals treated with antibiotics can also feedback into the human epidemiological environment.

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To address the positive and normative aspects of antibiotic use and identify the externalities involved, bioeconomic research has relied on simplified epidemiological models (for an exhaustive review on the economic literature of biological resistance, including insect resistance to genetically modified crops, see Laxminarayan and Herrmann 2015). Two different classes of biological models can be distinguished in the bioeconomic literature:

1. Deterministic compartment models of disease transmission, where individuals can be susceptible to infection (S), infected (I), or resistant to infection (R), as in the SIS or SIR model (e.g., Wilen and Msangi 2003)
2. Probabilistic models of antibiotic resistance (e.g., Laxminarayan and Weitzman 2002)

In deterministic models, antibiotic resistance is driven by natural selection and the emergence of "*de novo*" resistance, which is proportional to antibiotic use (Bonhoeffer et al. 1997). In probabilistic models, resistance may occur due to the mutation of bacteria. Clearly, all these mechanisms can drive antibiotic resistance, rendering the quality of any normative or positive bioeconomic analysis contingent on the specificity and representativeness of the biological model used.[2]

The seminal paper by Laxminarayan and Brown (2001) analyzes the optimal use of two antibiotics to fight the propagation of infection over time, when the economic objective is to minimize the intertemporal social cost of infection. Each antibiotic is assumed to have its own resource pool of antibiotic effectiveness.[3] When the cost of infection and treatment cost are not an issue, the antibiotic with the highest level of antibiotic effectiveness should be used first until that point in time when both antibiotics have the same level of effectiveness. As of this point, antibiotic use is such that the levels of antibiotic effectiveness remain identical for both. When there is a higher treatment cost of infection with a particular antibiotic, this antibiotic should not be used initially. Optimal use involves using only the cheaper antibiotic at first, lowering consequently its level of antibiotic effectiveness. It is only when the opportunity cost of using only the cheaper antibiotic becomes too important that both antibiotics should be used jointly. Because of the economic intertemporal optimization, these results differ from those obtained in the epidemiological scenarios of Bonhoeffer et al. (1997), who found joint antibiotic use preferable to using one sole antibiotic during an initial phase.

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2 Antibiotic susceptibility, the mirror image of antibiotic resistance, is generally defined as the proportion of infected individuals in the overall infected population that are infected with the drug-susceptible strain. An alternative, but not equivalent, measure of antibiotic resistance is related to the number of antibiotic doses necessary to cure an infection (Howard 2004).

3 The model is derived under the simplifying assumption that there is no cross resistance, nor multidrug resistance, as well as a zero fitness cost.

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Wilen and Msangi (2003) present a bioeconomic model in which only one antibiotic is available to fight a given infection. However, here, antibiotic effectiveness is considered a renewable resource: resistant bacteria suffer a fitness cost because they die at a higher rate than susceptible bacteria when no antibiotic treatment is applied. Hence, a low enough antibiotic use allows antibiotic effectiveness to recover.[4] Wilen and Msangi show that the optimal path is characterized by treating the overall infected population during an initial period, followed by a singular, interior control, where only a fraction of the infected population gets treated. Such a particular treatment rate tends to balance the selective pressure exactly due to antibiotic use and the fitness cost of resistance.

Herrmann and Gaudet (2009) extended the model by Wilen and Msangi (2003) and, in addition to the normative analysis, conducted a positive analysis in which antibiotic producers have open access to a renewable, common-pool resource. This market structure represents a benchmark for a generic industry in which no patent protects access to the resource pool. Hence, no producer has an incentive to preserve antibiotic effectiveness by lowering its sales, as this benefit would have to be shared with all the other producers, and thus is another example of the tragedy of the commons. In their model, Herrmann and Gaudet (2009) show that depending on the production cost, which at equilibrium equals the price of the antibiotic, antibiotic effectiveness may be higher or lower than what would be socially optimal in the steady state. The intuition behind this result is that a high price for the antibiotic lowers the quantity in demand. This benefits the maintenance of antibiotic effectiveness, but it does not account for the positive externality which results from antibiotic use: fighting the infection.

In another scenario, Herrmann (2010) considered what happens when a monopolist sells an antibiotic, while a patent is pending, to protect market access. Under this type of market structure, no externality or free-riding problem in relation to the pool of antibiotic effectiveness exists, at least as long as the resource pool associated with the patented antibiotic is not connected to any other antibiotic. In contrast to the social optimum, however, antibiotic effectiveness as well as infection are desirable resources, from the monopolist's point of view, because they represent the quality and potential market size of the drug, respectively. This study shows that the monopolist may want to preserve the antibiotic effectiveness and infection at higher levels. Toward the end of the patent, the monopolist becomes more myopic and prices the antibiotic by giving less weight to the intertemporal aspects of antibiotic effectiveness and infection. The divergence between viewing infection as a valuable resource from the firm's point of view versus undesirable from a social point of view

[4] Whether the fitness cost of resistance is positive, zero, or even negative is an empirical question (for a review, see Herrmann and Laxminarayan 2010). A recent publication shows that the fitness cost can indeed be negative (Roux et al. 2015).

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becomes apparent when the possibility of patent extensions are considered in response to the problem of antibiotic resistance. Herrmann (2010) shows that a longer patent extension is socially desirable when the prevalence of infection is less an issue or antibiotic resistance is high.

In a more stylized biological model, Mechoulan (2007) also identified the divergence between a monopolist and the "social planner" by showing that the monopolist does not find it profitable to eradicate the disease even though it may be socially desirable to do so. In a highly stylized model that ignores the evolution of infection, Tisdell (1992) showed that a monopolist may indeed correct for the problem of antibiotic resistance, as the monopolist tends to fix higher prices, which lowers antibiotic use, and the monopolist causes less antibiotic resistance. This is a well-known result in public or environmental economics: one distortion (here, the market distortion due to monopoly) may compensate exactly for another distortion (here, antibiotic effectiveness, which is a public good). Clearly, the stylized character of the epidemiological model has an impact on the results. In addition, not all models allow for the same epidemiological events (e.g., disease eradication), which makes the results obtained in the literature difficult to compare.

Considering this caveat on the precise epidemiological context, Laxminarayan and Smith (2006) obtained the general result that the cycling of two antibiotics to treat a given infection (i.e., switching from one antibiotic to another) is only optimal when two conditions are fulfilled: (a) fixed costs are present (e.g., to keep the antibiotic stocked in hospitals) and (b) switching costs from one antibiotic to another exist. This makes the antibiotic treatment cost function nonconvex. When there are no switching costs, a chattering control by instantly switching between one antibiotic and another would be optimal.

In another stylized model that focused on the rise of antibiotic resistance (and abstracted from the prevalence of infection), Laxminarayan and Weitzman (2002) analyzed the benefit of antibiotic treatment heterogeneity. The loss of antibiotic treatment susceptibility of an antibiotic is probabilistic (modeled as a Poisson process) and antibiotic treatment costs differ across antibiotics. Laxminarayan and Weitzman show that the policy of a first-line treatment, in which an infection is fought using the most cost-effective treatment, does not account for the externality of increasing the risk of resistance when concentrating on a single antibiotic. They show that less cost-effective antibiotics should also be part of a treatment policy, so as to diminish the overall risk of resistance: an optimal treatment policy is characterized by the additional treatment cost balancing exactly the benefit of reduced antibiotic resistance of the more cost-effective drug. This economic analysis is interesting because it is the first to capture the rise of resistance due to mutation. It hinges on the caveat that it remains static, in the sense that the optimal mix of antibiotics is not adjusted over time in response to a possibly changing environment. It also abstracts from the positive externality of antibiotic consumption related to the prevalence on infection.

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In light of their review (Laxminarayan and Weitzman 2002), the following research questions merit particular attention in the overlapping research field of economics and epidemiology:

- What is the "correct" biological model? Which level of abstraction is acceptable?
- How are resource pools in epidemiological models connected to one another?
- What are the existing substitute treatments among antibiotics and for antibiotics?

Providers of Antibiotics: The Role of Physicians and Hospitals

In developed countries, physicians generally prescribe antibiotics (and vaccines) to patients in both inpatient (hospital) and outpatient settings. One exception is in Greece, where antibiotics are able to be purchased "over the counter." Retail sales of drugs are more common in developing economies, such as India, and is characteristic of the absence of health insurance coverage for a large proportion of the population.

Incentives to prescribe antibiotics in out- and inpatient settings vary greatly (WHO 2014). Since antibiotic resistance is known to be a major problem in hospitals, hospital physicians need to be aware of antibiotic resistance, and good practice guidelines are necessary to avoid the overprescription of antibiotics. In outpatient settings, by contrast, regulations issued by public health agencies are needed to restrict possible overuse by individual physicians, as a means of countering antibiotic resistance.

Inpatient Settings

The intensive use of antibiotics in hospital settings to prevent infections during medical interventions is considered to be a driving factor behind the development of antibiotic resistance. To counteract this, Laxminarayan et al. (2007) found the effective control of the transmission of hospital-acquired infections to be one possible strategy for lowering antibiotic resistance in hospitals.

Whether a hospital has an incentive to control for hospital-acquired infections, especially antibiotic-resistant infections, depends on whether the additional costs related to the treatment of resistant hospital-acquired infections needs to be covered by the hospital or the patient via health insurance. The economic costs associated with antibiotic-resistant infections (e.g., vancomycin-resistant *Enterococci* or methicillin-resistant *Staphylococcus aureus*) have been well documented and account for higher morbidity, higher mortality, and prolonged hospital stays (Laxminarayan et al. 2007; WHO 2014). Even if hospitals are compensated for prolonged hospital stays, hospital-acquired

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infections lower the productivity of hospitals, thus lessening their ability to focus on first-line medical interventions for which patients are admitted.

Following arguments put forth by Laxminarayan et al. (2007), hospitals may choose to free ride on the efforts of other hospitals that actively engage in fighting antibiotic-resistant infections. This may be especially relevant in patient populations that fluctuate between hospitals (e.g., when a patient becomes infected in one facility and then visits other hospitals), thus creating a spillover effect. To control for hospital-acquired infections and lower their prevalence, direct incentives may be necessary to ensure quality in health care. For example, legislation could require hospitals to provide the public with information on how they manage antibiotic resistance.

Outpatient Settings

The prescription of antibiotics by individual physicians is generally done without testing for the infection's susceptibility, because such tests are costly and time consuming. Furthermore, patients tend to prefer an immediate prescription to satisfy the expectation for an earlier recovery. As a consequence, the prescription rate of physicians may be determined in a matching equilibrium between patients and physicians: if a physician's prescription rate were to be lower than expected, patients would turn to other physicians that prescribe at a higher rate.[5]

Howard (2004) showed that as the level of antibiotic resistance increases, physicians tend to prescribe newer, more expensive antibiotic drugs as first-line treatment. Such a resistance-induced substitution can imply important welfare costs as older, yet still effective drugs could have been used. The increasing use of broad-spectrum antibiotics as a response for high resistance levels to other antibiotics may counterbalance, in welfare terms, the beneficial effect of decreasing the overall use of antibiotics (Howard 2005). Clearly, prescription decisions taken by physicians also depend on their remuneration scheme as well as on health insurance coverage. Masiero et al. (2010) find empirical evidence that a fee-for-service and a salary remuneration are related to higher levels of antibiotic use compared to capitation compensation.

This analysis highlights the need to address the following research questions:

- What are the incentives and disincentives of hospitals to control for hospital-acquired infections?
- What kind of coordination is necessary between hospitals to optimize efforts to encourage cooperation in fighting regional prevalence of antibiotic resistant infections?

[5] Such a matching equilibrium has been described by J. Albert in a 2015 working paper, "Strategic Dynamics of Antibiotic Use and the Evolution of Antibiotic-Resistant Infections," where Albert determines the optimal number of providers (physicians) by accounting for arbitrage between temporarily lower prevalence of infection and higher antibiotic resistance in the future.

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- Can public information on the performance of hospitals, in terms of managing antibiotic resistance, sustain the right sorting of patients?
- Do economic agents utilize a sufficiently long planning horizon to account for cost-efficiency correctly?
- How does the retribution scheme of physicians affect the prescription of antibiotics?
- Is there any evidence that hospitals vary widely in hospital-acquired infections?

Patients' Demand for Antibiotics

Individuals suffering from bacterial infections are the ultimate end users of antibiotics. Their access to the resource pool of antibiotic effectiveness may, however, be limited by the practice of mandatory prescriptions and the access to and coverage of medical treatments (cost sharing) by health insurance plans.

From an individual patient's point of view, the effectiveness of antibiotic treatment is exogenous, and has been modeled in the literature as a quality aspect of the drug (Howard 2004; Herrmann 2010). When prescribed by a physician, an antibiotic treatment generally represents the optimal strategy for the individual patient, as the patient does not account for the negative externality of possible antibiotic resistance in the future.[6] As outlined above, overall antibiotic consumption creates a selective pressure for resistant bacteria. This selective pressure may be enhanced if patients do not comply with the antibiotic regimen or if resistance arises *de novo* (Bonhoeffer et al. 1997).

Given that antibiotic effectiveness represents a quality aspect of the antibiotic and may affect antibiotic demand positively, a feedback effect for society is created on the demand side that is beneficial: it may slow down the use of antibiotics, even in the case of open access occurring to the resource of antibiotic effectiveness. Indeed, the patients' willingness-to-pay for an antibiotic should be a function of its effectiveness. When antibiotic effectiveness decreases, so does the willingness-to-pay, which diminishes the antibiotic use, and hence slows down the decrease in antibiotic effectiveness. This pattern drove the results in Herrmann and Gaudet (2009) and allows convergence to a strictly positive steady-state level of antibiotic effectiveness (which may nonetheless be suboptimal), thus avoiding the complete exhaustion of antibiotic susceptibility. Such a feedback effect is akin to cases of more classical resources (e.g., halieutic ones). For instance, when consumers understand issues related to the well-being of dolphins, they are likely to reduce their consumption of tuna to reduce the risk imposed by tuna fisheries on the safety of dolphins. A similar effect relates to the consumption of fossil fuels and the consumers' willingness

[6] The decision to consult a physician, and purchase and take the antibiotic stems from a dynamic optimization problem. Indeed, an individual first has to decide whether to consult a physician or wait for the infection to clear naturally, which may depend on the morbidity cost.

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to pay extra for less-polluting fuels (e.g., biofuels). To which extent such quality consciousness enhances a more sustainable resource use is, however, an empirical question.

One way to reduce the demand for antibiotics resides in the avoidance of infection in the first place. Private decisions on social distancing on an individual level have been analyzed by Fenichel (2013) in a disease compartment model, where immunity to disease arises once an infected individual has recovered (i.e., in the case of viral infections). Following Fenichel (2013), public policies that demand ad-hoc distancing of infected individuals, but which do not account for the health status of individuals, may lead to welfare outcomes that are worse than decentralized outcomes in which each individual evaluates his/her own risk of becoming infected. This is because preventing immune individuals from coming into contact with others increases the likelihood of healthy individuals coming into contact with infected individuals.

Open research questions related to the demand of antibiotics include:

- How does awareness or information about antibiotic resistance affect outpatient demand?
- Is the patient able to wait so that antibiotic demand can be derived in a dynamic context, where the patient accounts for future levels of antibiotic effectiveness and disease prevalence?

Pharmaceutical Industry and the Innovation of Anti-Infective Drugs

In the past, the innovation of antibiotic drugs has followed the pace of increasing antibiotic resistance. Antibiotic resistance can even be considered as having spurred the innovation of new drugs: since the development of penicillin in 1928, 14 new classes of antibiotics have been developed. However, following Coates et al. (2011), the development of completely new antibiotic classes has failed in recent years because of their toxicity to humans. Becker et al. (2006) suggest that no new classes can be developed in the future, as all "broad-spectrum antibacterials have been discovered" (Becker et al. 2006:191). More recent research points to possible new avenues to combat the rise of antibiotic resistance of gram-negative bacteria. Future drugs may attack the protective barrier of bacteria, instead of the bacteria itself (Dong et al. 2014). However, before these drugs enter the market, time-consuming tests for drug approval must still be undertaken.

Given the difficult setting for the development of new antibiotic classes, antibiotic producers concentrate on the development of antibiotic analogues (which belong to existing antibiotic classes). Whether antibiotic analogues are necessarily linked to the same resource pool or whether antibiotics that belong to different antibiotic classes may be connected to a common pool remains an

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open epidemiological issue. Laxminarayan et al. (2007) propose grouping antibiotics in "functional resistance groups" because of possible inconsistencies that may occur between antibiotic classes and resource pools of effectiveness.

Clearly, incentives to innovate a new drug depend on the following:

1. Innovation costs need to be lower for antibiotic analogues, compared to antibiotic classes.
2. How a new drug will be possibly connected to a common resource pool shared with other antibiotics.
3. Which existing treatment substitutes are already available to limit the monopoly power due to patent protection.

Herrmann et al. (2013) analyzed in a stylized context how a pharmaceutical firm decides to distance its drug from a common pool of antibiotic effectiveness when no substitute treatment to the new drug is available. Here, markets are completely separated on the demand side, like antibiotic markets for use in animals and humans, whereas on the supply side they are only possibly connected.[7] While the patent holder of the new drug serves only one market, the other is served by a generic industry. Herrmann et al. find that a firm's incentive to incur a higher innovation cost is determined by the marginal impact that is avoided by the generic industry on the common resource pool of antibiotic effectiveness. Furthermore, the lower the distance of the new drug to the common resource pool of antibiotic effectiveness, the heavier the monopolist discounts its future profits.

The particular nature of antibiotics (i.e., linked on the supply side via common pools of antibiotic effectiveness and on the demand side via substitute treatments) creates potentially nontrivial strategic interactions between pharmaceutical producers. Indeed, an imperfectly competitive environment characterizes the pharmaceutical industry, such that each producer should account, at least to some extent, for the investment and pricing decisions related to antibiotics undertaken by its competitors.

As a result, as the developer of a new antibiotic drug is likely not the only claimant of the resource pool of antibiotic effectiveness to which the antibiotic is related, the question arises as to the optimal patent breadth of antibiotics.[8] Extending the breadth of antibiotic patents may collude with common antitrust laws, as mentioned by Laxminarayan et al. (2007). However, increasing the breadth of patents could increase welfare, because a sole claimant to the resource pool should care more for its sustainable management. Laxminarayan et al. (2007) go even a step further by claiming that *sui generis* rights (i.e., rights

[7] For an example of a possible link between the supply side (via a common pool) of antibiotic effectiveness and separated markets on the demand side, consider the case of the U.S. Food and Drug Administration, which withdrew in 2005 an antibiotic belonging to the quinolone class for use in poultry water to prevent the spread of fluoroquinolone-resistant infections in humans.

[8] The patent length is also an issue, as the clinical testing of antibiotics is time consuming.

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"of its own kind") over antibiotics could be attributed to antibiotic producers once patents have ended, in order to establish an ultimate claimant of the resource pool of antibiotic effectiveness.

Open research questions related to the pharmaceutical industry's incentive to innovate new anti-infective drugs include:

- What is the optimal patent length and breadth for new anti-infective drugs?
- How can we define functional groups among anti-infective drugs that are linked to common resource pools?
- How are new anti-infective drugs connected on the supply side, and how does this influence the incentives for innovation of new drugs?

Conclusion

If we are to preserve the achievements that have been made in public health, we need to combine our understanding of the private incentives of economic agents, which provide and use antibiotics and vaccines, with knowledge about ecology and evolutionary biology. In the past, the development of new antibiotic classes and analogues has been spurred by the evolution of antibiotic resistance. However, the pace of research and development has slowed down over recent years, making the resource pools of antibiotic effectiveness finite to some degree. Public intervention is necessary to correct private incentives that are using up this valuable resource, but this will not be easy to achieve as resource pools of antibiotic effectiveness cannot be controlled independently at local or national levels. Coordination, on both regional and national levels, is thus necessary and, for this, a global approach will be required. Such an approach has only been analyzed in a stylized macroeconomic model, where each country disposes of one resource pool of antibiotic effectiveness to affect, in turn, positively the health capital of its labor force (Rudholm 2002). Similar issues can be foreseen, related to the coordination among countries, as society confronts new, potentially fatal viral infections that can spread easily by modern means of transportation.

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