Medical Decision-Making by Patients and Providers under Uncertainty and in the Presence of Antibiotic Resistance

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by

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Abstract

We analyze the medical decision-making process, first from the perspective of a patient and then from the perspective of a health care provider. Using a decision-tree, we describe the different actions a mother can take to treat her daughter, who she suspects has *otitis media*—an ear infection. Next, we use comparative statics and numerical analysis to show how altering inputs (magnitude of infection probability, cost terms) can affect the outputs. Finally, we examine how different socioeconomic variables influence the mother's decision making process. With regard to the health care provider, we delineate the setting in which the physician operates and then derive the long run expected cost of providing health care that this physician seeks to minimize. Next, we set up the cost minimization problem and describe the optimal solution implicitly. Finally, we explain why this implicit characterization of the optimal solution is all that is possible analytically.

Keywords: Antibiotic Resistance, Decision-making, Healthcare Provider, Patient, Uncertainty

JEL Codes: I12, Q29

1. Introduction

Since the advent of penicillin in 1928, there are now a variety of antibiotics at our disposal which we regularly use to protect and cure individuals from bacterial infections. However, this ability to cure has come with costs. Antibiotic resistance is a real and imminent threat; it is the result of the misuse, or overuse, of antibiotics to treat illnesses. Studies have found that *Streptococcus pneumoniae, Streptococcus pyogenes,* and *Staphylococci,* organisms that cause respiratory and cutaneous infections, and members of the *Enterobactenaceae* and *Pseudornonas* families, which cause diarrhea, urinary infection, and sepsis are now resistant to almost all of the older antibiotics" (Neu 1992). The problem of antibiotic resistance has become so extreme that scientists have found strains of *Streptococcus aureus*---more commonly known as the strain of bacteria that causes "staph" infections---that are resistant to Vancomycin, which is considered to be one of the most potent antibiotics in the market (Gardete and Tomasz 2014). Antibiotic resistance is not just costly to health; it also results in financial costs. For instance, one estimate tells us that the annual deadweight loss associated with outpatient prescriptions for amoxicillin in the United States is US$ 225 million (Elbasha 2003).

A unique and good example of a common condition where antibiotic abuse is a real risk is that of an ear infection (*Otitis media*). An ear infection is a familiar ailment among children. Here, it is often caused by an upper respiratory viral infection such as the common cold or the flu but can also be caused by bacterial infections such as sinusitis or pneumonia. Unlike other common ailments such as *Streptococcal pharyngitis*, commonly known as "strep throat," there is no culture that can definitively confirm or deny the need to treat an ear infection with antibiotics. Thus, it is possible that doctors will prescribe antibiotics for an ear infection without knowing for certain whether or not that is the appropriate course of treatment, potentially giving rise to an environment that is ideal for the development of antibiotic resistance. There are two commonly prescribed treatments in the case of an ear infection: the first is "watchful waiting" where the child is not prescribed an antibiotic (the child may be prescribed an over-the-counter medication to manage symptoms) and a parent monitors the child's condition; the second is the prescription of an antibiotic.

Antibiotic resistance is not just an issue when it comes to common childhood illnesses or seasonal ailments. It can also be an issue that plagues less commonly thought of conditions such as acne. A common treatment for acne is an antibiotic, either in topical form or, in more severe cases, in oral form. Examples of such treatments are topical clindamycin or tetracycline, a class of drugs that includes doxycycline and minocycline. These treatments, which are quite common today, are gradually becoming less and less effective against acne. Typical acne, more commonly known as acne vulgaris, is caused by *Propionbacterium acnes*. *P. acnes* has recently been found to be more and more resistant to typical antibiotic treatment methods used in the last 30 years. The problem of resistance and how quickly this problem can develop is shocking. Studies have found that *P. acnes* develops resistance in 50 percent of individuals who use both oral and topical antibiotic treatment options (Swanson 2003). Another study found that 6.25 percent of individuals who had been on a short-term course of antibiotics (6-18 weeks) and 21.6 percent of individuals who had been on a longer course of antibiotics (18+ weeks) had developed resistance (Swanson 2003).

Contemporary research shows that bacteria are becoming resistant to existing antibiotics at a much faster rate than we can find ways to control this resistance and that there is now a pressing need to find alternate therapies (Amábile-Cuevas *et al.* 1995, McKenna 1998). The existing literature has documented the issue of antibiotic resistance—both its direct biological cause and its resulting effects. Research regarding patient and physician behavior in the face of antibiotic resistance is much more limited than research about antibiotic resistance itself. When looking at studies about patient behavior in the case of ear infections, researchers have found that socio-economic variables such as health insurance and education have an impact on patient satisfaction when the underlying diagnosis involves "watchful waiting" (Vouloumanou *et al.* 2009, Finkelstein *et al.* 2005). Other factors that are related to socio-economic factors include a parent's ability to take time off from work to care for a child, how much of a burden having a child at home is for the family, and the age of the child (Volulouumanou *et al.* 2009, Finkelstein *et al.* 2005). Research also shows that the parent-physician relationship is significant. One study found that patient satisfaction was unaffected by a treatment option but, instead, depended on whether the parent felt that the physician had spent an adequate amount of time with himself or herself and had a meaningful discussion with him or her about the treatment options (Mangione-Smith *et al.* 1999).

There is very little *theoretical* research that looks at a physician's decision-making when (s)he treats patients with antibiotics and resistance is an issue to contend with. In fact, most studies typically assume that all physicians behave in a similar manner which is the result of their prior medical training. A review of the literature shows that like patients, doctors are also susceptible to social pressures and differential expectations. For instance, one study found that the perceived pressure from a patient for a certain diagnosis affected the physician's decision about whether to prescribe antibiotics (Mangione-Smith *et al.* 1999). Another meta-analysis showed that phenomena such as confirmation bias, gambler's fallacy, hindsight bias, and anticipated regret all influence a physician's decision-making process (Bornstein and Emler 2001).

Existing studies about the behavior of both patients and physicians in the face of potential antibiotic resistance are typically *not* theoretical. Instead, they are either the result of surveys or focus groups or aim to generalize findings by performing a meta-analysis on pre-existing studies. The point we would like to emphasize is that there are very few studies in the literature that employ dynamic or stochastic *mathematical modeling*.[4] This is true even though some researchers have noted that such modeling permits researchers to have a stronger grasp of structures, interactions, and feedback loops present in complex systems (Manzo 2007). By utilizing mathematical modeling in our analysis of medical decision-making, we aim to fill a gap in the present literature.

More specifically, in this paper, we model medical decision-making under *uncertainty* from two different perspectives when antibiotic resistance is a potential problem. In section 2, we study a patient's perspective about whether or not to use an antibiotic treatment option. Using decision-tree analysis, we demonstrate the efficacy of our conceptual model. Next, we pose different questions and then demonstrate how differences in a patient's socio-economic background alters the nature of this patient's decision making. In section 3, we analyze a physician's decision-making when resistance to a prescribed antibiotic is an issue to contend with. Specifically, we examine some of the factors that go into a physician's decision-making process when this physician is interested in minimizing the long run expected cost of treating a patient. We explore the roles that sociological and economic variables such as the geographic location of a physician's clinic and the socioeconomic status of patients visiting the clinic play in influencing the physician's decision-making process. Finally, in section 4, we conclude and then delineate two ways in which the research described in this paper might be extended.

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See Furceri (2010), Kryzanowski and Mohsni (2010), and Chen *et al.* (2015) for alternate examples of empirical but not theoretical research on healthcare related issues.

2. Decision-Making under Uncertainty from a Patient's Perspective

2.1. The theoretical framework

Consider a scenario in which a parent (the mother) arrives at a medical clinic with her sick child (the daughter). The mother must decide what course of action to take given that she suspects her daughter has an ear infection. The mathematical analysis in this section is *static*. The reader should think of this scenario as one in which the mother's decision-making and the resulting payoffs to her and to her daughter occur in a *single* time period. That said, we recognize that many interesting aspects of medical decision-making from a patient's perspective have a temporal dimension to them. Therefore, we discuss this point in greater detail in section 2.4 below.

The mother has three possible options available to her. First, she can ask a physician in the clinic to treat her daughter with an antibiotic regardless of the result that a medical examination may yield. Second, she can first ask the physician to do a medical examination on her daughter and then request that an antibiotic be given only if the medical exam yields a positive result, i.e., a result that confirms her suspicion that her daughter has an ear infection. Finally, she can seek no formal medical attention and simply wait out the suspected illness---this is the case of "watchful waiting."

The above three possible courses of action give rise to specific consequences and these consequences are shown in detail in figure 1. It is important to understand that the mother's

Figure 1 about here

medical decision-making is *ex ante* in nature. This means that she makes a decision *before* the uncertainty about the outcome of this specific decision— and hence her ultimate payoff from this specific decision—is resolved. To see this clearly, consider the mother's decision to ask the physician to conduct a medical examination on her daughter. As shown in figure 1, this decision will yield either a positive or a negative result and either of these two possibilities will affect her eventual payoff that is shown in the last column on the right-hand-side (RHS) of figure 1. Even so, when the mother makes the decision to request a medical exam, she does *not* know which outcome—and hence which payoff—will materialize. Finally, observe from figure 1 that even the decision to seek no medical treatment can result in one of two possible outcomes and therefore one of two possible payoffs.

2.2. Decision-tree

Consistent with the description of the theoretical framework in section 2.1, we set up a decision-tree in figure 1 to illustrate the three options available to the mother and the payoffs to her—and to her daughter—that arise from the pursuit of each of these three options. When studying figure 1, the reader should keep the following five points in mind. First, if the daughter receives an antibiotic when she is not infected, then we assume that she will develop resistance to the antibiotic. This means that the antibiotic in question will not kill infections that she (the daughter) may get in the future. Specifically, the daughter will develop resistance with fixed probability $P_{AR} > 0$ and this will then result in additional costs for subsequent treatment that we denote by $C_{AR} > 0$. Second, if the daughter is infected and she receives the antibiotic then we assume that she will be cured immediately and that there will be no side effects. Third, if the daughter is infected but not treated then this infection will develop into some kind of complication and the treatment of this complication will cost $C_C > 0$. Fourth, the fixed probability that the daughter is infected before she receives any kind of treatment is $P_S > 0$ and this probability is known to her mother. We assume that P_S, or the likelihood of being infected, is a function of economic and sociological variables that are unique to the mother-daughter pair in our model. Finally, the cost of an antibiotic is $C_A > 0$, the cost of conducting a medical examination is $C_E > 0$, and the cost of watchful waiting is $C_W > 0$.

In addition to the costs and the probabilities specified in the previous paragraph, there also are benefit terms that we have specified in figure 1. In this regard, $B(treatment)$ is the benefit that the mother and her daughter experience as a result of a successful medical intervention using an antibiotic. Similarly, $B(no\ infection)$ is the benefit that the mother and her daughter experience when the daughter has no infection and hence an antibiotic is not needed to cure her. Note that all infections being discussed above refer to bacterial infections, not viral infections. Now, to show how alternate actions by the mother lead to distinct payoffs to the mother-daughter pair, we discuss some of the payoffs described in figure 1.

2.3. Alternate outcomes

Suppose that the mother goes to the medical clinic and requests a doctor to conduct a medical examination of her daughter. As shown in figure 1, this decision can result in two different outcomes and these outcomes in turn lead to two possible payoffs. The first outcome is that the doctor performs an examination and finds that the daughter's ear infection requires an antibiotic. In this case, the payoff to the mother is $C_E + P_S\{C_A + B(treatment)\}$. This payoff is numbered (4) in the table right after the decision-tree. In words, this payoff arises because of two reasons. First, the mother definitely pays the cost C_E of the medical examination. Second, she also pays the cost C_A of the antibiotic and her daughter obtains the benefit from the treatment denoted by $B(treatment)$ but these last two terms need to be weighted by the probability P_S that they are experienced.

Note that the mother could ask for a medical examination and this examination may reveal that her daughter does not have an ear infection. The resulting payoff in this case is

$C_E + (1 - P_S)B(no\ infection)$. This payoff is numbered (5) in the table right after the decision-tree. Here, the mother is still definitely paying the cost of the medical examination C_E but the benefit from not having an ear infection or $B(no\ infection)$ is weighted by the probability $(1 - P_S)$ that the daughter is not infected.

In contrast to asking for a medical examination, the mother may decide to not seek medical treatment and use "watchful waiting" to monitor her daughter's condition herself. This possibility is described by the third or bottom branch of the decision-tree. Choosing this course of action results in two possible outcomes. The first is the possibility that the daughter's illness will persist and that she will develop a complication such as rheumatic fever. When this happens, the payoff to the mother–daughter pair is the cost of the complication C_C multiplied by the probability P_S that this cost is incurred or $C_W + P_S C_{C.}$ The mother's decision to not seek any medical attention can also result in the daughter being cured of her own accord. The benefit from this outcome is $B(no\ infection)$ and the probability that this benefit will be incurred is $(1 - P_S)$. Therefore, the payoff to the mother-daughter pair in this instance is $C_W + (1 - P_S)B(no\ infection)$ and this payoff is numbered (7) in the table right after the decision-tree. We now discuss how changes in the infection probability P_S influence the mother's medical decision-making and the resulting payoffs.

2.4. Comparative statics

Using the method of comparative statistics—also known as sensitivity analysis—with the various payoffs in the figure 1 decision-tree, we can see how the payoffs (the endogenous variables of interest) are affected when the value of the infection probability P_S (the exogenous variable) changes.

As noted in the first paragraph of section 2.1, our mathematical analysis in this second section is static. Therefore, it is reasonable to suppose that P_S is fixed and exogenous. However, if we allow historical factors—that arise over multiple time periods—to influence the mother's decision-making, then, consistent with the discussion in the first paragraph of section 2.2, it would make more sense to think of P_S not as a fixed number but instead as a variable that is itself a function of economic and sociological variables. For concreteness, we suppose that the economic variable is income (I) and that the sociological variable is education (E). Put differently, when historical factors are allowed to influence the decisions that the mother is making, it makes sense to think of income and education as exogenous variables of interest. That said, we can now express P_S as

$$P_S = f(I, E), \tag{1}$$

where $f(\cdot)$ is the function that links the probability of being infected to one's family income and education. In our model, we assume that all else being fixed, as either income or education rises, the infection probability P_S goes down. Mathematically, we obtain[5]

$$\frac{\partial P_S}{\partial I} = \frac{\partial f(\cdot)}{\partial I} < 0 \tag{2}$$

and

$$\frac{\partial P_S}{\partial E} = \frac{\partial f(\cdot)}{\partial E} < 0. \tag{3}$$

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See Adler and Newman (2002), Finkelstein *et al.* (2005), and Hahn and Truman (2015) for a more detailed corroboration of the validity of these assumptions.

The logic behind the negative signs in equations (2) and (3) is as follows: as a family gets richer or more educated, this family acquires *better* knowledge about personal hygiene, nutritious meals, wholesome diets, and is therefore faced with a *lower* infection probability P_S for a family member such as a daughter. In contrast, when a family becomes impoverished or has a low level of education, this family is less well able to deal with medical ailments for a family member and hence the infection probability P_S is *higher*.

Given the discussion in the previous paragraph, when we lower the infection probability P_S, we are mimicking the effect of making a family richer or more educated. In contrast, when we raise P_S, we are mimicking the effect of making this same family poorer or less educated. In the remainder of this second section, we shall discuss the interplay between the mother's static or single time period decision-making—where P_S is fixed and exogenous—and the income and education variables that matter historically or over multiple time periods where P_S is more appropriately viewed as a function of income and education. Note that our thinking about the connection between income, education, and the infection probability P_S is supported by research. For example, a report published by the Royal College of Pediatrics and Child Health in the United Kingdom found that nearly two-thirds of pediatricians believe that food insecurity and homelessness contribute to the ill health of children while half of all pediatricians believe that financial stress also makes a significant contribution (Bulman 2017).

In order to further understand the relationship between P_S and the different numbered payoffs in figure 1, we shall, as an example, hold all other things fixed and take the derivative of the payoff numbered (3) in which the mother chooses to treat her daughter with an antibiotic because she believes her daughter has an infection. This gives us

$$\frac{\partial\{C_A+P_S B(treatment)\}}{\partial P_S} = B(treatment) > 0. \tag{4}$$

Equation (4) tells us two things. First, the relationship between P_S and this payoff is positive for all values of P_S between zero and one. Second, irrespective of whether a particular family has high or low socioeconomic status, as the probability of an infection rises, treatment with an antibiotic gives rise to a positive benefit denoted by $B(treatment)$.

Now, consider figure 2. This figure shows a cutoff point on the horizontal P_S axis.

Figure 2 about here

Consistent with our discussion earlier in this section, to the left of the cutoff point are families with relatively *high* socioeconomic status and hence they face a relatively *low* probability of infection. In contrast, to the right of the cutoff point are families with relatively *low* socioeconomic status and therefore they face a relatively *high* probability of infection. In addition, the point 0 on the horizontal axis corresponds to families that are either very wealthy or very well educated or both. In contrast, the point 1 on this same axis corresponds to families that are either impoverished or poorly educated or both. Note that our analysis thus far allows for the possibility that the magnitude of the benefit from antibiotic treatment, i.e., the size of $B(treatment)$ in the RHS of equation (4) is *larger* for a family with *low* socioeconomic status as opposed to one with high socioeconomic status. However, the opposite result is also possible. This means that of the two (high and low) socioeconomic groups under consideration, the question about which socioeconomic group benefits more from antibiotic treatment *cannot* be resolved definitively without making additional assumptions about how changes in the infection probability P_S affect the *slope* of the function describing the payoff numbered (3) in the table right after the decision-tree in figure 1.

We would like to emphasize the point that the impact of small changes in P_S on the payoff to the mother-daughter pair from the mother's choice of a treatment option is very *sensitive* to the specific treatment option chosen by the mother. We can show this in two steps. In the first step, observe from equation (4) that when the mother chooses to treat her daughter with an antibiotic and this daughter is infected, the impact of a small increase in P_S on the payoff numbered (3) in the table right after the decision-tree is *positive*. In the second step, consider the case where the mother once again chooses to treat her daughter with an antibiotic but the daughter is, in fact, not infected and hence develops resistance. The relevant payoff to focus on now is the one numbered (1) in the table right after the decision-tree. Mathematically, we get

$$\frac{\partial\{C_A+(1-P_S)P_{AR}C_{AR}\}}{\partial P_S} = \frac{\partial\{-P_S P_{AR}C_{AR}\}}{\partial P_S} = -P_{AR}C_{AR} < 0. \qquad (5)$$

Equation (5) shows that the impact of a small increase in P_S on the payoff is *negative*. This verifies the claim made in the first sentence of this paragraph.

We have shown how comparative statics can be used to shed light on some aspects of medical decision-making by the mother. We now show how simple numerical analysis can shed yet more light on the mother's decision-making when her focus is on minimizing a particular objective such as expected *cost*.

2.5. Numerical analysis

One question that can be asked, given the different payoffs in the figure 1 table is the following: what is the expected *cost* to the mother when she decides to treat her daughter with only an antibiotic and with no medical examination? Using the decision-tree, we see that in this case, there are three possible payoffs to consider and these payoffs are numbered (1), (2), and (3) in the table right after the decision-tree. Since our focus is only on the expected *cost*, we disregard the benefit terms in payoffs (2) and (3). This gives us $C_A + (1 - P_S)P_{AR}C_{AR}$ for payoff (1) and C_A for payoffs (2) and (3). Now, substituting the numerical values for the various probabilities and the cost terms given in table 1, we get

Table 1 about here

$$C_A + (1 - P_S)P_{AR}C_{AR} = 10 + 0.5 \times 0.2 \times 30 = 13, C_A = 10. \qquad (6)$$

A second question that can be asked is the following: given the three possible courses of action available to the mother, if her goal is to *minimize* the expected cost only then what is her optimal decision? From equation (6), we already know that the expected cost of treatment with an antibiotic is either 10 or 13. So, to answer the preceding question, we will need to calculate the expected cost of the medical examination and the expected cost of choosing not to treat the daughter.

When the mother chooses to have the physician conduct a medical examination on her daughter, the relevant payoffs to consider are the ones numbered (4) and (5) in the decision-tree. Since we are concentrating on *costs* we temporarily ignore the benefit terms in the two payoffs. This gives $C_E + P_S C_A$ for payoff (4) and C_E for payoff (5). Substituting the numerical values for the costs and the probability in these expressions from table 1, we get

$$C_E + P_S C_A = 8.5 + 0.5 \times 10 = 13.5, \ C_E = 8.5. \qquad (7)$$

The expected cost of not treating the daughter requires us to focus on the payoffs numbered (6) and (7) in the decision-tree. Once again, because our focus is on *costs*, we disregard the benefit term in payoff (7). This gives us $C_W + P_S C_C$ for payoff (6) and C_W for payoff (7). Substituting the numerical values from table 1 into the preceding two expressions, we obtain

$$C_W + P_S C_C = 17 + 0.5 \times 1000 = 517,\ C_W = 17. \qquad (8)$$

From an *ex ante* perspective, the mother does not know which of the three payoffs in equation (6) will actually arise were she to decide to treat her daughter with an antibiotic and with no medical examination. But the mother knows that $C_A + (1 - P_S)P_{AR}C_{AR} > C_A$. So, we can disregard the first payoff and focus only on payoffs (2) and (3). Without imposing additional structure on the problem, we can break the tie between payoffs (2) and (3) by supposing that they are equally likely. In this case, the mother's mean payoff from treating her daughter with an antibiotic only is $\frac{1}{2} \times 10 + \frac{1}{2} \times 10 = 10$. Similarly, looking at the case where the mother first has the physician perform a medical examination on her daughter, she can reason that $C_E + P_S C_A > C_E$. So, disregarding payoff (4), we focus on payoff (5) only for this case and the mother's payoff is 8.5. Finally, for the case where the mother does not treat her daughter, we have $C_W + P_S C_C > C_W$. As such, we now disregard payoff (6) and focus only on payoff (7). Hence, the mother's payoff is 17. Comparing these three payoffs, it is clear that the lowest cost is 8.5. So, if the mother's goal is to minimize *only* the expected cost she incurs then her optimal decision is to have the physician first conduct a medical examination on her daughter.

Is the mother's optimal decision given in the preceding paragraph sensitive to changes in the infection probability P_S? To answer this question concretely, observe from equations (6)-(8) that the infection probability does *not* appear in any one of the pertinent cost expressions. This tells us that when the mother focuses on costs *only*, her optimal decision is *invariant* to changes in the infection probability P_S. The reader should note that this result is *not* general. In particular, when the mother's focus changes from minimizing expected cost to maximizing the *net benefit* from alternate treatment options, it will be necessary to explicitly account for the benefit terms in the payoffs numbered (1) through (7). When this is done, changes in the infection probability P_S

will alter the *magnitudes* of the net benefit terms in the various payoffs. As such, the optimal course of action now will be a function of the magnitude of the infection probability P_S.

It is possible that a mother possessing less education and earning a lower income will want to pick the option of directly choosing the antibiotic without a medical examination. Such a mother may not have the money or the time to administer a "watchful waiting" diagnosis and she may also not be well informed about the costs of antibiotic resistance. To such a mother, the immediate, lowest cost option may well be to treat her daughter directly with an antibiotic. There is support for this line of reasoning in the work of Finkelstein *et al.* (2005). These researchers found that a parent who had a lower education level was more disappointed when a physician would not prescribe an antibiotic to his or her child. Finkelstein *et al.* (2005) also found that parents who had attained higher educational degrees were more knowledgeable about antibiotic resistance and were also more satisfied with a "watchful waiting" diagnosis. We now discuss medical decision-making under uncertainty from the perspective of a physician. The model we use to conduct the analysis is adapted from Batabyal and Beladi (2018).

3. Decision-Making under Uncertainty from a Physician's Perspective

3.1. Theoretical framework

Consider a geographic area known as Cornellville that has a population of infected individuals. For the purpose of the analysis, we shall focus on one representative individual with this infection from Cornellville who shall hereafter be known as the patient. For concreteness, we assume this patient is a man and that the physician under consideration is a woman. The patient comes to a local clinic seeking attention for a medical condition. The nature of this medical condition is such that the man's health deteriorates over time, but the *random* amount by which this deterioration occurs is unknown to the physician before an examination is conducted. In this scenario, the default treatment option for the patient is an antibiotic but this antibiotic is *not* always successful in treating the patient. Therefore, in what follows, we shall focus on some aspects of medical decision-making given that the default antibiotic has failed to treat the patient. It is important to note that the likelihood of a treatment being successful is *probabilistic*. In particular, the patient may develop resistance to an antibiotic being used and we shall be interested in exploring some of the implications of this possibility.

The patient comes to the clinic for routine check-ups at pre-determined points in time that are represented by $t = 0, 1, 2, \ldots$ In each time period between two successive check-ups, an organ in the patient's body incurs a random amount of damage and these damage amounts accumulate over time. At the check-ups, the physician examines the amount of accumulated damage the relevant organ has suffered. We assume that the random damage between successive visits to the physician's office can be described by independent random variables that have a common exponential distribution with mean $1/\beta$. A real life example of this kind of damage is when the intake of iron supplements results in iron deposits accumulating over time within the body.

When the patient comes to the clinic for his periodic check-ups, the physician is able to examine both the patient's health and the accumulation of damage to the relevant organ. The physician's ultimate goal is to cure the patient of his illness and as such, a related goal is to keep the total amount of damage in the patient's body lower than a critical level denoted by R. In this case, R represents the *resistant* state and reaching R means that the resistant state has been reached. This kind of thinking is consistent with previous research (Howard 2004). When the resistant state is reached, the physician switches the patient from his current treatment to an alternate antibiotic. The cost of switching is high and denoted by $C_R > 0$. Put differently, C_R is the cost the physician bears when the patient must be put on the alternate antibiotic treatment; it is not the cost of the alternate antibiotic treatment to the patient. From the physician's perspective, allowing the accumulated damages in the patient's body to reach the resistant state R is the worst possible outcome.

The physician also has the option of putting the patient on a non-antibiotic treatment regimen as long as the accumulated damage in the patient's body or r is less than R but greater than 0. From the physician's perspective, state $0\ (R)$ is the best (worst) possible state. In symbols, we have $0 \leq r \leq R$. We stress that state r refers to the cumulative amount of damage that the patient accumulates in his body and this damage is both measurable by and known to the physician upon the completion of a check-up.

When the cumulative amount of damage in the patient's body is r, the physician will prescribe the non-antibiotic treatment which has a cost of C_r and is *less* expensive than the alternate antibiotic and hence we have $0 < C_r < C_R$. Put differently, C_r is the cost that the physician incurs as a result of treating the patient with the non-antibiotic option in state r. The amount of damage incurred during successive visits to the physician's office is denoted by $r_0, r_1, r_2, \ldots$where r_0 is the total organ damage in the patient's body when visiting the physician's office at time $t = 0$, r_1 is the total or accumulated organ damage when visiting the physician's office at time $t = 1$, and so on and so forth. Because the successive damage amounts are random, they are not known precisely by the physician. This feature also explains why the physician is operating in an environment of uncertainty. Note that it is in the interest of both the physician and the patient to keep r low and, in particular, to ensure that the value of r does *not* reach or exceed the resistant state denoted by R. Also and in contrast with the section 2 analysis, we are now explicitly modelling the passage of time and hence our analysis is *dynamic*. The features of the problem that we have been discussing thus far are shown pictorially in figure 3. We now

Figure 3 about here

discuss a particular but informative application of this section's theoretical framework.

3.2. Specific application

Suppose that the infected patient described above is a patient who is suffering from moderate acne. Although acne is typically considered to be a cosmetic issue, it can be quite severe and hence require potent medication. This patient comes to a clinic to see a dermatologist. After examining the patient and his acne related history, the dermatologist decides to prescribe the patient a topical clindamycin gel, an antibiotic. After using this antibiotic for 9 to 12 weeks, the patient sees absolutely no improvement in his condition and hence both the dermatologist and the patient decide that this default treatment option is ineffective.

At this point, the dermatologist has a choice. She can either prescribe a non-antibiotic option, in this case a topical retinoid, or she can prescribe an oral antibiotic such as doxycycline. The latter treatment option can only be instituted once the patient's acne has reached the resistant state R, or in this case, cycstic/nodular acne. It is in the best interest of the dermatologist to keep r, or in this case the acne, as minimal as possible. A patient who is on the oral doxycycline will need to have a prescription that is filled on a monthly basis, meaning that the dermatologist must provide the patient with more frequent care than the topical retinoid which usually lasts a patient about three to six months, depending on usage. The cumulative damage that the dermatologist assesses at each visit, r, can be measured in terms of the new scarring that appears between successive visits and in terms of how active and numerous the current acne is. The amount of damage that the dermatologist finds during a visit in time $t = 0,1,2, \ldots$ is r_0, r_1, r_2, respectively. We now describe the "renewal-reward theorem" that will be used to derive the long run expected cost of providing medical treatment by the physician.

3.3. Renewal-reward theorem

The following description of the renewal-reward theorem is taken from Ross (2003, pp. 416-425). A stochastic process $\{Q(t): t \geq 0\}$ is said to be a counting process if $Q(t)$ denotes the total number of events that have occurred by time t. Now let X_1 denote the time or epoch at which the first event occurs. Further, for $q \geq 1$, let X_q denote the time between the $(q-1)th$ and the qth event. These $X_q, q \geq 1$, are known as the interarrival times. A counting process for which these interarrival times have an arbitrary distribution is called a renewal process.[6]

Consider a renewal process $\{Q(t): t \geq 0\}$ with interarrival times $X_q, q \geq 1$, that have cumulative distribution function $F(\cdot)$. Further, suppose that a monetary reward R_q is earned when the qth renewal is completed. Let $R(t)$, the total reward by time t, be given by $\sum_{q=1}^{Q(t)} R_q$. In addition, let $E[R_q] = E[R]$ and let $E[X_q] = E[X]$, where $E[\cdot]$ is the expectation operator. The renewal-reward theorem tells us that if $E[R]$ and $E[X]$ are finite, then with probability one,

$$lim_{t\to\infty} \frac{E[R(t)]}{t} = \frac{E[R]}{E[X]}. \tag{9}$$

So, if we think of a cycle being completed every time a renewal occurs, then the long run expected reward is the expected reward in a cycle divided by the expected amount of time it takes to complete this cycle. The renewal-reward theorem holds for positive rewards (revenue) and for negative rewards (costs). In addition, a renewal process is also a "regenerative process." We shall work with certain properties of an appropriately defined regenerative process to derive the physician's long run expected cost of providing medical treatment.

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Note that a renewal process is a more general stochastic process than either a discrete-time Markov chain (DTMC) or a continuous-time Markov chain (CTMC).

3.4. Expected cost function

To use the renewal-reward theorem, it will be necessary to first define two concepts from renewal theory (Ross 2003, chapter 7). The first concept is the renewal or mean value function (Ross 2003, pp. 403-404). This function, often denoted by $m(t)$, tells us the mean number of renewals by time t. The second concept is the excess variable (Ross 2003, pp. 424-425). The excess variable $y(t)$ tells us the random amount of time that has elapsed from epoch t until the next renewal after epoch t.

Let us now calculate the expected length of a cycle. The mean value function asks how many renewals have occurred with respect to time but in the setting of this third section, we are interested in how many renewals have occurred with respect to r, the cumulative amount of damage to the relevant organ in the patient's body. This means that the mean value function we are interested in is $m(r)$. We know from the discussion in section 3.1 that the random damage between successive visits by the patient to the physician's office is described by independent random variables that are exponentially distributed with mean $1/\beta$. Therefore, from Ross (2003, p. 405), we can tell that the mean value function in our case is

$$m(r) = \beta r. \tag{10}$$

In addition, given the exponentially distributed damage amounts, the excess variable $y(r)$ is also exponentially distributed with mean $1/\beta$. With these two pieces of information in hand, we infer that the average length of a cycle is

$$E[length\ of\ one\ cycle] = 1 + m(r) = 1 + \beta r. \tag{11}$$

Equation (11) shows that the expected length of a cycle depends on the mean value function $m(r) = \beta r$.

The next step in finding the long run expected cost function is to determine the expected cost of one cycle. To do this, we shall follow the thought process of the physician in the setting of this third section and then translate the resulting decisions into probabilistic terms. We know that the default antibiotic that the physician initially prescribed to the patient has been found to be ineffective. We also know that the patient will come to the physician's office to be examined at fixed points in time. If the physician finds the cumulative organ damage in the patient's body r to be anywhere between 0 and $R,$ then the patient is prescribed a non-antibiotic treatment. In contrast, if the patient is found to have cumulative organ damage that is either equal to or above the resistant state R then he is switched to an alternate antibiotic. This alternative is *costlier* than the non-antibiotic treatment option.

The physician's objective is to keep r low and in particular to ensure that r does not equal or exceed R. This means that whenever $r < R$, the patient will definitely be on the non-antibiotic treatment. With this information, we know that the cost C_r will appear in the numerator of the ratio describing the long run expected cost function in equation (9). The next step is to account for the chance that the cumulative amount of organ damage in the patient's body will exceed R. The way in which we shall do this is by determining the additional cost that will be incurred by the physician when she switches from the non-antibiotic treatment option to the alternate antibiotic and then weighting this cost by the probability that it will, in fact, be incurred. Doing this, the expected cost of one cycle is

$$E(cost\ of\ one\ cycle) = (C_R - C_r)e^{-\beta(R-r)} + C_r \tag{12}$$

In equation (12), the first part of the first term, $(C_R - C_r)$ accounts for the additional cost that will result from needing to switch from the non-antibiotic option to the alternate antibiotic. The second part of the first term or $e^{-\beta(R-r)}$ can be thought of as the probability that the cumulative amount of organ damage in the patient's body will equal or exceed R. All this is added to C_r, which is the cost of the non-antibiotic treatment option.

Now that both the expected cost of one cycle and the expected length of one cycle is known, it is possible to state the long run expected cost function. From equation (9), this function is the ratio of the two expectations found above. Therefore, dividing both sides of equation (12) by equation (11), the long run expected cost function is

$$Physician's\ long\ run\ average\ cost = \frac{(C_R - C_r)e^{-\beta(\mathrm{R}-r)} + C_r}{1+\beta r}, \tag{13}$$

with probability one. Now that we have obtained the long run expected cost function, we can set up and then use calculus to solve a cost minimization problem in which the physician chooses the value of the cumulative organ damage in the patient's body r to make the long run expected cost of providing medical treatment or the RHS of equation (13) as small as possible.

3.5. Cost minimization

The physician solves

$$min_{\{r\}} \left[\frac{(C_R - C_r)e^{-\beta(\mathrm{R}-r)} + C_r}{1+\beta r} \right]. \tag{14}$$

Differentiating the objective function in equation (14) with respect to the choice variable r gives us the first-order necessary condition for a minimum. After some algebra, the physician's long run expected cost of providing healthcare is minimal for the unique value of the cumulative amount of organ damage in the patient's body r^* that solves the equation

$$\beta r e^{-\beta(\mathrm{R}-r^*)} = \frac{C_r}{C_R - C_r}. \tag{15}$$

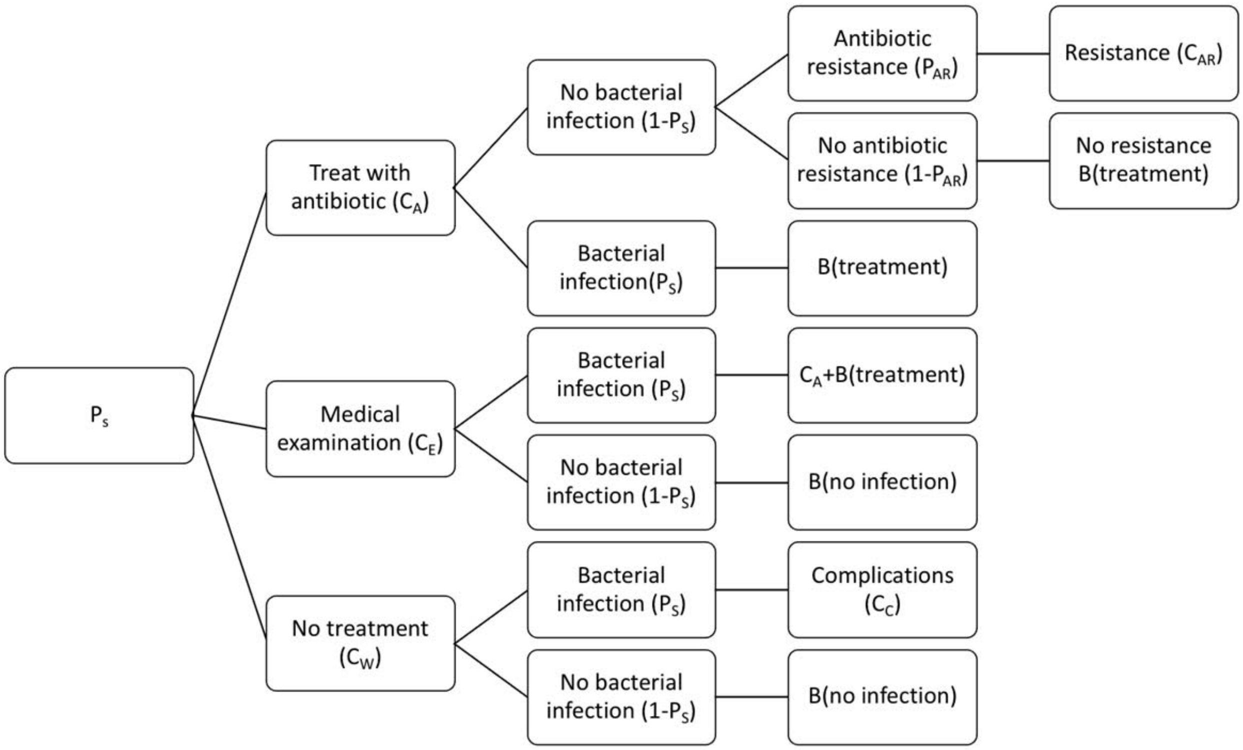
Two points about equation (15) are worth pointing out. First, the optimal r^* is given implicitly by this equation and it is not possible to explicitly solve for this r^*. Second, to make further progress with equation (15) it will be necessary to solve this equation numerically. This completes our analysis of medical decision-making in a probabilistic setting.

4. Conclusions

In this paper, we studied medical decision-making under uncertainty and in the presence of antibiotic resistance. In section 2, we first used a decision tree to describe the various actions that a mother could take to have her daughter treated for an infection that she suspects her daughter has. Next, we used comparative statics and numerical analysis to show how optimal actions were affected by the magnitude of the infection probability and the cost terms. Finally, we linked the discussion to economic and sociological variables and pointed out that a family's high or low socioeconomic status influences how this family evaluates the pros and cons of alternate treatment options.

In section 3, we studied medical decision-making by a health care provider. After describing the setting in which the physician operates, we discussed a specific application of the theoretical framework. We then used the renewal-reward theorem to derive the long run expected cost of providing health care that the physician sought to minimize. We set up the cost minimization problem and then described the optimal solution (r^*) to this implicitly. We took this course of action because it was not possible to solve for r^* explicitly. The approach used in this section shows one way to model and study a public policy issue of considerable importance, namely, how to provide health care to sick individuals at the lowest possible cost.

Here are two suggestions for extending the research described in this paper. First, consistent with our observation in the last paragraph of section 3.5, it would be worthwhile to determine whether methods of the sort utilized by Lin *et al.* (2017) or other similar methods can be employed to solve equation (1) numerically and to see how sensitive the obtained solution is to alternate specifications of, for instance, the parameter β. Second, it would also be interesting to use game theory---possibly as in Greenberg *et al.* (2002)---to analyze the patient-physician interaction as a game in which both players interact with each other repeatedly over time. Studies of medical decision-making by patients and physicians that incorporate these aspects of the problem into the analysis will provide further insights into the provision of health care in the presence of antibiotic resistance.



Reading the right-most boxes in Figure 1 from top to bottom	
1	$C_A + (1 - P_S)P_{AR}C_{AR}$
2	$C_A + (1 - P_S)(1 - P_{AR})[B(treatment)]$
3	$C_A + P_S[B(treatment)]$
4	$C_E + P_S[C_A + B(treatment)]$
5	$C_E + (1 - P_S)[B(no\ infection)]$
6	$C_W + P_S C_C$
7	$C_W + (1 - P_S)[B(no\ infection)]$

Figure 1: The decision-tree for the mother

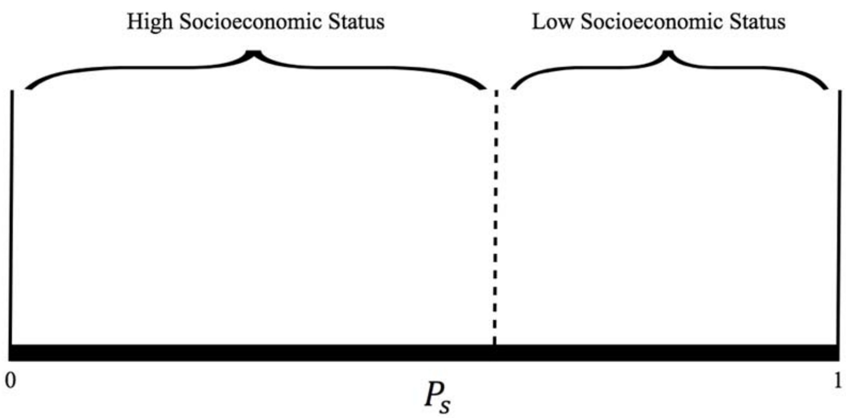


Figure 2: Families with high and low socioeconomic status

P_S	P_{AR}	C_A	C_E	C_W	C_{AR}	C_C
0.5	0.2	10	8.5	17	30	1000

Table 1: Numerical values of costs and probabilities

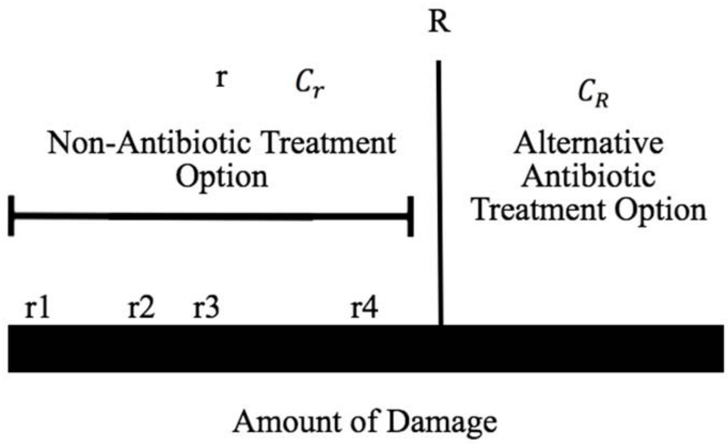


Figure 3: Treatment options depending on the cumulative amount of organ damage

References

Adler, N.E., and Newman, K. 2002. Socioeconomic disparities in health: Pathways and policies, *Health Affairs*, 21, 60-76.

Amábile-Ceuvas, C.F., Cárdenas-Garcia, M., and Ludgar, M. 1995. Antibiotic resistance, *American Scientist*, 83, 320-329.

Batabyal, A.A., and Beladi, H. 2018. Probabilistic approaches to cleaning the Ganges in Varanasi to attract tourists. Forthcoming, *Natural Resource Modeling*, https://onlinelibrary.wiley.com/doi/full/10.1111/nrm.12177

Bornstein B.H., and Emler A.C. 2001. Rationality in medical decision making: a review of the literature on doctors' decision-making biases, *Journal of Evolution in Clinical Practice*, 7, 97-107.

Bulman, M. 2017. Poverty and low income is 'making children sick', warn pediatricians, *The Independent*, May 11.

Chen, M., Lin, Y., Tseng, C., and Chen, W. 2015. Bubbles in healthcare: Evidence from the U.S., U.K., and German stock markets, *North American Journal of Economics and Finance*, 31, 193-205.

Elbasha, E.H. 2003. Deadweight loss of bacterial resistance due to overtreatment, *Health Economics*, 12, 125-138.

Finkelstein J.A., Stille C.J., Rifas-Shiman S.L., and Goldman D. 2005. Watchful waiting for acute otitis media: Are parents ready? *Pediatrics*, 115, 1466.

Furceri, D. 2010. Stabilization effects of social spending: Empirical evidence from a panel of OECD countries, *North American Journal of Economics and Finance*, 21, 34-48.

Gardete, S., and Tomasz, A. 2014. Mechanisms of vancomycin resistance in *Staphylococcus aureus*, *Journal of Clinical Investigation*, 124, 2836-2840.

Greenberg, J., Luo, X., Oladi, R., and Shitovitz, B. 2002. (Sophisticated) stable sets in exchange economies, *Games and Economic Behavior*, 39, 54-70.

Hahn, R.A., and Truman, B.I. 2015. Education improves public health and promotes health equity, *International Journal of Health Services*, 45, 657-678.

Howard, D.H. 2003. Resistance-induced antibiotic substitution, *Health Economics*, 13, 585-595.

Kryzanowski, L., and Mohsni, S. 2010. Capital returns, costs and EVA for Canadian firms, *North American Journal of Economics and Finance*, 21, 256-273.

Lin, S., Wang, S., Chen, C.R., and Xu, L. 2017. Pricing range accrual interest rate swaps employing LIBOR market models with jump risks, *North American Journal of Economics and Finance*, 42, 359-373.

Mangione-Smith R., McGlynn E.A., Elliott M.N., Krogstad P., and Brook R.H. 1999. The relationship between perceived parental expectations and pediatrician antimicrobial prescribing behavior, *Pediatrics*, 103, 7111.

Manzo, G. 2007. The progress and "urgency" of modeling in sociology. The concept of "generative modeling" and its implementation, *L'Année sociologique*, 2007, 13-61.

McKenna, J. 1998. *Natural alternatives to antibiotics*. Avery Publishing Group, Garden City Park, NY.

Neu, H.C. 1992. The crisis in antibiotic resistance, *Science*, 257, 1064-1073.

Ross, S.M. 2003. *Introduction to Probability Models,* 8th edition. Academic Press, San Diego, CA.

Swanson, J. 2003. Antibiotic resistance of Propionibacterium acnes in acne vulgaris, *Dermatology Nursing*, 15, 359-362.

Vouloumanou E.K., Karageorgopoulos D.E., Kazantzi M.S., Kapaskelis A.M., and Falagas M.E. 2009. Antibiotics vs placebo or watchful waiting for acute otitis media: A meta-analysis of randomized controlled trials, *Journal of Antimicrobial Chemotherapy*, 64, 16-24.