Alternate Strategies for Managing Resistance to Antibiotics and Pesticides[1]

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Abstract

How should one manage the problem of resistance to antibiotics and pesticides? The formal modeling of this question is very much in its infancy. Therefore, we construct a dynamic and stochastic model of antibiotic or pesticide use to investigate the relative merits of two kinds of treatment options for overseeing the problem of resistance. In particular, we identify a likelihood function and then, *inter alia*, we show that this function has an important bearing on how we might best address the problem of resistance.

Keywords: Antibiotics, Management, Pesticides, Resistance, Uncertainty

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1. Introduction

Our era is sometimes called the "life sciences era." As the medical and the biological sciences have advanced, so has the ability of humans to successfully control a variety of deleterious organisms. Indeed, with the passage of time, humans have used a variety of antibiotics and pesticides to cure humans, animals, and plants of a whole host of previously lethal diseases. A good example of an antibiotic that has been widely used to cure all manner of infections including staphylococci causing infections is penicillin. Similarly, the so called *Bt* plant pesticides are prominent examples of pesticides that have been engineered to express the *Bacillus thuringiensis (Bt)* δ endotoxins that effectively attack and kill a prominent pest, namely, the European corn borer (Secchi and Babcock (2003)).

Although humans have enjoyed remarkable success in mitigating the detrimental effects of bacteria and agricultural pests, it is now becoming increasingly clear that this success has not come without a cost. Consider the case of antibiotics. As noted by Garrett (1994), Elbasha (2003), and Howard (2004), the fundamental problem is this: When antibiotics eliminate drug susceptible bacterial strains, they create a fertile setting for drug resistant strains to prosper. As a result, the effectiveness of antibiotics is reduced by repeated use and the rate of this reduction is often rapid. This is the problem of *resistance* to the use of antibiotics and a similar problem arises with the repeated use of pesticides.

In a fairly comprehensive study, the Institute of Medicine (1992) noted that multiple drug resistance induced by the use of antibiotics can lead to treatment costs of $150,000 per patient. The reader should note that this figure is an order of magnitude *higher* than the costs of traditional treatment. Similarly, in the German context, Fleischer and Waibel (2003) have documented a case in which the cost of maize herbicide use *increased* from less than DM 40 million in 1987 to about DM

111.7 million in 1993. Only a few years after the introduction of the first antibiotic, penicillin, in the late 1940s, penicillin resistant infections caused by the bacterium *Staphylococcus aureus* (*S. Aureus*) began to emerge. As Bren (2002) has noted, these so called "staph" infections are varied and they can range from urinary tract infections to bacterial pneumonia. Methicillin, one of the most potent antibiotics available to treat "staph" infections is now no longer effective against some strains of *S. aureus*. In fact, very recently, it has been reported that some strains of *S. aureus* are now resistant to the antibiotic Vancomycin. This means that even Vancomycin—one of the most lethal antibiotics around—may be in danger of losing its effectiveness against some kinds of "staph" infections.

Because of this unfortunate state of affairs, for well over a decade now, concern about the effects of increasing resistance to antibiotics has been growing. The fact that there are now so many concrete instances of resistance to antibiotics has led several writers—see Amabile-Cuevas (1997), Buhner (1999), and McKenna (2003)—to focus explicitly on *alternate* treatment options to antibiotics. The discussion in this and the previous paragraph leads to two noteworthy findings. First, the economic cost of resistance to antibiotics and pesticides is non-negligible and is in fact likely to be substantial. Second, for quite some time now, there has been increasing concern in the world about the *cost of antibiotic treatment* relative to the *cost of treatment by alternate means*. A theoretical discussion of this second finding will form the centerpiece of our subsequent analysis in this paper.

Given the salience of antibiotic and pesticide resistance, one can ask what researchers have contributed to increasing our understanding of this problem. In this regard, two observations are pertinent. First, although there does exist a medical and biological sciences literature on this subject, as Rowthorn and Brown (2003, p. 43) have noted, "epidemiologists and biologists in the research community have not responded by building optimization models." Second, despite the fact that there

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is a clear economic dimension to the problem of antibiotic and pesticide resistance, optimal "human drug use has been addressed within an economic context by only a handful of economists" (Wilen and Msangi (2003, p. 19)).

Some of the most noteworthy contributions by economists on the subject of resistance are contained in the recent edited book by Laxminarayan (2003).[4] Many of the papers in this book construct and analyze theoretical models of antibiotic and pesticide use and management. Using dynamic analysis, Rowthorn and Brown (2003) point out that a social planner ought to begin antibiotic use by exclusively using the antibiotic that is effective against the bacterial strain that is the most prevalent. However, if this antibiotic is also the more expensive one, then the above strategy may or may not continue to be an optimal strategy. Laxminarayan and Weitzman (2003) use a static framework and show that although treatment homogeneity is valued in the medical profession, when the possibility of resistance is acknowledged, there are circumstances in which it makes more sense to treat an infectious disease with a combination of antibiotics. Morel *et al.* (2003) study the regulation of *Bt* corn in the presence of pesticide resistance. Their probabilistic analysis tells us that a transgenic crop ought to be released into the environment only if the irreversible costs are lower than the sum of the irreversible benefits and the present value of an infinite stream of instantaneous additional net benefits.

Given the documented concern about the costs of treatment with antibiotics relative to the costs of treatment with alternate options, the general purpose of this paper is to conduct a

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Hueth and Regev (1974), Brown and Layton (1996), and Laxminarayan and Brown (2001) are three important papers on the subject of resistance that appeared before Laxminarayan (2003). These three papers and the relevant medical and biological sciences literature on resistance are discussed by the authors of the individual chapters in Laxminarayan (2003). Therefore, readers interested in a more detailed review of the literature than we provide in this paper should consult these references.

comparative *theoretical* analysis, in a stochastic setting, of the conditions under which treatment with alternate means—involving no use of antibiotics—is more desirable than treatment with antibiotics. Specifically, because there are virtually *no* stochastic analyses of this question, we wish to show how stochastic modeling can shed valuable light on this antibiotic use versus no antibiotic use question. We stress that our objective in this paper is *not* to conduct either an empirical or a simulation analysis of the above question. Further, in our subsequent discussion, we shall identify and discuss salient cost terms, a parameter, and a likelihood function that *are* location specific. Even so, the reader should understand that the purpose of such identification is to point to those aspects of the problem that, while being location specific as far as *magnitudes* are concerned, are germane in general. Concretely, what this means is that our analysis will *not* be concerned with empirical details about things such as the social infrastructure or the geographic environment of a particular locality. In addition, our use of the phrase "as far as magnitudes are concerned" above, is intended to point out that the actual sizes of the cost terms and the pertinent parameter will typically vary from location to location.

Now it turns out that very recently, Wilen and Msangi (2003) have addressed aspects of this antibiotics versus no antibiotics use question, albeit in a non-stochastic or *deterministic* setting. These researchers use an optimal control framework to compare and contrast the properties of what they call "interventionist" and "ecological" strategies. The interventionist strategy always uses an antibiotic to treat an ailment and the ecological strategy is a no treatment strategy.[5] Which strategy ought a health care provider to use to cure an ailment? Wilen and Msangi (2003) show that the answer to this question depends on the magnitude of the treatment *cost* parameter. When this magnitude is low, the

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[5] As Wilen and Msangi (2003, p. 19) explain, the ecological policy is non-interventionist in the sense that when this strategy is used, a disease is allowed "to progress in a manner dictated by the natural interaction among bacteria exhibiting interspecific and intraspecific competition."

interventionist strategy leads to lower total treatment and damage costs. In contrast, when this magnitude is high, the ecological strategy results in lower aggregate treatment and damage costs.

In the "real world," a health care provider typically makes decisions about the antibiotic versus no antibiotic use question in an environment of *uncertainty*. Particularly, when a non-antibiotic course of treatment is used, this provider will typically not know—or know only imperfectly—what the likelihood of success is.[6] Therefore, in this paper, we extend the Wilen and Msangi (2003) analysis by introducing *uncertainty* into the analysis. Specifically, we ask two questions. First, how does the presence of uncertainty affect the answer to the choice question that we posed in the previous paragraph? Second, in a stochastic framework, are costs still salient in distinguishing between the two strategies, or, in addition to costs, is some other aspect of the problem just as important in helping a health care provider choose between antibiotic and non-antibiotic courses of treatment? By answering these two questions, we show how theoretical analysis, and in particular stochastic modeling, can help shed light on the practical issue of choosing between antibiotic and no antibiotic treatment options.

The rest of this paper is organized as follows: Section 2 describes a dynamic and stochastic model of antibiotic or pesticide use. Section 3 first analyzes interventionist and non-interventionist strategies (to be explained in the next section) for overseeing the problem of resistance. Next, this section identifies a particular likelihood function and it shows that in addition to cost considerations,

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In the rest of this paper, to illustrate our theoretical points, we shall frequently refer to one specific but very common ailment, namely, acute otitis media or AOM. AOM is a middle ear infection that may cause a change in the normal eardrum, which is located at the inner end of the ear canal. Now, to see the points that we have been making in the text of the paper, note that because of the problem of resistance, it is sometimes suggested that instead of treating AOM with an antibiotic such as amoxicillin, a non-antibiotic option such as homeopathic treatment ought to be considered. However, as Jacobs *et al.* (2001) have clearly pointed out, one of the problems that has prevented the widespread use of homeopathy to treat AOM is the *uncertainty* concerning the likelihood of success when this non-antibiotic option is used.

whether the problem of resistance is best addressed with an interventionist strategy or a non-interventionist strategy depends fundamentally on this likelihood function. Finally, section 4 concludes and discusses ways in which the research of this paper might be extended.

2. The Theoretical Framework

We now begin our analysis by adopting a stochastic modeling approach. The model of this paper is based on previous research by Antelman and Savage (1965), Ross (1983, chapter 6), and Batabyal and Yoo (1994). At the outset, the reader should note that from a modeling perspective, the questions of the development of resistance to either an antibiotic or to a pesticide are formally equivalent. Therefore, even though in what follows we shall describe our model in terms of antibiotic use, the model is equally pertinent to the case in which a pesticide is being used.

Consider a specific geographic area in which there exists a population of infected individuals. These individuals seek treatment for their ailment at a health care facility such as a physician's office or a hospital. We assume that it is standard practice in this health care facility to treat relevant ailments with an *interventionist* strategy that involves the use of an antibiotic. This assumption is consistent with standard medical practice in the United States and in large parts of western Europe.[7] To see this clearly, suppose the malady under consideration is AOM. In this case—also see footnotes 6 and 7—it is common to attempt to cure this ailment by prescribing the antibiotic amoxicillin. In fact, as Laxminarayan and Weitzman (2003) have pointed out, in 1997, nearly 60% of all cases of AOM in the United States were treated with amoxicillin. This example is indicative of our general point that the default treatment of choice in the majority of ailments in the United States and western Europe is an antibiotic and, hence, in what follows, we call this default selection the *interventionist* strategy.

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[7]
For a more detailed corroboration of this claim in the case of AOM, see Jacobs *et al.* (2001) and Bosker (2004).

The fundamental stock variable that an antibiotic affects is what we shall call the stock of drug susceptibility. Conceptually, this stock is very much like an exhaustible natural resource stock. Just as repeated extraction draws down the stock of an exhaustible resource such as coal, similarly, repeated use of an antibiotic degrades the stock of drug susceptibility. This phenomenon essentially describes an economic case of declining marginal benefits. It is important to understand that this degradation process is typically stochastic and *not* deterministic. We shall account for this feature by thinking of the stock of drug susceptibility as a stochastic process that can exist in one of many possible states. To this end, let state 0 be the best possible state. In other words, this state corresponds to the highest possible level of the stock of drug susceptibility. Further, to model the probabilistic degradation process, we suppose that the stock of drug susceptibility changes state in accordance with a Brownian motion process with drift $\beta > 0$. [8]

With repeated use of an antibiotic, our Brownian motion process changes state and eventually it gets to state *r*. This is the *resistant* state and the idea here is that once this state is reached, the default antibiotic that is currently being used is useless for subsequent treatment. When this happens, our medical facility must use a new interventionist strategy, i.e., a different antibiotic to treat the ailment in question. When this is done, our Brownian motion process is assumed to return to state 0. In other words, the stock of drug susceptibility is, once again, as high as it could possibly be. [9] We

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[8]

Note that unlike our paper, most of the extant literature—see Wilen and Msangi (2003) and Rowthorn and Brown (2003) for examples—has modeled this degradation process as a deterministic process. For more on the Brownian motion process, see Ross (1983, chapter 6) and Ross (2003, chapter 10).

[9]

In the "real world," it is possible that when bacteria are resistant to drug "A" then they will also be partially resistant to drug "B." If this is in fact the case in a specific instance and an interventionist course of action is taken, then, with the passage of time, a substitute for drug "B" will have to be found. Although what we have just mentioned is a possibility, the reader should note that this is certainly not inevitable. To see this, consider, once again, the case of AOM. As Bosker (2004) has pointed out, when treating AOM with an interventionist strategy, the default antibiotic is typically amoxicillin. When resistance to amoxicillin is an issue, the "different antibiotic" that we have just talked about is often chosen from the trinity of azithromycin, cefuroxime, and ceftriaxone.

shall denote the cost of using this new interventionist strategy by c^r.

Let us now delineate the *non-interventionist* strategy for treatment. The reader should note that we are using the label "non-interventionist" in a general way. Therefore, following Wilen and Msangi (2003), one non-interventionist strategy would be a no treatment strategy. However, in the context of this paper, homeopathic, herbal, or other natural treatments, in addition to doing nothing, are all non-interventionist strategies. In other words, a non-interventionist strategy is a no antibiotics strategy. Put somewhat differently, a non-interventionist strategy is essentially the "passive" counterpart of an active treatment strategy. It comprises a rather heterogeneous class of medical options ranging from no antibiotics provision to homeopathic treatments. We shall treat this class as a single class, but without loss of generality, a set of specific non-interventionist strategies may be identified and analytically treated in our subsequent modeling efforts. Clearly, our health care provider may choose to treat the ailment in question with a non-interventionist strategy before the Brownian motion process hits state r. In other words, this provider may choose to eschew use of the antibiotic and treat the ailment in question with a non-interventionist strategy before the resistant state for the default antibiotic that is currently being used is reached.

As long as the resistant state r has not been reached, we suppose that the default antibiotic is successful in treating the relevant ailment with probability one.[10] However, to keep the problem interesting and to be consistent with actual practice where there typically tends to be greater uncertainty about the success of less used non-antibiotic treatment options, we suppose that a success score of one is not the case with the non-interventionist strategy. In particular, if the state of the

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This "success with probability one" supposition may be a little too rigid. One way to account for this issue would be to specify and work with an appropriate probability function—in addition to the one we employ—in the analysis.

Brownian motion process is k and the non-interventionist strategy is used, then this strategy will be successful in treating the ailment with probability $p(k)$ and it will be unsuccessful with probability $1 - p(k)$. This likelihood function is explicitly a function of the *state* in which the non-interventionist strategy is used. However, because these alternate states indirectly proxy the biological and the social aspects of the treatment choice question, the likelihood function $p(\cdot)$ itself also indirectly accounts for these biological and social aspects. Note that this likelihood function $p(\cdot)$ will typically vary depending on the ailment being analyzed. Now, if the non-interventionist strategy is successful in treating the ailment then our Brownian motion process returns to state 0. In contrast, if this strategy is unsuccessful in treating the ailment then the Brownian motion process is assumed to go to state r.[11] The cost of attempting to cure the ailment in question in state k with the non-interventionist strategy is c^k.

In the second paragraph of this section, we noted that our analysis concerns a "specific geographic area." What this means is that the cost terms (c^r, c^k), the drift parameter β, and the likelihood function $p(k)$ are *specific* to this geographic area. Put differently, the cost terms, the drift parameter, and the likelihood function are *local* in nature and we are *not* saying that local conditions do not matter. Further, when the geographic area under consideration is changed, the magnitudes of (c^r, c^k, β) may well change and so may the nature of the likelihood function. The reader should note that our analysis in this paper is fully compatible with such local variation in the magnitudes of (c^r, c^k, β) and in the likelihood function. Our task now is to determine whether the interventionist strategy or the

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[11] We realize that the failure of the non-interventionist strategy does not necessarily mean that our Brownian motion process must go to state r. We make this assumption mainly to keep the subsequent mathematics from getting unduly complicated. Indeed, in principle, it is possible to focus on the case in which our Brownian motion process goes to some intermediate state m, where m is worse than k but better than state r.

non-interventionist strategy minimizes the long run expected cost per time.

3. Interventionist versus Non-Interventionist Strategies

3.1. The long run expected cost per time

The issue of the cost of medical treatment has been the subject of intensive economic research. In this regard, various alternative methodologies may be distinguished. In this paper, to compute the pertinent cost function, we shall use renewal theory.[12] Further, we shall restrict attention to non-interventionist strategies that attempt to treat the ailment when our Brownian motion process is in state k, where $0<k<r$. Given this restriction, the reader will note that returns by our Brownian motion process to state 0 constitute renewals. Therefore, we can use the well known renewal-reward theorem[13] to compute the long run expected cost that we seek.

Now, if we think of a cycle being completed every time a renewal occurs, then the renewal-reward theorem tells us that the long run expected reward is given by the expected return earned in a cycle divided by the length of this cycle. The reader should note that this last sentence about the long run expected reward is *not* a hypothesis of ours. Instead, it is one way of stating what the renewal-reward theorem tells us. In this paper, the object of interest is a cost, i.e., a negative reward. This notwithstanding, we stress that the renewal-reward theorem continues to apply.

Adapting the renewal-reward theorem to the problem we are analyzing, we get

$$Long\ Run\ Expected\ Cost = \frac{E[Cost\ per\ Cycle]}{E[Length\ of\ Cycle]}, \tag{1}$$

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[12]

Excellent textbook accounts of renewal theory can be found in Taylor and Karlin (1998, chapter 7) and in Ross (2003, chapter 7).

[13]

For more on the renewal-reward theorem, see Ross (1983, p. 78) or Ross (2003, p. 417). This theorem has been used previously in the literature to model all manner of natural resource and environmental phenomena. See Batabyal and Yoo (1994), Batabyal (1999), and Batabyal and Beladi (2002) for more details.

where $E[\cdot]$ is the expectation operator. It is straightforward to compute the numerator on the right-hand-side (RHS) of equation (1). Some reflection tells us that the expected cost per cycle equals $c^k + \{1 - p(k)\}c^r$. Therefore, in symbols we have

$$E[Cost\ per\ Cycle] = c^k + \{1 - p(k)\}c^r. \tag{2}$$

The computation of the expected length of a renewal cycle is more complicated. We proceed as in Batabyal and Yoo (1994). Let us denote the expected time it takes for our Brownian motion process to reach state k with the function $g(k)$. Now, because a Brownian motion process has independent and stationary increments,[14] for any two states k and l, we can write

$$g(k + l) = g(k) + g(l). \tag{3}$$

Equation (3) and the aforementioned properties of Brownian motion processes together tell us that the function $g(k)$ is linear and specifically that $g(k) = a \cdot k$, where a is a constant. Now, following the procedure described in Batabyal and Yoo (1994), we can tell that the constant $a = 1/\beta$ and hence $g(k) = k/\beta$. This last finding allows us to conclude that

$$E[Length\ of\ Cycle] = \frac{k}{\beta}. \tag{4}$$

Now, using equations (2) and (4) together, we have

$$\{Long\ Run\ Expected\ Cost\}_{NI} = \frac{E[Cost\ per\ Cycle]}{E[Length\ of\ Cycle]} = \frac{\beta[c^k + \{1 - p(k)\}c^r]}{k}. \tag{5}$$

According to equation (5), the long run average cost of treating the ailment under consideration with

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[14]

For more on these concepts, the reader should consult Ross (1983, chapter 6) and Ross (2003, chapter 10).

the *non-interventionist* strategy is given by the ratio of the weighted sum of the two cost terms c^k

and c^r to the state k, $0<k<r$, in which this strategy is utilized.

Our next task is to determine the long run expected cost for the interventionist strategy. For

this strategy, it should be clear to the reader that $E[Cost\ of\ Cycle]=c^r$. Similarly, following the logic

of the derivation that led to equation (4), we infer that $E[Length\ of\ Cycle]=r/\beta$. Therefore, putting

these two pieces of information together, we deduce that

$$\{Long\ Run\ Expected\ Cost\}_I=\frac{E[Cost\ per\ Cycle]}{E[Length\ of\ Cycle]}=\frac{\beta c^r}{r}. \qquad (6)$$

In words, equation (6) tells us that the long run average cost of treating the ailment under study with

the *interventionist* strategy is given by the ratio of the product of the drift parameter of our Brownian

motion process β and the cost of using a new interventionist strategy c^r to the resistant state r.

Inspecting equation (5) it is clear that for a *given* likelihood function $p(k)$, we can always use

calculus to minimize this long run expected cost function. This notwithstanding, we now provide two

examples to highlight an important point and that point is this: The *choice* between the interventionist

strategy and the non-interventionist strategy (see equations (5) and (6)) depends in large part on the

likelihood function $p(k)$.

3.2. The likelihood function and its salience

In our first example the likelihood function is $p(k)=1-k/r$. In this case $1-p(k)=k/r$.

Substituting this last expression in equation (5) and then simplifying, we get

$$\{Long\ Run\ Expected\ Cost\}_{NI}=\frac{\beta c^k}{k}+\frac{\beta c^r}{r}>\frac{\beta c^r}{r}=\{Long\ Run\ Expected\ Cost\}_I. \qquad (7)$$

Equation (7) clearly tells us that when the likelihood function is $p(k) = 1 - k/r$, the optimal course of action for our health care provider is to *always* use the interventionist strategy, i.e., always use an antibiotic. In this case, it makes no sense to use the non-interventionist strategy because this strategy results in higher long run expected costs. If this example were about pesticide use then, in this setting, we would say that a pesticide regulator ought *never* to use organic fertilizer (a non-interventionist strategy). Instead, (s)he ought to continue to use the currently used pesticide.

As a second example, consider the probability function

$$p(k) = \begin{cases} \dfrac{e^{-\theta k} - e^{-\theta r}}{1 - e^{-\theta r}} & if\ 0 < k < r \\ 0 & if\ k \geq r. \end{cases} \tag{8}$$

In this case, let us first substitute the value of $p(k)$ from equation (8) into equation (5). This gives us

$$\{Long\ Run\ Expected\ Cost\}_{NI} = \frac{\beta[c^k + \dfrac{c^r(1 - e^{-\theta k})}{1 - e^{-\theta r}}]}{k}. \tag{9}$$

Now, as in the first example, the health care provider ought to pursue the interventionist strategy if the RHS of equation (9) is greater than $\beta c^r / r$, the long run expected cost with the interventionist strategy.

Suppose, for the moment, that the non-interventionist strategy is optimal. Then, the optimal course of action for our health care provider can be determined by differentiating the RHS of equation (9) with respect to k and then simplifying. This tells us that our health care provider ought to use the non-interventionist strategy in state k^* where k^* satisfies

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$$\theta k^* e^{-\theta k^*} + e^{-\theta k^*} = \frac{c^r + c^{k^*}(1 - e^{-\theta r})}{c^r}. \tag{10}$$

Wilen and Msangi (2003) showed that in a *deterministic* setting, the choice between the interventionist strategy and the non-interventionist strategy depends on the magnitude of the treatment cost parameter. Our analysis shows that in a *probabilistic* setting, the answer to this choice question depends not only on cost considerations, i.e., on c^k and c^r in equations (5) and (6), but *also* on the nature of the likelihood function $p(k)$. We now have answers to the two questions we posed in the second last paragraph of section 1.

Our primary theoretical finding in this paper is that in a *specific* geographical area or *locality*, when (i) resistance to antibiotics is an issue and (ii) decisions are made in an environment of uncertainty, the question as to whether it makes more sense to use an interventionist or a non-interventionist treatment option depends fundamentally on the costs of the two treatment options and on the provider's *ex ante* uncertainty about the likelihood of success when (s)he uses a non-interventionist strategy. The reader should note that this finding is *not* just of theoretical importance but also of great practical significance. We have already documented (with citations) the practical salience of *costs* in section 1 and hence we shall not repeat this point here.

We now use the ailment of AOM to stress the practical relevance of the uncertainty aspect of our story. Because of resistance to amoxicillin and to some other antibiotics, health care providers have pondered the usefulness of non-interventionist strategies such as homeopathy to cure AOM. Now, our theoretical analysis tells us that a key determinant of the usefulness of homeopathy ought to be the probability function $p(\cdot)$ describing the likelihood of success when this homeopathic option is used to cure AOM. Is there any real evidence to support this contention? The answer is yes. For

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instance, in a private pediatric practice in Seattle, in an attempt to determine the above mentioned likelihood of success or the $p(\cdot)$ function, Jacobs *et al.* (2001) studied 75 children between the ages of 18 months and 6 years who had been diagnosed with AOM and then treated with homeopathic medicine. Friese *et al.* (1996) and Barnett *et al.* (2000) have made similar attempts to determine, respectively, the likelihood of success or the $p(\cdot)$ function for homeopathic treatment options in specific parts of Germany and the United States.

4. Conclusions

In this paper, we introduced uncertainty into the analysis and thereby generalized the Wilen and Msangi (2003) study of the choice between the interventionist strategy and the non-interventionist strategy in dealing with the problem of resistance caused by the repeated use of antibiotics and pesticides. Specifically, we asked and answered two questions. First, we showed exactly how the presence of uncertainty affects the answer to the aforementioned choice issue. Second, we pointed out that in a stochastic framework, the answer to the above choice question depends not only on cost considerations but also on the likelihood of success or the $p(\cdot)$ function when the non-interventionist strategy is used. Finally, we provided citations and "real world" evidence to substantiate our claim about the salience of cost considerations *and* the likelihood of success function.

The analysis contained in this paper can be extended in a number of directions. In what follows, we suggest five possible extensions. First, the reader will note that we modeled the probabilistic movement toward the resistant state with a Brownian motion process. As such, it would be useful to investigate the extent to which the results of this paper hold when alternate stochastic processes are used to model the random movement toward the resistant state. Second, it would be

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useful to compare the approach of this paper—in which, outside the resistant state, the default antibiotic is successful in curing the ailment under study with certainty—with an alternate approach in which the default antibiotic's success is probabilistic and not deterministic. Third, an important and promising research direction would be to position this paper's analysis, with its focus on costs, onto an alternate analysis in which the explicit focus is on human health because lifetime additions have clear personal benefits over a long time period. Fourth, subsequent research might also highlight related issues such as the motives for accepting interventionist or non-interventionist strategies (see Travisi *et al.* (2004)). Finally, given the salience of the likelihood function $p(\cdot)$, more experimental research is needed to obtain an appropriate and solid statistical basis for its specification. Indeed, there is much scope for innovative behavioral and statistical research in the new field of resistance economics.

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