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MEDICAL TECHNOLOGY ADOPTION, UNCERTAINTY, AND IRREVERSIBILITIES: IS A BIRD IN THE HAND REALLY WORTH MORE THAN IN THE BUSH?

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SUMMARY
The influence of current medical technology adoption decisions on the use of future potential interventions is often overlooked. Some health interventions, once exercised, restrict future potential interventions for both related and unrelated medical conditions. For example, treatment of a patient with an antibiotic may lead to resistance in that patient that precludes future treatment with the same or related compounds. This irreversibility raises the value of treatment modalities that preserve future treatment options. Surprisingly, partial reversibility with or without learning can either increase or decrease this value, depending on the distribution of patient types within the treated population. Evaluations that ignore these option values miss an important part of the welfare equation that is becoming increasingly important as individuals live longer and the stock of medical treatments increases. Copyright © 2009 John Wiley & Sons, Ltd.

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1. INTRODUCTION
The global policy environment that governs the approval and price setting process for new pharmaceuticals has shifted its orientation from an almost exclusive focus on safety to the orientation that is increasingly preoccupied with the ‘value’ of new products. As a result, we have witnessed the rise of cost–effectiveness analysis and other economic valuation techniques as important tools for the evaluation of new medical interventions. In resource constrained environments, this emphasis on value is an important step for achieving more efficient outcomes.

However, the metrics employed for determining the value of new medical technologies often produce measures that do not accurately capture the full costs or benefits of a new technology, and thus its true contribution to social welfare. One important dimension of value typically overlooked by traditional evaluation approaches relates to the influence of current medical technology adoption on the effectiveness of future potential interventions.\textsuperscript{1} Some health interventions, once exercised, restrict future potential interventions for both related and unrelated medical conditions.

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\textsuperscript{1}The general point that current treatment decisions affect the likelihood of developing future medical conditions has received considerable attention in the health technology assessment literature (see, for example, Weinstein \textit{et al.}, 1980; Meltzer, 1997). Here we focus on the ‘irreversible’ influence of current treatment decisions on the effectiveness of treatment for future diseases, and thus the value associated with preserving treatment options in the future.
For example, treatment of certain types of cancer patients with a bone marrow transplant and massive doses of chemotherapy will reduce the patient’s ability to tolerate and respond to chemotherapy in the future, should some form of cancer recur (Schouten et al., 2000; Messori et al., 1997). Coverage and adoption of this course of treatment may be the best decision, but clearly its influence on the availability of future treatment protocols and the effectiveness of alternate, option-preserving treatments should be incorporated in the treatment decision. Drugs that are subject to resistance are another example. Indeed, these concerns may help explain why there is still no consensus about when to start therapy in HIV patients (Cohen, 2000; Harrington and Carpenter, 2000). Some advocate the ‘hit hard and hit early’ approach, which suggests the initiation of complete treatment at the time of diagnosis in order to prevent the disease from progressing. Others are concerned that starting therapy at early stages, when T-cell counts are high and viral loads are low, may lead to the development of viral resistance to these drugs and related compounds. These clinicians advocate waiting until the disease reaches a more advanced stage to initiate therapy so that future therapeutic options can be preserved, although the disease may progress to an advanced stage more rapidly.

This problem of current decisions influencing the availability of future potential interventions has received considerable theoretical attention in the environmental economics literature (Arrow and Fisher, 1974; Hanneman, 1989; Kolstad, 1996) as well as the more general literature on economic investments (Henry, 1974; for a good review, see Pindyck, 1991). Since actions taken today involve some irreversible transformation of the set of available interventions in the future, this phenomenon has become known as the irreversibility problem. The benefits associated with actions that preserve treatment choices in the future, above and beyond the direct value associated with those actions, are referred to as the option value of the intervention. Numerous empirical studies have shown that investment rules that ignore this option value can be grossly in error (see, for example, McDonald and Siegel, 1985; Pindyck, 1988).

Incorporating option values in medical technology evaluations is potentially important for several reasons. First, this setting is one where there is tremendous uncertainty about the demand for future products. When we begin treating a population of individuals, we do not know what additional conditions they will develop in the future. Since new diseases are constantly emerging, we do not even necessarily know the nature of these future conditions. Moreover, recent improvements in life expectancy, which increase the opportunity for new conditions to arise – especially those associated with aging such as cancer and dementia – make option values in this context an especially important piece of the valuation equation. Second, despite brisk growth over the past several decades in the number of treatments available for a wide range of conditions, treatments generally share a fairly small set of common mechanisms of action, making interdependencies especially likely. Third, ignoring option values during the drug approval and reimbursement setting process could result in disincentives to create socially valuable technologies. Finally, unlike many private investment decisions, decisions taken by national governments may be effectively irreversible for political reasons. Once medical technologies have been authorized for public consumption, it is extremely difficult to limit their use.

In the health technology assessment literature, only one study has explicitly addressed these issues of irreversibility and option valuation (Palmer and Smith, 2000). In that study, the authors focus on the timing of health investments and whether it makes sense to delay adoption of a new technology in anticipation of the exogenous arrival of new information about its value. While the prospects for delaying investments has potentially important implications for decision making, delay is often not feasible in this setting, especially on the timescale under which we expect new information to arrive.

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2This is an especially acute problem when drug approval/coverage is based on head-to-head comparisons of drugs since a welfare-enhancing drug can appear to be inferior to existing treatments when option values are not included in the assessment.
In this paper, we take a different approach, analyzing situations where current treatment decisions have irreversible implications for the treatment of future diseases, patients are heterogeneous in their risk of developing these diseases, and decision makers are choosing between competing interventions with differing intertemporal consequences. We find that irreversibility raises the value of treatment modalities that preserve future treatment options, but that introducing some reversibility can either increase or decrease this value, depending on the distribution of patient types. We also examine the relationship between these values and the biologic and economic parameters that characterize any given set of technologies.

This paper is organized as follows. The following section provides a simple illustration of the irreversibility problem. Section 3 develops a formal model, analyzing the cases of complete irreversibility, partial irreversibility without learning, and partial irreversibility with endogenous learning. A discussion of the results and conclusions are presented in Section 4.

2. IRREVERSIBILITY AND INTERTEMPORAL UNCERTAINTY: A SIMPLE ILLUSTRATION

In this section, we develop a very simple and stylized example to illustrate the role that uncertainty and irreversibility can play in determining the value of a particular medical intervention. For simplicity, we suppose that people live for only two periods, that the discount rate is zero, and that all treatment costs are equal and negligible. Consider a chronic disease \( X \), which first occurs in period 1 and lasts two periods. Suppose that there are two choices in treating disease \( X \), denoted by \( T_1 \) and \( T_2 \), respectively. Patients with disease \( X \) treated with \( T_1 \) gain six health units in each period. Patients treated with \( T_2 \) gain four health units in each period. A traditional economic analysis would indicate that patients should be treated with \( T_1 \) in both periods, as illustrated in Figure 1 (with purely dominated strategies demarcated by short parallel lines).

Now consider an acute disease, \( Y \), which may occur in period 2. There is only one treatment (\( T_Y \)) for disease \( Y \). Patients who contract \( Y \) lose eight health units in the period in which the disease occurs. Patients who are treated with \( T_Y \) recover all of these units. Clearly, treatment with \( T_Y \) is strongly preferred to non-treatment for those patients with condition \( Y \).

The problem of irreversibility occurs in circumstances when these two situations are combined and the treatments are inter-related. Suppose that patients who, in period 1, contracted disease \( X \) and were treated with \( T_1 \) cannot tolerate \( T_Y \) (i.e. \( T_Y \) is ineffective in treating \( Y \)) if they later develop disease \( Y \). Let \( p \) denote the probability of developing disease \( Y \), which we will assume is independent of developing (or treating) disease \( X \). In this case, \( T_2 \) has two values associated with it – one due to its effectiveness in treating \( X \) and another due to it preserving the option to effectively treat \( Y \). The treatment decision in this case is illustrated in Figure 2. When patients are offered \( T_1 \) in the first period, it will always be optimal to offer \( T_1 \) again in the second period, although the overall benefit of this treatment strategy is clearly diminished for cases where disease \( Y \) develops. When patients are offered \( T_2 \) in the first period, the arrival of disease \( Y \) will dictate the second period protocol. If \( Y \) does not arrive, patients will switch to \( T_1 \) in the second period since there is no benefit from option preservation at this point. If \( Y \) does arrive, then patients are treated with \( T_2 \) and \( T_Y \).

The incremental value of \( T_2 \) (relative to the value of \( T_1 \)) can be expressed as the difference in expected effectiveness between starting with \( T_2 \) and providing patients with \( T_1 \) in both periods: 

\[
[p \cdot (8) + (1 - p) \cdot (10)] - [p \cdot (4) + (1 - p) \cdot (12)].
\]

This value reflects both the direct treatment benefits of \( T_2 \) for condition \( X \), as well as the value of preserving the option to use \( T_Y \) in period 2, which is known as the option value associated with \( T_2 \). While this option value will always increase the value of \( T_2 \) relative to \( T_1 \), it will not always be the case that this ‘extra’ value is enough to justify its use. In this

Note that we are being intentionally vague about our quality-of-life measure so as to abstract away from the specific assumptions associated with conventional outcome measures, such as the quality-adjusted life year.
simple example, $T_2$, which is an inferior treatment for disease $X$ alone, would only be the preferred treatment option if the probability of developing disease $Y$ were greater than one-third.\(^4\)

It is interesting to note that, particularly in our simple example, the interdependencies in the treatment value create a potential coordination problem. The treatment $T_2$ only has a value if $TY$ exists and likewise $T_2$, the option-preserving treatment for $X$, is necessary for $TY$ to be profitable. Unless these treatments are developed by the same firm, current anti-trust statutes will make it quite difficult for firms to invest optimally. Thus, the benefits from fostering competition through limits on coordination across firms may need to be balanced against the costs imposed through the loss of innovations due to firm uncertainty about their ability to successfully capture option values. As we move to the less stylized models that follow, this coordination game becomes more complex.\(^5\) As such, regulators may need to rely on coarser methods to incorporate option values that help overcome these challenges. For example, a new treatment that operates on a different biophysical relationship than the existing ones, even if it is

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\(^4\)This calculation presumes a risk-neutral decision maker who is only concerned with average outcomes. Decision makers in the medical context are often risk averse (Graff Zivin, 2001) in which case the threshold probability of disease $Y$ that would make $T_2$ the preferred treatment would be less than one-third.

\(^5\)In this case, the value of $T_2$ still depends on the availability of $T_Y$, but the degree to which the value of $T_Y$ will depend on the availability of $T_2$ will depend upon the population-level distributions of diseases $X$ and $Y$ and the degree to which they overlap.
no more effective, might receive a value ‘premium’ because that diversity offers the option of alternative approaches should adverse treatment interactions later be discovered.

3. MODELING TREATMENT VALUES WHEN ACTIONS ARE IRREVERSIBLE

More generally, option value can be quantified and incorporated in cost–effectiveness analyses by explicitly formulating a multiperiod, dynamic decision model that attends to uncertainty and the potential role of irreversibility. In this section, we will analyze three cases – complete irreversibility, partial irreversibility, and partial irreversibility with learning. While the first two could be viewed as special cases of the third, we develop them separately to highlight important insights under each type of scenario.

As in our earlier stylized example, we examine decisions to treat chronic disease $X$ when decisions to treat it can affect the prospects for treating acute condition $Y$ should it develop. The two treatments for disease $X$ are denoted by $T_1$ and $T_2$ and the treatment for disease $Y$ is denoted by $T_Y$. To simplify things, the value of each treatment is expressed in terms of net benefits, i.e. the value of health benefits generated by treatment minus the costs of that treatment.$^6$ The net benefits from treatment with $T_1$ is denoted by $B_1$ and the net benefits from treatment with $T_2$ is denoted by $B_2$, where $B_2 = \pi B_1$ and $\pi < 1$. The net benefit from $T_Y$ for those on $T_1$ is $B_{Y1}$ and the net benefit for those on $T_2$ is $B_{Y2}$, where $B_{Y1} = \omega B_{Y2}$ and $\omega < 1$. In other words, $T_2$ is an inferior treatment for condition $X$, but yields better results should it need to be combined with $T_Y$. Thus, there is an option value associated with using $T_2$, but that option comes at a cost.

3.1. The uncertain arrival of disease $Y$

We begin by defining the process governing the incidence of disease $Y$ in the future. Let $\gamma$ be a biological marker of disease $Y$, such that individuals enter the disease state when $\gamma \geq \tilde{\gamma}$. The growth rate in this marker is modeled as an increasing function of the current marker level and time. Owing to idiosyncratic exposures and other mitigating factors, this growth rate is also stochastic. Formally, the variable $\gamma$ is modeled as a geometric Brownian motion process with a drift component of the following form:

$$d\gamma = a\gamma dt + \sigma\gamma dz$$  \hspace{1cm} (1)

where $a$ is the intrinsic growth rate of the marker, $dt$ is an increment of time, $\sigma$ is a variance coefficient, and $dz$ is the increment of a Wiener process.

Applying Ito’s lemma to Equation (1) to obtain an expression for the distribution of the marker at time $t$ yields the following:

$$\gamma_t \sim LN[\gamma_0 e^{at}, \gamma_0 e^{2at}(e^{\sigma^2t} - 1)] \hspace{1cm} (2)$$

where $\gamma_0$ denotes initial marker levels at the time of the forecast. Future levels of the marker are distributed lognormally as a function of current levels, the drift parameter, variability in growth, and time. Since Equation (2) probabilistically defines the point at which the marker will exceed the threshold value for disease, $\tilde{\gamma}$, it should be viewed as a characterization of the age-specific disease incidence distribution for condition $Y$. We let $q_t$ denote the probability that individuals contract disease $Y$ in period $t$, i.e. the probability that $\gamma_t \geq \tilde{\gamma}$.

3.2. Complete irreversibility

We begin with the simplest and most extreme case, where the impacts of using $T_1$ on the effectiveness of $T_Y$ are completely irreversible and agents cannot perform tests to improve their knowledge about the

$^6$The general insights of the model remain unchanged if the costs and benefits of treatment are measured separately. In this case, treatments would be compared with one another in terms of their incremental cost effectiveness.
expected arrival of \( Y \). Since the downstream impacts of ever receiving \( T_1 \) are permanent, it will never make sense to switch from initial treatment regimens. Patients initiated on \( T_1 \) will receive that treatment in perpetuity and the same will be true for patients initiated on \( T_2 \). As such, the decision maker will use the forecast about the arrival rate of disease \( Y \) to calculate the expected present discounted value (PDV) of each treatment regime and select the one with the highest return. The PDV for each treatment can be expressed as follows:

\[
V_1 = \int_0^\infty [(1 - q_t)B_1 + q_t \omega B_{Y_2}]e^{-\delta t}
\]

\[
V_2 = \int_0^\infty [(1 - q_t)\pi B_1 + q_t B_{Y_2}]e^{-\delta t}
\]

where \( \delta \) is the discount rate.

Let \( \tilde{\gamma}_0 \) denote the baseline level of the biological marker for \( Y \) that equates (3) and (4) such that decision makers are indifferent between the two treatment regimes. For patients with \( \gamma_0 > \tilde{\gamma}_0 \), \( T_2 \) will be the preferred option since \( V_2 > V_1 \). For those with \( \gamma_0 < \tilde{\gamma}_0 \), \( T_1 \) will be preferred. We will refer to these individuals as ‘high-risk’ and ‘low-risk’ patients, respectively.

3.3. Partial irreversibility without learning

In this version of the model, we relax the assumption of complete irreversibility by assuming that the negative impacts of \( T_1 \) on the effectiveness of \( T_2 \) are temporary. In particular, we model a cooling off period of length \( n \) such that \( T_2 \) is fully effective after \( n \) consecutive periods of treatment with \( T_2 \). Since agents still cannot perform tests to update their knowledge about the arrival of \( Y \), the least sophisticated treatment protocol would start patients on \( T_1 \) and switch them to \( T_2 \) when disease \( Y \) arrives. Under such a protocol, patients will pay a ‘penalty’ for \( n \) periods while they are waiting for the cooling off period to end.

Of course, decision makers can use the information that they have about the expected arrival rate of disease \( Y \) to do better than simply waiting for it to arrive before switching to \( T_2 \). The optimal strategy requires switching when the expected marginal benefit of one more period of \( T_1 \) is exactly equal to the expected PDV of adopting \( T_2 \) now.\(^7\) These values are expressed as the following equations, respectively:

\[
\int_0^1 [(1 - q_t)B_1 + q_t \omega B_{Y_2}]e^{-\delta t} + \int_1^{n+1} [(1 - q_t)\pi B_1 + q_t \omega B_{Y_2}]e^{-\delta t} + \int_{n+1}^\infty [(1 - q_t)\pi B_1 + q_t B_{Y_2}]e^{-\delta t}
\]

\[
\int_0^n [(1 - q_t)\pi B_1 + q_t \omega B_{Y_2}]e^{-\delta t} + \int_n^\infty [(1 - q_t)\pi B_1 + q_t B_{Y_2}]e^{-\delta t}
\]

Letting \( \tilde{t} \) denote the time at which (5) and (6) are equal, the value of the optimal treatment regime under partial irreversibility can be expressed as follows:

\[
\int_0^\tilde{t} [(1 - q_t)B_1 + q_t \omega B_{Y_2}]e^{-\delta t} + \int_{\tilde{t}}^{n+\tilde{t}} [(1 - q_t)\pi B_1 + q_t \omega B_{Y_2}]e^{-\delta t} + \int_{n+\tilde{t}}^\infty [(1 - q_t)\pi B_1 + q_t B_{Y_2}]e^{-\delta t}
\]

Patients are offered \( T_1 \) for the first \( \tilde{t} \) periods, after which point they switch to \( T_2 \). The first term reflects the expected returns under \( T_1 \), the second term reflects the expected penalty associated with the cooling off period, and the third term reflects the expected returns under \( T_2 \) for the remainder of time.

\(^7\)Note that this characterizes the optimal interior solution where both treatments are used. A corner solution where patients exclusively receive \( T_1 \) or \( T_2 \) could also arise when the probability-adjusted costs associated with the inferior treatment of \( Y \) are extremely high or low, respectively.
It is now instructive to compare the value of \( T_2 \) under complete irreversibility with its value under partial irreversibility. This value is derived by comparing Equations (4)–(7). The change in this value associated with the move from complete to partial irreversibility can be expressed as follows:

\[
\int_0^{\hat{t}} [(1 - q_t)(1 - \pi)B_1]e^{-\delta t} + \int_0^{\hat{t} + n} [q_t(o - 1)B_{Y_2}]e^{-\delta t}
\]  

(8)

Since the first term is positive and the second is negative, the sign of (8) is ambiguous. For those patients that would have received \( T_2 \) under complete irreversibility, the move to partial irreversibility lowers the value of that treatment, i.e. the sign of (8) is negative. To see this, it is helpful to re-express (8) in the following manner:

\[
\int_0^{\hat{t}} [(1 - q_t)(1 - \pi)B_1 + [q_t(o - 1)B_{Y_2}]]e^{-\delta t} + \int_{\hat{t}}^{\hat{t} + n} [q_t(o - 1)B_{Y_2}]e^{-\delta t}
\]  

(9)

The choice of \( T_2 \) under complete irreversibility implies that the value of Equation (4) is greater than the value of Equation (3), which in turn implies that the first term in (9) is negative. Since the second term is also negative, the value of \( T_2 \) to these patients is necessarily lower under partial reversibility. For those patients that would not have received \( T_2 \) under complete irreversibility, the move to partial irreversibility has an ambiguous effect on its value. When the cost of the cooling off period captured in the second term in (9) is smaller than the relative value of the advantage of \( T_1 \) over \( T_2 \), the value of \( T_2 \) for those patients that would not receive it under complete irreversibility increases in a world of partial irreversibility. If the cooling off costs are larger than the benefits that would be received from introducing \( T_2 \), then the value of \( T_2 \) again decreases under partial irreversibility.8

The intuition for these results relies on the recognition that the introduction of partial irreversibility has two distinct effects, as illustrated in Figure 3. First, it reduces the amount of ‘wasteful’ \( T_2 \) that needs to be offered to patients to ensure that they can be effectively treated for condition \( Y \) when it arrives. This yields changes on the intensive margin, since under partial reversibility these individuals no longer need to initiate treatment of \( T_2 \) at time zero. Second, by reducing this ‘wasteful’ spending, the use of \( T_2 \) may become attractive for some patients who did not find it attractive under complete irreversibility when the effective costs of using \( T_2 \) were higher. This yields changes on the extensive margin, since a subset of patients that would not have received any \( T_2 \) under complete irreversibility will receive some when irreversibility is partial. Clearly, the overall impact of a move to partial irreversibility on the value of \( T_2 \) will depend on the distribution of patients in each of these groups.

In addition to comparing the value of \( T_2 \) across scenarios, we can also examine how that value depends on underlying economic and biologic parameter values. Recall that \( \hat{t} \) represents the optimal time period to switch from \( T_1 \) to \( T_2 \), which is determined by equating (5) and (6). Thus, \( \hat{t} \) is implicitly determined by the following equation:

\[
\int_0^1 [(1 - q_t)(1 - \pi)B_1]e^{-\delta t} + \int_{n+1}^{n+1} [q_t(o - 1)B_{Y_2}]e^{-\delta t} = 0
\]  

(10)

where the first expression in Equation (10) represents the benefits of not switching to \( T_2 \) now, while the second expression represents the costs of not switching now. These latter costs accrue in the future, as not switching today means one extra period of cooling off starting \( n \) periods from now. Since \( \hat{t} \)

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8In this last case, the value of \( T_2 \) is going from negative under complete irreversibility to more negative under partial irreversibility. If we view the value of \( T_2 \) as bounded from below at zero, then the value of this treatment will be the same for these types of patients under both scenarios.
corresponds to the threshold period after which one would switch to $T_2$, we can interpret decreases in $\tilde{T}$ with respect to other parameter values as indicating more use, and thus a higher value, of $T_2$.

It is straightforward to show the rather intuitive result that the value of $T_2$ is increasing in $\pi$ and $n$ and decreasing in $\omega$ and $\delta$. The second treatment is more attractive when its relative advantage in interacting with treatment for $Y$ is larger (smaller $\omega$) and less attractive when its relative disadvantage in treating condition $X$ is larger (smaller $\pi$ or $n$ or larger $\delta$). In other words, $T_2$ is more attractive when the option value associated with its use is higher, but less attractive when the costs of the option are higher. Since the advantages of the second treatment accrue in the future, higher discount rates diminish the value of the option, making the second treatment less attractive.

We can also examine the role of those parameters that determine the annual incidence rates for disease $Y$. The value of $T_2$ is increasing in $\gamma_0$, $\alpha$, and $\sigma$. The parameter $\gamma_0$ – the baseline level of the biologic indicator – can be viewed as a measure of an individual’s idiosyncratic, time-independent risk of developing $Y$. Individuals at high risk for $Y$ due to early life exposures or genetic factors have a higher $\gamma_0$, and thus place a greater value on $T_2$. As such, societies with more high-risk individuals will also place a higher value on $T_2$. The drift parameter $\alpha$ indicates how quickly, on average, the biologic indicator for disease $Y$ grows. The variance parameter $\sigma$ captures the uncertainty around the precise level of $\alpha$, which in the geometric Brownian motion framework grows over time. Higher levels of $\alpha$ or $\sigma$ increase the probability that $Y$ arrives sooner and make $T_2$ more attractive. Derivations are provided in the Appendix.

3.4. Complete irreversibility with learning

The models developed up to this point have assumed that decision makers have basic knowledge about the population-level incidence of disease $Y$, but that they have no means of updating that knowledge with information about individual patients until the disease actually arrives. For example, patients may be given dual energy X-ray absorptiometry scans to monitor bone mineral density that allows health-care providers to alter treatment protocols as they progress through various stages of osteopenia. Here, we introduce the possibility of a test that can be performed to measure levels of the biologic indicator for $Y$ within patients. Given a cost $c$ to execute the

Note that (10) defines an interior solution, such that the comparative statics discussed in the following paragraphs are limited to changes on the intensive margin. They describe changes in the option value associated with $T_2$ in response to parameter changes that are sufficiently small to ensure that some use of $T_2$ remains optimal.
test, the optimal moment to perform that test, which we will denote by \( \hat{t} \), is implicitly defined by the following equation:

\[
\int_0^1 [(1 - q_t)(1 - \pi)B_1]e^{-\delta t} + \int_n^{n+1} [q_t(1 - \pi)B_{12}]e^{-\delta t} - c = 0 \tag{11}
\]

The decision maker will perform the test precisely at the moment where the net benefits from waiting one more period to switch equal the costs of the test. If the test reveals that the biologic indicator is higher than was expected, the decision maker will switch earlier than if using the population arrival rates. If the test reveals that the biologic indicator is lower than expected, the decision maker will wait, performing the test again when the equality in Equation (11) holds given the new expectation about the evolution of \( \gamma \). A formal derivation of the value of \( T_2 \) in this setting necessitates the imposition of more structure on the realizations of \( \gamma \) revealed by the test, but the impacts are fairly intuitive. Since switching early, absent disease, will happen no earlier than \( \hat{t} \), but switching late is essentially unbounded, the introduction of learning will lower the overall option value of \( T_2 \) for those that would have received it under partial irreversibility, absent learning. Moreover, increases in the cost of the test make deviations from the expected protocol under partial reversibility without learning less likely and thus increase the value of \( T_2 \). The responsiveness of the value of \( T_2 \) with respect to underlying parameters remains qualitatively the same.

4. CONCLUSIONS

For many physicians, the observation that current medical treatment decisions have repercussions for the treatment of health conditions in the future is an obvious one that often factors into their clinical decision making, albeit heuristically. Yet, such considerations form no part of health-care technology assessment calculations at societal or sub-societal levels, leading to potentially significant mischaracterizations of the treatment value.\(^{10}\) While it is difficult to systematically assess the size of the bias induced from ignoring option values, the only empirical study in the health domain found an increase in consumer willingness-to-pay of approximately 53\% when option values were considered (Smith, 2007). Growth in the availability of treatments for chronic diseases that require interventions in perpetuity, along with general increases in life expectancy, suggests that the impact of omitting option values from evaluations will only become larger.

In this paper, we developed a formal valuation model that attends to these intertemporal dependencies by explicitly modeling the uncertain arrival of a future disease that can be treated with varying degrees of effectiveness depending on current treatment decisions. Several key insights emerge. Irreversibility raises the value of the option-preserving treatment. The existence of an option value—that value above and beyond the direct value of treatment for the current condition—means that a seemingly inferior treatment may be the superior choice when considering lifetime welfare. Optimal decision making requires a careful comparison of the ‘costs’ of a less effective treatment for a condition today with the ‘benefits’ of more effective treatments for conditions in the future. The size of the option value, and thus the degree to which valuations that ignore it are miscalculated, depends critically on the relative effectiveness of treatments, the likelihood of diseases arriving in the future, the extent to which current interventions limit the ability to treat these future conditions, and the relevant discount rate.

Comparing treatment values under complete irreversibility with a scenario where irreversibility is only partial reveals a more nuanced role for option values. For those patients at high risk for the future

\(^{10}\)Indeed, the recent move toward value-based pricing under Pharmaceutical Price Regulations Scheme in the UK calls for therapeutic reference pricing that appears to explicitly ignore the differential value of products within a therapy class (Towse, 2007).
disease, the value of the option-preserving treatment falls when irreversibility is incomplete, while the value increases for those at low risk. These impacts are best viewed as the intensive and extensive margins associated with the move to partial irreversibility. Value is falling on the intensive margin since we no longer need to provide these patients with the option-preserving treatment from the moment they begin treatment. On the other hand, value is increasing on the extensive margin because some patients that were not well served by a lifetime of the option-preserving treatment now find its use for a spell worthwhile. In a world with patients that are heterogeneous in their risk for future diseases, the distribution of patient types will determine whether the option-preserving treatment is more valuable in an environment of partial or complete irreversibility. Each of these impacts is compounded when a test for future disease progression is introduced.

The intuition for these results is deepened when we recognize that one of the principal features driving our results is that health risks for future diseases increase with age, a characteristic that accurately describes the incidence profile for many diseases throughout the world. When patients are heterogeneous in early environmental exposures or their genetic predisposition to disease, older low-risk patients are conceptually akin to younger high-risk patients since both have similar risks of developing disease in the coming years. The key distinction is that under complete or near-complete irreversibility, low-risk patients must begin the option-preserving treatment when they are young, which is precisely when the treatment is least valuable. Only in the cases where future disease is both very likely and of significant consequence, i.e. when the option value is very large, will it make sense to place low-risk patients on this option-preserving regimen. As the ‘costs’ of reversing current treatment impacts fall, it becomes more feasible to provide the option-preserving treatment to these low-risk individuals at a later age, even if the impacts of future disease are modest.

The biggest obstacle to translating theory to practice is the intensive data requirement, which in some cases would require coordination across firms whose products might interact, and would greatly increase drug evaluation costs regardless. As discussed earlier, one coarse but easy solution to overcome this challenge that relies on the spirit of the model developed in this paper is to provide a valuation ‘premium’ for treatments that rely on new therapeutic mode of action, with the idea that a diversified portfolio of interventions will enhance social welfare by providing more alternatives for treatment. Our basic framework of option valuation also highlights potentially important macro-level strategies to improve social welfare through medical technologies. Research investments that focus on transforming irreversibility from complete to partial could generate large social benefits. This is particularly true for the nearly invisible case where most of the population is at low risk for future diseases. Clearly, investments in the development of alternative treatments for future diseases are also important, but the return to such investments will hinge critically on the degree of irreversibility in the system. At a broader policy level, our model clearly points toward support for research that strengthens our etiologic and epidemiologic understanding of disease and its evolution over time, which stands in contrast to approaches that focus on investing in disease treatments for the sole purpose of reducing the onset and severity of symptoms. Modifying the simple model developed in this paper to directly assess the value of such strategies is an important area for future research.

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APPENDIX A

Totally differentiating (10) and applying the implicit function theorem tell us how the optimal treatment switching period \( t \) changes in response to changes in other parameter values of interest. Increases in \( t \) should be interpreted as decreases in the value of \( T_2 \) since less of it will be used by patients.

Letting

\[
X = -\left[ \frac{d q_t}{d t} (1 - \pi) B_1 \right] + \int_{n}^{n+1} \left[ \frac{d q_t}{d t} (\omega - 1) B_{Y_2} \right] e^{-\delta t} < 0
\]

we obtain the following:

\[
\frac{d \tilde{t}}{d \pi} = -\frac{[(1 - q_t) B_1]}{X} < 0 \quad (A1)
\]

\[
\frac{d \tilde{t}}{d \omega} = -\frac{\int_{n}^{n+1} [q_t B_{Y_2}] e^{-\delta t}}{X} > 0 \quad (A2)
\]

\[
\frac{d \tilde{t}}{d \delta} = -\frac{\delta \int_{n}^{n+1} [q_t (\omega - 1) B_{Y_2}] e^{-\delta t}}{X} > 0 \quad (A3)
\]

\[
\frac{d \tilde{t}}{d X} = -\frac{[q_n (\omega - 1) B_{Y_2}]}{X} < 0 \quad (A4)
\]

The value of \( T_2 \) is increasing as its effectiveness in treating condition \( X \) increases (A1) and as the cooling off penalty becomes larger (A4). The value of \( T_2 \) is decreasing as \( T_1 \) has less severe negative interactions with the treatment for \( Y \) (A2). The value of \( T_2 \) is also decreasing in the discount rate (A3).

Turning our attention to the parameters governing the arrival rate of disease \( Y \), we can also obtain the following:

\[
\frac{d \tilde{t}}{d q_t} = -\frac{[(dq_t/d\gamma_0)(1 - \pi) B_1] + \int_{n}^{n+1} [(dq_t/d\gamma_0)(\omega - 1) B_{Y_2}] e^{-\delta t}}{X} < 0 \quad (A5)
\]

\[
\frac{d \tilde{t}}{d \gamma_0} = -\frac{[(dq_t/d\gamma_0)(1 - \pi) B_1] + \int_{n}^{n+1} [(dq_t/d\gamma_0)(\omega - 1) B_{Y_2}] e^{-\delta t}}{X} < 0 \quad (A6)
\]

\[
\frac{d \tilde{t}}{d \sigma} = -\frac{[(dq_t/d\sigma)(1 - \pi) B_1] + \int_{n}^{n+1} [(dq_t/d\sigma)(\omega - 1) B_{Y_2}] e^{-\delta t}}{X} < 0 \quad (A7)
\]

Since the probability of disease \( Y \) arriving in period \( t \) is increasing in the baseline biologic indicator, the average growth rate of the biologic parameter, and the variance in the growth rate of the biologic parameter, the value of \( T_2 \) is increasing in each of them.

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