

# TREATMENT DECISIONS WHEN THERE ARE MULTIPLE OPTIONS

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## Abstract

This paper suggests a simple framework for analyzing treatment decisions when a patient is faced with multiple options, all of which are uncertain, and differ in terms of duration, side-effects, and outcomes. The model allows for a fallback plan if the first treatment fails so that simply ranking treatments by their expected return is not optimal. The optimal treatment plan is patient specific. A treatment that may yield a high recovery rate may not be chosen if it is accompanied by strong side effects, A treatment that has a low probability of high return may be chosen if it costless, but a play-safe treatment with a higher probability of a lower return may be chosen once cost considerations are taken into account. The implied heterogeneity in patients' choices are consistent with survey and clinical evidence. A treatment plan that is optimal for the 'representative patient' may well be suboptimal for few individuals.

Keywords: patients' preference, side-effects, decision making

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## 1 Introduction

We all get sick. Most illnesses can be treated by several options. If the problem is back pain, we can take over the counter anti-inflammatory drugs, undergo physiotherapy, see a chiropractor, or undergo surgery. For more serious illness such as cancer, clinically tested options include surgery, radiation, chemotherapy, and oral medication, though it is often the case that only one treatment can be taken at a time. Experimental drugs, complementary and alternative (CAM) treatments are sometimes used to supplement and even replace conventional treatment. The single treatment constraint may be necessary to avoid conflicts amongst treatments, or because financial constraints prohibit multiple treatments simultaneously.

The notable aspect here is that these medical treatments have different risks, ex-ante success rates, treatment horizons, side-effects, and financial costs. Patients are often willing to pay out-of-pocket for treatments that are either not covered by insurance plans or do not have scientifically scrutinized evidence of success. For example, experimental drugs are not always paid for, but there is no shortage of patients who are willing to participate in the trial programs. On the other hand, sometimes patients prefer not even to be treated at all. Why do they do so, and are such decisions optimal? More generally, how do patients make medical treatment choices? When might a patient agree to a treatment that has an average chance of achieving an average outcome, and when might a patient agree to a treatment that has a small chance of being extremely effective?

The objective of this paper is to suggest a simple framework for analyzing the treatment decision focusing one particular aspect:- which treatment to take first when there are multiple fallback options. The sequence of treatments will be referred to as a treatment plan. The problem is one of dynamic decision under uncertainty. Although the tools for analysis is simple and the problem is similar to consumer decisions in many ways, treatment decisions seem not to have been analyzed in a formal economic framework. Zeckhauser and Sommers (2007) introduced the principles of decision making in a recent article intended for medical professionals, emphasizing 'probabilities' and 'preferences' as the two components of decision making. While they sketch the idea of how a treatment decision would be solved using tools that economists would use, we work out one such application.

The problem under consideration is similar in some ways to that of portfolio choice in which an agent decides how much to invest in assets with different risk and payoff characteristics. The primary difference is that in portfolio decisions, all asset types can be chosen simultaneously. Here, treatment is administered sequentially:- try treatment A first, if it does not work, try treatment B. The problem also bears some resemblance to that of a two-arm bandit in which a decision is made

each period whether to explore a new alternative. Weitzman (1979) considered the optimal order of choices to take. His Pandora's rule is to always open the box with the highest reserve value. By this rule, it is optimal to first sample those options drawn from distributions which are more spread out in the hope of striking rich early and ending the search, all things equal. In that problem, agents stop searching when all the remaining boxes have a lower reserve value than the best reward that has been secured. This problem differs from ours in several ways. In Weitzman's problem, once a box is opened, it remains opened, and the individual is faced with an increasingly small set of choices. In our problem, a treatment can be used repeatedly, and the stopping rule is implicit: a patient stops treatment only if he has recovered, or when he can no longer be treated. More importantly, the fallback option in Weitzman's problem is the highest value of the boxes sampled to date. The individual has the option to not accept the prize after the box is opened. In contrast, patients do not have this option. If one chooses an option that say, results in liver damage, one has to live with that damage. The fallback treatment takes as starting point the health status left by the previous treatment.

Our analysis can also be seen as an elaboration of Grossman (1972). In that model, which is often the building block for analyzing issues pertaining to health spending, health is treated like a durable good that depreciates over time. Health care investment is an activity that combines medical services and other inputs to increase the health stock, or at least, to slow or stop the depreciation process. Households choose the level of medical care, which subsequently determines utility. However, the model is silent on what type of treatments are made. Treatment of all types are subsumed under the investment spending on health. But the same level of medical care can be achieved by many treatment options. Two patients taking two different options may have different speed to recovery and absorb different risks, even though their investment spending is the same. Our analysis digs deeper into what underlies health investment of the standard model.

One method that is often used to guide the medical decisions tree analysis. A decision tree describes how patients in one health state might end up in other states over a fixed time period. It is a systematic method for identifying a strategy that will most likely reach a certain goal. A static decision trees, which does not allow for a switch in option, evaluates the steps in the decision and its consequences, taking into account the probability of the outcome, the resource cost, and utility. The final utility of a decision is obtained by multiplying all the probabilities along the branches until the terminal node is reached. The order that these branches are evaluated does not matter. Our focus is on the sequence of treatment to take, and as such, each option cannot be evaluated independently of the other. Markov decision trees are more general and allow transitions during a series of short intervals. They are still not designed to study how agents choose which treatment

to pursue first.

Doctors are often confronted with the need to adjust the choice of the next treatment in light of the patient's previous reactions and current state of health, a process also known as a dynamic treatment regime. There is active research by biostatisticians to estimate the parameters of the decision rule from observational data, see for example Murphy (2003). However, doctors and patients need not come to the same decision. A doctor may be constrained to follow options provided by the insurance company, while the patient might be willing to pay out of pockets for other options. A doctor might be risk averse and choose a treatment that is slow to take effect, while the patient might be more willing to aim for a fast relief. A doctor might also be conservative and choose strategies that work for the average patient, while the patient might be willing to try more aggressive strategies. Furthermore, a doctor might (and should) be highly concerned about survival rate, while the patient might take into account the quality of life after treatment. Some studies have reported that patients do not always agree with what physicians assumed, see e.g. Fraenkel et al. (2004). Interestingly, studies have found that when doctors are confronted with multiple options, physicians can have difficulty deciding between different medications and may recommend doing nothing, see Redeimeier and Shafir (1995). On the other hand, patients feel that no action is not an option as they have to be proactive and do something, Fagerlin et al. (2005).

We analyze the problem from the patient's perspective. We take as given that the physician has conveyed pertinent information regarding the costs and benefits to the patient whose job is then to find a plan that would maximize his/her well-being. As we will see, the optimal treatment plan will be different for different patients. A treatment plan that works for the 'representative patient' will often be suboptimal. Tradeoffs between the quality and length of life, as well as side effects, often determine which treatment would be optimal for a specific patient. Before turning to a simple model that guides our thoughts on some of the issues discussed, we first present a brief review of what is known about patients' preferences..

## **2 Survey and Clinical Evidence**

Treatments can differ in many dimensions. For example, radical options such as radiotherapy and surgery that remove vital organs exist along side with gentle options such as oral medication and non-invasive surgery. It is unlikely that a choice that dominates in every dimension exists. Understandably, many studies aim to establish the best average treatment. For example, Coco (2007) studied treatment options for acute otitis media (middle ear inflammation) in children aged 6 months to 12 years. He compared the cost and utility of four strategies: watchful waiting (72 hour observation and return to clinic if symptoms persist), delayed prescription (observe and

collect prescription if the symptoms persist), routine treatment of amoxicillin for 5 days, and routine treatment of 7 to 10 days. Costs consideration include parental work time lost and non-health care expenses (such as transportation). The benefits of treatment include absence of the symptoms and decreased likelihood of future episodes of the disease, while the primary side effect is gastrointestinal discomfort. Upon weighing the effectiveness of each treatment, the associated costs and benefits, the analysis finds that a 7 to 10 days treatment of amoxicillin and delayed prescription are the better of the four options. The 10 day treatment, while more effective, is also the most costly. Delayed prescription is more economical not just because of less use of antibiotics, but also because of fewer office consultations. Studies of this nature often recommend a treatment that is best 'on average'. But individuals may weight the attributes of each treatment differently. Whether the average treatment is desirable for a specific patient very much depends on the patient's preference.

Various studies have solicited patients' preferences by asking whether they want to forgo or continue treatments. Such studies often find that patients have a strong distaste for negative side-effects. Fraenkel et al. (2004) found that while a variety of medications are available to relieve pain of older patients with arthritis, people would rather be safe than sorry:- they often choose treatments with fewer side effects (such as a cream) rather than the ones that may work better but decrease their quality of life (such as highly toxic pills).

The strong aversion against negative side-effects is also reported amongst patients with more serious illnesses. In a survey that interviewed male prostate cancer patients, Bryan et al. (2004) found that patients are willing to trade-off as much as 18 months of life-expectancy to relief side-effects. McQuellon et al. (1995) studied data on patients with metastatic breast cancer in the U.S. who either had mastectomy or lumpectomy plus radiation as primary treatment, and were told of a life expectancy of 18 months. They assessed patients' preference towards four clinical scenarios with different side-effects for a 50% chance of increasing life expectancy. They found that the greater the toxicity potential of the treatment, the less likely were patients willing to accept the treatment. Almost all patients would accept treatment for a 5-year increase in length of survival, but only 34-85% of patients would take therapies for a 6 month addition to life expectancy. Only 15% of patients would prefer high-risk treatment for an additional month of living. Younger patients are more willing to take risky treatments. Interestingly, over 75% of the patients would take treatment just to relieve symptoms even if it does not prolong life, and most would also take treatment even without symptoms related to metastatic disease.

Side-effects appear to weigh in heavily in patients' preference, whether patients are young or old. Sculpher et al. (2004) studied 129 men with non-metastatic prostate cancer age 70 years and over. The objective of the study was to assess patients' trade-offs between the risks and benefits of

alternative therapies, some more radical than others. Patients who were interviewed were presented with eight attributes (side-effects) of the treatment, ranging from diarrhoea to sex drive, physical energy life expectancy, and out of pocket expenses. Patients were then asked to make discrete choices of the pairwise attributes. Probit regressions were then used to estimate the effect of each attribute on the probability of choosing the treatment, as well as the marginal rate of substitution between the attributes. The male patients were found willing to trade-off some life expectancy to be relieved of side effects. On average, they were most willing to give up life expectancy to avoid limitations of physical energy and least willing to avoid hot flushes.

Fried et al. (2002) interviewed a sample of 226 patients 60 years or older, and who were diagnosed with cancer, congestive heart failure, and other serious illnesses. These patients, who were aware of their limited life expectancy, were asked their treatment preference given the different burden it imposed, different possible outcomes, and the likelihood of these outcomes. A high burden treatment might involve long hospitalization in possibly an intensive care unit, complex tests, and surgery. The study found that almost all participants choose a low-burden therapy that would restore their health if the alternative of no treatment would imply death. However, if the low burden treatment involves an outcome associated with cognitive impairment, almost 90% of the respondents no longer want to be treated. The study establishes that preferences change in response to the burden of treatment, the outcomes, and the likelihood of outcomes.

The distaste for side effects also appears in studies conducted in other countries. Using data on Australian women with Stage I and II breast cancer, Mastaglia and Kristjanson (2001) found that women who had breast conserving treatment tends to rate the surgeon's preference as being important in decision making relative to women who underwent radical mastectomy. The study also finds that patients tend to opt for conservative treatment, especially when there is a lack of difference in long term survival between the different types of surgery.

While most of the above studies indicate a clear preference of patients against treatments with strong side effects, Winter and Parker (2007) found that less healthy people are more eager to try life-prolonging treatments compared to healthier ones. Matsuyama et al. (2006) also found that the attitude of those near the end of life might be different. Based on a literature search from 1980 to the present, these authors found that many patients would choose chemotherapy for a small benefit in outcome. Adverse effects at such a stage of the disease become less of a concern for patients than for the health care providers. This suggests that a decision optimal for health providers need not be optimal for patients.

The studies referenced above suggest that the magnitude of side-effects is an important concern for patients in treatment choice. Yet, these studies do not usually proceed to map patients' pref-

erences to optimal treatment. An exception is Sommers et al. (2007), who pointed out that many patient decisions (at least regarding prostate cancer treatment) are based on anecdotes, friends' experience, physicians' recommendations that depend on the specialty of the physician in question, and these decisions need not be optimal for the patient once his personal preferences are taken into account. The study first elicited the preference of 156 patients with localized prostate cancer for four treatments and then used a decision model implemented in Excel to determine the optimal treatment under different clinical scenarios and patients' preferences. They found that radical treatments are better for younger patients and those with more aggressive tumors regardless of their preferences. On the other hand, a less aggressive treatment is a better option for patients with low risk tumors of any age. Their main conclusion is that selecting treatment based on average preferences leads to suboptimal choices for 30% of patients. Accounting for heterogeneity in the preference of individuals in making treatment decisions is thus important.

The brief review of evidence above suggests that costs, benefits, duration, and side effects are the key components of decision making. We now develop a simple model to show how these factors can generate heterogeneity in a particular aspect of treatment:- which treatment to take first. The order of treatment is rarely analyzed even amongst more formal analysis of medical decisions, such as tree analysis. Yet in real life situations, patients using knows that if one treatment fails, another treatment can be attempted. Accounting for the fallback option in treatment selection is a unique aspect of the model.

### 3 The Model

Let  $H_{it}$  be an indicator of health status for individual  $i$ . An individual is healthy if  $H_{it}$  exceeds some threshold  $H^*$ , which we will normalize to 1. An individual dies if  $H_{it}$  falls to zero. When  $H_{it} \leq H^*$ , the individual needs to 'repair' himself by seeking medical treatment. Utility is a function of consumption and health but health-related decisions are separable from the consumption decision. This can be justified by assuming that individuals perform two-stage budgeting; resources are allocated to health care first, and the residual is allocated to consumption. If  $U(C_{it}, H_{it}) = u(C_{it})v(H_{it})$ , where  $v(H_{it})$  is monotonically increasing in  $H_{it}$ , then  $H_{it}$  acts like a 'taste shifter'. Whereas standard taste-shfters are assumed to evolve exogenously, individual decisions will alter the evolution of  $H_{it}$ . In this analysis, we simply assume  $v(H_{it}) = H_{it}$ .

Consider now individual  $i$ , who is diagnosed with an illness. He is given  $K$  treatment options, indexed by  $k = 1, \dots, K$ . There does not exist a perfect treatment that can restore health in one period with perfect certainty. No treatment is always possible. This option, referred to in medical science as 'watchful waiting', is index by 0. Patients also do not want to be over-treated, so they

chose options that bring them closest to  $H^*$ . We also assume that patients are not 'confused' when confronted with multiple options.

Assume for simplicity that each option has two outcomes:– health will improve at rate  $\mu_k^G$  with probability  $p_k$ , and at rate  $\mu_k^B$  with probability  $1 - p_k$ . By assumption,  $\mu_k^G > \mu_k^B$ , and we will accordingly call  $\mu_k^G$  the good outcome under treatment  $k$ . We also assume treatments can do no harm in the sense of making one even less healthy. Thus,  $\mu_k^B > 0$  for all  $k$ . For a given treatment  $k$ , the expected gross return (or outcome) is

$$\mu_k = p_k \mu_k^G + (1 - p_k) \mu_k^B.$$

To complete the description, treatment  $k$  takes  $\Delta_k$  periods to complete, and is associated with side-effects of  $\delta_k$  per time period. Side effects make an individual feels unpleasant and will be treated like a negative return to health. The longer is the treatment, the higher is the level of discomfort that the side effect inflicts. It is also possible to interpret  $\delta_k$  as the rate of time preference. An impatient patient will dislike the treatment just like a side effect, and impatience also serves the purpose of lowering the return to the treatment. It can be argued that  $\delta_k$  is individual specific as individuals have different tolerance for pain. For now, we will simplify analysis by assuming that the same side-effect is felt by all individuals.

Taking  $H_{it}$  as given, the health status upon completion of treatment  $k$  in the good and bad states are respectively,

$$\begin{aligned} H_{it+\Delta_k} &= H_{it} R_k^G, & R_k^G &= (1 + \mu_k^G - \delta_k \Delta_k) \\ H_{it+\Delta_k} &= H_{it} R_k^B, & R_k^B &= (1 + \mu_k^B - \delta_k \Delta_k). \end{aligned}$$

The net return in the two states depend not only on the direct benefit from the treatment, but also on the side-effects that will be incurred over the treatment period. It will be convenient to define expected net return as

$$R_k = p_k R_k^G + (1 - p_k) R_k^B.$$

For a treatment to be effective, the post-treatment health status  $H_{it+\Delta_k}$  has to be no lower than  $H_{it}$  in expectation.

Patients are assumed to know the cost, the side-effects, the duration of the treatment, and the outcome in different states. Myopic patients would simply choose a treatment with the highest net return. But it is hard to imagine that patients, especially those with serious illness, actually behave this way. Patients usually know that the number of treatments they can realistically attempt is quite small, as they have neither the time nor the resources to try all options. Patients usually have a fallback plan in mind and take a 'one step at a time' attitude to observe the progression

of the latest treatment. Specifically, I assume that if the first treatment is successful, the patient sticks with the plan and repeats the treatment. If it is unsuccessful, he tries a different option. These considerations suggest a two period model in which the length of the period depends on the treatment being undertaken. The state variable for the problem is health status,  $H_{it}$ . Let  $\mathcal{K} = \{0, 1, \dots, K\}$  be the action space. Let  $d_t = (a_t, a_{t+\Delta_{a_t}}^e)$  be the decision taken time  $t$ . It consists of an action  $a_t \in \mathcal{K}$ , and a fallback action  $a_{t+\Delta_{a_t}}^e$  taken at some future date that depends on the outcome of  $a_t$ . The objective is to find  $d_t^*(H_{it}) = \arg \sup_{d_t} E(Y|H_{it}, d_t)$  subject to an ‘over-treatment’ constraint that discourages treatment well above  $H^*$ , where  $Y$  is outcome at  $t + \Delta_{a_t}$  if the treatment  $a_t$  is successful, but is outcome at  $t + 2\Delta_{a_t} + \Delta_{a_t}^e$  if the fallback option is exercised. The optimal decision can be found by enumerating all possible actions directly.

### 3.1 No Cost Treatments

It is useful to first consider the decision problem without cost considerations, which may arise if all treatments are covered by insurance plans, for example, so that costs do not affect marginal decisions. Let  $\bar{V}_i(k, j)$  be the valuation of plan  $(k, j)$  by individual  $i$ , obtained by proceeding with treatment  $k$  first, and with treatment  $j$  as the fallback option. Then

$$\begin{aligned} \bar{V}_i(k, j) &= p_k (R_k^G)^2 H_{it} + (1 - p_k) H_{it} R_k^B \left[ p_j R_j^G + (1 - p_j) R_j^B \right]. \\ &= p_k (R_k^G)^2 H_{it} + (1 - p_k) H_{it+\Delta_k} R_j. \end{aligned} \quad (1)$$

When the outcome from treatment  $k$  is good, the patient knows he responds to the treatment and is willing to accept the same treatment in the next period. Since  $H_{it+\Delta_k} = H_{it} R_k^G$  is the health status after one treatment in the good state,  $H_{it+2\Delta_k} = (R_k^G H_{it}) R_k^G$  is the health status after two good treatments of option  $k$ . When treatment  $k$  results in a bad outcome, the patient proceeds to the next treatment taking  $H_{it+\Delta_k} = H_{it} R_k^B$ , the health status after the first treatment, as given. The quantity  $\bar{V}_i(k, j)$  will also be referred to this as the reserve value of health from treatment plan  $(k, j)$ . Notice that repeating option  $k$  even after it fails is not ruled out. The optimal treatment plan is the  $(k, j)$  pair that maximizes  $\bar{V}(k, j)$  over all  $k, j = 1, \dots, K$ .

Now  $H_{it}$  does not depend on  $j$  and  $k$  and  $R_j$  can be ranked. Absent cost considerations, the optimal plan simplifies to evaluating the return from treatment  $k$  this period and the best overall treatment next period. Let  $R_* = \max_j R_j$ . Then

$$k^* = \operatorname{argmax}_{k=0, \dots, K} \bar{V}_i(k, *) = p_k (R_k^G)^2 H_{it} + (1 - p_k) R_k^B R_* H_{it}$$

with the side constraint that for all  $k'$  satisfying  $\bar{V}(k', *) > H^*$ ,  $k^*$  is chosen such that  $\bar{V}(k^*, *) - H^*$  is minimized to prevent individuals from being over treated. The key to the decision is  $p_k$ ,  $R_k$  and

$\delta_k$ . From

$$\begin{aligned}\frac{\partial \bar{V}_i(k, *)}{\partial p_k} &= ((R_k^G)^2 - R_k^B R_*) H_{it} \\ \frac{\partial \bar{V}_i(k, *)}{\partial R_k^G} &= 2p_k R_k^G H_{it}, \\ \frac{\partial \bar{V}_i(k, *)}{\partial \delta_k} &= -2p_k R_k^G \Delta_k H_{it} - (1 - p_k) R_* \Delta_k H_{it},\end{aligned}$$

we see that an increase in  $p_k$  increases  $\bar{V}_i(k, *)$  only if

$$(R_k^G)^2 > R_k^B R_*.$$

Since  $R_k^G > R_k^B$ , the condition will hold if  $R_k^G > R_*$ , or equivalently,  $R_k^G - R_* > (1 - p_*)(R_*^B - R_*^G)$ . Since  $R_*^B < R_*^G$  by assumption, a sufficient condition for an increase in  $p_k$  to increase the reserve value of treatment  $k$  is  $R_k^G > R_*$ . The condition fails only when the best treatment unambiguously dominates  $k$ . This happens when  $p_k < p_*$ ,  $R_k^G < R_*^G$ , and  $R_k^B < R_*^B$ .

The risk-return trade-off concerns balancing a treatment with a lower probability of success against one with a higher expected return. Treatment  $j$  with  $p_j = p_k + \varepsilon$  but  $R_j^G = R_k^G - \varepsilon$  will be valued more than treatment  $k$  if  $(R_k^G)^2 - R_k^B R_* > 2p_k R_k^G$ . Essentially, this depends on the difference in two period returns from the two strategies. As  $R_k^G$  is in turn a function of  $\mu_k^G$ ,  $\Delta_k$  and  $\delta_k$ , a treatment with a high  $\mu_k^G$  will be discounted if it takes a long time to implement because  $\Delta_k$  lowers  $R_k^G$ . The trade-off between  $p_k$  and  $R_k^G$  evidently does not depend on  $H_{it}$  because  $\bar{V}_i(k, *)$  is linear in  $H_{it}$ . Thus, absent treatment costs, the risk-return trade off only depends on the parameters of the treatment and has no individual specific element.

Whether individuals are willing to accept stronger side-effects  $\delta_k$  for a high  $p_k$  is determined by  $\frac{\partial \bar{V}_i(k, *)}{\partial p_k}$  relative to  $\frac{\partial \bar{V}_i(k, *)}{\partial \delta_k}$ . The required condition

$$(R_k^G)^2 - R_k^B R_* > (2p_k R_k^G + (1 - p_k) R_*) \Delta$$

is more likely to hold the higher is  $R_k^G$  relative to  $R_*$  and the smaller is  $R_k^B$ , and the shorter the duration of the treatment.

Consider the following three-option example, all with the same side effect of  $\delta_k = .02$ .

$k$	$p_k$	$\mu_k^G$	$\mu_k^B$	$\Delta_k$	$\mu_k$	$R_k$
1	0.600	0.500	0.100	5.000	1.340	1.213
2	0.400	0.400	0.300	3.000	1.340	1.262
3	0.200	0.700	0.200	2.000	1.300	1.249

Plan 1 has a high probability of a moderate return but it also has a good chance of a very low return, and it takes the longest time to complete. Plan 2 is ‘average’ by all counts. It has a fair

chance of two fairly similar returns and it takes a moderate time to administer. Plan 3 has a low probability of striking a high return and a high probability of a low return, but it takes only a short time to complete. Notably, plan 2 ranks first both in terms of expected gross return  $\mu_k$  and net expected return  $R_k$ . The reserve value matrix assuming  $H_{it} = .5$  is as follows:

Table 1a: No cost,  $H_{i0} = .5, \Delta = (5, 3, 2)$

$k \setminus j$	1	2	3
1	0.796	0.805	0.803
2	0.794	0.812	0.807
3	0.827	0.850	0.843

The optimal dynamic decision is to take plan 3 first, followed by plan 2. The reason is intuitive. Plan 3 has a small chance of striking high. As treatment is costless by assumption, there is little to loose by trying plan 3. The solution has the flavor of Pandora’s rule, which is to choose the option with the highest reserve value. In our model, this means that a riskier option will be tried first in the hope of early recovery, all things equal. But the treatment 4 will loose its appeal if it takes a long time to administer. For example, if we change  $\Delta$  from (5,3,2) to (4,3,3) the reserve values become

Table 1b,  $H_{i0} = .5, \Delta = (4, 3, 4)$

$k \setminus j$	1	2	3
1	0.828	0.833	0.820
2	0.803	0.812	0.789
3	0.796	0.807	0.779

The increase  $\Delta_k$  coupled with a decrease in  $\Delta_3$  now makes (1,2) the preferred plan. Notice also that for both values of  $\Delta_k$  considered above, treatment 2 was not the first choice even though it has the highest expected return. The reason is that there is an option value in saving the best for the last. One may get more out of the best treatment by waiting.

### 3.2 Costly Treatment

In reality, there can be substantial variation in treatment cost. Denote unit treatment cost by  $\phi_k$ . Total treatment cost is assumed to be individual specific and is higher the more unhealthy is the individual. Let

$$\Phi_{ik}(H_{it}) = (H^* - H_{it})\phi_k.$$

The optimal treatment plan is now defined by

$$(k^*, j^*) = \underset{j=0, \dots, K, k=0, \dots, K}{\operatorname{argmax}} V_i(k, j)$$

where

$$\begin{aligned}
V_i(k, j) &= -\Phi_{ikt}(H_{it}) + p_k \left( (R_k^G)^2 H_{it} - \Phi_{ikt+\Delta_k}(H_{it}R_k^G) \right) \\
&\quad + (1-p_k) \left[ H_{it}R_k^B \left( p_j R_j^G + (1-p_j)R_j^B \right) - \Phi_{ijt+\Delta_k}(R_k^B H_{it}) \right] \tag{2}
\end{aligned}$$

where  $\Phi_{ikt}(H_{it})$  is total cost of adopting the first of treatment  $k$ ,  $\Phi_{ikt+\Delta_k}(H_{it}R_k^G)$  is the cost of the second treatment give a health status of  $H_{it}R_k^G$  at the end of the first successful treatment, and  $\Phi_{ijt+\Delta_k}(R_k^B H_{it})$  is total cost of treatment  $j$ , given health status upon realizing the bad outcome of treatment  $k$ . Treatment cost introduces an individual specific component to the problem as the cost incurred depends on how far is  $H_{it}$  from  $H^*$ . As the net return to the fallback treatment is now individual specific, we need to evaluate  $V_i(k, j)$  for all  $(k, j)$  and for all  $i$ . It is useful to rewrite  $V_i(k, j)$  as

$$\begin{aligned}
V_i(k, j) &= p_k(R_k^G)^2 H_{it} + (1-p_k)H_{it}R_k^B R_j \\
&\quad - \phi_k(H^* - H_{it}) - (1-p_k)\phi_j(H^* - R_k^B H_{it}) - p_k\phi_k(H^* - R_k^G H_{it}) \\
&= p_k(R_k^G)^2 H_{it} + (1-p_k)H_{it}R_k^B R_j - H^* \left[ \phi_k(1+p_k) + (1-p_k)\phi_j \right] \\
&\quad + H_{it} \left[ \phi_k(1+p_k R_k^G) + (1-p_k)R_j^B \phi_j \right]
\end{aligned}$$

The first two terms in  $V_i(k, j)$  are the same as in  $\bar{V}_i(k, j)$  when treatment is costless. Treatment cost adds the last two terms to the valuation problem. The first of these two terms is the same for all individuals, but the last term is individual specific. The trade-offs between outcome, risk, cost and side-effect can be obtained from

$$\begin{aligned}
\frac{\partial V_i(k, j)}{\partial p_k} &= ((R_k^G)^2 - R_k^B R_j)H_{it} + \phi_j(H^* - R_k^B H_{it}) - \phi_k(H^* - R_k^G H_{it}) \\
\frac{\partial V_i(k, j)}{\partial R_k^G} &= 2p_k R_k^G H_{it} + H_{it}\phi_k p_k \\
\frac{\partial V_i(k, j)}{\partial \phi_k} &= -(H^* - H_{it}) - p_k(H^* - R_k^G H_{it}) \\
\frac{\partial V_i(k, j)}{\partial \phi_j} &= -(1-p_k)(H^* - R_k^B H_{it}). \\
\frac{\partial V_i(k, j)}{\partial \delta_k} &= -H_{it}\Delta_k \left( p_k(2R_k^G + \phi_k) + (1-p_k)(R_j + \phi_j) \right)
\end{aligned}$$

It will be useful to define

$$Z_{it}(k, j) = (\phi_k R_k^G - \phi_j R_k^B) - h_{it}(\phi_k - \phi_j)$$

where

$$h_{it} = \frac{H^*}{H_{it}}$$

is one plus the deviation of health status from optimal. An increase in  $p_k$  is desirable if

$$(R_k^G)^2 > R_k^B R_j - Z_{it}(k, j).$$

Treatment costs evidently changes individuals' valuation of risk. Even if  $(R_k^G)^2 > R_k^B R_j$ , a condition that would increase  $V(k, j)$  when  $\phi_k = 0$ , an increase in  $p_k$  may not increase  $V_i(k, j)$  anymore. It depends on  $Z_{it}(k, j)$ , and thus on relative cost, return in both states, as well as health status. If  $\phi_k < \phi_j$ , the condition is more likely to hold for unhealthy individuals with high  $h_{it}$  as they enjoy not only a more certain return, but also a larger one.

Individuals are willing to incur a higher  $\phi_k$  for a higher  $p_k$  if

$$(R_k^G)^2 - R_k^B R_j > h_{it}(1 + p_k) - (1 + p_k R_k^G) - Z_{it}(k, j).$$

The inequality is more likely to hold when the alternative treatment does not appear promising, that is, when  $R_j$  is low. Paradoxically, the more unhealthy the patient, the higher is  $h_{it}$ , the less likely will he pay more for a more predictable return.

Individuals will accept a more predictable treatment (higher  $p_k$ ) for a less effective one (lower  $R_k^G$ ) if

$$(R_k^G)^2 - R_k^B R_j > 2p_k R_k^G + \phi_k p_k - Z_{it}(k, j).$$

This 'arbitrage' condition is again individual specific, as the net cost of taking more risk depends on individual's health status prior to treatment. For the same cost structure, a healthy individual with a small  $h_{it}$  has a large  $Z_{it}$  and will be more likely to accept a higher risk for a higher return. Unhealthy individuals with a large  $h_{it}$  who would have accepted the trade-off when treatment is costless (ie.  $(R_k^G)^2 - R_k^B R_j > 2p_k R_k^G$ ) may refuse to accept the lower risk if  $\phi_k$  is sufficiently high.

As discussed earlier, patients are averse to the side-effects of treatments. In this model, individuals are willing to endure a higher side effect  $\delta_k$  for a higher  $p_k$  if

$$(R_k^G)^2 - R_k^B R_j + Z_{it}(k, j) > \Delta_k \left( p_k(2R_k^G + \phi_k) + (1 - p_k)(R_j + \phi_j) \right).$$

This marginal rate of substitution is individual specific in view of  $Z_{it}(k, j)$ . Compared to the condition when the treatment was costless, costly treatment adds a term to the left and one to the right hand side. Patients may well change their mind about the tolerance for side effects once costs are taken into account. A long duration and a high cost will make it less likely for the patient to endure more side effects for a higher  $p_k$ .

We now return to the example above when (3,2) is optimal. Suppose that unit cost for the three treatments are  $\phi_1 = .25, \phi_2 = .50, \phi_3 = .3$ , respectively. The valuation matrix at  $H_{i0} = .5$  is:

Table 2a:  $H_{it} = .5$

$k \setminus j$	1	2	3
1	0.572	0.532	0.569
2	0.551	0.378	0.419
3	0.630	0.538	0.581

The best treatment outcome of (3,1) leaves the individual with a reserve health value of .630. Even though plan 1 does not offer the highest expected return nor is it the shortest in duration, it is cost effective for what it can offer. Evidently, (3,2) is no longer optimal for any value of  $\phi_3$ ,

To see the sensitivity of the optimal choice to health status, consider now a less healthy individual with  $H_{i0} = .3$ . Then

Table 2b:  $H_{i0} = .3$

$k \setminus j$	1	2	3
1	0.143	0.079	0.134
2	0.211	-0.173	-0.100
3	0.282	0.227	0.109

In the absence of treatment costs, this individual would have chosen (3,2), giving  $\bar{V}(3,2) = .510$ . But notice that with positive treatment costs, the valuations are all below the beginning health state of 0.3. The amount of ‘repair’ that this individual needs to undertake is so high that his total treatment cost cannot be justified relative to the benefit he receives. No treatment thus becomes desirable. On the other hand, for a healthier individual with  $H_{i0} = .8$ , we obtain

Table 2c:  $H_{i0} = .8$

$k \setminus j$	1	2	3
1	1.216	1.211	1.223
2	1.062	1.205	1.199
3	1.152	1.004	1.289

For the assumed parameters, the highest reserve value can be obtained by repeated use of treatment (3,3). But since  $H^* = 1$ , he would be ‘over-treated’ if he follows the plan. Instead, plan (3,2) will be chosen since full health can be restored more quickly. Treatment costs can give rise to the paradoxical situation that the healthier patients gets treated while the sick do not.

To assess how treatment costs and side effects affect marginal decisions, we take a random draw of 100 individuals with different initial health states. When there is no side effect ( $\delta_k = 0$ )

and treatment is costless ( $\phi_k = 0$ ), Plan (2,1) was chosen by all. If we put in treatment cost of (.25, .5, .3), 54% choose (1,1), 24% chooses (3,1), while 22% choose to do nothing. If we now change  $\delta_k$  from zero to  $\delta_k = [.07, .06, .12]$ , 75% choose to do nothing, while 25% choose (2,2). Individual decisions are affected as much by costs as they are by the side-effects they have to endure.

### 3.3 Heterogeneous Reaction to Treatments

So far, the only source of heterogeneity is individual's health status, and  $\delta_k$  has been used as our catch-all variable for the rate of time preference and side-effects. While  $\delta_k$  varies across treatments, it is the same for all patients. Some patients may be more tolerant of lengthy treatments, while others may prefer a 'quick mix' even if the side-effects might be unpleasant. Some patients may also have stronger reactions to certain drugs than others. A convenient way to capture heterogeneity in patients of such nature is to allow  $\delta_k$  to be individual-specific. Replacing  $\delta_k$  by  $\delta_{ik}$  has the consequence of making the net return to treatment  $k$  individual-specific:

$$R_{ik}^G = 1 + \mu_k^G - \delta_{ik}\Delta_k \quad R_{ik}^B = 1 + \mu_k^B - \delta_{ik}\Delta_k.$$

Naturally, there will now be an individual specific expected return, viz  $R_{ik} = p_k R_{ik}^G + (1 - p_k) R_{ik}^B$ . The valuation function when treatment is costless is now

$$\bar{V}_i(k, j) = p_k (R_{ik}^G)^2 H_{it} + (1 - p_k) H_{it} R_{ik}^B R_{ij}.$$

Letting  $R_{i*} = \max_j R_{ij}$ , the individual's problem reduces to

$$\bar{V}_i(k, j) = p_k (R_{ik}^G)^2 H_{it} + (1 - p_k) H_{it} R_{ik}^B R_{i*}.$$

As  $R_{i*}$  varies across individuals, two individuals with the same health status may now choose different treatments. Consider again the costless treatment example in Table 1. One individual has  $\delta_k = .02$  for all  $k$  as in Table 1a, while the other has  $\delta_{ik} = .05$  for all  $k$ . For this individual, the valuation matrix becomes

Table 3a: No cost,  $H_{i0} = .5$ ,  $\delta_{ik} = .05$ ,  $\Delta = (5, 3, 2)$

$k \setminus j$	1	2	3
1	0.595	0.614	0.618
2	0.646	0.682	0.690
3	0.695	0.742	0.751

While the individual with  $\delta_{ik} = .02$  chooses (3,2) (as seen from Table 1), the individual with  $\delta_{ik} = .05$  chooses (3,3). They choose different treatment plans because the individual with  $\delta_{ik} = .02$

has  $R_{ik}$  of 1.3950, 1.3664, 1.2687, respectively. The individual with  $\delta_{ik} = .05$  has of  $R_{ik}$  1.049, 1.157 and 1.179. respectively. The expected return to treatment 3 is higher than 2 when  $\delta_{ik} = 0.05$ , making treatment 3 now the desired follow-up plan.

If we now make option 3 more time consuming by changing  $\Delta_3$  from 2 to 4, as in Table 1b, we obtain the following valuation matrix:

Table 3b: No cost,  $H_{i0} = .5$ ,  $\delta_{ik} = .05$ ,  $\Delta = (4, 3, 4)$

$k \setminus j$	1	2	3
1	0.656	0.666	0.650
2	0.664	0.682	0.653
3	0.631	0.653	0.618

The optimal choice for this individual is now (2, 2) instead of (1, 2). Heterogeneous preferences can thus lead to variation in treatment choices.

In practical situations, each treatment will likely have multiple side-effects. Then  $\delta_{ik}$  would be a weighted average of the various effects, where the weights could arguably be individual specific. More dispersion in optimal choices could emerge. There may also be variations in the structure of insurance plans, and individuals' marginal value of money. For someone with an unlimited budget, treatment costs might well be irrelevant to decision making.

#### 4 Discussion and Conclusion

Our simple model has several predictions. First, patients face a risk-return, a return-side-effects, as well as a cost-return tradeoff. A treatment with a high probability of an average outcome may be bypassed in favor of one with a low probability of a strongly favorable outcome. A treatment with a high gross return can be sub-optimal if it has strong side-effects and/or has a long duration. Patients may favor a treatment with a less effective outcome for a less costly treatment. Second, the optimal treatment plan is person specific. It depends on the severity of the illness, as represented in our model by  $H_{it}$ , and also on individual preferences, as indicated in our model by  $\delta_{ik}$ . A treatment plan based on the parameters of a 'representative' patient will, in general, be suboptimal. Our simple analytical model thus generates predictions that are qualitatively consistent with the main result of Sommers et al. (2007), namely, that the optimal treatment often depends on individual patient preferences and cannot be determined just by evaluating the clinical scenario.

Our analysis can also shed some light on why patients are sometimes willing to use comprehensive and alternative treatments. According to Vital and Statistics (2004) published by the CDC, some 62% of adults in the U.S. use some form of CAM. In Canada where the provincial health

plan provides conventional health services to every citizen, use of chiropractic services is even more prevalent. At face value, patients seem willing to pay to supplement or replace the free services that they are entitled to. It has also been reported that half of HIV-infected Americans use alternative medicine to supplement or replace antiretroviral drugs. In our model, seeking alternative treatment may be desirable if it has smaller side effects, or it makes a patient 'feels good', which would raise the net return to treatment.

We have assumed  $v(H_{it}) = H_{it}$  so that expected utility increases in proportion with  $H_{it}$ . It can be argued that patients have a reservation point for their health. Consider for example  $v(H_{it}) = H_{it}^\alpha$  if  $H_{it}$  exceeds some lower threshold  $\underline{H}$ , and  $v(H_{it}) = -\gamma H_{it}^\alpha$  when  $H_{it}$  falls below the threshold. If patients' valuation depends on how sick they are, then a patient that is somewhat sick will make a different choice as a patient that is very sick. Winter and Parker (2007) found evidence in support of prospect theory. Integrating such preferences into an analytical model would be useful to better understand how optimal decisions differ the standard paradigm.

Spending on health care is an issue that concerns patients, insurers, and policy makers alike. Insurers inevitably want to authorize treatments only when they are necessary. If the patient's preference for treatment does not coincide with the treatment undertaken, a market should exist for providing specific services. Ultimately, it is the patients' characteristics that will induce such demand. Our analysis shows that heterogeneity in the characteristics of patients can give rise to individual specific treatment choices. A plan that works for the average person may in fact be suboptimal for everyone. If doctors and insurers provide treatments that work for the average patient, patients may indeed seek alternative and complementary treatments to complement suboptimal treatment plans.

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