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Patients' Perceptions and Treatment Effectiveness

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Abstract

An extensive literature relating patients' expectations to treatment outcomes has not addressed the determinants of these expectations. We argue that treatment history is part of a reference point that influences patients' expectations of how effective further treatment might be, thus influencing whether to proceed with additional treatment or not. We hypothesize that those patients with unsuccessful prior treatments have diminished expected improvement from subsequent treatments. Prospect theory provides a theoretical foundation for reference frame effects, and the model is tested with data on patients diagnosed with idiopathic intracranial hypertension. Our results support the reference frame hypothesis.

Keywords: Prospect Theory, Treatment Outcomes, Treatment History, Misclassification, Monotone Rank Estimator

JEL codes: C14, C25, I12

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Introduction

For some illnesses or health disorders, treatments are palliative rather than curative. One commonly used measure of treatment effectiveness when conditions are without clear objective symptoms is self-reported changes in disease status. Prior experience with, and earlier treatment for, the condition contributes to a frame of reference that may affect a patient's perception of how much further treatment will improve his or her[1] health status. More specifically, by affecting patients' expectations about how effective a treatment might be, this reference point influences whether a patient pursues an additional treatment, as well as subsequent perceptions of how effective that treatment is. Although there is an extensive literature on how patient expectations influence treatment outcome(s) and recovery speed, to our knowledge no existing research tests how prior treatment impacts reference point effects. The purpose of this paper is to explore how reference points affect the perceived effectiveness of medical treatments.

The literature regarding the relationship between expectations and health is extensive, but many of these studies focus only on the fact that a connection exists, and not on the causal relationship (Carver et al., 1994; Frey et al., 1985; Koller et al., 2000).[2] For example, Miceli and Castelfranchi (2002) speculate on the psychological effects of combining forecasts of future events with hopes and fears, both before and after the event occurs.

Another line of research finds that positive expectations speed recovery (Scheier, 1989 and Scheier and Carver, 1987 for coronary bypass surgery; Frey et al., 1985 for recovery from accidents; and Kalauokalani et al., 2001, for low back pain). Others find that positive expectations improve patients' perceptions of subjective health (Carver et al., 1994 for breast

[1] The data include both male and female patients. For convenience only the female pronoun is used in the remainder of this paper.
[2] For summaries of the earlier literature see Ditto and Hilton (1990), Jones (1982), and Jones (1990).

cancer patients; Llewellyn-Thomas, Thiel, and McGreal, 1992 for the general assessment of one's own health; and Koller et al., 2000 for the quality of life of cancer patients).

None of these studies, however, address what determines expectations of treatment outcomes. We argue that prior treatment provides a frame of reference which, along with other personal characteristics, affects patients' baseline expectations of treatment success, which in turn influences their perceived effectiveness of that treatment. We expect that patients with unsuccessful prior treatments have a frame of reference leaving them less likely to expect improvement from subsequent treatments. We use Prospect Theory (Kahneman and Tversky, 1979) to model frame of reference effects on subsequent treatment and expectations of effectiveness. We test the implications of the model using the Monotone Rank Estimator (MRE) (Cavanagh and Sherman, 1998) with data on patients diagnosed with idiopathic intracranial hypertension (IIH).[3] The results support the proposition that prior treatment failure or success impacts a patient's reference point, which in turn influences her perceptions about the effectiveness of subsequent treatments.

The remainder of this paper is organized into five sections. In the next section we describe our model of treatment choice. Successive sections discuss an application, our empirical methods and estimation results. We finish the paper with conclusions and implications for future research.

Frame of Reference and Treatment Choice

Prospect theory (PT) was introduced as an alternative to expected utility theory (Von Neumann and Morgenstern, 2004) for modeling decisions under risk when those decisions are dependent

[3] See Appendix A for a detailed explanation of this disorder.

on a frame of reference.[4] Unlike expected utility theory where values are placed on final states, PT assumes that individuals assign values to gains and losses relative to a reference point. The frame of reference can in principle influence the valuation of possible outcomes, the subjective probabilities of treatment effectiveness, and risk preferences. In our model we focus on how a patient's reference point affects her expectations of treatment success, thus determining the path of treatment, and, for subjective outcomes, the perceived success of treatments after the treatments have been pursued.

The value of a given prospect is measured by

$$V(x,p;y,q)=\pi(p)v(x)+\pi(q)v(y), \tag{1}$$

where x and y are potential outcomes that occur with probabilities p and q, respectively. The decision weights, $\pi(\cdot)$, measure not only the impact of the perceived (as opposed to actual) probabilities on the overall valuation of the prospect, but also the influence of factors such as ambiguity. Kahneman and Tversky (1979) argue that in most cases $\pi(p)<p$, and $\pi(p)+\pi(1-p)<1$, but that small probabilities tend to be overweighted so that $\pi(p)>p$ if p is small.

The value function $v(\cdot)$ measures the value of gains and losses relative to the reference point. This function is believed to be concave for gains and convex for losses, giving it an S-shape, as illustrated in Figure 1. Consistent with the literature (Kahneman and Tversky, 1979), we assume that the function passes through the reference point, and is steeper for losses than gains, reflecting risk aversion. The overweighting of low probability events and the

[4] A revised version titled "cumulative prospect theory" (Tversky and Kahneman, 1992; Wakker and Tversky, 1993), applies to uncertain and risky prospects with multiple outcomes. Under the extended theory decision weights are applied to cumulative, as opposed to individual, probabilities. However, the extension gives the same results as the original theory for all two-outcome and mixed three-outcome prospects. This paper focuses on three-outcome prospects, hence the earlier version of Prospect Theory (Kahneman and Tversky, 1979) is sufficient for our purposes.

underweighting of high probability events is what can cause some people to be risk seeking for potential losses and risk averse for potential gains.

Many of the PT applications in health care focus on the effects of information framing on medical decisions (McNeil et al., 1988). Meyerowitz and Chaiken (1987) find that the use of negatively framed information leads to increased breast self-examination. Rothman et al. (1993) further corroborate the importance of framing by demonstrating that negative framing may be more effective in encouraging behaviors that are seen as risky (for example being tested for a sexually transmitted disease), while positive framing may be more effective in encouraging preventive behavior (for example, practicing safe sex). Block and Keller (1995) show that negative (positive) framing may be more persuasive when the perceived efficacy of a solution is low (high). In more recent work, Rasiel et al. (2005) use PT to rationalize risk-seeking behavior among terminally ill patients. They suggest that patients' reference points differ due to factors such as pre- and post-diagnosis life expectancies which therefore affect the chosen treatment paths.

Unlike traditional PT models, which have the reference point affecting the valuation of outcomes (Lenert et al., 1999; Treadwell and Lenert, 1999), we focus on how a patient's reference point influences the subjective expectations of treatment success, thus determining the path of treatment, and impacting the perceived success of treatments after they have been pursued.

A Prospect Theory Model of Treatment Choice

Patients choose a treatment path if they expect it to have a positive impact on their current health status. We assume that an individual's expectations of post-treatment disease status depend on her subjective probabilities of treatment effectiveness, which in turn are influenced by her reference point. The reference point for our purposes is the patient's current status and the successfulness of her earlier treatments. We assume there are three possible outcomes of treatment: the patient improves (*b* = "better"), the patient remains the same (0 = "no change"), and the patient worsens (*w* = "worse").

These assumptions give us the following equation:

$$V(b,p;w,q;0,r) = \pi(p)v(b) + \pi(q)v(w) + \pi(r)v(0). \quad (2)$$

The value $v(b)$ is the value a patient places on feeling better relative to her current status, which occurs with objective probability p. This is a gain in well-being, so $v(b)$ is positive. On the other hand, $v(w)$ is the value placed on feeling worse relative to her current status, and occurs with probability q. This is a loss in well-being and therefore $v(w)$ is negative. A third possibility is that the patient observes no change from her current situation with a resulting value of $v(0)$, and probability $r=1-p-q$. One might initially expect $v(0)$ to equal 0, but values are affected by the reference value, and as a result $v(0)$ could be negative if the current situation is relatively poor compared to earlier states, although $v(0)$ would still exceed $v(w)$. We hypothesize that $0 \geq v(0) > v(w)$ because a typical individual seeks medical treatment to improve her condition, contingent upon the outcomes of previous treatments. We further maintain that losses are feared at least as much as gains are valued, so the absolute value of $v(w)$ will equal or exceed that of $v(b)$ given a one unit change in disease status.

The decision weights, $\pi(\cdot)$, are the subjective probabilities of each outcome. Thus (2) represents the individual's subjective valuation of the treatment outcome. As such, a negative (positive) overall value indicates that the individual perceives a negative (positive) valuation of pursuing further treatment. A zero value indicates a perceived neutral valuation of receiving subsequent treatment. To a large extent the final value will depend on the relative magnitudes of the decision weights. For example, we know that if a patient anticipates an equal one unit change in disease status one way or the other (i.e. b = -w), if $\pi(p) \leq \pi(q)$, and if $v(0) = 0$ or $\pi(r)=0$, or both, the overall prospect valuation from (2) would be negative due to the absolute valuation of a loss being at least equal to that of a gain.

Assuming medical treatment is voluntary, all individuals agreeing to a treatment should have a positive subjective valuation at their reference point of the outcome; that is, $V(b,p;w,q;0,r) = \pi(p)v(b) + \pi(q)v(w) + \pi(r)v(0) > 0$. Assuming that $v(0)$=0 or $\pi(r)$=0 or both, this means $\pi(p)v(b) > -\pi(q)v(w)$, or the subjective weighted gain from improving b units must exceed the subjective weighted loss from regressing w units.[5] Because $v(w)$ is negative, the right hand side of the inequality is positive. The inequality can then be rearranged to

$$\pi(p)/\pi(q) > -v(w)/v(b). \qquad (3)$$

Equation 3 implies that a treatment is pursued only if the subjectively weighted probability of a gain relative to that of a loss exceeds the ratio of the (absolute) utility value of a loss divided by the utility value of a gain. In terms of our specific application this has an interesting interpretation. For any given values of *v(w)* and *v(b)*, treatment is more likely to be pursued if there is only a relatively small subjective probability of the treatment leading to a worse outcome.

Acetazolamide is the drug generally viewed as the most effective form of treatment for IIH, and is usually the first treatment pursued. Other medicinal options are generally reserved for patients who cannot tolerate acetazolamide. If medication is ineffective, subsequent

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[5] Even though the model is conditioned on the assumption that v(0) = 0, it is a trivial extension to extend the results to the non-restricted case. The math is available upon request from the authors. Also, as we mentioned above, v(0) is most likely less than zero, otherwise treatment would not be sought. This assumption essentially allows us to group v(0) and v(w) and analyze the probability of feeling better relative to not feeling better.

treatment normally involves an invasive procedure such as neurosurgical shunts. In Appendix A we discuss in more detail how the treatment path for IIH follows a specific sequence, but here, consider hypothetically two types of individuals, assuming all individuals place the same value on a one unit deviation from the reference point, regardless of what that point is. Patient A is initially prescribed a medication of some sort; however, due either to its ineffectiveness or the individual's inability to tolerate it, the patient is then given an invasive procedure. Patient B on the other hand, for some reason moves directly to an invasive procedure. Keeping in mind that treatment paths are being evaluated at a point in time after the previous treatment results have been observed, we expect that because they have different frames of reference due to different treatment paths, these two individuals will have different perceived valuations for the probability of success of the invasive procedure. Given that A has already experienced a failed treatment we anticipate that person B would have a higher perceived probability ratio of success to failure. This implies the following:

$$[\pi(p)/\pi(q)]_B > [\pi(p)/\pi(q)]_A. \qquad (4)$$

One testable hypothesis implied by (4) is that prior failed treatment makes it less likely that individuals will pursue subsequent treatment. Unfortunately we do not have the necessary data to test this hypothesis. If, as the existing literature contends, expectations directly influence perceived treatment outcomes (Carver et al., 1994; Llewellyn-Thomas, Thiel, and McGreal, 1992; Koller et al., 2000), an additional testable hypothesis implied by equation (4) is that patient A will be less likely to report an improvement in disease status from the invasive treatment, having already suffered a failure. We do have the data to test the following hypothesis.

Hypothesis 1: All else equal, a patient who has received more (fewer) failed treatments will be less (more) likely to report an improvement from the latest treatment.

In our application to IIH, hypothesis 1 suggests that among patients who received a medicinal prescription other than acetazolamide, those who had an initial unsuccessful experience with acetazolamide should be less likely to report an improvement in disease status than those who only had the alternative prescription.[6] Furthermore, among patients who eventually received an invasive procedure, those who received only the invasive procedure will be most likely to report an improvement, followed by patients who first had an alternative prescription, then individuals who were treated with acetazolamide before receiving the procedure, and finally patients who had both acetazolamide and an alternative prescription before receiving an invasive procedure. The reason we expect patients who had acetazolamide prior to an invasive procedure to have a lower probability ratio than those who had an alternative prescription before a procedure is because acetazolamide is widely believed to be the most effective form of therapy for IIH. We therefore expect patients who experienced a failure of this drug to be even less likely to anticipate an improvement from subsequent treatment. To summarize: patients with fewer failed treatments will be more likely to report an improvement in the latest treatment than those having experienced more failed treatments.

[6] In our application to IIH our ordering assumes that the acetazolamide was ineffective from its initial use. If acetazolamide was at first effective and improving a patient's condition, but over time lost its effectiveness, the ordering of anticipated probabilities may be opposite what we discuss here.

Data

Data for this study come from the Intracranial Hypertension Registry.[7] The Registry gathers information from individuals diagnosed with intracranial hypertension and their physicians. Patients are admitted to the Registry on a voluntary basis, however confirmatory data from at least one of the patient's physicians is required for admission to the Registry.

Because participation in the Registry is voluntary and either self or physician initiated, the patients in the Registry may not be representative of the entire population of IIH sufferers. At the time of this study the Registry contained information from 732 IIH patients. This study focuses solely on patients in the Registry who reported a disease status relative to their pre-diagnosis condition. Individuals who did so rated their relative health status on a scale of 0 to 10, 5 being "no change". Our primary variable of interest, *better*, is a binary variable created from this scale. Patients who had a rating between 6 and 10 were given a value of 1, and based on the assumption that patients would most likely place a negative value on observing no change in their disease status, patients who claimed a status of "no change" or "worse" are grouped into a "not-better" category and coded as 0. One hundred fifty-one observations remained after deleting missing values, the majority resulting from patients who did not report a post-treatment disease status. Descriptions of the variables used in this study are contained in Table 1.

Patient socioeconomic variables include real income earned from the last year worked *(Earnings)* and a collection of binary variables: whether the patient has health insurance *(Health_Ins),* whether the patient is working *(Working),* whether or not the patient is in a medical profession *(MedDv),* whether the patient has vision problems, *(Vision),* is obese *(Obese),* or

[7] The registry is co-sponsored by the Intracranial Hypertension Research Foundation of Vancouver, Washington and the Casey Eye Institute at the Oregon Health and Science University (OHSU). http://www.ihrfoundation.org/news/registry.asp

suffers from headaches *(Headache)*. *Male* and *White* are dummy variables indicating the gender and race of the patient.

Each patient was placed into one of 8 treatment categories. *AcetaRx* indicates that the patient had been prescribed acetazolamide as well as an alternative medication. *AcetaInv* and *RxInv* identify patients that received an invasive procedure in addition to acetazolamide or an alternative medication, respectively. *Invasive, Rx,* and *Aceta* are all binary variables which equal one if the patient received only the given treatment. *AcetaRxInv* indicates whether the patient received all three forms of treatment. Patients who did not receive any of the above treatments serve as the base case. A dummy variable was also created to identify patients who attempted weight reduction (*Diet*), because diets are often recommended by physicians due to the apparent link between obesity and IIH.

Summary statistics for the sample and the Registry can be found in Table 2. As shown by the t-test results in Table 2, the sample does not appear to be representative of all patients in the Registry. Most mean values differ at $p \leq 0.10$. However, our sample does appear to be fairly representative of the population of all IIH patients, the statistics for which are also presented in Table 2. We therefore argue that sample selection bias that may exist due to self-selection into this sample is likely to be relatively small. Sixty-seven percent of the patients in our sample experienced vision problems, 85% suffered from headaches at some point, and 49% were obese at the time of diagnosis. Roughly 93% of our sample is female and 92% is white.

Forty-seven percent of our sample had attempted weight reduction (*Diet*), 9% had been prescribed only acetazolamide (*Aceta*), 5% had only been on an alternative form of medication (*Rx*), and 25% only received an invasive procedure (*Invasive*). Five percent of our sample had been on both acetazolamide and an alternative prescription (*AcetaRx*), 21% had taken both of these and received an invasive procedure (*AcetaRxInv*), 14% had been on acetazolamide and received an invasive procedure (*AcetaInv*), while 17% had taken an alternative form of medication and had an invasive procedure (*RxInv*).

Empirical Methods

Our model implies that an individual pursues a subsequent treatment only if her ratio of the subjectively weighted probability of a gain relative to that of a loss exceeds the ratio of the (absolute) utility value of a loss divided by the utility value of a gain. That, in turn, influences a patient's probability of assessing a taken treatment as effective, leading to hypothesis 1 that patients with fewer failed treatments are more likely to report an improvement from their latest treatment. The empirical results are conditioned on a point in time after treatment paths have been observed, so the treatment paths can be represented in the model by dummy variables. Our dependent variable is the patient's self-assessed post-treatment disease status. Because this binary variable is created by imposing a chosen cutoff point on the 0-10 scale variable measuring the patient's perceived health status,[8] there may be some miscoding, and thus misclassification, of the dependent variable. That is, the variable measuring the patient's true subjective outcome from the treatment is latent. The relationship between the patient's subjective outcome and the observed response is

$$\Pr\left[\left(\frac{\pi(p)}{\pi(q)} > \frac{v(w)}{v(b)}\,\middle|\, z\right)\right] \Rightarrow \Pr(T = 1) \rightarrow R\begin{bmatrix}1\\0\end{bmatrix} \Rightarrow R^*\begin{bmatrix}1\\0\end{bmatrix}, \qquad (5)$$

[8] See the discussion of the dependent variable in the Data section.

where z is a vector of patient characteristics, including treatment history, T=1 implies that a given treatment was chosen, and R is the measured result. R^* represents the latent dependent variable denoting true subjective gains.

Ordinarily a binary logistic or probit regression would be performed in this case to analyze the probability of a patient feeling *better* relative to *not-better*. However, as mentioned above, one potential problem with this model is that the dependent variable is subject to misclassification error. Failure to control for this when estimating a discrete-response model via traditional techniques such as Logit or Probit, can result in inconsistent estimates (Hausman et al., 1998). Abrevaya and Hausman (1999) recommend using the semiparametric MRE as an alternative to parametric estimation. Unlike the parametric approach, semiparametric estimation does not require that the mismeasurement be modeled correctly in order to obtain consistent estimates. Therefore, the MRE is used to adjust for the potential misclassification bias.[9]

For each model, we estimate the probability that a status of *better* occurs as a function of a linear index in the following patient characteristics and treatment variables: *Male, White, Earnings, Health_Ins, Working, MedDv, Vision, Obese, Headache, Diet, Rx, Aceta, Invasive, AcetaRx, AcetaRxInv, RxInv, and AcetaInv.*

To test hypothesis 1, the effects of the relevant treatment paths on the dependent variable are tested against each other. A Wilcoxon signed-rank sum test, the nonparametric alternative to the paired t-test, is performed on the linear index $\mathbf{X}\hat{\boldsymbol{\beta}}$ from two regressions, one where the two treatment variables being tested enter the regression separately and one where they are combined to form one variable. This test consists of ranking the absolute differences between each pair of $\mathbf{X}_i\hat{\boldsymbol{\beta}}$s and calculating the Wilcoxon signed-rank statistic to test whether the median difference is

[9] See Appendix B for a detailed discussion of the MRE. Jason Abrevaya's MRE code can be obtained at: http://www.krannert.purdue.edu/faculty/abrevaya/rankest.txt.

zero. If the restriction is valid, the sum of the ranks for the positive differences should approximately equal the sum of the ranks of the negative differences. A rejection of the null hypothesis that the median $\mathbf{X}_i\hat{\boldsymbol{\beta}}$s are equal, i.e. $\mathbf{X}_i\hat{\boldsymbol{\beta}}^{MRE}_{Unrestricted} = \mathbf{X}_i\hat{\boldsymbol{\beta}}^{MRE}_{Restricted}$, implies that the effects of the two treatment variables being tested are significantly different, and thus can be compared to one another.

Results and Discussion

Results from the MRE model can be viewed in Table 3. Health insurance (*Health_Ins*) has a positive influence on disease status, and its estimate is the largest among all explanatory variables. Patients in the medical profession (*MedDv*) and those who are obese are also significantly more likely to report an improvement in disease status. The remaining significant patient characteristic variables, *Male, White, Earnings, Working, Vision,* and *Diet,* negatively affect the probability of *better* being reported by the patient.

In terms of the seven primary treatment variables, we are most interested in comparing the magnitudes of the effects that the previous treatments have on the probability that a patient claims a status of *better* relative to *not better*.[10] Patients who received only acetazolamide (*Aceta*) show a highly significant increase in the probability of reported improvement. This group has the largest coefficient estimate of all the treatment variables. Individuals who had taken acetazolamide as well as a different medication (*AcetaRx*) have the second largest estimate, followed by those who only had an alternative medication (*Rx*), then patients who received acetazolamide as well as an invasive procedure (*AcetaInv*), those who only had an invasive procedure (*Invasive*) are next, then patients who received a medication other than acetazolamide

[10] This is possible because all of these variables are binary and share the same omitted category.

in addition to an invasive procedure (*RxInv*), and finally patients who received all three forms of treatment (*AcetaRxInv*). All of these estimates are positive. The expected and actual orderings of the treatment variables are displayed in Table 4.

Our primary hypothesis is that patients with unsuccessful prior treatments have a frame of reference leaving them less likely to expect improvement from subsequent treatments, and therefore less likely to report an improvement in disease status. As shown in Table 4, our results indicate two failures out of six tests of this hypothesis: using acetazolamide prior to another treatment appears to increase a patient's reported improvement from the subsequent treatment. That is, patients who had acetazolamide prior to receiving a different prescription are more likely to claim a status of *better* than those who only had the alternative medication. The same is true of patients who had acetazolamide and an invasive procedure versus those who bypassed the medication and went straight to an invasive procedure. As we noted earlier, this might indicate that for many of the patients acetazolamide was initially effective, giving them a frame of reference that the disease symptoms are treatable, but that they were unable to tolerate acetazolamide for an extended period of time due to its side effects (Wall, n.d.; IHRF, 2007c). The ordering suggested in equation 4 appears to hold for the remainder of the patients. That is, patients who only had an invasive procedure are most likely to report an improvement, followed by patients who first had an alternative prescription, and finally, patients who had both acetazolamide and an alternative prescription before receiving an invasive procedure.

Except for the case of acetazolamide we have support for our primary hypothesis, and as explained, the failure of our hypothesis for the case of acetazolamide could be due to its outstanding effectiveness at reducing CSF within the skull (Gücer and Viernstein, 1978; Lubow and Kuhr, 1976; Rubin et al., 1966; Tomsak et al., 1988). Further support for this conjecture comes from the fact that the treatment group consisting of patients who were only prescribed acetazolamide is by far the most likely to report an improvement in disease status. The coefficient estimate for this group is over twice as large as the estimate for patients who in addition to having had acetazolamide were prescribed an alternative form of medication.

Two additional insights about the treatment of IIH come out of our analysis. The first is that attempted weight reduction is the only form of treatment to decrease the probability that a patient would end up in the *better* category. When considering how difficult dieting is for most people and the low success rate that exists among dieters, this result is not surprising.[11] Dieters tend to be frustrated with unsuccessful results, leaving them with lower expectations for the treatment's effectiveness.

Perhaps our finding with the most important policy implications is that patients with health insurance are significantly more likely to perceive an improvement than those without it. This may be due to the fact that the nature of the disease leads physicians to treat symptoms rather than the root cause, which is expensive, and those with health insurance would be more likely to be able to afford an extensive set of treatments over an extended period of time.[12]

Among the other variables in the model, higher earnings slightly decreases the probability of a *better* status, individuals with a history of vision problems and those who were working prior to IIH interfering with their daily life are also significantly less likely to report an improvement in post-treatment disease status, as are males and whites. Patients in the medical profession and those who are obese are more likely to report an improvement. The results discussed in this paragraph are difficult to explain; however, they may deserve further attention.

[11] The long term success rate among all dieters is only 31%. For females the success rate is only 27%. (Kruger et al., 2006).

[12] See Rosenman, et al. (2008) for a detailed discussion on the economic costs of IIH.

Conclusions

We provide a conceptual basis for how prior treatment failure or success along with other factors can influence a patient's reference point that helps determine expectations and decisions on future treatment, empirically demonstrate support that a patient's prior treatment failure or success may impact her perceptions about the effectiveness of subsequent treatments, and identify other factors that might influence patients' reference points and perceptions. The finding that prior treatment results affect the perceived success of subsequent treatments is important for physicians to know when prescribing additional treatment. Physicians play a large role in providing information, and this knowledge would be very useful when prepping patients for whether or not the subsequent treatment will be effective. The health insurance finding suggests that it may be especially important for patients diagnosed with idiopathic disorders where treatment is focused on symptoms to have good health insurance coverage if they are going to experience at least a perceived improvement in health status.

One of the primary shortcomings of our analysis is that our data come from a voluntary, self-reported registry. While the data are likely to be quite accurate, they may not be representative of the population of IIH sufferers as a whole with respect to some variables. Based on the variables we were able to compare, our sample does appear to be fairly representative of the population of all IIH patients (see Table 2). However, this potential registration bias may still limit some of our findings, particularly those associated with the race and gender of the patients. Additionally, we are not able to explicitly control for the costs of IIH, which may influence the decision making process, nor does our study account for all other comorbidities that might occur because of IIH. Finally, our data limitations require an empirical analysis that relies on indirect evidence. Our empirical approach requires we assume that prior expectations of how successful a treatment will be are matched by *ex post* perceptions of treatment effectiveness. A more direct test would utilize the implications from equation (4) and compare directly how prior unsuccessful (or successful, for that matter) treatment influences patients' perceptions of expected success of subsequent treatment, and therefore, their propensity to have the treatment.

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Table 1
Data Descriptions

Better	Binary variable indicating patient's disease status. Equals 1 if patient perceived themselves as better off than they were prior to diagnosis.
Male	Binary sex variable, equals 1 if patient is male
White	Binary race variable, equals 1 if patient is white_non Hispanic
Earnings	Real income values from the last full year the individual worked.
Working	Binary variable, equals 1 if patient was working the year prior to symptoms interfering with daily life
Health_Ins	Binary variable, equals 1 if patient has health insurance
MedDv	Binary variable indicating whether or not the patient has a background in health care
Vision	Binary variable, equals 1 if patient suffered from problems with vision
Obese	Binary variable, equals 1 if patient was obese at time of diagnosis
Headache	Binary variable, equals 1 if patient suffered from headaches at any time
Diet	Binary variable, equals 1 if patient attempted weight reduction
Invasive	Binary variable, equals 1 if patient underwent a surgical procedure, including subsequent lumbar punctures, but was not on medication for IIH.
Rx	Binary variable, equals 1 if patient was prescribed a medication for IIH other than acetazolamide, but did not receive acetazolamide, nor a surgical procedure
Aceta	Binary variable, equals 1 if patient was prescribed acetazolamide, but did not receive additional medication for IIH, nor a surgical procedure
RxInv	Binary variable, equals 1 if patient was prescribed a medication other than acetazolamide and underwent a surgical procedure, but did not receive acetazolamide.
AcetaRxInv	Binary variable, equals 1 if patient was prescribed a medication other than acetazolamide in addition to acetazolamide, and underwent a surgical procedure.
AcetaRx	Binary variable, equals 1 if patient was prescribed a medication other than acetazolamide in addition to acetazolamide, but did not undergo a surgical procedure.
AcetaInv	Binary variable, equals 1 if patient was prescribed acetazolamide and underwent a surgical procedure, but did not receive additional medication for IIH.

Table 2
Summary Statistics

	Sample				Registry			
Variable	**N**	**Mean**	**St. Deviation**	**Coeff. Of Variation**	**N**	**Mean**	**St. Deviation**	**Coeff. Of Variation**
$Male_a^{***}$	151	0.0662	0.2495	376.7493	732	0.1393	0.3465	248.6950
$White_b^{*}$	151	0.9205	0.2714	29.4799	732	0.8784	0.3270	37.2294
Earnings	151	6425.6000	5216.2400	81.1791	152	6410.3100	5202.3500	81.1560
Health_Ins	151	0.9205	0.2714	29.4799	194	0.9330	0.2507	26.8692
Working	151	0.8278	0.3788	45.7588	176	0.8239	0.3820	46.3697
MedDv	151	0.2252	0.4191	186.1214	196	0.2296	0.4216	183.6509
$Vision_c^{***}$	151	0.6689	0.4722	70.5939	732	0.5246	0.4997	95.2623
$Obese_d^{***}$	151	0.4901	0.5016	102.3463	732	0.1803	0.3847	213.3465
$Headache_e^{***}$	151	0.8477	0.3605	42.5306	732	0.2910	0.4545	156.2035
Diet***	151	0.4702	0.5008	106.5022	732	0.1708	0.3766	220.5140
Rx	151	0.0464	0.2110	455.0667	732	0.0191	0.1371	716.6301
Aceta**	151	0.0861	0.2814	326.8968	732	0.0355	0.1852	521.4498
Invasive***	151	0.2517	0.4354	173.0176	732	0.4194	0.4938	117.7395
AcetaRx	151	0.0464	0.2110	455.0667	732	0.0178	0.1322	744.1999
AcetaRxInv***	151	0.2119	0.4100	193.4823	732	0.0724	0.2593	358.1738
RxInv***	151	0.1656	0.3729	225.2465	732	0.0642	0.2453	382.0263
AcetaInv***	151	0.1391	0.3472	249.6347	732	0.0560	0.2301	410.8128

* implies Ho: Sample Mean = Registry Mean, rejected at significance level of 10%

** implies Ho: Sample Mean = Registry Mean, rejected at significance level of 5%

*** implies Ho: Sample Mean = Registry Mean, rejected at significance level of 1%

a) Incidence of IIH for men is approximately .3/100,000, compared to 1/100,000 women (Binder et al., 2004).

b) There is no evidence to suggest that race or ethnicity are significant determinants of IIH (Goodwin, 2006).

c) Approximately 20% - 68% of all patients with IIH experience vision problems (Binder et al., 2004).

d) Obesity is believed to be a risk factor for IIH, especially for women, with the incidence increasing from 1/100,000 to approximately 19/100,000 for obese females between the ages of 20 – 44 (Binder et al., 2004; IHRF, 2007b).

e) Approximately 90% of all patients with IIH experience headaches (Binder et al., 2004).

Table 3
MRE Results

	Dependant Variable = Better	
Parameter	**Estimate**	**95% Confidence Interval**
Intercept	------	---------
	------	---------
Male	-0.0881**	[-0.2250, -0.0250]
	(0.0651)	
White	-0.1244**	[-0.2099, -0.0079]
	(0.0595)	
Earnings	-5.1E-07**	[-6.82E-07, -5.1E-07]
	(2.0473)	
Health_Ins	0.7468***	[0.4382, 0.8684]
	(0.1354)	
Working	-0.0054**	[-0.0143, -0.0003]
	(0.0044)	
MedDv	0.0045*	[-0.0010, 0.0072]
	(0.025)	
Vision	-0.1259**	[-0.1749, -0.0273]
	(0.0440)	
Obese	0.1011*	[-0.0005, 0.1997]
	(0.0594)	
Headache	0.0634	[-0.0232, 0.1153]
	(0.0415)	
Diet	-0.1194**	[-0.2457, -0.0305]
	(0.0628)	
Rx	0.2063**	[0.0033, 0.2657]
	(0.0845)	
Aceta	0.4918***	[0.3398, 0.7892]
	(0.1311)	
Invasive	0.0598**	[0.0022, 0.0646]
	(0.0199)	
AcetaRx	0.2801**	[0.0098, 0.3324]
	(0.0989)	
AcetaRxInv	0.0250**	[0.0011, 0.0308]
	(0.0094)	
RxInv	0.0411**	[0.0014, 0.0619]
	(0.0206)	
AcetaInv	0.0766*	[-0.0104, 0.1037]
	(0.0346)	

Standard errors are in parentheses.

*Statistical Significance based on 90% confidence interval

**Statistical Significance based on 95% confidence interval

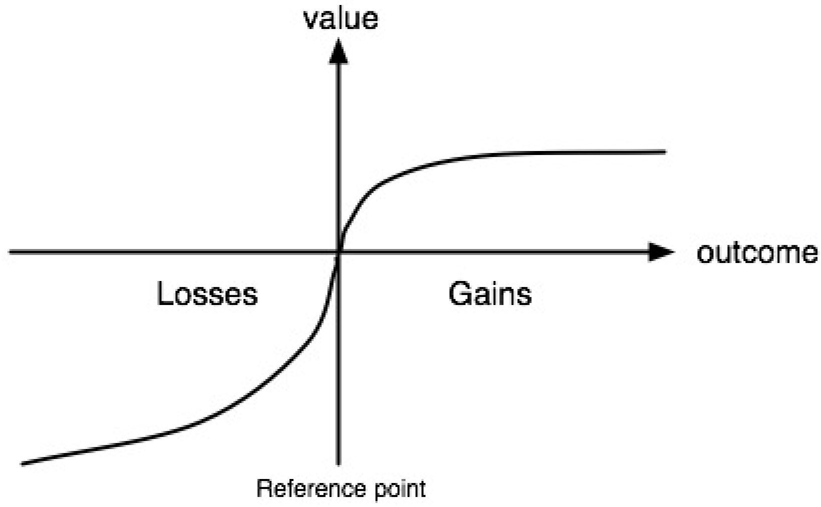
***Statistical Significance based on 99% confidence interval

Table 4

Hypothesis	p-value	Result	Expected Ordering	Actual Ordering
Rx > AcetaRx	<.0001	AcetaRx > Rx	Aceta	Aceta
Invasive > RxInv	<.0001	Invasive > RxInv	Rx	AcetaRx
Invasive > AcetaInv	<.0001	AcetaInv > Invasive	AcetaRx	Rx
Invasive > AcetaRxInv	<.0001	Invasive > AcetaRxInv	Invasive	AcetaInv
RxInv > AcetaRxInv	<.0001	RxInv > AcetaRxInv	RxInv	Invasive
AcetaInv > AcetaRxInv	<.0001	AcetaInv > AcetaRxInv	AcetaInv	RxInv
			AcetaRxInv	AcetaRxInv

Note: p-values are for Wilcoxon signed rank sum test of the null hypothesis that the effects of the two treatment paths on the dependent variable are equal.

Figure 1



Appendix A

Idiopathic Intracranial Hypertension

Individuals afflicted with intracranial hypertension suffer from elevated cerebro-spinal fluid (CSF) pressure in the skull. There are 2 types of intracranial hypertension (IHRF, 2007d). The first is *primary or idiopathic intracranial hypertension (IIH).* As the name implies, IIH arises spontaneously from an unknown cause. The other is *secondary intracranial hypertension,* which is associated with, and usually a side effect of, an identifiable cause such as a different disease, an intracranial blood clot, or certain drugs (IHRF, 2007a). The most common symptoms of increased intracranial pressure are headache and papilledema (Binder et al., 2004). The latter is particularly problematic due to the fact that over time swelling of the optic disc can lead to blindness or irreversible deterioration of vision (Giovannini and Chrousos, 2005).

Because the causes of *secondary intracranial hypertension* are known, its treatment can be tied to the patient's primary condition, and thus treated relatively effectively even though the prevalence of the disease is unknown. In this study we focus on IIH. IIH is most common among women of child-bearing age and occurs at an approximate rate of 1/100,000 (Binder et al., 2004); roughly 3 times that of males. Obesity is thought to be a risk factor for IIH, especially among women. The rate increases approximately 19 fold for females between the ages of 20 – 44 who are diagnosed as obese (Binder et al., 2004; IHRF, 2007b). However, while gender is a significant determinant of IIH, there is little evidence to suggest that race or ethnicity are significantly correlated with IIH (Goodwin, 2006).

There are several common treatments for idiopathic intracranial hypertension. Pharmaceutical treatments of IIH usually employ different types of diuretics, most commonly carbonic anhydrase inhibitors which reduce the production of CSF. Medications of this type are the only ones known to be effective (Binder et al., 2004). Acetazolamide (originally sold under the trade name Diamox) is the most common medication of this sort, and the primary drug used to treat IIH. Its success in treating IIH has been well documented (Gücer and Viernstein, 1978; Lubow and Kuhr, 1976; Rubin et al., 1966; Tomsak et al., 1988). Another diuretic that has been shown to lower intracranial pressure is furosemide (Lasix). However, this drug does not appear to be as effective as acetazolamide, and in most cases is prescribed to individuals who cannot tolerate the latter (Binder et al., 2004; Gans, 2005). Other medicinal options do exist; however, little, if any, clinical evidence exists to support their efficacy (Friedman, 2005).

Due to the link between weight gain and IIH, physicians often recommend weight loss programs as a form of treatment. Previous studies have shown that weight loss appears to be an effective treatment for IIH (Johnson et al., 1998; Kupersmith et al., 1998). However, the importance of weight loss in this context remains unclear (Ball and Clarke, 2006; Binder et al., 2004).

Sugerman et al. (1995) report systematic improvement in patient symptoms following gastric bypass surgery[13]. Newborg (1974) documents resolution of papilledema in 9 patients after being treated with a diet alone. However, the small sample size prevents these results from being generalized to the entire population afflicted with IIH.

Surgical processes are generally reserved for patients who do not respond well to medicinal treatments. There are 2 primary types of surgery that can be performed. The first is optic nerve fenestration, where an incision is made in the sheath surrounding the optic nerve to relieve papilledema. The second involves the use of neurosurgical shunts, which are used to drain the CSF into another area of the body (IHRF, 2007c). The principle types of shunting

[13] All of the patients in that study were on acetazolamide at one time, and it is unclear whether they continued to take the drug after surgery.

procedures used to treat IIH are lumboperitoneal (LP) and ventriculoperitoneal (VP), although LP shunts are used most often as they are easier to insert (Binder et al., 2004; Friedman and Jacobson, 2004). Revisions are quite common with both procedures. LP shunts have a revision rate somewhere between 38% and 64% (Friedman and Jacobson, 2004). VP shunts appear to have a slightly lower revision rate in the range of 23% to 41% (Bynke et al., 2004; Lund-Johansen et al., 1994; Maher et al., 2001).

Repeated lumbar punctures are sometimes used as a surgical alternative. However, according to Binder et al. (2004), this is a less than ideal approach to treating IIH and should only be used as an emergency measure for patients who experience a sudden loss of vision resulting from serious cases of papilledema. Curry et al. (2005) maintain that the best surgical procedure for IIH remains unknown.

Appendix B

Monotone Rank Estimator (MRE)

The following model is based on Abrevaya and Hausman (1999), and is an extension of Han's (1987) *generalized regression model.* The latent dependent variable is as follows:

$$R^* = g(x\beta_0, \varepsilon), \tag{6}$$

where ε is an *i.i.d.* error disturbance, and *g* is an unknown function containing strictly positive partial derivatives at every point. The distribution of *R* then has the following c.d.f:

$$F_{R|R^*}(n \mid d) = \Pr(R \le n \mid R^* = d), \tag{7}$$

where *n* and *d* represent potential values for the dependent variable. For a model with a binary dependent variable, the probabilities of misclassification are:

$$\alpha_0 \equiv \Pr(R = 1 | R^* < 0) \tag{8}$$

$$\alpha_1 \equiv \Pr(R = 0 | R^* > 0)\,. \tag{9}$$

The conditional c.d.f. becomes

$$F_R(n \mid R^*, d < 0) = \begin{cases} 0 & if \quad n < 0 \\ 1 - \alpha_0 & if \quad n \in [0,1) \\ 1 & if \quad n \ge 1 \end{cases} \tag{10}$$

$$F_R(n \mid R^*, d \ge 0) = \begin{cases} 0 & if \quad n < 0 \\ \alpha_1 & if \quad n \in [0,1) \\ 1 & if \quad n \ge 1 \end{cases}. \tag{11}$$

To estimate the parameters we use the MRE, which is a rank estimator for semiparametric monotonic linear index models. The MRE consists of a vector $\hat{\beta}^{MRE}$ that maximizes the following objective function:

$$S^{MRE}(b) = \sum_i M(R_i) \cdot Rank(x_i b) \tag{12}$$

over the set $B \equiv \{b \in \Re^l : |b_l| = 1\}$, where $\Re$ represents the real line, M is an increasing function in R, $\boldsymbol{X'\beta}$ is the linear index, l represents the number of covariates in x, and $|b_l|$ is the determinant of the b vector. Two comments are in order here. First, note that because the MRE is based on a rank-order process, there is no need to explicitly include an intercept in $x_i b$. Second, equations (10) and (11) imply that the stochastic-dominance conditions are fulfilled when $(1-\alpha_0) > \alpha_1$, which if it holds implies consistency of the parameter estimates.

The *Rank* function is defined by:

$$x_{i1}b < x_{i2}b < ... < x_{in}b \Rightarrow Rank(x_{im}b) = m. \tag{13}$$

Some examples of functions for M are given by Cavanagh and Sherman (1998). For robustness, $M(R) = Rank(R)$, for efficiency $M(R) = R$, or an intermediate alternative would be $M(R) = a\{R < a\} + R\{a \le R \le b\} + b\{R > b\}$, such that a and b are real numbers and $a < b$. By using a semiparametric approach we may be sacrificing some efficiency relative to a correctly specified parametric model (Powell, 1994); therefore, we used the second option to increase the efficiency of our estimates. Finally, the primary condition for consistency is that $\mathrm{E}[M(R)|X]$ is a nonconstant increasing function of $X'\beta$; however, a sufficient condition for consistency is that the distribution of R for a higher R^* first order stochastically dominates that of an R associated with a lower R^*.