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Value of Information on Preference Heterogeneity and Individualized Care

Anirban Basu, PhD, David Meltzer, MD, PhD

Background. Cost-effectiveness analysis traditionally focuses on identifying when treatments are cost-effective based on their average benefits and costs in the population. However, there may be considerable value in identifying when treatments are cost-effective for individual patients given their preferences or other personal attributes. **Objectives.** To present a theoretical framework to assess the potential value of identifying cost-effective treatments for individual patients given their preferences and to compare the value of individualized treatment decisions with the value of treatment decisions based on traditional population-level cost-effectiveness analysis. **Methods.** The authors calculate the expected value of individualized care (EVIC), which represents the potential value of providing physicians information on the preferences of individual patients, such as quality-of-life (QOL) weights, so as to make individualized treatment decisions. They also show how EVIC varies with insurance structures that do not internalize relative costs of treatments. They illustrate this theory using an example in which physicians

make treatment choices for 65-year-old prostate cancer patients. **Results.** The value of identifying cost-effective treatments at the individual level for 65-year-old prostate cancer patients in the United States is about \$70 million annually. This is more than 100 times the \$0.7 million annual value of identifying the cost-effective treatment on average for this population. However, failure to internalize costs almost eliminates the value of individualized care. **Conclusions.** The value of individualizing care can be far greater than the value of improved decision making at the group level. However, this can vary immensely with insurance. EVIC can provide a guide as to when the high value of individualized care may make population-level decision making especially at risk of providing poor guidance for coverage decisions. Future studies of the value of individualized care should also consider baseline levels of individualization of care. **Key words:** preferences; value of information; individualization of care; quality of life; prostate cancer. (*Med Decis Making* 2007;27:112-127)

Physicians and other health care providers often aim to provide individualized care to their patients in order to enhance the welfare of their patients. To achieve this, the physician spends time with a patient to learn about his or her clinical conditions, characteristics, and preferences, all of which would enable the physician to better assist patients in making the optimal choice concerning their care. This physician-patient interaction is one of the central issues in medical decision making.¹⁻³ However, in most clinical settings, physicians do not have the time or the resources to use all observed information on the patient, let alone obtaining all relevant information about the patient. In such scenarios, physicians may make treatment decisions without taking into account the levels of certain characteristics of an individual patient, which may

play a part in shaping up the outcome for that patient. Alternatively, physicians may acknowledge that these characteristics affect outcomes but use their prior beliefs on the levels of these characteristics for treatment decisions. In either case, failing to base treatment decisions on the information of the individual patient may lead to suboptimal outcomes.

Consider the case of patient preferences that play a critical role in determining the quality of life for the patient and therefore directly influence treatment selection. In most clinical situations, formal methods to assess patient preferences are not used. Physicians may still incorporate patient preferences in their decisions by learning about these preferences through informal communication with the patient. Physicians may also decide to use typical preferences for patients with similar demographic and/or clinical characteristics (a paternalistic population-based approach).⁴ Whatever the baseline level of communication, a case

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can be made that better outcomes for an individual patient might be attained by incorporating their individual preferences in the decision-making process.

In this article, we estimate the value of optimal decision making based on a paternalistic population-based model and compare it to the additional gains that can be obtained through improved decision making based on incorporating individual-level values of heterogeneous parameters such as preferences in the decision-making process. For the sake of illustration, throughout this article, we use patient preferences, as measured by quality-of-life weights for various health states, as the heterogeneous parameters based on which individualized treatment decisions are expected to be made. However, the methods we develop here can be widely applied to identify areas where substantial gain can be achieved by accounting for variability in other individual-level attributes that might affect the costs and/or benefits of treatments, such as comorbid illnesses or genotype.

We term the gain from improved decision making at the individual level the *expected value of individualized care* (EVIC). Concretely, physicians might be viewed as pursuing individualized care using a variety of decision aids that are designed to reveal information on patients' values and preferences to physicians. These decision aids are often expensive both in terms of program development and implementation and in time costs for patients and physicians. Therefore, to decide how to best allocate limited resources toward decision aids and other approaches to providing individualized care, it is important to have information on the potential social value of such endeavors and which dimensions of patient preference are most valuable to

elicit. The EVIC approach provides a way to quantify the value of individualized care and therefore provides a guide to setting priorities for individualized information elicitation across clinical conditions and institutional contexts. We also discuss how to account for how preexisting levels of individualized decision making by physicians and patients can alter the gains of optimal individualized decision making.

To the extent that such decision aids provide updated information on the benefits and costs of treatment decisions, they can be considered to be similar to a diagnostic test. Accordingly, the EVIC approach can be viewed as an approach to valuing a correct "diagnosis" of a patient as having preferences (or other attributes) that would cause him or her to favor a given therapeutic option. Furthermore, EVIC can provide a guide as to when population-level decision making may be especially at risk of providing poor guidance for coverage decisions because of failure to account for the value of individualized decision making.

Throughout this article, we use the net health/monetary benefit criteria to assess value. That is, we calculate the value of paternalistic or individualized decision making based on the treatment prescribed to an individual patient under each process and the net monetary benefits associated with this treatment for that patient. We study how this valuation is modified by certain insurance structures that minimize the incentive to internalize relative costs of treatments, such as full insurance that eliminates all patient costs of care. That is, how does the EVIC change when physicians ignore costs and make decisions based on only health benefits?

This article is structured as follows. In the next section, we develop the theory behind the EVIC and how it is affected by insurance structures that minimize the incentive to internalize the costs of treatments. Then we illustrate the concept of EVIC using a decision model for cost-effectiveness of treatments in prostate cancer that incorporates heterogeneity in preferences and variations in insurance coverage. We restrict our analysis to 65-year-old men with moderately differentiated cancer. We also compare the value of identifying treatments that are cost-effective on average with the value of identifying treatments that are cost-effective at the individual level. In addition, we discuss methods that can be used to adjust EVIC calculated earlier to reflect the incremental value of improved information in the context of baseline levels of communication between patients and physicians that produce partial individualization of care. The last section concludes.

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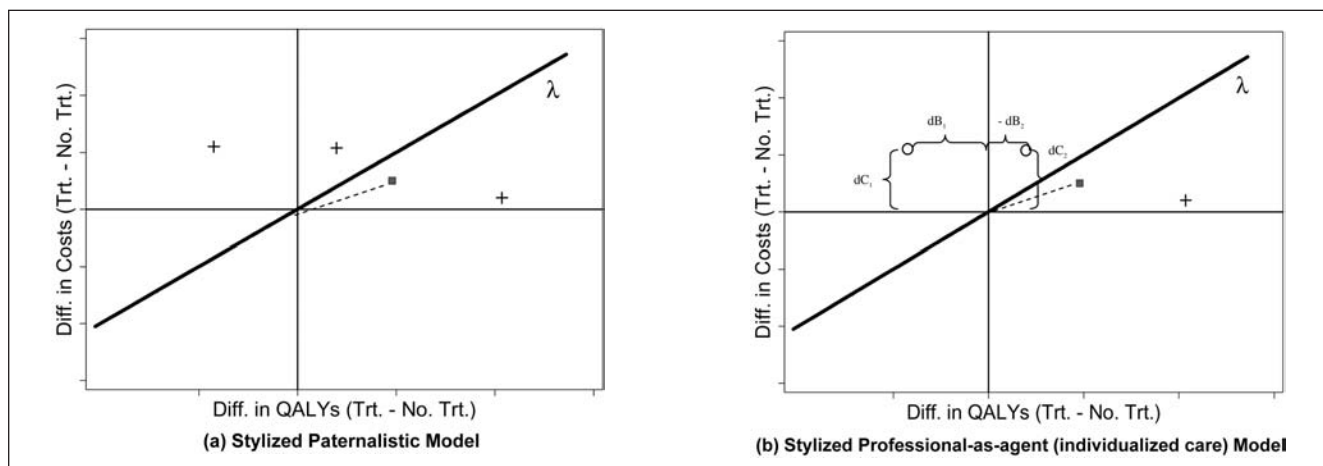


Figure 1 Illustration of the concept of expected value of individualized care (EVIC). λ = threshold cost-effectiveness ratio; o = physician's choice is no treatment; + = physician's choice is treatment. ■ = mean incremental costs and benefits. QALY, quality-adjusted life year.

THEORY OF THE EXPECTED VALUE OF INDIVIDUALIZED CARE

The Conceptual Framework

Figure 1 illustrates the conceptual framework that motivates our calculations of the expected value of individualized care. Assume there are 3 representative patients in the population confronting a clinical decision with 2 options. In all the graphs throughout this article, we use a “+” to denote that a patient received a treatment and an “o” to denote that a patient did not receive treatment (i.e., no-treatment option). These patients differ in their preferences but are otherwise homogeneous (i.e., the distributions of costs and benefits among these 3 patients are assumed to be generated by the differences in their preferences). The mean incremental cost and benefits among these 3 patients are given by the solid black square. The slope of the dotted line joining the origin to the solid square gives the incremental cost-effectiveness ratio. The slope of the solid line, denoted by λ , indicates the marginal societal willingness to pay for an improvement in health outcome under the societal perspective. As drawn, it indicates that the treatment is the cost-effective option given the threshold value of λ . Under the paternalistic model, the physician fails to incorporate variation in individual preferences in the process of decision making and prescribes the treatment to all 3 of the patients based on a favorable cost-effectiveness ratio for the treatment over the no-treatment option. Therefore, Figure 1a shows all 3 patients with the “+” symbol. On the contrary, under the individualized

care model, if the preferences of these patients are incorporated in the decision-making process, then the optimal choices for patients 1 and 2 would be no treatment (as indicated by the “o” symbol in Figure 1b). Thus, under the individualized care model, the total additional value obtained by incorporating individual patients' preferences in the decision process is given by the cost savings ($dC_1 + dC_2$) and the net benefits ($dB_1 + (-dB_2)$) of patients 1 and 2 in choosing no treatment over treatment (Figure 1b), although, on average, treatment is the cost-effective one in the population. The average per patient additional value ($\{[dC_1 + dC_2]/\lambda + [dB_1 + (-dB_2)]\}/3$) is the EVIC and is interpreted as the cost of ignorance of preference heterogeneity or the benefits of individualized care. Based on this simple idea, in the following section, we develop a general model for EVIC for the entire patient population facing multiple treatment options.

The Modeling Framework

The 4 assumptions that are inherent in both the paternalistic model and the individualized care model are that 1) patients differ in their preferences but are otherwise homogeneous (i.e., if preferences between patients were the same, then the optimal treatment would be the same for all these patients). 2) Individual patient preferences are not directly observed by physicians, although physicians know about the population distribution of preferences (later, we relax this assumption by considering the case in which physicians may engage in communication with the patients about their preferences, so the decision-making process

becomes closer to individualized care than paternalistic care). 3) Physicians make treatment decisions, and 4) patients accept the physician’s treatment prescriptions. In any particular clinical situation, let the patients face multiple treatment options $j(j=1, \dots, J)$. Assume that patients are heterogeneous in preferences as reflected by a vector $\theta = (\theta_1, \theta_2, \dots, \theta_j)$ of parameters that determines their net health benefits (NHB_j) from any treatment j . Net health benefits of a treatment is the net value the treatment produces in terms of benefits (often quality-adjusted life years [QALY]). It is the difference between the benefits from the treatment and the benefits-equivalents of the costs of the treatment. The latter is obtained by dividing costs by λ , which is the marginal social willingness to pay for health improvement. The joint distribution of θ in the population is given by $p(\theta)$.

Under the paternalistic model, physicians are unaware of the values of θ for individual patients but base their decisions on the distribution $p(\theta)$. Thus, physicians may choose the treatment that maximizes expected net health benefits and prescribe it to all patients. Hence, the average per patient societal value (V) obtained from physician’s choice under asymmetric information is given by

$$V(\text{Paternalistic}) = \max_j \int_{\theta \in \Theta} \text{NHB}(\theta) p(\theta) d\theta. \tag{1}$$

This scenario is conceptually similar to one illustrated in Figure 1a, which shows the incremental costs and benefits of treatment over no treatment, where each patient faces these 2 options. Under the paternalistic model, assume that treatment produces the *maximum expected net health benefits* and therefore that physicians prescribe treatment to all patients (all “+”). Here the expectation is taken over all patients in the population.

Under the individualized care (IC) model, individualized care is attained by identifying patient-level preferences, which can be viewed conceptually as eliciting individual values of θ and physicians using these individual levels for θ to make treatment decisions. Thus, physicians choose different treatments for different patients so that the net health benefits are maximized for each patient given his or her true value of θ . Hence, under the IC model, the average per patient societal value (V) obtained is the expected maximum net health benefits, as given by

$$V(\text{IC}) = \int_{\theta \in \Theta} \{\max_j \text{NHB}(\theta)\} p(\theta) d\theta. \tag{2}$$

This is shown in Figure 2a (conceptually similar to Figure 1b) for a 2-treatment world, where the physicians are able to choose the optimal treatment for each individual patient based on the patient’s true value of θ . Thus, physicians prescribe “no treatment” to all individuals above the threshold line and treatment to all patients below the threshold line.

The EVIC is then given by

$$\begin{aligned} \text{EVIC} &= V(\text{Individualized Care}) - V(\text{Paternalistic}) \\ &= \int_{\theta \in \Theta} \{\max_j \text{NHB}(\theta)\} p(\theta) d\theta \\ &\quad - \max_j \int_{\theta \in \Theta} \text{NHB}(\theta) p(\theta) d\theta. \end{aligned} \tag{3}$$

Thus, EVIC is the expected costs of ignorance of patient-level heterogeneity and represents the potential (though not the maximal) value of research to elicit information on heterogeneous parameters that helps to convey individualized information about each patient to the physician compared to optimal population-level decision making implicit in the paternalistic model. Because the individualized care model represents efficient outcome for each patient individually, the potential EVIC will always be nonnegative.

EVIC without Internalization of Relative Costs of Treatments

Typical health insurance covers the marginal costs of treatments and therefore does not provide incentives for patients and physicians to internalize the relative costs of treatments when making treatment decisions. We denote this scenario by *no cost internalization* (no-CI). In this case, the average societal value per patient that is obtained from the physician’s choice under the paternalistic model is given by

$$\begin{aligned} V_{\text{No-CI}}(\text{Paternalistic}) &= \left\{ \max_j \int_{\theta \in \Theta} B_j(\theta) p(\theta) d\theta \right\} \\ &\quad - (1/\lambda) \int_{\theta \in \Theta} C_k(\theta) p(\theta) d\theta, \end{aligned} \tag{4}$$

*If population-level decision making is suboptimal, the value of optimal individual-level decision making would be greater than the EVIC. On the other hand, if physicians are already making individualized treatment decisions to some degree, the value of providing symmetric information would need to be reduced to reflect baseline levels of communication between the patients and physician. This issue is discussed further in the section on measuring baseline levels of communication and weighting EVIC.

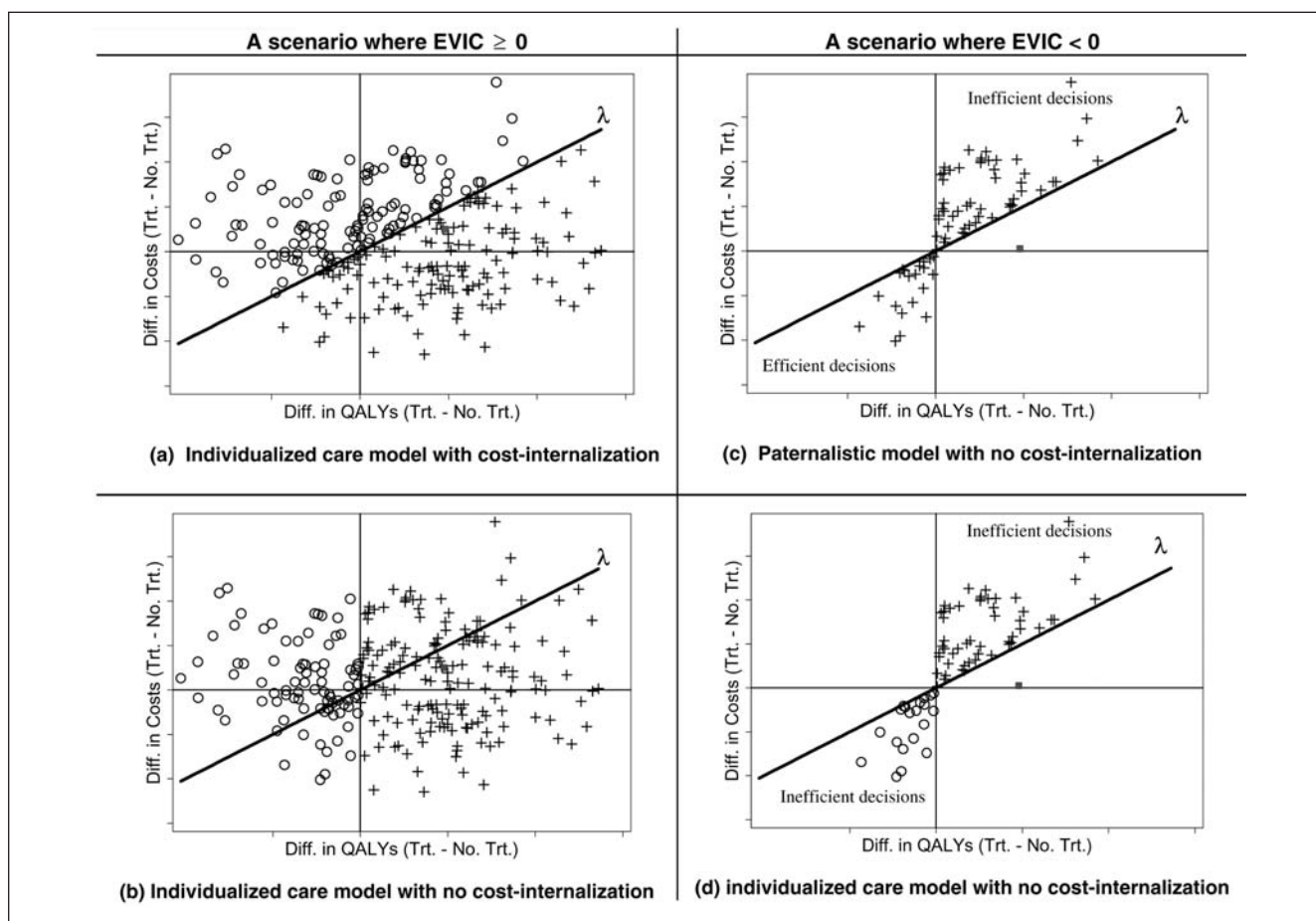


Figure 2 Individualized care model with and without cost internalization under different distributions of costs and benefits. λ = threshold cost-effectiveness ratio; o = physician's choice is no treatment; + = physician's choice is treatment. QALY, quality-adjusted life year.

where $B_j(\theta)$ and $C_j(\theta)$ are the benefits and costs of treatment j at a particular preference value of θ , and treatment k is the one that produces the maximum expected health benefits and not the maximum expected net health benefits. The illustration of this scenario is similar to that in Figure 1a, in that the physician prescribes treatment to all patients, assuming that treatment produces the *maximum expected health benefits*.

However, if physicians practice individualized care and choose different treatments for different patients that maximize health benefits for each patient given their personal value of θ but does not account for costs, then the average per patient societal value obtained is

$$V_{\text{No-CI}}(\text{IC}) = \int_{\theta \in \Theta} [\{\max_j B_j(\theta)\} - (1/\lambda)C_{k'(\theta)}(\theta)] p(\theta) d\theta, \quad (5)$$

where treatment $k'(\theta)$ is the one that produces the maximum health benefits at each level of θ . This scenario is illustrated in Figure 2b, in which physicians choose the treatment that maximizes benefits for each patient. For example, in Figure 2b, all patients with negative incremental benefits are given no treatment, whereas all patients with positive incremental benefits are given treatment. Therefore, the EVIC under no cost internalization is given by

$$\begin{aligned} \text{EVIC (No-CI)} &= V_{\text{No-CI}}(\text{Individualized care}) - V_{\text{No-CI}}(\text{Paternalistic}) \\ &= \int_{\theta \in \Theta} [\{\max_j B_j(\theta)\} - (1/\lambda)C_{k'(\theta)}(\theta)] p(\theta) d\theta \\ &\quad - \left\{ \max_j \int_{\theta \in \Theta} B_j(\theta) p(\theta) d\theta \right\} - (1/\lambda) \int_{\theta \in \Theta} C_k(\theta) p(\theta) d\theta. \end{aligned} \quad (6)$$

This can be interpreted as the potential value of attaining individualized care within a health insurance structure that does not provide incentive to internalize relative costs. Note that, in this case, even if treatment choices were made after ignoring costs, the estimate of EVIC is based on the net health benefits (including costs) conditional on treatment choices.

Although EVIC is always expected to be nonnegative with cost internalization, EVIC with no cost internalization may be less than, equal to, or greater than zero. This is because individualized care based on preferences from patients may sometimes lead to inefficiencies if the marginal costs of treatments are not internalized. This situation is illustrated in Figure 2c,d. Assume that the patient population is such that the distributions of a patient's incremental costs and benefits between treatment and no treatment are shown in Figure 2c,d. Also, assume that decision making happens with no internalization of costs. Although Figure 2c illustrates the paternalistic model under this scenario, Figure 2d illustrates the individualized care model. In order to obtain the efficient outcome from the societal point of view, patients above the threshold line should get no treatment, and those below the threshold line should get treatment. Assume that, based on the distributions illustrated in Figure 2c, treatment provides the maximum expected health benefits. Therefore, under the paternalistic model with no cost internalization, physicians will prescribe treatment to all the patients. This choice is inefficient for patients in the northeast quadrant above the threshold line (Figure 2c) because for them, treatment is expensive and provides only small benefits. However, this choice is efficient for patients in the southwest quadrant below the threshold line (Figure 2c) because for them, treatment saves costs and produces only small harm. Under an individualized care model with no cost internalization (Figure 2d), because physicians will base their choices between treatment options on individual levels of benefits, they will prescribe no treatment for patients in the southwest corner and choose treatment for patients in the northeast quadrant. However, these choices are the opposite of the socially efficient choices in both the quadrants. Thus, in this situation, individualized care (Figure 2d) will lead to greater inefficiency than paternalism (Figure 2c). Therefore, the potential societal value of the program that facilitates elicitation of individual-level preferences and encourages physicians to use them in order to make individualized treatment decisions will be negative in this case.

Population EVIC and Parameter-Specific EVIC

The annual EVIC (with or without cost internalization) of the population can be calculated using the formula $EVIC(pop) = EVIC * I$, where I is the incidence of the condition for which the treatment might be applied in the patient population per year.

Analogous to the expected value of perfect information (EVPI) methods, parameter-specific EVIC can also be calculated. The goal of these estimates is to rank and identify those heterogeneous parameters whose values are most important for the physicians to make efficient decisions for individual patients. The EVIC for any 1 parameter θ_i among the vector of parameters θ is calculated as follows:

$$EVIC_{\theta_i} = EVIC - \int_{x \in \theta_i} p_i EVIC(\theta_i = x) d\theta_i. \quad (7)$$

Here, p_i represents the marginal probability distribution of parameter θ_i . The second term in the above expression represents the EVIC calculated, holding θ_i constant at any specific value of x and then taking the expectation of these EVICs over all possible values of θ_i . Thus, the second term represents the expected value of information on all the remaining parameters in the model as the true value of θ_i is always known. The EVIC for parameter θ_i is therefore the difference in EVIC for all parameters in the model and EVIC for all parameters except for θ_i in the model.

EVIC IN PROSTATE CANCER TREATMENTS AND THE EFFECTS OF NO COST INTERNALIZATION

Model

We illustrate the EVIC calculations using a decision model developed by Meltzer and others⁵ to address cost, effectiveness, and cost-effectiveness of treatments in prostate cancer (PC). This model possesses several advantages over currently published decision models in PC. Specifically, the advantages are due to modeling the following aspects: 1) tumor heterogeneity and progression rates by grade, 2) misclassification of tumor stage due to the discrepancy between clinical and pathologic stage, 3) the ability of screening and treatment to affect the prevalence of prostate cancer, 4) the effects of benign prostatic hypertrophy (BPH) and other prostate symptoms on the detection of prostate cancer, and 5) the potential

effects of treatment on quality of life, as measured by quality-adjusted life expectancy. These aspects enable modeling of the natural history, screening, and treatment of prostate cancer more accurately than previously and are better situated for cost-effectiveness analyses.

We restrict treatment choices to 3 options—watchful waiting, radical prostatectomy, and external-beam radiation therapy—and for the purpose of illustration in this article, we restrict our analysis to 65-year-old men with moderately differentiated cancer. The model⁵ includes the effects of prostate cancer and treatment on quality of life, survival, and costs. Complications varied by treatment include impotence, urinary incontinence, urethral stricture, bowel dysfunction, metastasis, and death. Moreover, we consider anxiety from prostate cancer spread or recurrence as a complication reflecting the uncertainty underlying prostate cancer treatments. Psychological anxiety following diagnosis of prostate cancer is 1 aspect of quality of life that has been neglected by all previous cost-effectiveness studies. Anxiety may stem from 2 factors—lack of information on the stage and grade of the cancer (i.e., whether it is clinically localized) and concern that the cancer may become incurable if not treated immediately. No literature on prostate cancer could be identified that elicits quality-of-life (QOL) weights corresponding to the patients' health state involving anxiety, let alone their effects on quality-adjusted life expectancy. Moreover, this anxiety is expected to change by treatment type if the cancer were more likely to be eliminated. We address this issue as follows. If patients are detected with prostate cancer, their baseline QOL is equated to this anxiety QOL in the absence of any other side effects. If they are treated successfully with surgery, we assume that the cancer could be removed with certainty, and the patient's QOL will become 1.0 (full health) in the absence of any other side effects. In the case of radiation therapy, although the cancer may be fully cured, there is no way to ascertain this with a certainty, and therefore the patient's QOL is given a weight = $(1 + \text{Anxiety QOL})/2$ in the absence of any other side effects. We estimated all parameters of interests in the model via extensive literature review, meta-analysis, secondary data analysis, and mathematical modeling.⁵ Except for the QOL weights for the different health states described above, we hold all other parameters at their estimated mean values.

We obtain individual-level QOL weights for different health states through an ongoing pilot project at the University of Chicago led by William Dale. Individual utilities are elicited from prebiopsy, pretreatment

subjects using an established computer-assisted utility elicitation program, Program to Survey Preferences by Evaluating Quality of Life Tradeoffs (ProSPEQT). Time-tradeoff method is used to elicit utilities for the health states of anxiety, metastasis, impotence, urinary incontinence, and bowel dysfunction. QOL weights on urethral stricture were not collected, and so we rely on published information for this health state. Complete data were obtained from a sample of 47 subjects with mean age of 65 years (SD = 7.7), 53% whites, and 71% married. We combine these data with prior information from published results on QOL weights following a Bayesian method to obtain the joint posterior distribution for the QOL weights. Details of this estimation can be found in the appendix.

Results

Table A1 of the appendix reports the description of individual-level QOL data from our pilot study, whereas Table A2 reports the prior information from the published data on various QOL weights. Finally, Figure A1 shows the posterior distributions obtained for each QOL weight. A sample of 1000 replicates is drawn from the joint posterior distribution of QOL weights and is propagated through the model to get the distributions of costs and benefits for 65-year-old men with moderately differentiated prostate cancer under each treatment. Note that costs are not modeled as a function of QOL weights, and hence they do not vary with different values of QOL weights within any treatment group.[†]

Table 1 presents the results based on mean costs and benefits. Radiation appears to be the cost-effective treatment on average at the population level and also the most beneficial. Figure 3a shows the distribution of mean net health benefits (in terms of QALYs, where $E(\text{NHB}) = E_0(\text{Benefits}) - \text{Cost}/\lambda$). It shows that under the paternalistic model, when a physician tends to make a decision based on maximum expected net health benefits, radiation would have been the optimal choice across most threshold values. Only at threshold

[†]It should be noted here that we use these simulated distributions of QOL weights for the purpose of illustration only. Much more individual-level data are needed to properly characterize the true population distribution of QOL weights. For example, although the sample from our pilot study has a mean age of 65 years, it may not be representative of the 65-year-old cohort facing treatment choices because QOL weights may vary over the age of the patient. Therefore, the following results should be interpreted in terms of the methodological contributions that EVIC makes and not as substantive results.

Table 1 Cost-Effectiveness and EVIC Results

Cost-Effectiveness Results Based on Mean Costs and Effectiveness				
Treatment	Costs ^a	QALYs ^a (SD)	ICER (\$/QALY)	
Watchful waiting	4745	5.42 (0.22)	—	
Surgery	26,161	5.57 (0.15)	142,773 (not CE ^b)	
Radiation	26,703	5.86 (0.11)	49,904 ^c	

Expected Value of Symmetry of Information				
Threshold →	With Cost Internalization		Without Cost Internalization	
	50,000/QALY	100,000/QALY	50,000/QALY	100,000/QALY
EVIC(pop) ^d	70.5	9.0	0.9	1.2
EVIC(pop) ^d : specific parameters				
Anxiety	62.1	2.8	0.2	0.3
Impotence	23.8	0.1	0.4	0.5
Bowel dysfunction	16.1	-1.0	-0.2	-0.2
Urethral stricture	13.4	-1.4	-0.3	-0.3
Incontinence	7.3	-0.5	-0.1	0.0
Metastasis	4.5	0.1	0.0	0.0

EVIC, expected value of individualized care; QALY, quality-adjusted life year; ICER, incremental cost-effectiveness rate.
a. Costs are in 2003 dollars. Both costs and QALYs are discounted at a 3% interest rate.
b. Not cost-effective based on the \$100,000/QALY threshold.
c. Compared to watchful waiting.
d. In millions of dollars; incidence rate: 550/100,000; US pop 65: 4.33 million.

values less than \$50K/QALY does watchful waiting become the optimal choice. Figure 3b reports the acceptability curves for different treatments over a range of threshold values. It shows that there is strong evidence of popularity of watchful waiting below the \$25K/QALY threshold and for radiation therapy above the \$75K/QALY threshold. At $\lambda = \$50K/QALY$, the choice of the physicians to apply radiation to all patients would have been suboptimal for about 50% of the patient population, in whom watchful waiting is the optimal treatment of choice. This suggests the importance of the need for individualized decision making based on preferences. Note that, conditional on the distribution of QOL weights used here, surgery does not appear to be cost-effective for most replicates across any threshold value.

Table 1 reports the population EVIC under different scenarios discussed in the previous section at 2 threshold values of \$50,000 and \$100,000. The annual EVIC of the population is calculated using an incidence rate of moderately differentiated cancer of 550 per 100,000 in the 65-year-old male population (SEER database, 1995) and a US population of 4.33 million men aged 65 years (US Census, 2000). The results (Table 1 and Figure 3d) indicate that the potential value of individualized care for 65-year-old prostate cancer patients is

maximized at the \$50K/QALY threshold and is about \$70 million. Because most of this population of patients is covered by Medicare, EVIC under no cost internalization may be the more appropriate measure to value research. In this case, no cost internalization seems to affect EVIC considerably. Results in Table 1 and Figure 3d suggest that in the Medicare population, programs directed toward eliciting utilities from patients and encouraging physicians to use them to make individualized decisions may not be valuable if physicians do not internalize costs at the individual level (Figure 3c). Therefore, from a societal perspective, the incentive to facilitate individualized care based on preferences is low in this scenario.

Furthermore, we find that anxiety and impotence QOL weights are the most relevant preference measures to elicit from the patient under both scenarios, with and without cost internalization (Table 1). When costs are internalized, information on individual anxiety appears to be more important than impotence. However, when costs are not internalized, impotence QOL seems to gain precedence over anxiety. This is because, when costs are internalized, the primary choice between treatments in prostate cancer lies between watchful waiting and more aggressive treatments such as radiation or surgery. In this

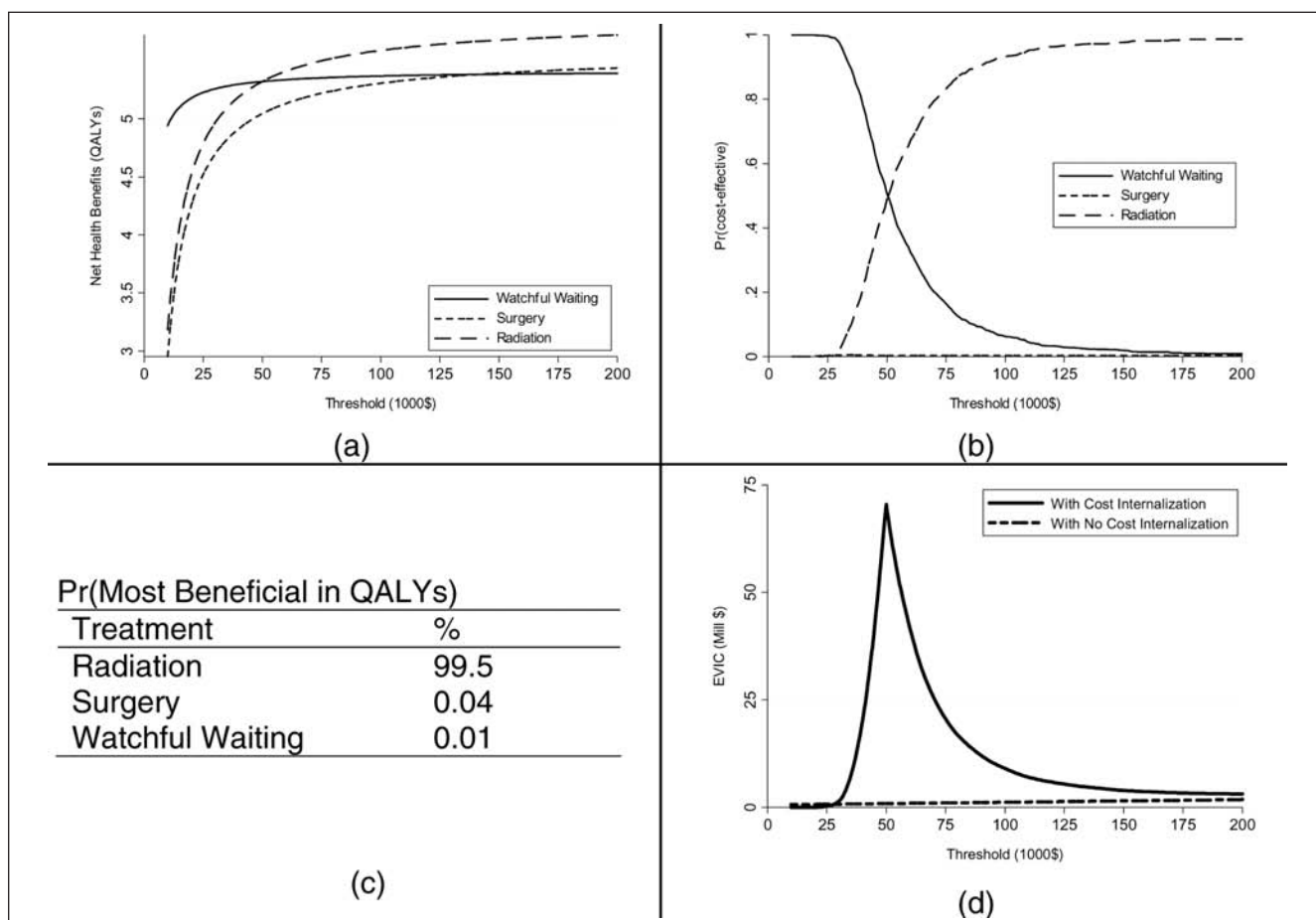


Figure 3 (a) Distribution of mean net health benefits across treatments over different threshold values. (b) Acceptability curves—proportion of replicates who find a specific treatment to produce the maximum net health benefits. (c) Percentage of replicates who find a specific treatment to produce the maximum health benefits in terms of quality-adjusted life years (QALYs). (d) Expected value of individualized care (EVIC) with cost internalization and without cost internalization across a range of threshold values (λ).

case, preference about anxiety is critical to determine the cost-effective treatment. On the other hand, when costs are not internalized, the primary choice lies between surgery and radiation, and then preferences on impotence, which is a side effect of these treatments, are critical in making the choice.

The value of preference elicitation on incontinence, bowel dysfunction, and urethral stricture appears to be negative (implying inefficiency in the economic sense) when there is no cost internalization. This corresponds to the previous discussion on negative EVIC. Here, unlike the distributions of Figure 2c,d, a different set of distributions for costs and benefits produces negative EVIC. Incorporating individual preferences on these treatment side effects results in positive incremental costs while incremental benefits range from large and negative to

small and positive for a substantial portion of the patient population. Also, these patients may lie above the threshold line, indicating that watchful waiting may be the cost-effective option at the individual level. Given the distribution of benefits, watchful waiting may also be the cost-effective option under the paternalistic model (i.e., average incremental benefit is negative), which would indicate that efficient outcomes may be obtained for most patients without using their individual preferences. However, if physicians base their decisions on individual levels of benefits, as under the individualized care model, then they might prescribe treatment to those patients who enjoy positive, albeit small, benefits from treatment. This will result in inefficiency that leads to negative EVIC for these side effects of treatments.

VALUE OF IDENTIFYING COST-EFFECTIVE TREATMENT ON AVERAGE VERSUS IDENTIFYING COST-EFFECTIVE TREATMENT AT THE INDIVIDUAL LEVEL

Over the past decade, a very large body of research has focused on the economic evaluations of medical technology.⁶ However, most of this research is devoted to identifying the single most cost-effective treatment *in the population*. For example, most cost-effectiveness studies in prostate cancer are focused on identifying if surgery or radiation is more cost-effective than watchful waiting based on average estimates of incremental costs and benefits. In contrast, a smaller, though still sizable, body of research has focused on improving decision making at the individual patient level.⁷⁻⁹ In this section, we examine how the value of identifying the best single treatment at the population level compares to the value of identifying the most cost-effective treatment at the individual level.

Figure 4a shows the net cost matrix (NCM) for a given threshold value of λ . The rows of this matrix represent the optimal treatment based on patient preferences. The columns represent the treatment prescribed to the patients. Therefore, the cell (i, j) of the NCM represents the average net cost per patient of prescribing treatment j to patients for whom the optimal treatment is treatment i . For example, at $\lambda = \$50K/QALY$, the average per patient cost of prescribing radiation to patients for whom the optimal treatment is also radiation is 0, and the average per patient cost of prescribing surgery to these same patients is \$10,612. Figure 4b,c represents the probability matrix (PM) for $\lambda = \$50,000/QALY$. The rows and columns of the PM have the same interpretation as that of NCM. The cell (i, j) of the PM represents the proportion of the whole patient population for whom treatment j has been prescribed when treatment i was their optimal treatment. The total expected cost ($E\{\text{Net Cost}\}$) under any model (paternalistic or individualized care) is computed as

$$E\{\text{Net Cost}\} = \sum_{j=1}^k \sum_{i=1}^k PM_{ij} \cdot NCM_{ij}, \tag{8}$$

where k represents the total number of treatment choices.

Note that conducting traditional cost-effectiveness analyses, primarily under the paternalistic model, aims to answer the following question: what is the additional value of prescribing the treatment that is cost-effective, on average, over doing nothing (or

prescribing watchful waiting) to all patients? Based on the results of our decision model (Figure 3b), we find that at $\lambda = \$50K/QALY$, watchful waiting is optimal for 50.7%, radiation is optimal for 48.9%, and surgery is optimal for 0.4% of the patients. Under the paternalistic model, if every patient were getting watchful waiting, then PM cells (W, W) , (R, W) , and (S, W) would take on the values of 50.7%, 48.9%, and 0.4%, respectively (Figure 4b). Therefore, $E\{\text{Net Cost}\}$ in this scenario is $0.489 \cdot 5912 + 0.004 \cdot 23,981 = \2987 per patient. Based on identifying radiation to be the cost-effective therapy on average, if every patient gets radiation under the paternalistic model, then the PM cells (W, R) , (R, R) , and (S, R) would take on the values of 50.7%, 48.9%, and 0.4%, respectively (Figure 4b). Therefore, $E\{\text{Net Cost}\}$ in this scenario is $0.507 \cdot 5811 + 0.004 \cdot 3073 = \2958 per patient. Thus, the value of identifying the cost-effective treatment on average amounts to about $(\$2987 - \$2958) = \$29$ per patient, which at the population level amounts to about \$0.7 million.

We now compare this with the value of identifying the cost-effective treatment at the individual level. Under the individualized care model, because optimal treatment is achieved for each individual patient, cell $(W, W) = 50.7\%$, cell $(R, R) = 48.9\%$, and cell $(S, S) = 0.4\%$, respectively (Figure 4c). Therefore, under the individualized care model, the $E\{\text{Net Cost}\}$ is always 0 as it achieves individualized care and efficient outcome for each patient. Therefore, the additional value of achieving individualized care amounts to \$2958 per patient that corresponds to a population estimate of \$70.5 million. This is about 100 times the value of identifying cost-effective treatment on average, an exercise that the research literature on cost-effectiveness analysis has primarily focused on over the past decade. This suggests a very important potential implication—that even if radiation appears to be cost-effective on average, there may be potentially large benefits of not basing coverage decisions on this information if coverage will encourage use by people who might not benefit greatly from radiation. This is potentially a very important concern with the application of cost-effectiveness methods, and we discuss this point in detail in our discussion section.

MEASURING BASELINE LEVELS OF COMMUNICATION AND WEIGHTING EVIC

The potential EVIC calculated above represents the potential value of individualized care when the baseline level of communication between the physicians and the patients is represented by the paternalistic

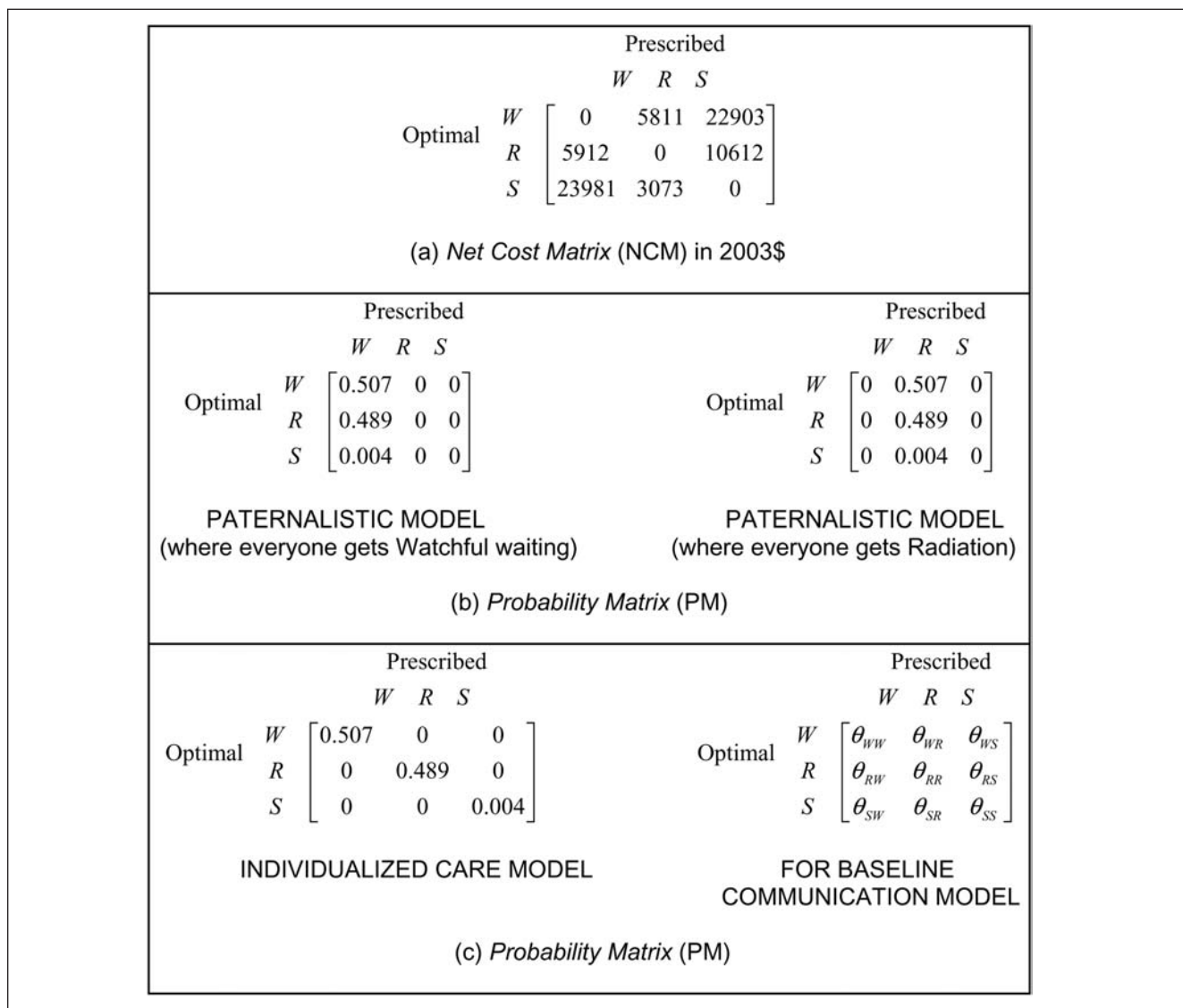


Figure 4 Illustration of the framework for calculating baseline levels of communication-weighted expected value of individualized care (EVIC) using the example of prostate cancer treatments. *W*, watchful waiting; *R*, radiation; *S*, surgery; θ , elements in the probability matrix.

model. Generally, baseline levels of communication between a physician and a patient depend on a variety of factors such as patient education, awareness and demographics,^{10,11} duration of the physician-patient relationship,¹² the setting in which care is given,¹³ and the use of decision aids.¹⁴ Consequently, physicians may be able to successfully assess patient preferences without any explicit mechanisms in place. This will tend to weight the potential EVIC toward 0. On the other hand, physicians may try to assess patient preferences but do a poor job. For example, Wennberg¹⁵

found that, in the context of selecting prostate cancer treatments, doctors cannot predict patient preferences unless they explicitly ask the patients for their preferences. This in turn will tend to weight the potential EVIC to be larger. Therefore, because the assumption of a paternalistic model for the baseline levels of communication may be violated in practice, measuring these baseline levels of communication are important to obtain the weighted EVIC. The weighted EVIC would then represent the maximal value of individualized care, conditional on current baseline levels of

communication, which may be achieved by altering any or all of the characteristics that improve baseline levels of communication.

A baseline probability matrix (Figure 4c) may be obtained by measuring the baseline levels of communication between the physician and the patient. One can then calculate the weighted EVIC

as $E\{\text{Costs}\} = \sum_{j=1}^k \sum_{i=1}^k \theta_{ij} \cdot \text{NCM}_{ij}$. In general, we would

expect the weighted EVIC to be greater than the potential EVIC, if the off-diagonal elements of the PM, which also corresponds to high cost estimates in NCM, are nonzeros and the diagonal elements are close to zeros. The findings of Wennberg¹⁵ suggest that, in the context of prostate cancer, weighted EVIC may be even greater than the potential EVIC reported here.

A weighted EVIC estimate without cost internalization may be obtained analogously using the PM corresponding to treatment prescriptions that are based only on benefits. Note that the net cost matrix (NCM) remains the same matrix as with the cost internalization scenario.

DISCUSSION

Physicians and other health care providers often aim to provide individualized care to their patients to enhance the welfare of their patients. Patients’ preferences play a critical role in this individualization. A wide range of efforts in shared decision making have been developed to facilitate transmission of information between patients and physicians for this reason. However, there is an important need to quantify the potential social value of such endeavors and the types of patient preferences that are most valuable to elicit. The concept of EVIC that we introduce here represents the potential value that society is willing to pay so that individually efficient decisions can be made.

Our results have several implications for societal welfare generated by the application of technology assessment. Table 2 illustrates the 4 states of the world based on different processes of decision making and denotes the corresponding societal welfare for these processes as A, B, C, and D. We have established in this article that individualized treatment choices with cost internalization produce the maximum welfare (C) that is at least as large as that produced by population-level treatment choice with cost internalization ($C \geq A$). It is also well known that, in the absence of external benefits to treatment, population-level treatment choice with cost internalization produces welfare as large as

Table 2 Welfare Outcomes Corresponding to Type of Decision Making

	Cost Internalized	Cost Not Internalized
Population	A	B
Individualized	C	D

population-level treatment choice without cost internalization ($A \geq B$). We have also shown that welfare from individualized treatment choices without cost internalization can be less than the population-level treatment choice without cost internalization ($D < = > B$). However, there is no general result that relates A, B, to D. This indicates that although there may be substantial value of individualizing care if costs are internalized, it is an empirical issue whether traditional population-level cost-effectiveness analysis with cost internalization is welfare enhancing compared to individualized decisions in the absence of cost internalization.

The empirical approach of EVIC is similar to the proposed calculations of EVPI on uncertain parameters.¹⁶ Both valuations can be used to inform future research in their respective fields. However, the interpretation of EVIC is different from that of EVPI. EVPI is the expected costs of uncertainty in parameters that are unknown to both the physician and the patient. It represents the maximal value of research to acquire additional information on those uncertain parameters, which helps to enrich the information that both the physicians and the patients do not currently possess. In fact, EVPI assumes that the parameter of interest has a fixed value in the population and that an infinite sample will eliminate the uncertainty in estimating that fixed value. Conversely, EVIC is the expected costs of ignorance of patient-level preference heterogeneity and represents the potential (though not necessarily the maximal—see footnote *) value of research that helps to elicit individualized information on heterogeneous parameters that can be used to make individualized decisions. Also, the heterogeneity parameters of interest are random; hence, rather than larger samples, individualized elicitation will reveal the true values of these parameters, thereby enabling individualized decision making.

In this article, we focus on a simple framework to calculate EVIC, which results in several limitations. In this base case, we assume that the baseline levels of communication follow a paternalistic model. In practical settings, this assumption is likely to be violated; therefore, one needs to calculate a weighted EVIC to properly inform resource allocation decisions by

measuring and weighting the potential EVIC, given the actual treatment choices that are made with existing baseline levels of communication between patients and physicians.

Second, in deriving our analysis, we have neglected the idea that elicitation of preferences might be costly. Indeed, in practice, the costs of eliciting preferences may be quite high, thereby negating the value of individualized care based on these preferences. Hence, individualization based on these preferences, though potentially valuable, may not always be worthwhile. Such an assessment would require comparing the EVIC to the cost of preference elicitation, which could vary across different clinical scenarios. However, even in the case that the cost of preference elicitation exceeds the value of individualization, EVIC still can provide a guide for resource allocation by identifying the cases in which preference elicitation has the most potential to produce value if the costs of preference elicitation can somehow be reduced, perhaps through computerized decision aids or other low-cost approaches to attempt to better individualize care.

Another limitation relates to our data on QOL weights. We have simulated the distribution of QOL weights for different health states in prostate cancer based on a small pilot data set, published means, and noninformative priors. However, refining the posterior distributions of these QOL weights using more detailed empirical data elicited from individual patients should be of high priority as that would more appropriately represent the true heterogeneity in patient preferences. First, it is important to account for correlation between QOL weights for an individual. For example, people who have a very low threshold for bearing pain (i.e., have low metastatic QOL weight) may also be the ones with high anxiety for metastasis (i.e., have low anxiety QOL weight). Therefore, eliciting information on one health state may also provide information on preferences about a second health state, thereby reducing the value of further elicitation of patient preferences on additional health states. Second, care should be taken in disentangling the first-order uncertainty (representing variability in preferences, an attribute that we are interested in for this application) from the second-order uncertainty (generated via measurement error). Often, these 2 types of uncertainties are separated using longitudinal data. However, for QOL weights, repeated measures must be taken within short periods of time to rule out the effects of adaptation.

We have also assumed a net health benefit approach that is grounded in expected utility theory. However, while making individual-level decisions, expected utility theory is often violated. However, the general

framework presented here can be easily modified to use other indirect utility measures for individual decision making, such as those based on prospect theory.¹⁷ Furthermore, in this article, we allow objective units of benefits to vary across individuals but value these benefits using the same threshold value ($1/\lambda$) for each individual in the society. Thus, our measure of benefits is independent of the individual constraint on the ability to pay. Alternatively, one can allow even these thresholds to vary across individuals (like in a cost-benefit analysis), effectively producing a set of thresholds ($1/\lambda_i$) for each individual. Such weights could reflect differential social valuation of health outcomes across persons or differences in endowments in a market context. Our article does not attempt to compare the normative question of whether one should assign such differential valuations of benefits to different patients. Rather, it provides an analysis of how to make better informed resource allocation decisions for any given set of threshold values.

Next, we have assumed that only patient preferences play a role in the optimal choice of treatments. However, physician preferences may also play a critical role in this decision-making process. For example, in certain complicated health states, patients may be less aware of the intricacies of that health state, and therefore their a priori QOL weight would be a biased estimate of how they would feel if they truly experienced that health state. In this situation, physicians may be better able to predict the QOL weight for that health state. One can easily extend the model presented here to incorporate the interactions between physician and patient preferences, where individualization is accomplished by allowing the physician's preferences to be refined in part by individual patients' preferences as prior information.

Finally, we note that the method of EVIC presented in this article has much broader applicability than measuring the value of individualization of care based on patient preferences. First, as noted above, when EVIC is large, there is extra reason for caution in limiting coverage of a treatment because there may be individuals who would benefit greatly from the treatment if they were to receive it. Whether these additional benefits translate into enhanced societal welfare would depend on who actually receives the treatment and is an empirical question that relates to important empirical issues such as patterns of self-selection.¹⁸ This particular use of EVIC suggests a broader set of areas in which EVIC could be useful in identifying areas where substantial gains can be achieved by accounting for variability in attributes—be those attributes of patients, a system, or an environment—and therefore serve as an effective

guide to resource allocation decisions in that area. For example, one can potentially use these methods to calculate the value of transmitting information on variability in drug efficacy and side effects to patients, thereby quantifying the value of direct-to-consumer advertising. Yet another example would be calculating the value of providing clinical risk information to patients based on demographic or genetic heterogeneity so that the optimal amount of resources can be directed toward communicating the most relevant risk information to the patients.

APPENDIX
Bayesian Framework for Distributions of QOL
Weights in Prostate Cancer

We used Bayesian methods to obtain the joint posterior distribution ($g(\vec{\theta}) = g(\theta_1, \theta_2, \dots, \theta_6)$) of QOL weights for different health states (anxiety, metastasis, impotence, incontinence, bowel dysfunction, and urethral stricture), where ($g(\vec{\theta})$) is given by

$$g(\vec{\theta}) \propto \prod_{m=1}^M L_m(\vec{x}|\vec{\theta}) \prod_{k=1}^6 f(\theta_k). \tag{A1}$$

Here, L_m is the likelihood of the data given any function of parameters $h_m(\vec{\theta})$ for study m ($m = 1, \dots, M$). The prior distribution of each parameter θ_k ($k = 1, 2, \dots, 6$) is given by $f(\theta_k)$. We model the observed QOL weight for health state k for individual i as a beta distribution.

Table A1 Description of Individual-Level Quality-of-Life Weights from Pilot Data

Health State	<i>n</i>	Mean	SD	Median
Impotence	47	0.804	0.252	0.885
Incontinence	47	0.710	0.308	0.800
Bowel dysfunction	47	0.616	0.340	0.635
Advanced metastatic cancer	47	0.365	0.328	0.270
Anxiety	47	0.800	0.235	0.870

$$y_k^i \sim \text{Beta}(\alpha_k, \beta_k) \tag{A2}$$

We will drop the subscript k notation from here for the sake of clarity. Here, our parameter of interest, θ , is given by $\alpha/(\alpha + \beta)$, which represents the true QOL weight parameter for this health state that is random in the population. The likelihood function is therefore defined as

$$L(x|\alpha, \beta) \propto \prod_{j=1}^n y_j^{\alpha-1} (1 - y_j)^{\beta-1}. \tag{A3}$$

Description of individual-level QOL weight is given in Table A1.

Prior information is obtained for published QOL weights on the interested health states. We use reported mean and variance estimates of QOL weight from the published literature and calculate a weighted mean (m) and variance (v) for each utility measure.

Table A2 reports these results. Assuming that the individual QOL weights that generated these statistics

Table A2 Prior Information from Published Data on Quality-of-Life (QOL) of Prostate Cancer Health States

Health State	Sample Size	QOL Mean (Var)	Weighted Mean (Var ^a)	Reference	$\tilde{\alpha}$	$\tilde{\beta}$
Impotence	31	0.71 (0.048)		20		
	31	0.69 (0.048)		21		
	10	0.74 (0.081)	0.706 (0.051)	22	2.134	0.894
Incontinence	31	0.62 (0.073)		20		
	31	0.57 (0.010)		20		
	10	0.68 (0.100)	0.607 (0.049)	22	2.340	1.516
Bowel dysfunction	10	0.45 (0.010)	0.45 (0.010)	22	10.690	13.060
Urethral stricture	10	0.60 (0.010)	0.60 (0.010)	22	13.800	9.200
Metastasis	31	0.47 (0.063)		20		
	31	0.42 (0.068)	0.445 (0.065)	20	1.256	1.566
Anxiety	—	—		No information	1.000	1.000

a. Weight mean = $m = \sum_{m=1}^M n_m \bar{y}_m / \sum_{m=1}^M n_m$, and weighted variance = $v = (N)^{-1} \sum_{m=1}^M n_m \{v_m + (\bar{y}_m - m)^2\}$, where $N = \sum_{m=1}^M n_m$ and $v_m =$ study-specific variance.

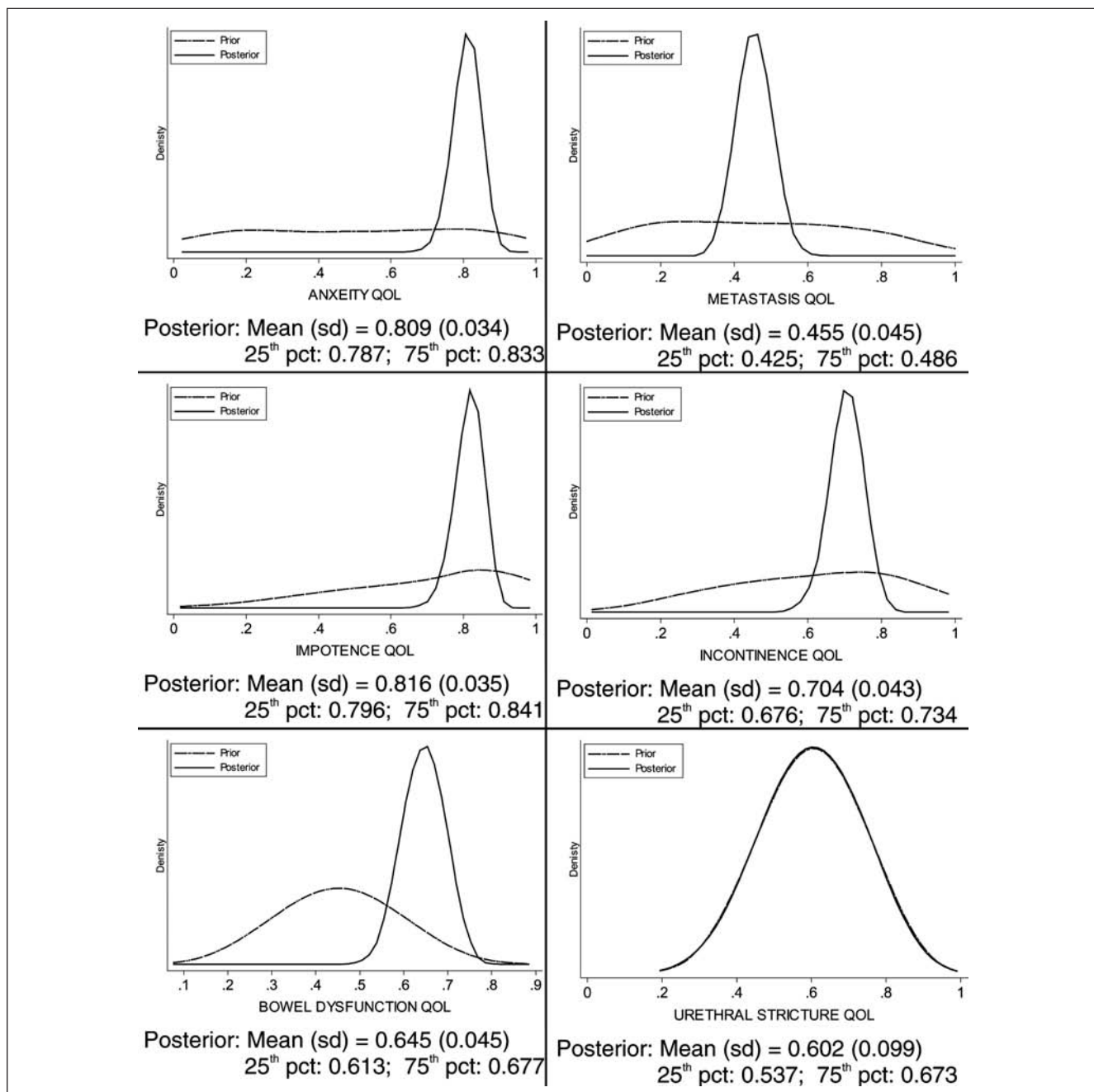


Figure A1 Posterior distributions of quality-of-life (QOL) estimates based on published data.

were also distributed as beta, we can use the mean and variance estimates and convert them into prior information on α and β . For example, the mean of the beta distribution is given by $E(\cdot) = \alpha/(\alpha + \beta)$, and the variance is given by $Var(\cdot) = \alpha\beta/(\alpha + \beta)^2(\alpha + \beta + 1)$. We can get an estimate of α and β by equating

$$\alpha/(\alpha + \beta) = m \Rightarrow \alpha = \beta m/(1-m) \tag{A4}$$

and

$$\alpha\beta/(\alpha + \beta)^2(\alpha + \beta + 1) = v. \tag{A5}$$

Replacing α from (A1) in (A2) and solving for β and α yields

$$\begin{aligned}\tilde{\beta} &= (1-m)[(m(1-m)/v)-1] \text{ and} \\ \tilde{\alpha} &= m[m(1-m)/v]-1.\end{aligned}\tag{A6}$$

Based on (A6), we estimate the prior values of $\tilde{\alpha}$ and $\tilde{\beta}$ for each utility measure, which is shown in Table A2.

The prior information on $\tilde{\alpha}$ and $\tilde{\beta}$ is now entered as the mean of the gamma priors for α and β so that

$$\begin{aligned}\alpha &\sim \text{Gamma}(0.01\tilde{\alpha}^2, 0.01\tilde{\alpha}) \text{ and} \\ \beta &\sim \text{Gamma}(0.01\tilde{\beta}^2, 0.01\tilde{\beta}),\end{aligned}\tag{A7}$$

where $E(\alpha) = \tilde{\alpha}$ and $\text{Var}(\alpha) = 100$, signifying a diffuse distribution. Moments for β are determined analogously.

We use Gibbs sampling,¹⁹ a Markov chain Monte Carlo (MCMC) algorithm implemented in WinBUGS, to obtain the posterior distributions of these parameters. Five chains were run simultaneously, starting from values dispersed over the domain space of the parameters. The first 1000 iterations are used as burn-ins. Autocorrelation is observed for the next 1000 iterations to monitor independence across the sampling process. The MCMC results show reasonably quick convergence (assessed via the Gelman-Rubin statistic) and good mixing of the independent chains (results omitted in this article for space constraints). Minimal autocorrelation was found between subsequent draws for each chain, and consequently no thinning was done. A sample of 1000 observations (200 from each of the 5 chains) was obtained from the stationary distributions of θ^7 , where each observation consists of parameter estimates drawn from the joint posterior distribution of the parameters. Figure A1 illustrates the posterior distributions and descriptive statistics of the QOL parameters.

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