

# The Challenge of Individualizing Treatments for Patients With Breast Cancer

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ONE OF THE MOST COMPLEX CHALLENGES CLINICIANS and their patients with breast cancer face is to determine a treatment plan for disease with relatively favorable prognosis. Advances in treatment have improved life expectancy, but these advances have come at a steep price because treatments impose substantial morbidity and burden on patients and their families. Concerns about the potential harm of treatments have increased as population-based screening has identified an increased number of breast cancer patients with relatively favorable prognosis.<sup>1</sup> These concerns have motivated several initiatives to reduce morbidity and treatment burden.

However, powerful drivers of aggressive treatment thwart these efforts. Payment structures can favor use of more aggressive locoregional and systemic therapies. The sensitivity of evaluative tests has increased uncertainty about the extent of disease, which may trigger more aggressive surgical treatment. Low treatment thresholds based on clinical guidelines may leave little room to omit therapy in patients with more favorable prognosis. Social consequences of the treatment decision also favor aggressive treatment. Clinicians are concerned that they can be faulted if all possible therapies are not used and an adverse outcome occurs. On the other hand, clinicians are frequently praised for a favorable outcome after treatment, although in most cases the more aggressive treatment was unlikely to have made the difference. For example, on average, 87 of 100 patients with invasive breast cancer with favorable prognosis treated with locoregional and endocrine therapy alone will be disease free and alive at 10 years compared with 89 of 100 patients for whom chemotherapy was added.<sup>2</sup> Yet most of those women who underwent chemotherapy will attribute their disease-free survival in part to more aggressive therapy and praise their physicians for curing them.

Individualized care is achieved when the right evaluative tests are used the right way; receipt of therapy is largely driven by evidence-based clinical indications; and patients are informed and their preferences are incorporated into those decisions. Individualizing treatment is challenging be-

cause expected net benefit of different treatment options is often small and difficult to formulate. Furthermore, different locoregional and systemic treatment options are linked in complicated ways. Synthesizing this interplay into a treatment plan is challenging because different specialists direct the various treatments, and recommendations are based on complicated clinical information that is revealed variably over time.

It is difficult for patients to formulate preferences for treatment under challenging circumstances. In this context, patients may deploy complex mental processes to make judgments. Haidt<sup>3</sup> uses the metaphor of a rider and an elephant to characterize a key dichotomy in these dual mental processes. The rider represents the conscious higher brain function that directs deliberative, systematic thinking. The elephant represents the more primitive, often dominant, subconscious lower brain function that controls intuition and visceral reactions. A number of powerful factors limit the rider's capacity to process information in the treatment decision context, including lack of understanding of probabilities and the difficulty of considering the interplay between the likelihood of an event and its (imagined) consequence. These factors constrain the role of deliberative, systematic reasoning in formulating preferences for treatment.

Several heuristics—mental shortcuts—reduce the burden imposed by more deliberative mental processes.<sup>4</sup> Two heuristics in particular influence cancer treatment decisions and influence patient preferences for aggressive therapy. Risk aversion (the preference for a smaller certain gain over a larger but more uncertain one) influences patient decisions. Patients with a strong aversion to risk may choose more aggressive therapy because they focus on the uncertainties about probability and consequences of recurrence. These patients may choose mastectomy over breast-conserving surgery because removal of the breast gives them “greater peace of mind” about recurrence even though both options confer the same net benefit. Anticipated regret is another heuristic that strongly favors aggressive treatment. The prospect of regret over omitting therapy if recurrence

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were to occur may motivate patients to choose chemotherapy because “if I have a recurrence, I will know I did everything I could.” Anticipated regret is a particular problem because most people struggle with predicting their emotional responses to future events. Most important, both heuristics divert attention from the net benefit of treatment because they focus on overall recurrence, which precludes consideration of other risks, such as the adverse effects of aggressive therapy.

Patient involvement in treatment decisions has been promoted on ethical grounds<sup>5</sup> and improves patient satisfaction.<sup>6</sup> However, while autonomy is valued, it may be easily relinquished when decision making is difficult because the more choices confronted, the less patients want to choose.<sup>7</sup> Deferring to standards or rules is a powerful strategy to make the challenges of difficult decision making more manageable. Thus, it is not surprising that physicians remain a dominant influence in directing receipt of therapies for patients with breast cancer and those with other cancers.

Although many factors influence physician recommendations, it is particularly important to understand how clinical guidelines and consensus statements are formulated and used because they will play an increasing role as personalized cancer medicine advances. Guidelines strongly influence recommendations because they simplify the decision process for both patient and physician and provide norms that help diminish clinician concerns about the social consequences of “failure to treat.” Choice and interpretation of evaluative tests account for much of the variation in application of guidelines to individual patients. Patients are vulnerable to variation in which tests are performed and how the results are interpreted. Thus, understanding how evaluative tests are used is critical for better individualizing treatments. Yet much more attention is paid to treatments than to the quality of the clinical information that directs their use.

Although extent of disease remains an important determinant of treatment, tumor biology–based tests have increased in importance because in combination with other clinical information they provide additional information that helps guide therapy in individual patients.<sup>8</sup> Advances in use of tumor markers have the potential to reduce morbidity and burden of the treatment of invasive breast cancer by increasing the accuracy of prediction of net benefit in individuals. Additionally, these tests may be less prone to measurement error than current methods to determine extent of disease (imaging and lymph node histology) because they are performed in more centralized laboratory settings where processing of results is more easily observable and standardized.

There are limitations of patient-directed treatment decisions in the context of an increasingly complex treatment decision-making process. In particular, physicians should

be aware of the difficulties patients face when using quantitative risk information to formulate preferences for treatments. Physicians should pay greater attention to the critical need to address heuristics that focus on disease recurrence rather than the much smaller marginal benefit of treatment. The increasingly frequent practice of performing contralateral prophylactic mastectomy in a patient with breast cancer with virtually no possibility of the procedure further reducing breast cancer–specific mortality is an example of the need to disentangle the clinical and psychological factors driving this decision. Surgical intervention involving removal of an unaffected breast in this context speaks less to long-term emotional well-being than to powerful heuristics that drive decisions about the treatment.

However, the most potent opportunities to better individualize treatments are largely in the hands of physicians. A high priority is to reduce the unwanted variation in receipt of testing and interpretation of results. The increasing importance of tumor biology over extent of disease in directing systemic therapy holds the promise of improving the accuracy of evaluative testing while at the same time reducing unwanted variability in measurement of disease. But the rapid adoption of newer tests such as magnetic resonance imaging to evaluate locoregional treatment options, in the face of uncertain benefit,<sup>9</sup> indicates that clinicians need to address test measurement and clinical utility.

Strategies to improve the deliberation process include building multidisciplinary clinician models of treatment decision making that can reassure patients about the process of recommendations; encouraging more time to make treatment decisions; and incorporating patient decision tools that can increase the salience of the clinical information and help clarify patient values and preferences.

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