New Study Suggests Causal Relationship Between Drop in Breast Cancer Rate and Reduction of Prescriptions for Hormone Replacement Therapy

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The issues relating to evidence-based medicine continue to make the news. On Friday, Dec. 15, 2006, news surfaced of a study conducted by investigators affiliated with M.D. Anderson Cancer Hospital on the U.S. breast cancer rate.1 According to the article, the U.S. breast cancer rate dropped by seven percent in 2003.2 Such a figure is significant enough regardless of the reasons offered for the decline, but the investigators offered a “striking” suggestion for the primary cause of the steep decrease: “women’s abandonment of menopause hormones after a large study was stopped the year before because the pills were increasing health risks.”3

That large study, conducted by the Women’s Health Initiative (“WHI”), was halted on the recommendation of the data safety and monitoring board because women receiving the active drug had an increased risk of invasive breast cancer . . . and an overall measure suggested that the treatment was doing more harm than good.”4 These findings surprised investigators given that as many as thirty eight percent of postmenopausal women were using hormone replacement therapy (“HRT”), with one HRT medications, Premarin, being the second most frequently prescribed medication in the U.S. in 2000.5

Providers had issued prescriptions for HRT for millions of women in the belief that it might help reduce the risk of certain kinds of cancer. Yet this belief had simply not been confirmed by the best kind of evidence. And now we hear the news that the most plausible single factor explaining the highly statistically significant drop of seven percent in the 2003 U.S. breast cancer rate is the fact that providers ceased writing the prescriptions and women stopped taking them.6

There are several important points worth thinking about here. First, it is all too easy in hindsight to attack the prescribers. The observational evidence was quite consistent (though again, no randomized controlled trials on outcomes and efficacy had been performed before prescribing practices changed),7 and was based on an entirely

1 Todd Ackerman, Breast Cancer Rate Dropped with Halt in Hormone Use, HOUS. CHRON., Dec. 15, 2006, at A10.
2 Id.
3 Id.
5 Fletcher and Colditz, supra note 4, at 366.
6 Ackerman, supra note 1, at A10.
7 I should hasten to add that I am not granting randomized controlled trials (“RCTs”) hegemony in an evidence hierarchy. There are all sorts of different questions relevant to clinical practice that RCTs would
reasonable pathophysiological model: premenopausal women generally had much less coronary disease than postmenopausal women. Given that model, it would have been quite reasonable for a clinician to prescribe HRT prior to the WHI study of 2002. Thus it is inadvisable or at least somewhat unfair to use the results of the latest study to retrospectively castigate prescribers for issuing so many prescriptions for HRT. Second, the study is just that – one study, and given how complex and multifactorial cancer causation is (and not to mention how poorly understood it is), attributing a seven percent drop in the U.S. breast cancer rate even primarily to the reduction of HRT prescriptions is likely to invite controversy. In short, medical causation is a notoriously tricky concept.

However, there remain several important bioethical and health policy questions raised by the study. First, breast cancer treatment in the U.S. has been plagued with an alarming recurrence of such “inductive mistakes” throughout much of the twentieth century (and into the twenty-first). Jay Katz details some of these early debates, arising with the radical surgical approach pioneered and favored by William Halsted and his followers. Eventually, when conservative surgery combined with radiation proved therapeutic in certain circumstances, truly acrimonious debates flared up between the proponents of radical surgery and the proponents of conservative surgery plus radiation.

The problem, as Katz defines it, is not so much that the best evidence regarding breast cancer treatment was uncertain. Rather, the problem was that both sides to the debate refused to acknowledge the uncertainty, and “rabid[ly]” stuck to their conviction as to the optimality of their preferred treatment, whatever that preference was. Such convictions led countless numbers of women to elect a procedure (radical surgery) on the recommendations of providers who likely refused to even acknowledge the possibility that other treatments might prove just as beneficial without the risks and suffering that would seem to attend radical surgery.

A similarly sad story underlies the controversy over the use of autologous bone marrow transplants combined with high-dose chemotherapy, in which women with late-stage breast cancer sued their insurers and HMOs for refusing to cover the use of the procedure. Some courts ruled in favor of the plaintiff in these cases, and yet a major study in 1999 showed that the procedure was not efficacious as to the cancers for which

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8 I am indebted to Dr. Howard Brody for this point.
10 Id. at 178.
11 This, of course, is not to deny that radical surgery has saved and will continue to save lives in treating breast cancer. Nor is it to suggest that radical surgery is not best treatment in certain circumstances. Nevertheless, the considerable scientific evidence amassed on the subject does not indicate that radical surgery is definitively more beneficial than other forms of treatment for certain kinds of breast cancer. See id. The point here revolves around clinical uncertainty, which was generally not acknowledged in breast cancer treatment, at least according to Katz. Id.
13 Id.
the regimen was being used.\textsuperscript{14} This means that it is possible that some women suffered and perhaps even had their death hastened via the procedure, which has a high mortality rate,\textsuperscript{15} for few benefits, if any (at least in terms of outcomes). To make matters worse, the pressure to confirm efficacy for a regimen that was already being prescribed and that was making headlines likely had some effect on a South African investigator's decision to falsify data in favor of efficacy in the 1999 study.\textsuperscript{16}

Thus, while it is entirely legitimate to argue that prescribers ought not be retrospectively castigated for prescribing HRT prior to the WHI study, there nevertheless seems to be a troubling recurrence of a clinical willingness to prescribe and perform interventions for breast cancer treatment in the absence of solid proof of efficacy that likely end up doing more harm than good. Further study of exactly why and how this happened is imperative, especially because the clinical uncertainty surrounding breast cancer is hardly a thing of the past. Gina Kolata reported in May of 2006 on the severe – and perhaps even increasing – uncertainty that attends the use of chemotherapy in breast cancer treatment.\textsuperscript{17} Her article reveals much frustration on the part of both physicians and patients, quoting the director of a breast cancer advocacy group as concluding that “You're going to get a lot of information. Trust your gut. Nobody has the answers.”\textsuperscript{18}

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\item Id.
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