



CASE STUDIES IN SOCIAL MEDICINE

## Contingent Knowledge and Looping Effects — A 66-Year-Old Man with PSA-Detected Prostate Cancer and Regrets

Robert Aronowitz, M.D., and Jeremy A. Greene, M.D., Ph.D.



In 2006, Mr. B., a 66-year-old economics professor, learned from his general internist that his prostate-specific antigen (PSA) level was 4.5 ng per milliliter, up from 3.0 ng per milliliter the previous year. His urologist, who found only mild prostatic enlargement on examination, confirmed an elevated PSA level and recommended a biopsy. Mr. B. consented. Two of 12 biopsy specimens showed cancer, with a Gleason score of 7. After presenting the options of radical prostatectomy, radiation, and active surveillance, the urologist indicated a strong preference for surgery, while acknowledging that it could lead to impotence and incontinence. Before consenting, Mr. B. met with a medical oncologist to discuss the option of active surveillance.

Knowing that Mr. B. had a back-

ground in quantitative social science, the oncologist sent two relevant research articles to Mr. B. by email before his appointment. The studies, which had begun before PSA screening became routine, showed a clear survival benefit for surgery in men with localized cancer. These studies, plus the oncologist's review of expert guidelines, led him to recommend surgery or radiation.

Influenced by this evidence, by a colleague's recent painful death from prostate cancer, and by his wife's strong opinion that he should "do everything" to avoid death from prostate cancer, Mr. B. underwent robot-assisted radical prostatectomy. Afterward, he had urinary incontinence, which slowly resolved, and impotence that has continued despite several rehabilitation programs and pharmaceu-



tical interventions. His PSA has remained at the zero-to-negligible level.

Mr. B. initially saw his impotence as the unfortunate effect of a rational decision that may have saved his life. But in 2009, early results in two large, randomized, controlled trials of PSA screening showed equivocal or no benefit. The rationality of Mr. B.'s decision to undergo surgery now seemed to be undermined by earlier decisions that he'd made casually: consenting to the initial PSA test and to the biopsy. His doubts increased when, a few years later, a trial that began after PSA screening became routine revealed no overall survival benefit of surgery over active surveillance for localized disease. Mr. B. struggled to understand how the data he'd reviewed just a few years earlier had made him confident about surgical intervention.

### Social Analysis Concepts: Contingent Knowledge and Looping Effects

A social medicine perspective attends to all the ways in which social conditions shape health, disease, and recovery — including the production, circulation, and consumption of medical knowledge. As social responses to disease, screening and diagnostic technologies can change the behavior of people by reclassifying them (in this case, as “cancer patients”), transforming the meaning of the disease category and knowledge about the safety and efficacy of preventive and therapeutic interventions.

The resulting instability of medical knowledge will not be solved by medical progress. Many therapeutic decisions are made under conditions of uncertainty and with the knowledge that future studies could upend practice

patterns. Clinicians know that medical knowledge is constantly changing and that facts considered unassailable can be reversed by new trends.<sup>1</sup> We often assume that this process is due to progress, that researchers are constantly honing our knowledge, getting ever closer to universal truths about health and disease. Mr. B.'s case, however, highlights a different way in which medical knowledge can change: the largely social processes by which we identify diseases can transform diseases themselves.

The label “prostate cancer” was applied to a different group of people before widespread PSA screening than it was afterward. As new clinical trials and guidelines shift (and typically expand) the population receiving a diag-

nosis or treatment, they also change the epidemiologic and clinical profiles of the disease in question. As philosopher of science Ian Hacking has noted, categories such as prostate cancer, breast cancer, hypertension, and diabetes are not stable objects but “moving targets because our investigations interact with them, and change them.”<sup>2</sup> Hacking uses the term “looping effects” (see box) to describe feedback cycles like those through which the naming of disease reshapes the epidemiology and clinical profile of disease.

Social responses have radically reshaped the diagnosis, therapeutics, and prognosis of prostate cancer. At the simplest level, changes in screening practices in the early PSA era expanded the

**A substantial portion of our knowledge about disease, treatment, and prognosis is contingent, meaning that many perceived medical truths may eventually be determined to be false. “Looping effects” describes the ways in which feedback patterns among diagnosis, therapeutic interventions, and health behaviors influence the natural history and prognosis of diseases. Knowledge produced by our investigations and interventions changes the way we diagnose and treat people, which in turn transforms the epidemiology and clinical profile of disease itself.**

category of “people with prostate cancer” to include many asymptomatic people. This change in the groups deemed to be affected by prostate cancer shifted knowledge about its prognosis and treatment. Until the 1980s, prostate cancer typically presented as a painful, metastatic, and often incurable disease. After a few years of PSA screening, the typical presentation occurred at a localized, curable stage. Case fatality rates plummeted, and survival rates approached 99%. Observers of these transformations casually linked them to the efficacy of PSA screening and subsequent medical and surgical interventions.

### Clinical Implications

Careful thought about feedback loops and the contingency of medical knowledge may lead to insight into the social processes that can transform clinical and epidemiologic patterns, magnify

PSA screening diffused quickly, independent of any rigorous evidence from clinical trials.

Part of this apparent progress was propelled by a self-reflexive loop. Widespread screening can cause lead-time bias (earlier diagnoses without longer overall survival) and overdiagnosis (more people labeled with disease but without clinical benefit). As screening increases the denominator of people with prostate cancer, survival rates necessarily improve and case fatality rates fall. People attribute these trends to the biologic efficacy of screening and radical interventions, even if no such efficacy exists, which leads to more screening and active treatment, better apparent survival rates, and so on. Mr. B. and his doctors were unaware that their own decisions and behaviors and those of millions of others were creating the conditions that made screening and early intervention seem to “work.” In addition, they believed that something named “cancer” should not be left in the body, since cancer progresses and kills if not detected early and extirpated.

Naming a condition “cancer” produces further changes in people’s beliefs and actions, and ultimately in the biologic processes in patients’ bodies, by generating fear that leads to more radiation, chemotherapy, and surgery.<sup>3</sup> Such fear is evident in Mr. B.’s wife’s feeling that “everything” should

be done to fight cancer, which overshadows any cooler assessment of benefits and harms. Fear underlies Mr. B.’s desire to avoid the regret he anticipates feeling if he chooses less aggressive treatment and ends up with a terminal condition. By assuming that “a cancer is a cancer” (despite evidence that prognosis greatly depends on how pathology is detected and diagnosed), many cancer prevention and intervention efforts blind us to the potential harms of framing the problem as “cancer” in the first place.


Mr. B.’s regrets were not simply attributable to newer medical insights calling into question his past decisions. He believed that he might have chosen differently, or at least approached active surveillance less fearfully, had doctors described his biopsy findings, which were unlikely to lead to metastasis and death if untreated, without using the word “cancer.” And he wished he’d been aware that he and his doctors were participating in powerful self-reinforcing social processes, instead of attributing the improvement in prostate cancer prognosis to the direct biologic effects of screening and treatment. This attribution, along with the economic calculus in which vested interests and malpractice fears favored increased screening, allowed Mr. B.’s internist to order his initial PSA test without much discussion with Mr. B.

fears, and lead to overuse of interventions of negligible value. Such insight underscores that medical knowledge, though contingent, is not arbitrary. Understanding the structured, historical patterns that

shape our beliefs and practices can improve decision making and health policies. Fostering a critical, historically informed approach to medical knowledge (one that includes the consensus of special-

ist organizations) can help us identify and thoughtfully respond to the distorting role of fear in medical decision making and the iterative social processes that may result in overestimating the efficacy and safety of aggressive and expensive practices.

1. Physicians can work to counteract the downsides of looping effects that occur when the act of diagnosis leads to behavioral change. A group of leading clinicians and researchers recently proposed renaming cancers and precancers that are unlikely to cause harm if left untreated as “indolent lesions of epithelial origin.”<sup>4</sup> They hoped that such renaming might reduce

 An audio interview with Dr. Aronowitz is available at NEJM.org

the influence of fear on decision making and policies. Though there has been little response to this proposal, such relabeling

seems like a promising strategy. Other shifts in the framing of dilemmas posed by aggressive screening and radical treatment have made a difference. The terms “overdiagnosis” and “overtreatment” — and the reframing of certain interventions in terms of “choosing wisely” — have helped make diagnostic and therapeutic decisions less automatic and active surveillance a more plausible option.

2. Clinicians can strive to reduce the “evidence-free” spread of purportedly risk-reducing interventions. The social as well as the biologic effects of medical technologies should be considered carefully when they are first approved and disseminated. By the time Mr. B. was making his decision, it was too late for him to resist the powerful clinical consensus that PSA

screening and radical treatments for screening-detected cancers were helpful practices. If we understand how upstream factors beyond biologic efficacy and safety have influenced the diffusion of interventions such as PSA screening, perhaps we will exercise special caution in evaluating the unintended consequences of future tests and treatments — and seek better evidence of efficacy and safety before mass implementation.<sup>5</sup> When considering new screening tools that have powerful social as well as biologic effects (such as identifying millions more people as having disease), we should be mindful both of the power of such interventions to alter mass beliefs and behavior and of the vested interests that benefit from widespread interventions even if patients do not.

## Case Follow-up

Mr. B. has coped with his regret by becoming more cautious about other medical interventions. He does not attribute his cancer-free survival to screening and surgery, and he no longer calls himself a “cancer survivor.”

The patient’s initial and identifying characteristics have been changed to protect his privacy.

The editors of the Case Studies in Social Medicine are Scott D. Stonington, M.D., Ph.D., Seth M. Holmes, Ph.D., M.D., Michelle

Morse, M.D., M.P.H., Angela Jenks, Ph.D., Helena Hansen, M.D., Ph.D., Jeremy A. Greene, M.D., Ph.D., Keith A. Wailoo, Ph.D., Debra Malina, Ph.D., Stephen Morrissey, Ph.D., Paul E. Farmer, M.D., Ph.D., and Michael G. Marmot, M.B., B.S., Ph.D.

Disclosure forms provided by the authors are available at NEJM.org.

From the University of Pennsylvania, Philadelphia (R.A.); and Johns Hopkins University, Baltimore (J.A.G.).

1. Prasad V, Cifu A. Medical reversal: why we must raise the bar before adopting new technologies. *Yale J Biol Med* 2011;84:471-8.

2. Hacking I. Making up people. *Lond Rev Books* 2006;28(16-17):23-6.

3. Aronowitz R. Risky medicine: our quest to cure fear and uncertainty. Chicago: University of Chicago Press, 2015.

4. Esserman LJ, Thompson IM, Reid B, et al. Addressing overdiagnosis and overtreatment in cancer: a prescription for change. *Lancet Oncol* 2014;15(6):e234-e242.

5. Rosenberg CE. The therapeutic revolution: medicine, meaning, and social change in nineteenth-century America. *Perspect Biol Med* 1977;20:485-506.

DOI: 10.1056/NEJMp1811521

Copyright © 2019 Massachusetts Medical Society.