
The Mortality Effect: Counting the Dead in the Cancer Trial

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In its attempt to recruit patients with late-stage and metastatic renal cancer for a new trial of an experimental cancer treatment, Oxford Biomedica took the standard form of asking and answering an array of imagined patient questions in its patient pamphlet. The trial was organized as a standard randomized control trial (RCT), in which one group of patients would receive the new treatment and the other group would be given the standard treatments. No one would know which group they were in until the end of the trial, at which time the survivors would be counted, the side effects measured, and a decision made about whether to take the drug to the next stage of testing.

Among the questions appears one that addresses the key issue patients must struggle with when considering signing up themselves, and their caretakers, for a trial that will take a great deal of time and energy at what will likely be the end of their lives. The pamphlet puts the question in this form: “What happens if I get placebo and TroVax® is then shown to work?” Although the five-year survival rate for metastatic renal cancer is less than 5 percent, the answer to the question is given as: “If the study shows TroVax® prolongs survival and you received the placebo, you will be given the opportunity to be treated with TroVax®, *following regulatory approval.*”¹ As with the vast majority of such trials, the drug was

I want to thank audiences at the University of California, San Francisco; the University of Michigan; and Harvard University, as well as Gail Hershatter, Sharon Kaufman, Jake Kosek, Michelle Murphy, Diane Nelson, Elizabeth Roberts, Elaine Scarry, Derek Simons, Sylvia Sokol, Miriam Ticktin, Fred Turner, Kate Zaloom, the editors and reviewers of *Public Culture*, and the many people who have discussed cancer with me from so many angles. This article is dedicated to the Oxidate Working Group.

1. Patient Information Leaflet FINALver.1.0, TroVax Renal Immunotherapy Survival Trial TRIST™ (accessed August 12, 2007). My italics.

found to be ineffective; the trial was canceled after nearly a third of the patients died.² To say, then, that the answer given to this imaginary patient question foregrounded hope would drastically understate the politics of recruitment for trials of experimental treatments for late-stage cancer.

The pamphlet might, after all, have had the imaginary patient ask: “What if I were in the TroVax group and it were shown *not* to work, or to work but with impossibly brutal side effects? Would I be paid for my time, which would be expensive, since there isn’t much left?” But the gut-splitting effect of the question and answer as given lies in its elision of two simple but critical facts. First, a person with metastatic renal cancer has virtually no hope of surviving long enough for this drug to come to market. Nevertheless, the inevitable deaths serve a critical role in the trial. Second, the vast majority of cancer drug experiments do not prolong survival. While diminishing this fact may well underwrite a patient’s search for a miracle cure, the question and answer rely on a serious misrecognition and misrepresentation of the temporal scope of the trial in relation to its mortal subjects.

Together, these effects result in a sort of ghosting of the lives that move through these trials; deaths maintain an everywhere and nowhere quality, even as they hold the statistics and results of the trials in place. I refer to this ghosting as the “mortality effect,” which I will elucidate through an analysis of how these cancer deaths, removed from particulars of individuals, produce paradoxical subject positions for the vast range of players involved in cancer culture. Consider, for example, that the immortal and mystical survival prognoses given to individuals at diagnosis require deaths to predict lives; they rely on an impossible future thinking since, as I have explored elsewhere, an individual does not 70 percent die, he or she lives or dies. Here I examine the infinite time line and life-or-death binary of the mortality effect as structured by the firm logic of the randomized control trial. But my concern with tracing one of the many paradoxes of cancer culture also includes an argument about the science. The logics and paradoxes I trace cannot be dismissed as merely cultural, for they fundamentally affect, justify, and enable the actual chemicals that are pumped into peoples’ bodies.

This recruitment pamphlet offers insight into one of many ways that both patients and oncologists are invited to live in a space organized through both hope and progress as virtually inescapable, ubiquitous tropes. Venues as distinct as marches for a cure, fund-raisers for children’s camps, and clinical interactions between doctor and patient parry the concept of hope. As cancer scholars

2. Action to Cure Kidney Cancer, www.ackc.org/trovax (accessed June 16, 2009).

Mary-Jo DelVecchio Good, Ilana Löwy, Helen Valier, and Carsten Timmermans note, the RCT plays a critical role in such infrastructures, building on a cultural presumption of progress in cancer treatment and providing the basis for highly protocol-driven treatments for cancer.³ The RCT method offers a site in which the structures of hope and future orientation are produced, represented, and deployed through the wider culture of cancer and its treatments and therefore offers a critical site of the cultural production of cancer. My ethnographic, literary, and historical research bears out the further observation that not only participation in trials but the very form and phantasmic role of the trial centrally structure experiences and understandings of cancer not only through the production of statistics about risk and prognoses but also in the ways some people with cancer orient themselves toward possible participation in future trials, in the ways people research their own and others' disease (through drug selection, for example), in advertisements for cancer drugs, and in doctor-patient interactions.

No doubt the ubiquitous requirements for hope serve the interests of obscuring both cancer's profitability and scientific uncertainty. Such obfuscation takes place through insidious slippages with a series of consequences. A lecture given at the annual San Antonio Breast Cancer Symposium (SABCS) in 2007 strikingly captured the temporal fissure I take as central to my analysis. Introducing his research with a roundabout acknowledgment, verging on thanks, of the people who partake in such trials, Mitchell Dowsett declared, "1,050 people would have to relapse before we had data."⁴ Neither Dowsett's translation of lives into data, nor the third-person voice of the "would have to," nor the transference of people's

3. Mary-Jo DelVecchio Good, "The Biotechnical Embrace," *Culture, Medicine and Psychiatry* 25 (2001): 395–410; Ilana Löwy, *Between Bench and Bedside: Science, Healing, and Interleukin-2 in a Cancer Ward* (Cambridge, Mass.: Harvard University Press, 1996); Helen Valier and Carsten Timmermans, "Clinical Trials and the Reorganization of Medical Research in Post-Second World War Britain," *Medical History* 52 (2008): 509. Cancer trials have often "delivered at best marginal benefits" with controversial endpoints and success difficult to assess. "Nevertheless, such controversy did not undermine the progress of the clinical trial as an increasingly essential feature of clinical bio-medical research" (Valier and Timmermans, "Clinical Trials," 501–2). "One of the new technologies that changed the face of clinical research was the clinical trial. The meaning of clinical trials has changed significantly since the 1950s. . . . Arguably this is a consequence of repeated reports on hopes associated with new experimental treatments since the 1960s (especially for childhood cancers) and the rigorous promotion of the randomized controlled trial as the gold standard of modern clinical research" (509).

4. Mitchell Dowsett, "William L. McGuire Memorial Lecture: Biomarking the Estrogen Dependence of Breast Cancer" (lecture presented at the San Antonio Breast Cancer Symposium [SABCS], San Antonio, Tex., December 14, 2007). The SABCS is the main forum in which breast cancer study results and interim research findings are presented each year.

lives into terms of ownership over data fully accounts for the startling effect of this remark. Rather, the temporal shiftiness creates a counterfactual disjuncture: one knows only after the data are in that 1,050 recurrences were suffered. Yet Dowsett's phrasing implies advance knowledge of the 1,050 recurrences. A subject in the trial may have hoped to be in the nonrecurrence group, yet after the data were in, the subject would know which group he or she had been in. These central, structuring temporal paradoxes of cancer culture—its inevitability, its predictability, the possibility and impossibility of early detection, the mystery of relapse—form the counterfactual hopes and histories made so vivid in these different views on the trial.

Here I suspend questions of whether the trial methodology itself works, or whether it would work if there were better oversight, exactitude, or basic science. Rather, I analyze the RCT as an actual, material, *present* structure—as a representational form—in and through which people live and die, and in and through which people eke out an understanding about the disease, medicine, and mortality. In examining the centrality of RCTs as a primary material practice in which cancer patients are constituted as material and conceptual objects and subjects, I aim to better understand how cancer is lived and reproduced in the United States.⁵

Because futurity so centrally informs American understandings of cancer research, fund-raising, survivorship, and treatment, the argument I pose may seem both counterintuitive and in some way abhorrent. As I have witnessed many times in talks and academic reviews, hope as a charitable emotion, a life raft, or a habit is not given up easily. One dispenses with it personally, analytically, and politically at one's peril, regardless of survivor status, not only because of its obvious attraction but because of the identity politics that so often adheres to efforts to speak and write about cancer.

So to be clear, I do not question the intent of oncologists. Oncologists, like other experts, practice their profession for various reasons, both complementary and contradictory and with greater or lesser skill, which I neither question nor affirm. Similarly, I remain agnostic on questions of hope, survival, and treatment. I point no fingers at researchers, at people choosing among a sparse set of treatments, or those raising money for more research, camps, awareness, or rides to the hospital. Many patients, caretakers, and doctors tell their stories sincerely and sympathetically, albeit with a great deal of anger, trust, frustration, resignation,

5. Cancer trials differ from most other disease and drug trials in that they are typically not outsourced, though they may take place at several medical centers.

and grief, and this affect and these emotions remain central to any possibility of understanding the cultural traumas of cancer and the high stakes in this mode of critique.⁶ I am not arguing that the personal and social costs of cancer research are too high (though they are), and I am not attempting to determine how such an assessment should be made. I am not arguing that people are dying from chemotherapy and not from cancer (though many do); indeed, the complication in determining cause through ideologies of natural cancer and scientific treatment protocols holds a critical spot in the story about the ethics and cultural constitution of the dying body. Finally, I am not arguing that the logic directing the trials is nonsensical or inefficacious or that they should be banned. I provide no alternative format for drug testing.

Rather, I explore how the organizing structure of the trial arranges and comprehends its mortal subjects by relying on affective economies such as hope, progress, and futurity. These undergird the format and emanate further into moral and cultural understandings of cancer and into judgments prevalent among the lay and expert communities about how to live with cancer. Such analysis has consequences for how suffering counts, as I examine below in thinking about treatment injury, and for how cancer research has been institutionalized in research and clinical medicine. Furthermore, such affective economies influence what chemicals are used in treatment, for example, high-dose chemotherapy (HDC) and anthracyclines. The use of such chemicals offers an opportunity to rethink not only the ethics of how dying bodies are constructed but basic concerns of science and technology studies such as how to weigh the dangers of chemical intervention against so-called natural cancers. The actual people who make these decisions are missing from these accounts or papered over with epithets of their bravery and courage.⁷

Given that in the United States more than half a million people die of can-

6. Lauren Berlant writes of obesity as a form of “slow death,” by which she means “the physical wearing out of a population and the deterioration of people in that population that is very nearly a defining condition of their experience and historical existence” (“Slow Death,” *Critical Inquiry* 33 [2007]: 756). Cancer, like obesity, may be thought of as a form of slow death in that it can be analyzed and understood as related to forms of violence distributed in arbitrary and not so arbitrary ways and as a by-product of systems that require consumers and exposures.

7. Affective economies and RCT-based medical practice furthermore provide a basis on which to think through the recursive phenomena of what medical historians refer to as the increasing alienation of medical care: the treatment of and by strangers. Good finds that most people in America die under the direction of a physician who has known them for less than thirty-six hours (“The Biotechnical Embrace,” 408). RCTs provide one place to see further how strangers, now as numbers, provide the grist for calculations in ways that have created industries often quite separate from cancer survival and treatment.

cer each year, 12 million survivors are produced, and one in thirty-nine people under the age of forty is diagnosed with cancer, virtually everyone in the country has lived through cancer, in some proximity. Yet very few languages attempt to grapple with this central trauma of American life. As a multibillion-dollar industry, proliferating cancer cultures demand anthropological analysis. Within this morass of big money and big suffering, the hegemonic tropes of hope, charity, the good death, and cure seriously misrepresent, obscure, and play down the deeply political character of the disease.

The TroVax pamphlet cited above does not tell the stories about the difficulty of getting into trials or how it feels to be presented a series of chemotherapy options and survival statistics by a physician in a clinical setting and asked to choose one. One does not learn about the last-ditch efforts of people flying with their oxygen tanks to Texas or Argentina in their last months and weeks, or taking the carefully researched stacks of trial reports or printed trial numbers diligently inscribed on a folded sheet of paper into the doctor's office and hearing the doctor say, "Oh, no one followed that up," or, "That's just not what we do here," or, "There were not enough people in the trial to draw any conclusions," or, "Yes, but those results are controversial, so we don't give that treatment," or, "Yes, but the population was too varied to be of use in your case," or, "Yes, but your insurance will not pay for that treatment." These are stories I have collected, but their confusion and heartbreak pose only the latest in a long history of the rise and fall of various "miracle" cures, from radium pills to letrozole, interferon, Gc-MAF, to hundreds more, and the hundreds of thousands of patients who have taken them, often at great physical and financial cost. The stories demonstrate the excruciating positions of both patients and physicians who represent, manage, and attempt to communicate, on a daily level, information and speculation about diseases and potential treatments under conditions in which little is known, much data are collected, and much is hoped for.

If these stories make evident the vast rifts in the ideals of cancer treatments and trials and the phantasmic role they play for cancer patients to the extent that "I need a trial" sometimes substitutes for "I need a cure," they also attest to the centrality of the trial format to the experience and culture of cancer.⁸

8. Only recently have patient advocacy groups been allowed at oncology conferences, and their admission is strictly regulated; it certainly is not genuinely participatory. At the SABCS meetings every December, for example, patient advocates each evening may listen to a panel of medical experts who translate the events of the day into lay language. The week I attended, the tone was sometimes condescending and sometimes simply explanatory, but the forum was never taken as an open exchange among knowledgeable participants in the cancer complex.

The RCT, as the gold standard of evidentiary medicine, refers to an experimental method in which two similar groups given different treatments are compared to measure the efficacy of the treatment. In human trials, a group of people with something to be treated or measured will enter the trial, which may have certain controls for age, race, or disease characteristics.⁹ Individuals are then randomized into two different groups (the passive voice is appropriate here), one that takes the placebo or standard of care treatment and the other that receives the new treatment.¹⁰ Upon completion of an amount of time, the researchers compare the groups' data using highly specialized and often controversial statistical methods.

Current literature on RCTs tends to fall into four categories. Many scientists claim that the objectification of the patient is an unfortunate but necessary by-product of the method.¹¹ Physicians often note that RCTs have led to improved patient care: survival rates for several types of cancer have skyrocketed thanks not only to new treatments but also to the RCT's ability to establish that new treatments are in fact better. Historians have demonstrated the difficulty in justifying the claim that RCTs have led to better medical outcomes in the context of the broader social history of medicine.¹² Anthropologists have further examined the cultural specificity of the trials and then of outsourcing trials in the search

9. For a history of how groups came to be included in trials through the 1980s and 1990s in problematic ways that correlated along the lines of identity politics, see Steven Epstein, *Inclusion: The Politics of Difference in Medical Research* (Chicago: University of Chicago Press, 2007).

10. On the history of placebo trials, cytotoxic drugs, National Cancer Institute research, and oversight by the Food and Drug Administration (FDA), see David Rothman and Harold Edgar, "Scientific Rigor and Medical Realities: Placebo Trials in Cancer and AIDS Research," in *AIDS: The Making of a Chronic Disease*, ed. Elizabeth Fee and Daniel M. Fox (Berkeley: University of California Press, 1992), 194–207.

11. As Ann Oakley points out, they purposely elide humans, both patients and doctors, by not allowing either to decide which treatment arm the subject will belong to, treatment or placebo ("Who's Afraid of the Randomised Controlled Trial? Some Dilemmas of the Scientific Method and 'Good' Research Practice," in *The Ann Oakley Reader: Gender, Women, and Social Science*, ed. Ann Oakley [Bristol, U.K.: Policy, 2005], 233–44). In this sense, the RCT dispensed with several key questions in human subjects research, such as who should receive new treatments (the doctor's friends) and where pools of human subjects should be drawn from (prisoners, cancer patients).

12. Ted Porter, *Trust in Numbers: The Pursuit of Objectivity* (Princeton, N.J.: Princeton University Press, 1995); Harry M. Marks, *The Progress of Experiment: Science and Therapeutic Reform in the United States, 1900–1990* (Cambridge: Cambridge University Press, 1997); Trudy DeHue, "Testing Treatments, Managing Life: On the History of Randomized Clinical Trials," *History of the Human Sciences* 12 (1999): 115–24; DeHue, "A Dutch Treat: Randomized Controlled Experimentation and the Case of Heroin-Maintenance in the Netherlands," *History of the Human Sciences* 15 (2002): 75–98.

for treatment-naive populations.¹³ Others focus on the ethics of the trials and the treatment of subjects, and a burgeoning literature addresses the on-the-ground efficacy of trials in terms of the slippages between theory and practice, the value of different statistical models, and the politics of pharmaceutical funding.¹⁴ These literatures critically engage the epistemology of the trials and how they have been corrupted by interests other than those of pure science.

By unpacking how late-stage cancer trials set up subject positions I aim for a different kind of analysis. Hope for the individual and progress for science usually justify the intensely dangerous or painful cancer treatments. In the RCT framework, ideally, many treated subjects get better and untreated subjects get worse. Thus a trial will require the ill health and the death of many of its subjects to provide for the investigator evidence of efficacious treatments. Yet while for decades and centuries, cancer patients have undergone risky and often horrific treatments, there has been very little progress in survival rates. This stasis would seem to undermine the forward-thinking logic of the RCT—a point that, while broadly noted, remains suspiciously absent from analyses of cancer culture.

Toxic treatments have simply been the presumed legitimate response to the “toxic cost of cancer.”¹⁵ Yet a growing number of historians trace the rise and fall of various cancer treatments. They examine in different ways how the bodies of cancer patients have been caught up and used in struggles that relate often only marginally to a larger cultural effort to find a cure for cancer. Sometimes well-intentioned local attempts to treat individual cases have had disastrous effects.

13. See, e.g., Vinceanne Adams, “Randomized Controlled Crime: Postcolonial Sciences in Alternative Medicine Research,” *Social Studies of Science* 32 (2002): 659–90; and Adriana Petryna, *When Experiments Travel: Clinical Trials and the Global Search for Human Subjects* (Princeton, N.J.: Princeton University Press, 2009).

14. Joseph Dumit, “Drugs for Life” (unpublished manuscript); Jill A. Fisher, *Medical Research for Hire: The Political Economy of Pharmaceutical Clinical Trials* (New Brunswick, N.J.: Rutgers University Press, 2009). Fisher has found that the fact that 75 percent of trials are run privately by for-profit pharmaceutical companies fundamentally influences medical research. A legal perspective on costs of human experimentation and ways of dividing them by comparing car accidents and medical experiments appears in Guido Calabresi, “Reflections on Medical Experimentation in Humans,” *Daedalus* 98 (1969): 387–405. For the bioethics angle, see, e.g., Andrew Feenberg, “On Being a Human Subject: Interest and Obligation in the Experimental Treatment of Incurable Disease,” *Philosophical Forum* 23 (1992): 213–30. For a more classically bioethical perspective, see George Weisz, ed., *Social Science Perspectives on Medical Ethics* (Dordrecht: Kluwer, 1990).

15. According to James Holland of New York City’s Mount Sinai Hospital: “Can it be more ethical to deny the possible good effects to most, by avoiding all toxicity in order to do no harm to one? The unmitigated disease must be calculated as a toxic cost of cancer. Underdosing, in an attempt to avoid toxicity, is far more deadly” (quoted in Rothman and Edgar, “Scientific Rigor and Medical Realities,” 196).

Barron H. Lerner describes the growing use through the mid-twentieth century of increasingly radical surgeries that cut out huge margins of the body, based on the theory that cancer spreads outward from an initial tumor. Eileen Welsome and Gerard Kutcher write about radiation experimentation that involves massive doses of radiation or the injection of radioactive elements, and Elizabeth Toon traces out how bodies with cancer have been caught in big professional shifts, such as the movement by radiologists to have radiation treatments added to the protocol despite major debates about its efficacy.¹⁶

In his remarkable history of breast cancer treatments, James S. Olson describes the women who had access to the latest, most aggressive treatments of their age as “a sisterhood of guinea pigs.”¹⁷ Such treatments involved the removal of the adrenal and pituitary glands, the cracking open of the sternum to remove the internal mammary chain, cauterization with hot irons, huge doses of radiation and X-rays, and surgeries that included the removal of ribs, collarbones, and shoulders in some cases following the discovery of tumors under a centimeter in diameter. Olson’s phrase to describe these women implies that they were used “like a guinea-pig as the subject of an experiment.”¹⁸ Unlike many treatments that use hired subjects or contract overseas for testing, experimental late-stage cancer treatments are often offered to Americans. Patients frequently request the most aggressive treatments. Indeed, I have heard the period after chemotherapy described many times as the hardest part of treatment, since the person must simply wait to see if the cancer returns. That is the only way to judge whether the treatment worked.

16. Barron H. Lerner, *The Breast Cancer Wars: Hope, Fear, and the Pursuit of a Cure in Twentieth-Century America* (Oxford: Oxford University Press, 2001); Eileen Welsome, *The Plutonium Files* (New York: Dial, 1999); Gerald Kutcher, “Cancer Therapy and Military Cold War Research: Crossing Epistemological and Ethical Boundaries,” *History Workshop Journal* 56 (2003): 105–30; Elizabeth Toon, *Breast Cancer Therapy and Experience in Postwar Britain* (New York: Palgrave Macmillan, 2009). The politics of cancer treatments happens in reverse as well; that is, as opposed to the adoption of treatments that increase survival only marginally, preventative measures can take a long time to be adopted. As Devra Davis shows, the broad adoption of the Pap smear to determine cervical precancerous polyps was delayed for decades because of professional debates about who would administer the tests and, Davis suggests, because of the huge amounts of money surgeons made by removing uteruses (*The Secret History of the War on Cancer* [New York: Basic Books, 2007]). For other explanations of the introduction of the Pap smear, see Kirsten E. Gardner, *Early Detection: Women, Cancer, and Awareness Campaigns in the Twentieth-Century United States* (Chapel Hill: University of North Carolina Press, 2006); and Adele Clarke and Monica Casper, “Making the Pap Smear into the ‘Right Tool’ for the Job: Cervical Cancer Screening in the USA,” *Social Studies of Science* 28 (1998): 255–90.

17. James S. Olson, *Bathsheba’s Breast: Women, Cancer, and History* (Baltimore, Md.: Johns Hopkins University Press, 2005), 84.

18. *Oxford English Dictionary*, 2nd ed. (1989), s.v. “guinea-pig,” def. 1b.

Cancer treatment philosophies of “aggressive” treatment provide one critical area in which to better understand and theorize the structures through which the contests between cancer the disease (nature) and treatments (technology) are made material through human bodies.

To be sure, the RCT and its use to test chemotherapy, pharmaceuticals, surgical techniques, and radiation virtually define oncology as a professional field. The growth of the profession and its rise in stature have been concurrent not with big improvements in survivorship, which have increased about 6 percent since 1975, but with more aggressive treatments, with people staying in treatment longer and undergoing more rounds of chemotherapy, and with an increase in the number and size of trials. As Nicholas Christakis writes in his study on prognosis in medicine, the “booming industry in clinical trials . . . supports increasing interest in the development and use of various prognostic staging systems and clinical markers.”¹⁹ The constant reporting of trial results in the news media suggests that they centrally shape Americans’ understandings of risk and causation, even to the extent that people carry the most excruciating self-blame and talk in the most crushed way about being blamed for their cancer, as if it were a result of having drunk too much milk or let their stress go uncontrolled: as if the cancer were their own fault. As one twenty-seven-year-old three-time cancer survivor said to me, “I hate it when people talk like that, it makes me feel bad, and it’s *too late for me.*”²⁰

The logic of the RCT offers an elegant simplicity, one so beyond reproach in its commonsensical grounding that even as the relevance of results and specific trials is hotly contested, the method itself serves as a tightly shut black box in medical discussions and debates. While some accounts attribute the first use of the RCT to efforts to eradicate scurvy through a comparative study examining lime consumption, the historian Harry M. Marks traces the contemporary hegemony of the method in medical research to agricultural studies, where it was developed by a geneticist and statistician, R. A. Fischer. In searching for a way of measuring the improvements of agricultural treatments, the most reliable data were found by dividing the land into strips and alternating a specific treatment—for example, fertilizer—with no treatment. This method, by producing multiple replications of a comparison, averaged out—thus canceling—random factors such as moisture or sun exposure, which might affect one patch of land more than the other

19. Nicholas Christakis, *Death Foretold* (Chicago: University of Chicago Press, 2001), 11.

20. This essay is based in part on my work with cancer survivors from 2005 to 2009. Unattributed quotations are drawn from this work.

if two large patches of land were simply compared over time. In this manner, the efficacy of the fertilizer could be judged against the other factors:²¹ the likelihood that the fertilizer would work on any individual sunny or windy patch of land could be recast as a population probability that the fertilizer would work on many of the land patches, where sun and wind were factored out of the equation. Researchers celebrate the method precisely for this ability to eliminate any factor other than the one they are testing.

RCTs are used to study many things, from the potential benefits of physical exercise and eating greens to proper dosing of medications. They have stood so firmly in the position of evidentiary standard for cancer chemotherapy trials—both witnessed explosive growth after World War II—that the method itself barely requires comment in the scientific literature. The common sense of the trial holds that a new drug will be tested on a randomly selected group of people who have a particular disease, while another group who have the same disease are given either a placebo or the previous standard of care. It would be unethical, for example, to have a trial that compared a group given a new chemotherapy to a group given none, if chemotherapy were the standard of care. Similarly, it would be unethical to let most types of cancers grow for very long, simply to “see” whether they were fast- or slow-growing cancers. Ideally a series of controls such as age, gender, or stage of disease will narrow the random factors, but often the quest for subjects requires that few controls are put on a group, affecting the clinical value of trial results, which requires the comparison of the population in the trial to the actual patient. Moving from Phase I to Phase III trials requires moving to progressively larger groups of people. At each phase, in theory, variations among people will cancel one another out—so the larger the group, the more accurate the trial.²²

The RCT literature takes remarkably lightly, and without comment, that patches of land translate into the self-evident unit of a person, that the disease can become a category with as much certainty as an agricultural pest or the natural

21. James Paul, Rachael Seibl, and Todd Prescott found in 2004 that the cumulative number of clinical trials yielded 65,886 controlled trials, of which 32,760 were randomized control trials (“The Internet and Clinical Trials: Background, Online Resources, Examples, and Issues,” www.ncbi.nlm.nih.gov/entrez/query.fcgi [accessed August 16, 2004]).

22. Causing and treating cancer are billion-dollar industries; Barbara Ehrenreich suggests that treatment alone costs \$12–16 billion annually in the United States (“Welcome to Cancerland: A Mammogram Leads to a Cult of Pink Kitsch,” *Harper’s*, November 2001, 51). I have heard it said that one leukemia patient puts \$6 million into the economy. Given the breadth of this industry (treatments, support groups, awareness posters, marches, basic research, pharmaceutical research, marketing, etc.), it is virtually impossible to assess the costs.

course of the growth of peas, and that treatment of mobile, complicated individuals can be understood as unproblematically as fertilizer on land. The facility of these translations offers a happy coincidence, much like the fact that the visibly obvious boiling point of water makes the perfect cup of tea or that the moon fits perfectly under the earth's shadow during an eclipse. Such coincidence enables the theoretical logic to stand up against actual practice. For example, often whole categories of terms such as what counts under "relapse-free survival" will vary from study to study or even within studies and among medical centers. This makes studies virtually impossible to compare, as oncologists readily admit. Sometimes people in the treatment group are not treated: the category is "intent to treat," rather than "actually treated." In histories of RCTs for many cancers one will find promising Phase I and Phase II trials for inexpensive drugs that were simply never picked up again or multimillion-dollar Phase III trials testing for incremental survival benefits.

The current common sense of trials, however, hides shifts in structures of knowledge collection such as the growth of statistics and what Ted Porter calls the "trust in numbers" over experience and other forms of knowledge.²³ Other historians have traced the professional battles and debates that came to favor the RCT methods. In short, belief in the RCT reflects a medical philosophy and a culture of health quite different from those of the nineteenth century, when an individual's physical and emotional constitution, more than particular disease characteristics, was thought to influence the course of the disease.²⁴ A nineteenth-century physician may not have understood the logic of the RCT, let alone taken it for granted as the primary—practically exclusive—means to medical evidence. Indeed, because of their commitment to ideas of clinical observation rather than statistics, several oncologists through the 1970s refused to give up the Halsted radical mastectomy despite trial evidence that, for all its brutality, removing muscle, tissue, and sometimes ribs bore no more lowered risk of recurrence than a simple mastectomy did. This fundamental belief in clinical care over statistics demonstrates how trust in these numbers had to be cultivated, as did the techniques of collection. Even so, clinicians sometimes rely on clinical experience and resist treating their patients based on trial results.²⁵

23. Porter, *Trust in Numbers*.

24. See, e.g., Charles Rosenberg, "The Tyranny of Diagnosis: Specific Entities and Individual Experience," *Milbank Quarterly* 80 (2002): 237–60.

25. Science and technology studies scholars have broached the question of responsibility by examining where explanations rest in cases of technological failure or disaster. I find increasingly that in oncology, explanations do not rest anywhere, which results in a shocking erasure of ques-

RCT logic reflects such a structuring principle of our time that some of its key paradoxes barely register: two groups compete, one wins. It's the logic of war: two sides competing for who can kill and injure the other; it's the logic of sport: two sides competing for goals, points, or marks.²⁶

In the RCT patients compete in a contest that exceeds their ability to compete; they will not even know which treatment they are getting. Despite the cultural energy expended on the rhetorics of personal battles against cancer, any question of patients' agency and the incredible exertions required on their part and the part of caretakers to withstand treatment will be elided. The success or failure of the treatment will be attributed solely to the treatment itself.²⁷ Indeed, one sees such critical omissions in other aspects of health care, as when doctor after doctor told one person dying of pancreatic cancer that "there is nothing more we can do for you," as if the caretaking work were, in fact, nothing.

The spectacle of the competition in the RCT lies only with the result, not with the life-or-death dramas it unfolds. In that sense, it stands at the crux of a counterfactual paradox: it relies on the elision of its conditions of possibility (the deaths of its human subjects). It steadies itself in this paradox by legitimating its dead through the future promise of a cure. Recall Dowsett: "1,050 people would have to relapse before we had data." Doctors overseeing RCTs stand in wait for these relapses, relapses that they presume would have happened anyway, regardless of their aggregation. One might draw an analogy to the organ transplant candidate waitlisted for a liver, literally waiting for someone else's fatal car accident or brain aneurysm, one that will spur a whole new round of productive events.²⁸

tions regarding issues such as early detection, misdiagnosis, and environmental causes of cancer, each of which is barely on the fringes of what counts as oncology in journals, at conferences, and in the clinic. Here I examine the possibility that these blind spots result from the hegemony of the method and the way that it structures its questions and assumptions as relentlessly future-oriented, diverting attention from the careful study and analysis of past failures, treatment injuries, and missed diagnoses.

26. These traits are expected of the diagnosed body, which in biomedicine will become at different points a work object, an object of curiosity, and a fleshy mound in need of infusion and alteration. This mound uneasily houses this thing—this data point—of "life," but it also provides the workaday object of medical providers who may see tens, or even hundreds, of such bodies in a day or week.

27. It is fascinating to note that this is in direct opposition to the "survivor" rhetoric, which fetishizes the role of individual agency, and I think that it is no accident that both of these versions of agency take place in the context of a natural and social history of confusion about the causes and mechanisms of cancer.

28. Another version of this self-abnegating nobility has been reported in the Canadian press in reference to a baby who will be a heart donor after her death: "She will leave behind more than just

In this way, the self-evident logic of the RCT manages the possibility—the virtual requirement—of the ill subject’s death, for nearly all of the subjects in trials of treatments for late-stage cancers will die. Even the demonstration of the most efficacious drug in the world will require the deaths of those in the untreated group. Thus the RCT asks its subjects to partake in the higher calling of what Michel Foucault might have called “collective living on.” He writes this paradox of individual sacrifice for the vision of a social form: “Go get slaughtered and we promise you a long and pleasant life.”²⁹ This critical disjuncture, the confusion between one’s own mortality and the longevity of the social, structures the population trade-offs in cancer research and treatment, yet so many cancer scholars who inscribe themselves in the position of survivor-researcher miss it.³⁰

I witnessed exactly this disjuncture at a lunch for cancer activists sponsored by Genentech. The representatives and scientists were attempting to recruit subjects, and they claimed that the success of leukemia drugs and survival rates in the 1960s and 1970s was because of the high rate of patients enrolled in trials—as opposed to only 3 percent of breast cancer patients participating in trials (a tired statistic trotted out in many such events). In fact, chemotherapy remains much more efficacious for liquid than for solid tumors. But Genentech’s representatives cajoled members of the audience not to let their diseases go uncounted, wasted, as missed opportunities that could be donated to the higher cause of Genentech’s shareholders.

The RCT asks cancer patients to undergo hardship for future patients, for a slim hope of a cure, or to do one’s bit for science and humanity. One person described to me how her mother participated in a trial for years, collecting and freezing her waste, explicitly as a noble endeavor done in the interests of future generations. This model relies on the promise of future progress and depends on an alliance

a heart-broken father and mother. Her parents will be the heroes behind her tragic sacrifice” (Don Martin, “Comment: Finding Good from Tragedy,” *National Post*, April 9, 2009).

29. Michel Foucault, “The Political Technology of Individuals,” in *Power*, ed. James D. Faubion, vol. 3 of *The Essential Works of Michel Foucault, 1954–1984* (New York: New Press, 1994), 405. Stuart Murray cites this quotation in a brilliant and suggestive piece, “Thanatopolitics: On the Use of Death for Mobilizing Political Life” (paper presented at the annual meeting of the American Political Science Association, Washington, D.C., September 1, 2005).

30. It is easy enough to reiterate these elisions by skipping the grief and moving straight into an academic argument. Maybe it is unavoidable; maybe the elision is the requirement of the academic narrative form. No one who writes about cancer can really escape the ways that language overwrites the helplessness and pain of mortality. The interpellation of the huge cancer statistics in the justification of research about cancer is horrifying, as if the large stats somehow ennobled researchers, justifying the bigness and importance of their work.

between patients and future patients. If the statement that “our ancestors died for this historic day” provides a way to mark the teleological culmination of nationalist history at a presidential inauguration, the request to participate in the RCT mirrors this standard political truism in American politics. The RCT offers the opportunity to have one’s disease and death stand in the service of a higher goal. It brings almost a military glory to an unfair, unfashionable death.³¹

The RCT works in the service—or, depending on how cynical you are, the lip service—of collective living on, but who and what do we miss by moving to that endpoint so quickly? Bodies lent to science suffer, and in many cases greatly, from cancer treatments, both standard and experimental treatments. Through its future-counterfactual promise, the RCT also dispenses with the questions of its own forms of violence; after all, its logics are corralled into the service of science, capital, and professional advancement, goals that do not in themselves correspond with cures or better treatments.

Margaret Edson’s play *Wit*, in documenting the death of an English professor from ovarian cancer and her course of a brutal experimental chemotherapy treatment, captures a set of miscommunications between doctor and patient that illustrate one facet of the paradox I unpack.³² The success of the play, and then the film, and its resonance for many of those involved in the cancer complex, was the way that it captured the physical and emotional costs of the logical mismatch between the objective account of the doctors and the required but disavowed subjective experience of the patient, who has to come to terms in the play with her own misrecognition of this mismatch in her professorial career. I have heard versions of this mismatch between doctors’ and patients’ accounts over and over again in cancer retreats and support groups; it is central to the trauma of cancer.

The point of the play was not that Vivian Bearing should have been cared for more empathetically or more respectfully by the treating physicians through the course of her treatment and death. Rather, the play explores how even had the medical community treated Bearing more compassionately, the system operates within the paradox of counting individual mortality through the immortal logic of

31. The following is a classic explication of this trade-off: “Society, having seen progress, asks not only for good care today, but for better care tomorrow and the medical profession has accepted this melioristic goal as legitimate and even obligatory. This has led to profound changes in a profession whose traditional commitment is to the individual patient. In order to give society the progress it demands for the future, we carry out clinical trials in which our patients of today become research subjects” (William J. MacKillop and Pauline A. Johnston, “Ethical Problems in Clinical Research: The Need for Empirical Studies of the Clinical Trials Process,” *Journal of Chronic Diseases* 39, no. 3 [1986]: 178).

32. Margaret Edson, *Wit* (New York: Sagebrush Education Resources, 1999).

the science itself. Bearing's doctors simply did not *need* to know anything about her except whether or not she would survive the experimental chemotherapy. She could have been *anyone* with ovarian cancer—the doctors did not care that she was Vivian Bearing, or that her cancer was diagnosed so late, or that she was the one in seven Americans who lives near a Superfund site. Regardless of whether she lived or died, useful data would have been produced.

In exchange for the deaths, the researcher renders them significant: he counts them. In counting them, he conjures a future—on the one hand, absorbing the individual into a yearned-for advantage and, on the other, further institutionalizing that fantasy of hope for the next generation of subjects. At the same time, the researcher will need to justify a new round of grant funding and consolidate his or her professional reputation: necessary aspects of the practice of science that help or hinder the effort to find the cure. And in the final write-up of the data, those who read them not only will not remember Bearing's name and profession but will not know her blood type, whether she smoked, whether the treatment was administered correctly, or even, likely, what may turn out for future researchers to be critical details of the cancer she had. Everything about her, except a check box on her cancer and another on her treatment, will be gone.³³

The RCT asks its subjects to join a program in which an individual body as a system of disease-flesh-treatment is converted into an abstraction that aggregates these components. The deaths in the trial swing both ways. Dowsett's 1,050 relapses were tallied from both groups: members of both the treatment and the placebo groups died.³⁴ It's nothing personal.

33. There are two ways of reading this aggregation. First, as I have argued elsewhere, the social logic of this leads to a way in which we come to live in populations and risk groups (S. Lochlann Jain, "Living in Prognosis," *Representations* 98 [2006]: 77–92). Second, actual clinical use in which an oncologist does his or her best to adjust a treatment to a patient is sometimes based on a trial's incredibly general terms, in which age, stage, and subtypes of cancer are not specific enough to draw conclusions from.

34. The vast numbers involved in the trials, the toxicity of the treatments for patients, the profits of drugs under patent for providers, and the incremental survival benefits consolidate cancer as a disease with a specific set of insights in relation to RCTs. This is different, say, from azidothymidine, or AZT, a drug that was designed two decades before the AIDS epidemic and that had no disease to work against until then. The efficacy of a drug so soon after the rise of the disease it is used to treat colors the cultural formations related to AIDS activism in ways that are insufficiently acknowledged in comparisons between AIDS and cancer activism. See Steven Epstein's rigorous account of AIDS activism's democratizing and lasting effect on RCTs in *Impure Science: AIDS, Activism, and the Politics of Knowledge* (Berkeley: University of California Press, 1996). I would argue that Epstein does not sufficiently recognize the efficacy of the medication in relation to the forms of and potential for activism.

In her analysis of war Elaine Scarry offers a unique insight into the political stakes of the way death can be separated from material, fleshy bodies. As she notes, bodies on both the winning *and* the losing side of the Civil War have been consolidated and explained as the price of freedom; in that sense, carcasses gain a mobility of attribution. She notes that the nonreferential character of the dead body “gives it a frightening freedom of referential activity, one whose direction is no longer limited and controlled by the original contexts of personhood and motive.”³⁵ This point is particularly salient in thinking through the nonreferential character of deaths in RCTs, for several reasons. First, we see this over and over again in how the statistics are rerun and debated and how the results are used for protocol or are redone or ignored. The trickiness and the politics of RCT research in light of incremental differences between drugs were hinted at by another doctor at the 2007 SABCS: “It is a great time to be a statistician.”³⁶ He was referring to the notorious difficulties in comparing RCTs and the facility with which results can be manipulated because of the variety of statistical methods. Second, where survival (and thus death) offers the endpoint of the trial, the questions of quality of life and quality of death ride in this framework of nonreferentiality.³⁷

When a person counts only insofar as he or she lives or dies, the medical descriptions of suffering shift nearly invisibly, often not for any conscious or vindictive reason but simply because they are not seen or made to count. The injuries,

35. Elaine Scarry, *The Body in Pain* (New York: Oxford University Press, 1985), 119.

36. Quoted in “Barbara Brenner’s Reflections on the 30th Annual San Antonio Breast Cancer Symposium—Day 2,” www.bcaction.org/index.php?page=2007-sabcs-day-2 (accessed March 6, 2008).

37. Elias Canetti writes that the commander of an army can appropriate all the dead bodies that result from his decision: “He commands; he sends his men against the enemy, and to their death. If he is victorious, all the dead on the battlefield belong to him, both those who fought for him and those who fought against him. . . . The significance of his victories is measured by the number of the dead” (*Crowds and Power*, trans. Carol Stewart [New York: Farrar, Straus and Giroux, 1960], 230). The dead come to belong to the person who counts; otherwise deaths are dispersed and inexplicable. Canetti also writes of the autocrat’s power over life and death. The autocrat “needs executions from time to time and, the more his fears increase, the more he needs them. His most dependable, one might say, his truest, subjects are those he has sent to their deaths” (232). See also Drew Gilpin Faust’s analysis of how the deaths related to the Civil War were understood: “The establishment of national and Confederate cemeteries created the Civil War Dead as a category, as a collective that represented something more and something different from the many thousands of individual deaths that it comprised. It also separated the Dead from the memories of living individuals mourning their own very particular losses. The Civil War Dead became both powerful and immortal, no longer individual men but instead a force that would shape American public life for at least a century to come. The reburial movement created a constituency of the slain, insistent in both its existence and its silence, men whose very absence from American life made them a presence that could not be ignored” (*This Republic of Suffering: Death and the American Civil War* [New York: Vintage, 2008], 249).

then, gain a frightening nonreferentiality and an ease of misrecognition in the name of future progress. Current suffering and the questions it raises are simply illegible: Is the suffering due to the initial (natural?) cancer or the treatment, are people dying of cancer or chemotherapy? To what extent is it acceptable, and who should decide? *How* are people living with, and dying of, cancer? The elision of these issues makes it easier to divert attention from other aspects of cancer production in the United States that are only barely tangentially associated with the profession of oncology: misdiagnosis, environmental causes, and early detection.

In this immutability the RCT shields its own God trick, its contingency on a sort of double logic of survivorship. In counting the dead on each side, the RCT logic simply offers an accounting: the 1,050 recurrences needed for the data were presumably going to happen anyway. The researcher has merely arranged these lives to figure out which treatments would be more promising, which pharmaceuticals more profitable. A final statistic will be bloodlessly inscribed by an omniscient observer, someone to weigh out the benefits and the costs of a new treatment. Future cancer patients will be invited to stare at these statistics and attempt to slot themselves into one side or the other in making decisions about treatments or whether to save money.

Over and above the shock and confusion generated by survival prognoses, one finds the violence and grieving of such elisions everywhere in patient-generated literature on cancer treatments. As he was dying of prostate cancer, Anatole Broyard wrote: “While he inevitably feels superior to me because he is the doctor and I am the patient, . . . I feel superior to him too, that he is my patient also and I have my diagnosis of him.”³⁸ Broyard diagnoses not only the fallacy of the objectivist stance of the one who expects to survive the trial but also the false sense of superiority marking the “previvor,” in that moment before fleshiness catches up to the physician. To Broyard, the physician is a priest who decries sin in the face of the black death before himself falling.³⁹

But Broyard’s high that comes with a firsthand knowledge of mortality does not quite explain the position demanded of the researcher, the counter of the dead. In big cancer trials the life span of the trial will exceed that of nearly everyone in it, and by necessity the survivors cannot be predicted in advance. Even in one of

38. Anatole Broyard, “The Patient Examines the Doctor,” in *Intoxicated by My Illness, and Other Writings on Life and Death* (New York: Clarkson Potter, 1992), 45.

39. Cliché might be considered, along with diagnosis and value-laden terms such as *patient*, as the linguistic philosopher J. L. Austin might describe it, a perlocutionary act, bringing one—by the very act of declaration—into a new subject position, one requiring a different set of customs, laws, ethics, and regulations.

the most successful cancer treatments ever, the use of Herceptin for a subset of breast cancers, many physicians expected another failure and expressed shock at the survival rates.⁴⁰ The investigator, as horrific as it may sound, simply needs the deaths of subject groups to complete the study. Thus doctors hold the awkward and horrible position of making their living through, that is, in needing, the deaths of their subjects.

Elias Canetti might describe the principal investigator of a large cancer trial as the ultimate survivor: “He is, as it were, an *innocent* hero, for none of the corpses are of his killing. But he is in the midst of the putrefaction and must endure it. It does not strike him down; on the contrary, one could say it is this which keeps him upright.”⁴¹ Doctors do not enjoy this position or necessarily profit from it (and neither do patients). But cancer deaths support the research and the researcher; they are productive, and they support whole industries and economies, however success is measured. Indeed, the more people die, the more the science becomes self-referential: the bigger a problem cancer becomes, the more trials we need. The point is not that the doctor inevitably gains from the patient’s suffering and death but that suffering and death undergird the system in ways that work differently for different participants. Subject positions are constructed through this model in such ways that some members become experts and others become in need of care; the ways that the model’s logics have been taken up in other cultural realms then shore up this notion of objectivity.

Shifting the question in this way enables several critical interventions that I will briefly note here before moving into a historical analysis of chemotherapy. First, we begin to see how the RCT creates a hierarchy, not just between the mortal and the survivors, but a temporal hierarchy, in which the mortality of some props up, or allows, the immortality of the others. This mortality effect, however inevitable, critical, and central to the RCT method, comes with its own politics. Second, its perceived objectivity erases the ways that the RCT produces cancer culture. The RCT provokes and elides these questions, central to the vast traumatic effects of cancer in America.

40. See Robert Bazell, *HER2: The Making of Herceptin, a Revolutionary Treatment for Breast Cancer* (New York: Random House, 1998).

41. This quotation is preceded by “His calm and imperturbability in the midst of putrefaction [are] characteristic of the hero. All the people in the world could lie rotting on top of him and he would still remain, also in the midst of universal corruption, upright and intent on his goal” (Canetti, *Crowds and Power*, 257).

Treatment Injury

Chemotherapy offers a necessarily harsh, toxic treatment, justified by the brutality of the disease. The high physical and social costs of the treatment, through the rituals of chemotherapy, present a social fact of cancer iterated in memoirs, support group discussions, graphic novels, and other cancer stories. First explored in the 1940s, following the chance observation that the blood and lymph systems of soldiers melted away after exposure to nitrogen mustard gas, the treatment still involves drastic side effects for many people even with vast improvements in antiemetics; theoretically, the drugs possess the maximum tolerable toxicity so as to have the best chance of killing cancers. Thus many chemotherapy drugs come with lifetime maximum doses.

Despite the term *targeted chemotherapy*, the treatment kills all quickly dividing cells in the body in the hope of killing the cancer cells; thus many healthy cells come under attack. In this sense, unlike surgery, the treatment offers systematic treatment and correlates with theories that cancer spreads throughout the body, in contrast to previous theories that cancer spreads outward from a localized tumor. Typical immediate side effects include intense nausea, bleeding mouth sores, and the deaths of quickly dividing cells such as those in hair follicles and those that produce white blood cells. Longer-term side effects can include leukemia, heart injury, fatigue, and cognitive impairment. The remarkable success of chemotherapy after World War II transformed once-deadly diseases such as leukemia, lymphoma, and testicular cancer into largely curable diseases and turned these cancers (and those who have survived them) into oncology poster children, propagating the promise that with enough funding and enough people signing up for trials, all cancers will be curable. Still, chemotherapies for cancers of the lung, pancreas, brain, and colon have not been as successful. Despite this dismal fact, not taking the therapy has something of a moral cast to it, as if it were an invitation to death by cancer, and for a doctor not to offer it for stage II, III, and IV cancers would constitute medical malpractice.⁴² Pursuing this example

42. One way to view this position is to juxtapose two noncontemporary articles, one by the journalist and researcher Rose Kushner and the other by the physician and historian Barron H. Lerner writing about her: Kushner, "Is Aggressive Adjuvant Chemotherapy the Halsted Radical of the '80s?" *CA: A Cancer Journal for Clinicians* 34, no. 6 (1984): 345–52, in which Kushner discusses the debates in oncology over the introduction of chemotherapy for breast cancer; and Lerner, "Ill Patient, Public Activist: Rose Kushner's Attack on Breast Cancer Chemotherapy," *Bulletin of the History of Medicine* 81 (2007): 224–40. Another way is to talk to people who discussed medical options with many physicians before deciding on a course of action and who later found that they had been dissuaded from what became the standard of care—some with regrets, some without.

demonstrates how treatment injuries become invisible, or are rendered invisible, as part of the benevolent intention of oncology.

The standard history of chemotherapy for breast cancer is narrated as follows. For breast cancer patients between stages I and III the same set of treatments are more or less given; in a twenty-first-century ritual, after surgery and before radiation, about one hundred thousand Americans a year receive chemotherapy treatment, and seven thousand to ten thousand derive some benefit from it. (In other words, some people will survive for years longer, while the great majority will not.) Oncologists acknowledge this limited success of chemotherapy and bolster it with treatments such as radiation and pharmaceuticals.⁴³ Oncologists have accepted an ethics of giving everyone chemotherapy: it will kill a few, it will injure many, but it will save others. It is a trade-off at the level of population, and it is measured by the chance of a favorable prognosis.

Chemotherapy for breast cancer was largely adopted in the United States in the late 1970s following a 1976 trial in Italy. With a fourteen-month follow-up of 386 initial patients, the trial demonstrated a small increase in survival and was hailed by the media as spectacular and monumental.⁴⁴ As the journalist and activist Rose Kushner documented at the time, and as the radiation oncologist and historian Gerald Kutcher has traced out since, controversy revolved around the trial's small number of patients and the combining of pre- and postmenopausal subjects. Nevertheless, as a result of the trial, the lack of other treatments, and the desire to demonstrate some medical progress, a combination therapy called CMF (cyclophosphamide, methotrexate, fluorouracil 5 FU) was adopted as protocol.⁴⁵

43. This is in part because treatments such as radiation and the use of hormones increase survival rates significantly over chemotherapy alone.

44. The Rose Kushner Archive, Schlesinger Library, Harvard University, has a collection of these news clippings. See also Gerald Kutcher, "Cancer Clinical Trials and the Transfer of Knowledge: Metrology, Contestation, and Local Practice," in *Devices and Designs: Medical Technologies in Historical Perspective*, ed. Carsten Timmermans and Julie Anderson (London: Palgrave, 2006), 212–29.

45. After a twenty-year follow-up study, some oncologists claim a marginal benefit of the CMF regime, while others claim that there was no survival benefit. Still others think that its success is contingent on the population of patients, depending on their pre- or postmenopausal status and on the kind and stage of cancer. "Statistics based on immature data are not necessarily significant," asserts Stuart G. Gilbert. "As an example, I cite the landmark 1976 report by Bonadonna and colleagues, which established adjuvant chemotherapy with cyclophosphamide, methotrexate, and fluorouracil (CMF) for node-positive breast cancer. They reported an extraordinary benefit in progression-free survival among postmenopausal patients at 27 months ($P = 0.001$). However, at 36 months, there was less benefit ($P = 0.16$), and at 20 years, there was no survival benefit from having received CMF" ("Trastuzumab in Breast Cancer," *Journal of the American Medical Association* 354 [2006]: 640).

Since the 1970s the one main change in the CMF regime has been the addition of a class of drugs called anthracyclines, which are given intravenously with a needle and known in medical circles as “the pink death.” One patient described anthracycline as “a big red burrito.” Though anthracyclines were discovered decades ago, the extremity of treatment-related side effects meant that little experimentation took place. Despite this hesitation in testing the drug, a 1998 study demonstrating a 4 percent survival increase when anthracyclines were added to the CMF treatment led to approval from the Food and Drug Administration (FDA) in 1999 and to widespread use of the drug.⁴⁶ For about ten years anthracycline treatment was the standard of care for breast cancer patients at stages II, III, and sometimes I, for it was hoped that treatment at those stages might bring these patients within the 4 percent who received some benefit.

This changed again in 2007, when a team led by Dennis Slamon, an oncologist at the University of California, Los Angeles, announced that they had found *which* people were likely to benefit from the more toxic chemotherapy of the anthracycline class of drugs.⁴⁷ In a presentation at the SABCS that year, Slamon claimed that “the use of anthracyclines in . . . treatment of all breast cancer is not supported by the existing data. Given the known long-term . . . toxicities of anthracyclines . . . other approaches to the . . . treatment of breast cancer should now be adopted.”⁴⁸ Indeed a breakthrough, as my interviews of oncologists during the meeting attest, this discovery will lead to a reduction in the number of people treated with anthracyclines. Ironically, while this is a promising development, it nullifies the only improvement in chemotherapy of the past thirty years,

Of course, what counts as “mature” data, when one is studying survival rates, remains an open question. Since the introduction of chemotherapy in 1976, there have been two critical breakthroughs, each contingent on the ability to distinguish the hormone status of breast cancer: the development of tamoxifen and then of aromatase inhibitors, typically prescribed for estrogen-positive cancers, and the development of trastuzumab for the use of HER2/neu-positive cancers. The success of these treatments resulted from Dennis Slamon’s discovery of the HER2/neu gene in 1986. This distinction in populations, critical to treatment regimens, was unavailable to the doctors leading studies in the 1970s, but it *was* available after 1986. In addition, it is possible to classify tumors even after the completion of trials if the tumors are kept.

46. The standard treatment became FAC (or FEC, depending on which anthracycline was used): fluorouracil, one of the anthracyclines, cyclophosphamide.

47. The indication is for HER2/neu-positive and topo-IIa-coamplified tumors; in 2008 the FDA approved a test for detecting the topo IIa amplification.

48. Dennis Slamon et al., “Role of Anthracycline-Based Therapy in the Adjuvant Treatment of Breast Cancer: Efficacy Analyses Determined by Molecular Subtypes of the Disease” (paper presented at the SABCS, San Antonio, Tex., December 13, 2007).

and so the vast majority of patients will now receive the same treatments that were used then, albeit with the addition of new pharmaceuticals such as tamoxifen and aromatase inhibitors.

Yet the discovery that the anthracyclines have virtually no benefit for so many patients means that since 1998 nearly a million people have been administered a toxic drug that has not helped them—a fact neglected at the conference. One might well wonder how the organization of these trials would allow this seemingly large and straightforward error in accounting. At the very least, the anthracycline treatment might have been tested separately on the two subcategories of breast cancer that have been identifiable since 1987, especially as this distinction is central to the course of treatments beyond chemotherapy. Data suggest that such population divisions would have rendered a very different set of results and treatments.

The success of the RCT method relies on a critical assumption: that the entities affecting all patients in a trial are similar enough that the patients can be said to have the same disease. Although some oncologists estimate breast cancer to comprise about two hundred diseases, most clinical trials combine even the known ways to distinguish the disease and the patients: by the disease's stage, by the pre- or postmenopausal status of the patient, and by the receptor status of the tumor. The anthracycline example demonstrates the politics of this approach and its pitfalls for patients.⁴⁹

In discussing the politics of diagnosis, Charles Rosenberg has examined the historical contingency of such diagnostic categorization. He writes that the diagnosis “labels, defines, and predicts and, in doing so, helps constitute and legitimate the reality that it discerns.”⁵⁰ Rosenberg's interest lies in examining how diseases are social entities, and his observation is useful in thinking about treatment injury and its role in constituting cancer as the horrific disease against which any treatment is acceptable and the cancer patient as one whose body is always already under attack.⁵¹ Rosenberg's point enables a better understanding, first, of how patient categories are constructed through the trials and then reconstituted

49. The distinctions in breast cancer trials make the results difficult to evaluate, because studies often combine stage I, II, and III diseases as well as women of different ages, in particular pre- and postmenopausal women.

50. Rosenberg, “Tyranny of Diagnosis,” 240.

51. Discussing how physicians approach diagnosis, T. M. Luhrmann writes: “As they memorize the hyperdetails of bodily process, they . . . turn the emotional horror of disease into a scientific entity. That transformation leaves the person and the pain out of illness” (*Of Two Minds: The Growing Disorder in American Psychiatry* [New York: Knopf, 2000], 87).

through the treatments and, second, of how the treatment of people with cancer as willing to undergo anything may lead to invisible medical violences. This latter assumption enables and justifies the continued constitution of control groups with inadequate controls.

In the case of anthracyclines, there was a 4 percent benefit in survival with the otherwise toxic drug, and so it is legitimate to weigh out the costs and benefits. In a way, the treatment was successful, since it offered any individual some population chance of survival benefit. Yet it was later found that most people who were given the drug would not have fallen into that 4 percent category. Before the field of cellular pathology enabled the identification of malignancy, a similar category confusion took place. Women with a variety of breast lumps frequently had mastectomies—at that time, before anesthesia and with high incidences of infections and death. (I bracket here a long history of misdiagnosis and complaints that were not taken seriously.) These radical treatments for what we now understand to be benign disease were often framed as the patient's only chance for survival. We now know that of the patients who survived the surgery, those with the benign lump were more likely to survive the disease and that the diagnostic category was far too broad.⁵²

Chance spread over population was misleading with the anthracyclines; a more finely calibrated study could have been done much earlier. But the scope and breadth of the treatment injury that resulted from the wide use of anthracyclines was barely mentioned at the SABCS. So how are these injuries explained away, and what can we learn by taking them seriously?

As I mentioned above, treatment injury is explained away through a relentless future thinking. The cost-benefit for people who will die anyway offers another explanation for justifying past and potential injury that bears consideration, because an ontology of cost-benefit necessitates a disavowal of the practices I trace out here: the production of subjects as members of these populations and the kinds of treatment injury that this subject production allows to be erased in the *name* of the individual's predicted future death and the population's future life.

Medical discourses have also occluded this confusion around diagnosis through a rhetoric of aggression. An oncologist at the SABCS, when asked about this news and how it would change his approach to treatment, told me that he would immediately stop using anthracyclines except for patients with advanced cancers. For them, he said, he would want to “shoot from both barrels.” This slippage between

52. Alternatively, a treatment that might have been highly successful for a few thousand people each year may have been abandoned because the market was not large enough.

specificity in diagnosis and the treatment's harshness (as opposed to its efficacy) has a remarkable history.

Taking stock of developments in thirty years of chemotherapy, a study published in 2006, twenty years after the discovery of the HER2/neu gene, reports: "The usual approach is to tailor the aggressiveness of the chemotherapy to the risk of recurrence. As compared with standard chemotherapy, aggressive chemotherapy is associated with a greater benefit, but also with more acute and long-term toxic effects. . . . Hence, patients at high risk for recurrence might be offered . . . an intensive anthracycline regimen."⁵³ The equation presented here skips the fact that aggressive treatments are associated not with some general form of "greater benefit" but with what is now believed to be efficacy for a very specific disease. In other words, the term *aggression* has been substituted for scientific precision in predicting the efficacy of the drug.

This confusion between toxicity and benefit was also central to the disaster of the experimental HDC treatment in breast cancer. That treatment involved removing in some cases a quart of the patient's bone marrow before giving a lethal dose of chemotherapy, keeping the patient in isolation to prevent infection, and then replacing the marrow. The procedure was in itself dangerous—in a Phase II trial, ten of the sixty-five patients died in treatment. Nevertheless, an estimated twenty-three thousand to forty thousand women in the United States received the treatment, using drugs that had been approved by the FDA for other purposes, before the completion of Phase III trials showed it to be of no benefit over standard chemotherapeutic treatments.⁵⁴

Some physicians believe that the HDC treatment became popular because of its profitability. But patients also wanted the treatment proffered as the most aggressive. As several people have explained to me, they wanted to know that they had done everything possible so they would have no regrets on their deathbeds. Treatment offers regret insurance.

The protocol model of cancer treatment constructs both its subjects *and* the disease, and the construction of a coherent concept of the disease is in some sense revived through these treatments that build on the battle metaphors, the measures of treatment as aggressive, the instructions to patients to be good soldiers.

53. Mark N. Levine and Timothy Whelan, "Adjuvant Chemotherapy for Breast Cancer—Thirty Years Later," *Journal of the American Medical Association* 355 (2006): 1920–22.

54. Richard A. Rettig, Peter D. Jacobson, Cynthia M. Farquhar, and Wade M. Aubry, *False Hope* (New York: Oxford University Press, 2007). For more examples of the extreme aggressiveness of cancer treatments, sometimes involving the surgical removal of body parts, see Lerner, *Breast Cancer Wars*.

Because the patients are understood as being in a battle for their lives, in a state of emergency, in some sense already dying—the treatments are always already warranted, even, as in the cases I outline here, when they kill the patients or when the physicians could have known better, sooner, with more carefully designed trials.⁵⁵ My goal here is not to argue that there is no role for the method (though I question its singular hegemony) or that there is some better method out there, though there may well be. Rather, the bumpy way in which RCTs work—often taking decades, mistaking diagnostic categories and groups, and rendering highly debated results—does not demonstrate the clear path toward progress that the reader of the TroVax pamphlet may be led to expect.⁵⁶

In her work examining the central role of injury in the settlement of disputes, Scarry offers a pivotal insight into how we might understand these treatment injuries. Why wage war, she asks. Why not use a chess game to settle an international dispute? In working this out, she examines the structured competition of out-injuring that is war and yet notes that accounts of war omit those very injuries. Injuries, she writes, are redescribed and hence invisible, or they are acknowledged but designated as a by-product, “something on the road to a goal, or something continually folded into itself as in the cost vocabulary, or something extended as a prolongation of some other more benign occurrence.”⁵⁷ Though not fully analogous, these routes are helpful in thinking about the stakes in reanimating the production of injury in oncology. In oncology injuries are elided through tropes of hope, the attribution of treatment-related deaths to new primary causes (leukemia becomes leukemia rather than radiation-based injury), the trope of aggression, the lack of attention to cancer causation and early detection, and population statistics

55. “The highly asymmetric characterization of survival and complications,” claims Kutcher, “typified the knowledge claims produced from clinical trials. On the one hand, the measure of success, the unit for comparing one treatment to another, was survival and its surrogate, disease-free survival. Almost the entire structure of the study, the whole of the statistical apparatus was designed to ensure that the reported survival differences were significant and not a consequence of hidden bias. Sophisticated statistical methods were developed to address pre-randomization, post-study stratification, and a host of other methodological difficulties, always with the goal of rooting out bias in reported survival. On the other hand, the analysis of complications had no such elaborate statistical paraphernalia to support it. Complications were presented as a stepchild of survival and characterized with qualitative terms like minimal and acceptable. This privileging of survival in the design and execution of clinical trials, however, . . . provided a limited measure for translating trial results into local practice” (“Cancer Clinical Trials,” 217–18).

56. Many treatment-related injuries are not attributed to treatments for the primary disease; for instance, leukemia and heart failure are most often considered primary causes of death themselves, rather than results of treatments for the initial cancer.

57. Scarry, *Body in Pain*, 80.

as a proxy for individual chances. After all, the war metaphor has been central to framing debates about cancer; the trope of aggression fits well into the life-or-death competition played out through the RCTs' competition to out-heal.⁵⁸ The tropes of competition and war fit so well into each other that they are difficult to see.

Yet they disguise several questions. What is the ethical difference between treatment injury and cancer injury? How long should the period be between distinctions in diagnosis and the continued use of prior categories in new trials? What is to be made of the fact that treatments at least as promising as anthracyclines never make it to the Phase III trials that cost so many millions of dollars to run? Where does responsibility rest for these injuries and false hopes and promises amid so much profit?

Conclusion

Typically, scientists interpret the RCT as a benign method. The fact that the method requires deaths of patients in one trial group is generally thought to be an unpleasant necessity of finding the facts, and the certainty that the deaths would happen anyway, in both groups, shore up the moral framing of the necessity of research. Inefficacies can be explained away as politics: as not having the right endpoints, the right statistical models, or the right controls, or as having too many economic interests polluting the data. If this is just the common sense of it, unpacking it further as I have done here opens a new view on the culture of cancer and the centrality of hope, risk, chance, and the nearly ritualistic comparisons of populations and individuals that virtually define contemporary cancer experiences. In my longer project I track how these numbers circulate through prognoses, medical malpractice litigation, cultures of chance and risk, pharmaceutical research economics, and quality-of-life measurements, all of which circulate also in affective economies of hope and progress.

Thinking about the RCT as a forward-driven representational form also challenges this division between science and politics. The basic tenet of the RCT, that people come to science as bodies whose characteristics can be averaged out, aggregated, and canceled out, assumes that actual individuals do not matter to the population-based basic science. This assumption seems to shift nearly impercep-

58. The term *out-healing* was coined by Elaine Scarry in a discussion in which I was trying out the following argument with her (Stanford Humanities Center, Stanford, Calif., February 26, 2008).

tibly to the supposition that no matter what, no matter which people come to the RCT, at the end we will have a chemical that either works or does not work.

This view misses the way that the cultures of disease fundamentally inform what science can be done.⁵⁹ The trial and its mode of objectivity rely on a temporal paradox that frames the mortality of the subjects against the immortality of the counters. The deaths of one group enable and justify the treatment injury of the other. Such justification makes perfect sense, and many patients do take the risks of treatment injury over the risks of cancer, even when the chances of cancer are low and those of treatment injury are high (neither alternative is well understood). But such a rough-cut comparison occludes two critical issues. First, it overlooks the dearth of oversight in the ways that control groups are constructed. The anthracycline example offers only one of many cases in which the diversity of people tested leads to vast treatment injury. The forming of such treatment groups may be innocent, unavoidable, or accidental—or the result of greed, sloppiness, or protocol. Either way, it comes with human and social costs that are not separate from the so-called real science of which chemicals are produced, how treatments are used, and what cancer looks like at the level of the social or through the collective of bodies that treatment produces.

Second, taking this seriously demonstrates that the natures and cultures of dividing cells, host bodies, chemical treatments, and injuries are in such constant flux, amid conditions of such uncertainty, that the explication of a causal factor is impossible to determine. The RCT's attempt to locate explanations in late-stage cancer trials can only ever be provisional, continually raising and evading the oncological and ethical status of the various actors constantly in play—from chemotherapy to ill people to capital.

The history of using cancer patients as guinea pigs for experimental treatments with radiation and chemical poisons—sometimes with their consent and sometimes not, sometimes leading to efficacious treatments but usually not, often producing enormous wealth for someone else—raises critical questions about the use of dying humans as experimental subjects, as natural resources, and as capitalist health care consumers. These questions cannot be asked if injuries and

59. In that sense, when Marks notes in passing that “I have yet to encounter a source that would tell me much about patients,” he suggests that these accounts might somehow simply be added to the story of the rise of RCTs (*Progress of Experiment*, 13). The inclusion of patient narratives in his account might have required him to write an entirely different history of RCTs from the remarkable one he provides, because the patient does not deal in the immortal gathering of populations and chance.

profits are explained away as side effects of failed but valiant attempts to find a cure.⁶⁰ For it is not simply that a certain chemical works on 4 percent of those who are given it, and works on a higher percentage of those with certain kinds of diseases. Where the “real” science lies at this level of uncertainty, when the categories of disease, treatment, and personal traits all compete for explanatory power, remains an open question. Through making categories and ascribing life-or-death consequences to those categories, the RCT method plays a central role in this recursive co-constitution of basic science.⁶¹

60. Moreover, treatments themselves may serve as shields for the uncertainty of oncology’s knowledge of cancer. If expertise is often based on claims of certainty, it may be easy for treatment to become a sort of proxy for certainty, where doing something is perceived by patients and physicians alike as better than doing nothing.

61. As one therapist who works exclusively with people with cancer told me: “People get treated for years, and the doctors are excited [that] people are ‘living’ longer with cancer. So they live longer on endless cycles of chemo, feeling sick and being tied to the cancer centers for years. I think there is a sacrifice of human dignity and a giving up of knowing what it is like to die without the horrendous effects of chemo, being bald, sick, etc., etc. The huge attachment to these treatments also forces communities to sacrifice caring for their members who are dying. Instead these people are trying to live and survive cancer and [are] dying in the process” (Janie Brown, founder and therapist of Callanish, Vancouver, B.C., pers. comm., January 13, 2006).

