

Introduction

Medicine has for long possessed the qualities necessary to make a science.¹

Bensalem will have an intellectual history consisting of the progress of science. It will have a social history consisting of the impact of science. It will, however, have no political history.²

“Modern” medicine, “scientific” medicine: the terms are virtually synonymous. The modernity of twentieth-century medicine consists of its reliance on the physical and biological sciences. Yet the association is deceptive, so familiar that it passes without further investigation. What does it mean, what should it mean, to call medicine a science? Is medicine dependent on science for its tools, its knowledge, or its methods? Is medicine scientific because physicians use an advanced technology, the x-ray, because they rely on a knowledge of pathology and radiology to interpret the image produced by the machine, or because of the rigor with which the technology and knowledge are used to arrive at clinical decisions?

From the seventeenth-century iatrochemist van Helmont through the twentieth-century educational reformer Abraham Flexner, it was generally believed that establishing medicine as a science meant grounding medical practices in one or more of the laboratory-based disciplines which study the functioning of biological organisms – biochemistry, physiology, genetics, immunology – disciplines which in turn were to be based on the sciences of physics and chemistry. Scientific medicine was a matter of applying at the bedside knowledge produced elsewhere, a conception of medical science that still thrives today.³

- 1 “Tradition in Medicine,” in *Hippocratic Writings*, ed. G. E. R. Lloyd (New York: Penguin Books, 1983), p. 71.
- 2 Samuel H. Beer, “Two Models of Public Opinion: Bacon’s ‘New Logic’ and Diotima’s ‘Tale of Love,’” *Political Theory* (May 1974), 166.
- 3 Claude Bernard’s *An Introduction to the Study of Experimental Medicine* (New York: Dover Publications, 1957), as introduced by L. J. Henderson in 1927, provides the locus classicus for twentieth-century proponents of this view. For a contemporary example, see George K. Radda, “The Use of NMR Spectroscopy for the Understanding of Disease,” *Science* 223 (August 8, 1986), 640. (The author is aptly titled Professor of Molecular Cardiology at the University of Oxford.) On the tensions among

2 Introduction

Historians of medicine have followed medical researchers in focusing on the laboratory sciences of the nineteenth and twentieth centuries: their practices, their organization, and their political ideals.⁴ Meanwhile, in this century, another interpretation of the project has been put forth: clinical medicine was, or could be, every bit as scientific as the research laboratory, if “scientific method” were directly applied to judging the results of medical treatment. Paramount among the means for placing medical practice on a scientific basis has been the controlled experiment.

This book examines the beliefs and activities of a disparate group whom I have labeled “therapeutic reformers,” individuals who sought to use the science of controlled experiments to direct medical practice. They range from the pharmacologist Torald Sollman, who for fifty-five years guided the American Medical Association’s Council on Pharmacy and Chemistry as it reviewed the claims drug manufacturers made for their products, to the gastroenterologist Thomas C. Chalmers, who once advocated that the very first patient to be treated with an experimental drug should be enrolled in a randomized controlled trial.⁵ This community of reformers includes individuals trained in the laboratory disciplines of pharmacology and physiology, clinical specialists whose interests range from the infectious diseases of syphilis and pneumonia to the chronic conditions of diabetes and heart disease, physicians and nonphysicians from the quantitative disciplines of statistics and epidemiology, practicing clinicians, government officials, and journal editors.

Historians of science and medicine are accustomed to studying groups bound by professional training and circumstance: the discipline of biochemistry, or the medical specialty of cardiology.⁶ This is not a history of clinical pharmacology or of biostatistics, although clinical pharmacologists and statisticians figure prominently in this story. Rather, the therapeutic reformers discussed here constitute a *political* community, a group joined by their belief in the power of science to unite

the laboratory sciences, see William Coleman, “The Cognitive Basis of the Discipline: Claude Bernard on Physiology,” *Isis* 76 (March 1985), 49–70.

- 4 Charles E. Rosenberg and Morris J. Vogel, eds., *The Therapeutic Revolution: Essays in the Social History of American Medicine* (Philadelphia: University of Pennsylvania Press, 1979); William Coleman and Frederick Holmes, eds., *The Investigative Enterprise: Experimental Physiology in Nineteenth-Century Medicine* (Berkeley: University of California Press, 1988); John Harley Warner, “Ideals of Science and Their Discontents in Late Nineteenth-Century American Medicine,” *Isis* 82 (September 1991), 454–478; Andrew Cunningham and Perry Williams, eds., *The Laboratory Revolution in Medicine* (Cambridge: Cambridge University Press, 1992); Adele Clarke and Joan H. Fujimura, eds., *The Right Tools for the Job: At Work in the Twentieth-Century Life Sciences* (Princeton: Princeton University Press, 1992).
- 5 Thomas C. Chalmers, “Randomization of the First Patient,” *Medical Clinics of North America* 59 (July 1975), 1035–1038.
- 6 See Robert E. Kohler, *From Medical Chemistry to Biochemistry: The Making of a Biomedical Discipline* (Cambridge: Cambridge University Press, 1992); W. Bruce Fye, *American Cardiology: The History of a Specialty and Its College* (Baltimore: Johns Hopkins University Press, 1996). For a study that takes the research group and research animal as the basis unit of analysis, see Robert E. Kohler, *Lords of the Fly: Drosophila Genetics and the Experimental Life* (Chicago: University of Chicago Press, 1994).

Introduction

3

both medical researchers and practitioners *despite* obvious differences of training and circumstance.⁷ Although connected in some cases by the accidents of personal biography, what binds reformers is the shared belief that better knowledge about the effects and uses of drugs will lead directly to better therapeutic practice.

My aim in the book is twofold. First, I wish to examine the changing character of reformers' efforts to direct clinical therapeutic practice. In the first half of the century, reformers depended on the integrity and expertise of individual researchers to produce reliable, untainted, knowledge about the effects of medical treatment. They relied on an organization of experienced researchers, the Council on Pharmacy and Chemistry, to sift and weigh the claims manufacturers offered about the effects of specific therapies on disease. U.S. Food and Drug Administration officials adopted the council's approach to judging the benefits and risks of treatment in their efforts to regulate the safety of new drugs during the 1930s and 1940s.

Reformers in the second half of the century abandoned their predecessors' trust in the judgment of experienced clinicians. In its place, they offered an impersonal standard of scientific integrity: the double-blind, randomized, controlled clinical trial. Yet despite obvious differences in their ideas about experiments, evidence, and clinical judgment, "methodological reformers" shared their predecessors' conviction that elevating the scientific standards of drug evaluation would lead directly to improvements in clinical practice.

Reformers' trust in the powers of science went hand in hand with a suspicion of the motives of business. Throughout the century, reformers have regarded evidence from corporate sponsored research as guilty until proven innocent. Early in the century, Progressive-era reformers warned that only an independent science of drug evaluation, securely controlled by the medical profession, could resist corporate impulses to "debauch our medical journals" and "taint our textbooks."⁸ In less colorful language, reformers' suspicions persist today, embodied in proposals that researchers identify any business interests in the products they study.⁹

7 For a related use of the notion of political identity, see John Harley Warner, "Remembering Paris: Memory and the American Disciples of French Medicine in the Nineteenth Century," *BHM* 65 (1991), 312–315.

8 George H. Simmons, "The Commercial Domination of Therapeutics and the Movement for Reform," *JAMA* 48 (May 18, 1907), 1645.

9 International Committee of Medical Journal Editors, "Conflict of Interest," *Ann Int Med* 118 (April 15, 1993), 646–647; "American Federation for Clinical Research Guidelines for Avoiding Conflict of Interest," *Clinical Research* 38 (April 1990), 39–40. For a survey of conflict of interest policies, see M. D. Witt and L. O. Gostin, "Conflict of Interest Dilemmas in Biomedical Research," *JAMA* 271 (February 16, 1994), 547–551. See also R. A. Davidson, "Source of Funding and Outcome of Clinical Trials," *Journal of General Internal Medicine* 1 (May–June 1986), 155–158; Paula A. Rochon, Jerry H. Gurwitz, Robert W. Simms, Paul R. Fortin, David T. Felson, Kenneth L. Minaker, and Thomas C. Chalmers, "A Study of Manufacturer-Supported Trials of Nonsteroidal Anti-inflammatory Drugs in the Treatment of Arthritis," *Archives of Internal Medicine* 154 (January 24, 1994), 157–163. On the history of corporate involvement in university drug research, see John P. Swann, *Academic Scientists and the Pharmaceutical Industry: Cooperative Research in Twentieth-Century America* (Baltimore: Johns Hopkins University Press, 1988).

4 Introduction

Reformers' appeals for an independent science of drug evaluation were integral to their political vision of the medical profession as a body united through science. Medicine's contemporary critics take the profession's scientific aspirations as both illusory and delusive: medicine is not, they argue, a science and its claims in this regard are chimerical.¹⁰ What such demystifying criticisms ignore is the role such visions of science have played within the profession itself.

Medical practitioners have always been divided by differences in formal training and professional opportunity. In the present century, the rapid pace of technological and scientific change has aggravated existing inequalities in the profession, between hospital-based physicians and community-based doctors, between specialists and general practitioners, between metropolitan and rural physicians.¹¹ Operating from the islands of academic medicine, therapeutic reformers offered practitioners the vision of a profession united by a faith in science which transcended all accidental differences of training and technological sophistication.¹²

Reformers' pursuit of a profession unified by science came at a price. Reformers believed that they need only provide physicians with a scientifically grounded knowledge of drugs' uses and effects to improve therapeutic practice. Until very recently, reformers have sidestepped the question of what to do about physicians who do not use drugs appropriately or prudently.¹³ Nor were reformers often successful in transcending the differences that divided researchers of diverse disciplinary backgrounds or between doctors who practiced under different material circumstances.

Reformers' need to create a "republic of science" continues to haunt contemporary efforts at therapeutic reform. Physicians dispute the relative merits of statistical and clinical expertise in evaluating medical treatments, while reformers find it difficult to define the point at which reasonable disagreement about

¹⁰ See E. Richard Brown, *Rockefeller Medicine Men: Medicine and Capitalism in America* (Berkeley: University of California Press, 1979); John Ehrenreich, "Introduction," in John Ehrenreich, ed., *The Cultural Crisis of Modern Medicine* (New York: Monthly Review Press, 1978), pp. 1–38.

¹¹ On the role of the nineteenth-century and early twentieth-century hospital in medical careers, see Charles E. Rosenberg, *The Care of Strangers: The Rise of America's Hospital System* (New York: Basic Books, 1987), pp. 58–68, 166–189. On divisions in the professional order and efforts to overcome them in the present century, see Rosemary Stevens, "The Curious Career of Internal Medicine: Functional Ambivalence, Social Success," in Russell C. Maulitz and Diana E. Long, eds., *Grand Rounds: One Hundred Years of Internal Medicine* (Philadelphia: University of Pennsylvania Press, 1988), pp. 339–364; idem, *In Sickness and in Wealth: American Hospitals in the Twentieth Century* (New York: Basic Books, 1989).

¹² The notion of science provides the basis for what Benedict Anderson calls, in the political context of modern nationalism, an "imagined" community. See his *Imagined Communities: Reflections on the Origin and Spread of Nationalism* (London: Verso Books, 1983). For an argument that the notion of a scientific community is a mid-twentieth-century invention, see David A. Hollinger, "Free Enterprise and Free Inquiry: The Emergence of Laissez-Faire Communitarianism in the Ideology of Science in the United States," *New Literary History* 21 (1990), 897–919. I am grateful to Bill Leslie for calling my attention to Hollinger's essay.

¹³ Jerry Avorn, "Drug Regulation and Drug Information – Who Should Do What to Whom?," *AJPH* 85 (January 1995), 18–19; Peter Temin, *Taking Your Medicine: Drug Regulation in the United States* (Cambridge: Harvard University Press, 1980).

therapeutic merit becomes irrational dissent from a scientific standard of practice.¹⁴ Should physicians be allowed to prescribe human growth hormone for children who are growing more slowly than their peers, but who show no signs of hormonal deficiency? What kinds of evidence are needed before physicians conclude that the use of calcium channel blockers for treating hypertension is unsafe? When should patients with HIV disease be allowed to take still experimental drugs?¹⁵

Invariably, such discussions involve questions of political values as well as scientific merit. Although the project of reforming professional therapeutic practice has always been a problem of political order as well as of science, reformers seem incapable of addressing matters of science and politics in the same breath. Part of my reason for writing this book is to suggest that the science and politics of therapeutic reform need not be as inimical as contemporary reformers sometimes suggest.

My second aim in the book is to chart the changing intellectual and social history of therapeutic experiments, from the early 1900s when the laboratory sciences provided the standard of the “well-controlled” experiment to the latter half of the century when the clinically based randomized controlled trial offered a new standard of scientific excellence. The controlled clinical trial has a history that, in the public health tradition, dates back at least to James Lind’s controlled test of lemons for scurvy prevention in the British Navy of the 1740s.¹⁶ Generally, physicians have focused their attention on a series of celebrated examples ranging

14 Alvan R. Feinstein, “An Additional Basic Science for Clinical Medicine. Parts I–IV,” *Ann Int Med* 99 (1983), 393–397, 554–550, 705–712, 843–848. On clinical controversies, see the discussion in Chapters 7 and 8.

15 On human growth hormone, see David B. Allen, C. G. D. Brook, N. A. Bridges, P. C. Hindmarsh, Harvey J. Guyda, and Douglas Frazier, “Therapeutic Controversies: Growth Hormone (GH) Treatment of Non-GH Deficient Subjects,” *Journal of Clinical Endocrinology and Metabolism* 79 (1995), 1239–1248; E. Kirk Neeley and Ron G. Rosenfeld, “Use and Abuse of Human Growth Hormone,” *Annual Review of Medicine* 45 (1994), 407–420. On calcium channel blockers, see Bruce M. Patsy, Susan R. Heckbert, Thomas D. Koepsell, et al., “The Risk of Myocardial Infarction Associated with Antihypertensive Drug Therapies,” *JAMA* 274 (August 23–30, 1995), 620–625; Curt D. Furberg, Bruce M. Patsy, and Jeffrey V. Meyer, “Nifedipine: Dose-Related Increase in Mortality in Patients with Coronary Heart Disease,” *Circulation* 92 (1995), 1326–1331; Lionel H. Opie and Franz H. Messerli, “Nifedipine and Mortality: Grave Defects in the Dossier,” *ibid.*, 1068–1073; Salim Yusuf, “Calcium Antagonists in Coronary Heart Disease and Hypertension: Time for Reevaluation?” *ibid.*, 1079–1082. On AIDS therapies, see Jeffrey Levi, “Unproven AIDS Therapies: The Food and Drug Administration and ddI,” in Committee to Study Biomedical Decision Making, Institute of Medicine, *Biomedical Politics* (Washington, DC: National Academy Press, 1991), pp. 9–37; Paul D. Stolley and Tamar Lasky, “Shortcuts in Drug Evaluation,” *Clinical Pharmacology and Therapeutics* 52 (July 1992), 1–3. See also the discussion in John Lantos, “How Can We Distinguish Clinical Research from Innovative Therapy,” *American Journal of Pediatric Hematology/Oncology* 16 (1994), 72–75.

16 For an account of Lind’s work which places it into context, see Ulrich Tröhler, *Quantification in British Medicine and Surgery 1750–1830, with Special Reference to Its Introduction into Therapeutics* (Ph.D. thesis, University of London, 1978), pp. 198–220. See also Alice Henderson Smith, “The Relative Content of Anti-scorbutic Principle in Limes and Lemons. B. Historical Inquiry,” *Lancet* ii (1918), 737–738. Earlier episodes of “controlled” tests sometimes cited seem to me to have far more to do with biblical traditions of trial by lots or, as in Ambroise Paré’s case, with the contemporary

6 Introduction

from Lind's field trial through the introduction of the "numerical method" in the Paris Clinic of the nineteenth century to the Medical Research Council's controlled trial of streptomycin for tuberculosis treatment in post-World War II Britain. These disparate episodes are then linked in a transhistorical narrative of antecedents deemed to constitute the history of the present-day randomized controlled trial.¹⁷ In turn, historians William Coleman, Ulrich Tröhler and George Weisz have treated several of these episodes in greater detail, without assuming the burden of a transhistorical narrative.¹⁸

My approach has been to focus on the activities, circumstances, and ideas of clinical researchers in situ, ignoring European (and American) antecedents except where they can be shown to have a direct influence on the practices and ideals of twentieth-century reformers active in the United States.¹⁹ The resulting account differs from earlier historical narratives in at least three ways. First, I have emphasized the changing meanings that researchers attached to terms such as experimental "controls" or "randomized" experiments. Second, I have given greater attention to the material circumstances under which researchers of successive generations worked, and to the effects of these circumstances on their ideas of experimentation. Successive approaches for producing and weighing evidence about the effects of drug therapies incorporated different assumptions about which group was best suited to perform such assessments: community-based physicians in the "collective investigations" of the preceding century, university-based specialists in the "cooperative studies" of the 1930s and 1940s, and the indispensable statisticians in the randomized clinical trials of the 1950s and beyond. The historical pathway to the latter was neither as smooth nor as direct as previous accounts suggest.

Third, this is quintessentially an American story. While the controlled clinical trial may be an international scientific accomplishment, the ways in which trials were organized and understood mark them as belonging to a particular place as

rhetoric of empirical versus learned medicine, than with subsequent developments of controlled experimentation in the nineteenth and twentieth centuries.

17 See, for example, J. P. Bull, "The Historical Development of Clinical Therapeutic Trials," *JCD* 10 (1959), 218–248; Abraham Lilienfeld, "Ceteris Paribus: The Evolution of the Clinical Trial," *BHM* 56 (1982), 1–18. The recent study by the historian J. Rosser Matthews, while adding both new episodes and considerable new detail to the canonical narratives of Bull and Lilienfeld, employs a similar approach. See *Quantification and the Quest for Medical Certainty* (Princeton: Princeton University Press, 1995).

18 See, in particular, Tröhler, *Quantification in British Medicine and Surgery* (n. 16); George Weisz, "Academic Debate and Therapeutic Reasoning in Mid-19th Century France," in Ilana Löwy, Olga Amsterdamska, John Pickstone, and Patrice Pinell, eds., *Medicine and Change: Historical and Sociological Studies in Medical Innovation* (Paris: INSERM, 1993), pp. 287–315; William Coleman, "Experimental Physiology and Statistical Inference: The Therapeutic Trial in Nineteenth-Century Germany," in Lorenz Krüger, Gerd Gigerenzer, and Mary S. Morgan, eds., *The Probabilistic Revolution* (Cambridge: MIT Press, 1987), vol. 2, pp. 201–208. See also William A. Silverman's exemplary case study of clinical evidence and clinical trials in post-World War II neonatology: *Retrolental Fibroplasia: A Modern Parable* (New York: Grunc and Stratton, 1980).

19 I discuss the historical literature on the nineteenth-century U.S. traditions in Chapters 1 and 2.

Introduction

7

well as time.²⁰ Historians of the United States will easily recognize the conviction of Progressive-era therapeutic reformers that science is a moral as well as an intellectual activity; the insistence of researchers in the 1920s and 1930s that new organizations were needed to conduct adequate studies of new drugs; and the almost paranoid obsession of researchers in the 1950s with purging subjectivity from controlled experiments. Other familiar features of the story include the influence of private organizations (the Council of Pharmacy and Chemistry) on public policy, and the enduring faith that the social and political obstacles to a rational therapeutics can be solved by better and more science.²¹

If I have anything to add to the conventional wisdom on twentieth-century U.S. history, it comes from my conviction that reformers were influenced less by the writings of public intellectuals or the irresistible forces of bureaucratization and professionalization than by intellectual traditions and circumstances particular to the local world of academic medicine. To paraphrase Marx, men make their own history but not under the circumstances described in the prefaces to history books. Perhaps that is why my scientists seem far more hostile to corporate America than prevailing historiography would predict; why their organizations are far less effective and enduring than proponents of the “organizational” synthesis might expect; and why my postwar bureaucratic state is far less heavy-handed (or effective) in furthering the cause of a rational therapeutics than neoliberal critics of the regulatory state might allow.²²

- 20 For analyses in a similar vein of comparable developments in Great Britain, see the forthcoming dissertations by Desiree Cox-Maximov, *The Making of the Clinical Trial in Britain, 1900–1950: A Cultural History* (Cambridge University), and Alan Yoshioka, *British Clinical Trials of Streptomycin: 1946–1951* (Imperial College).
- 21 On science, morality, and politics, see Charles Rosenberg’s *No Other Gods: On Science and American Social Thought* (Baltimore: Johns Hopkins University Press, 1978), pp. 1–21; David A. Hollinger, “Inquiry and Uplift: Late Nineteenth-Century American Academics and the Moral Efficacy of Scientific Practice,” in Thomas L. Haskell, ed., *The Authority of Experts: Studies in History and Theory* (Bloomington: Indiana University Press, 1984), pp. 142–156; Dorothy Ross, *The Origins of American Social Science* (Cambridge: Cambridge University Press, 1991). On organizations, see Louis Galambos, “The Emerging Organizational Synthesis in Modern American History,” *Business History Review* 44 (Autumn 1970), 279–290; idem, “Technology, Political Economy and Professionalization: Central Themes of the Organizational Synthesis,” *Business History Review* 57 (Winter 1983), 471–493. On private organizations and public policy, see the classic works of Grant McConnell, *The Decline of Agrarian Democracy* (Berkeley: University of California Press, 1953), and Philip Selznick, *TVA and the Grass Roots: A Study in the Sociology of Formal Organization* (Berkeley: University of California Press, 1949). For more recent work in this tradition, see J. David Greenstone, ed., *Public Values and Private Power in American Politics* (Chicago: University of Chicago Press, 1982). On objectivity in American social science after World War II, see Peter Novick, *That Noble Dream: The “Objectivity Question” and the American Historical Profession* (Cambridge: Cambridge University Press, 1988), pp. 281–360.
- 22 On science and the corporation, David F. Noble’s pathbreaking *America by Design: Science, Technology and the Rise of Corporate Capitalism* (New York: Alfred A. Knopf, 1977) remains unsurpassed. On organizations, see Louis Galambos, “The Emerging Organizational Synthesis” (n. 21), and Brian Balogh, “Reorganizing the Organizational Synthesis: Federal-Professional Relations in Modern America,” *Studies in American Political Development* 5 (Spring 1991), 119–172. Contrast Matthew E. Crenson’s and Francis E. Rourke’s views of the “inevitability” of postwar bureaucracy with Barry Karl’s views of the fragility of the prewar state. Crenson and Rourke, “By Way of Conclusion:

8 *Introduction*

My interest in the history of therapeutic reform dates to the late 1970s, when I was working with a group of statisticians, economists, and physicians at the Harvard School of Public Health. My colleagues were puzzled by the seeming indifference, if not hostility, of many clinicians to randomized controlled trials. I, in turn, was intrigued by the strength of my colleagues' belief in the power of evidence to transform clinical practice. Yet I would not have been able to follow up on the story had it not been for the emergence at that time of a new sociology of science, whose practitioners insisted that even orthodox science was fair game for social and historical inquiry, by researchers using the same tools in studying the "failed" sciences of the past, phlogiston and phrenology, as in investigating the "false" science of the present – cold fusion and the mysterious molecules of Dr. Benveniste.²³

From the study of scientific controversies, the new sociologists of science went on to inquire into the domain of scientific practice: the nature and organization of scientific work in different settings, the role of social conventions in stabilizing agreement about observed phenomenon, the diverse repertoire of resources scientists use in pursuing their work.²⁴ Each of these developments has left its mark on this book. Yet sociologists have focused almost exclusively on science's heartland, the laboratory, largely ignoring the domain of the clinic where the social character of the science conducted is perhaps too obvious to merit their attention.²⁵

Readers acquainted with the complex and sophisticated body of sociological

American Bureaucracy since World War II," in Louis Galambos, ed., *The New American State: Bureaucracies and Policies since World War II* (Baltimore: Johns Hopkins University Press, 1987), pp. 137–177; Barry D. Karl, *The Uneasy State: The United States from 1915 to 1945* (Chicago: University of Chicago Press, 1983).

- 23 For those who do not recall the incident, Benveniste and his colleagues found an immunological reaction even after diluting an antibody 10^{60} times. See E. Davenas, F. Bauvais, J. Amara, M. Oberbaum, B. Robinzon, A. Miadonna, A. Tedeschi, B. Pomeranz, P. Fortner, P. Belon, J. Sainte-Laudy, B. Poitevin, and J. Benveniste, "Human Basophil Degranulation Triggered by Very Dilute Antiserum against IgE," *Nature* 333 (June 30, 1988), 816–818. On cold fusion, see Thomas F. Gieryn, "The Ballad of Pons and Fleischmann: Experiment and Narrative in the (Un)Making of Cold Fusion," in Ernan McMullin, ed., *The Social Dimensions of Science* (Notre Dame, IN: University of Notre Dame Press, 1992), pp. 217–243. On symmetry in explaining "true" and "false" science, see G. Nigel Gilbert and Michael Mulkay, "Warranting Scientific Belief," *Social Studies of Science* 12 (1982), 383–408.
- 24 See especially Bruno Latour, *Laboratory Life: The Social Construction of Scientific Facts* (Beverly Hills, CA: Sage Publications, 1979); Peter Galison, "Bubble Chambers and the Experimental Workplace," in Peter Achinstein and Owen Hannaway, eds., *Observation, Experiment and Hypothesis in Modern Physical Science* (Cambridge: MIT Press, 1985); Karin Knorr-Cetina, *The Manufacture of Knowledge: An Essay on the Constructivist and Contextual Nature of Science* (Oxford: Pergamon Press, 1981). More recent work can be sampled in Andrew Pickering, ed., *Science as Practice and Culture* (Chicago: University of Chicago Press, 1992); David Gooding, Trevor Pinch, and Simon Schaffer, *The Uses of Experiment: Studies in the Natural Sciences* (Cambridge: Cambridge University Press, 1989).
- 25 See, however, the forthcoming work by Ilana Löwy, *Between Bench and Bedside: Science, Healing and Interleukin 2 in a Cancer Ward* (Cambridge: Harvard University Press, 1996); and the pioneering work of Leigh Star: Susan Leigh Star, "Simplification in Scientific Work: An Example from Neuroscience Research," *Social Studies of Science* 13 (May 1983), 205–229; idem, "Triangulating Clinical and Basic Research: British Localizationists, 1870–1906," *History of Science* 24 (1986), 29–48.

study on contemporary science may wonder what a historian has to add.²⁶ First is a greater awareness of the historical character of scientific inquiry. Sociologists have been at great pains to emphasize as well as analyze the social character of scientific knowledge. Yet for the historian, the notion that science is “social” is a truism: we are more interested in the different kinds of societies in which scientists work, the different forms of power and influence available to them, or in the fates of different sciences within a given society.

For example, clinical researchers in the 1930s and 1940s relied on inquiries they termed “cooperative investigations,” intended to transcend the limitations of isolated researchers in studying medical treatments. In the early 1930s, researchers emphasized the power of cooperative investigations to transcend the methodological vulnerability of individually conducted research, the use of idiosyncratic definitions of disease and treatment, and a reliance on small case series whose conclusions were easily affected by the ordinary cycles of spontaneous recoveries and remissions. During World War II, in contrast, researchers emphasized the greater efficiency of centrally planned cooperative investigations: their ability to quickly provide urgently needed answers to questions about the uses of new drugs. In two successive decades, contemporaries invested the same scientific activity with two very distinct meanings. Similarly, just as the resources available to cooperative investigations expanded enormously during World War II, as soon as the war was over, researchers resumed their search for new funding (and new justifications) for their research. It is difficult to understand the social character of cooperative investigations in either decade without exploring these differences in historical circumstances and meaning.²⁷

Contemporary sociological studies also invest science with great power. In one recent influential account, science is a “golem,” a powerful creature capable of running amuck. In another, it is a lever capable of lifting the world.²⁸ By contrast,

26 For a historian’s overview of recent work in the sociology of science, see Jan Golinski, “The Theory of Practice and the Practice of Theory: Sociological Approaches in the History of Science,” *Isis* 81 (September 1990), 492–505. For further discussion of the issues addressed here, see Harry M. Marks, “Other Voices: A Reply to Labinger,” *Social Studies of Science* 25 (1995), 329–334; idem, *Local Knowledge: Experimental Communities and Experimental Practices, 1918–1950*, a paper presented at the conference on Twentieth Century Health Sciences: Problems and Interpretations, University of California, San Francisco, May 1988.

27 For a thoughtful discussion of the limits of such historicizing, see Steven Shapin, “Discipline and Bounding: The History and Sociology of Science As Seen through the Externalism–Internalism Debate,” *History of Science* 30 (1992), 347–355.

28 Harry Collins and Trevor Pinch, *The Golem: What Everyone Should Know about Science* (Cambridge: Cambridge University Press, 1994); Bruno Latour, “Give Me a Laboratory and I Will Raise the World,” in Karin D. Knorr-Cetina and Michael Mulkay, eds., *Science Observed: Perspectives on the Social Study of Science* (London: Sage Publications, 1983), pp. 141–170. In his account of Louis Pasteur’s anthrax vaccine, Bruno Latour appears to recognize the significance of social engineering, when he notes that Pasteur’s vaccine never seemed to work outside the boundaries of the Francophone world. Yet within France, Latour makes Pasteur’s social engineering look so easy that a careless reader may easily come away with the wrong impression. For a critical discussion of Latour’s work emphasizing these issues, see Simon Schaffer, “The Eighteenth Brumaire of Bruno Latour,” *Studies in the History and Philosophy of Science* 22 (1991), 175–192.

10 *Introduction*

the sciences discussed in this book are weak, incapable of transforming the world of clinical practice as easily as reformers hope. The kind of social engineering that science requires to transform the world is, as sociologists *should* know, a far more difficult task in scale and complexity than physicists' no less ambitious efforts to measure gravity.

Since World War II, the organization and conduct of clinical experiments have been radically transformed by medicine's encounter with the discipline of statistics. When I began work on this project, the history of statistics after 1750 was best pursued by reading old statistical journals.²⁹ Now, the historian has a wealth of perspectives to chose from in seeking to understand the theory and practice of statistics in historical context. Nonetheless, there remain few historical guides to statistics after 1900, regardless of whether one is interested in debates among the high priests of statistical inference (R. A. Fisher, Jerzy Neyman, L. J. Savage) or the more mundane details of statistical practice in business, agriculture, or medicine.³⁰

I therefore chose a very narrow focus: to examine the ways in which ideas about randomized experiments and statistical analysis were introduced into clinical medicine, and the role professional statisticians played as allies of therapeutic reformers. My approach is premised on the convictions that ideas can best be studied in context, and that the administrative memo can reveal as much about the intellectual history of an era as the more formal treatises sometimes favored by intellectual historians.³¹ Other versions of the story can and hopefully will be written that give greater attention to statistics in other domains – the laboratory, the factory and the classroom – and other disciplines.

I have divided the book into two parts, corresponding to the two eras of therapeutic reform discussed above. Chapters 1 through 4 deal with the era of organizational reforms; Chapters 5 through 8 cover the era of methodological

29 In addition to the classic works of Westergaard and Todhunter, the collection of articles by Egon Pearson and Maurice Kendall was very useful: E. S. Pearson and Maurice Kendall, eds., *Studies in the History of Statistics and Probability* (London: C. Griffin, 1970), 2 vols. For seventeenth-century studies, see Ian Hacking, *The Emergence of Probability: A Philosophical Study of Early Ideas about Probability, Induction and Statistical Inference* (Cambridge: Cambridge University Press, 1975); Peter Buck, "Seventeenth-Century Political Arithmetic: Civil Strife and Vital Statistics," *Isis* 68 (1977), 67–84.

30 On statistics prior to 1900, see especially Stephen M. Stigler, *The History of Statistics: The Measurement of Uncertainty before 1900* (Cambridge: Harvard University Press, 1986); Lorraine J. Daston, *Classical Probability in the Enlightenment* (Princeton: Princeton University Press, 1988); Ian Hacking, *The Taming of Chance* (Cambridge: Cambridge University Press, 1990); Theodore M. Porter, *The Rise of Statistical Thinking, 1820–1900* (Princeton: Princeton University Press, 1986). For twentieth-century statistics, see the pioneering synthesis by Gerd Gigerenzer, Zeno Swijtink, Theodore Porter, Lorraine Daston, John Beatty, and Lorenz Krüger, *The Empire of Chance: How Probability Changed Science and Everyday Life* (Cambridge: Cambridge University Press, 1989).

31 If anyone should find this proposition disconcerting, I refer to the authority of Antonio Gramsci, for my therapeutic reformers certainly are among Gramsci's organic intellectuals, and to the historian William Bouswma, "From History of Ideas to History of Meaning," in idem, *A Usable Past: Essays in European Cultural History* (Berkeley: University of California Press, 1990), pp. 336–347.