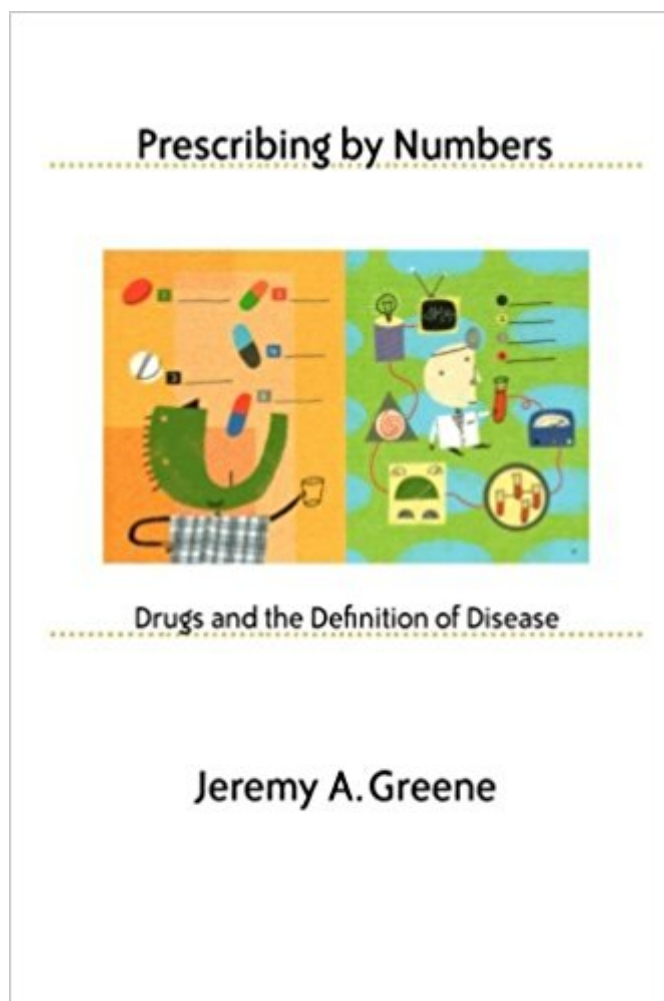


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# Prescribing By Numbers: Drugs And The Definition Of Disease



## Synopsis

The second half of the twentieth century witnessed the emergence of a new model of chronic disease—diagnosed on the basis of numerical deviations rather than symptoms and treated on a preventive basis before any overt signs of illness develop—that arose in concert with a set of safe, effective, and highly marketable prescription drugs. In *Prescribing by Numbers*, physician-historian Jeremy A. Greene examines the mechanisms by which drugs and chronic disease categories define one another within medical research, clinical practice, and pharmaceutical marketing, and he explores how this interaction has profoundly altered the experience, politics, ethics, and economy of health in late-twentieth-century America. *Prescribing by Numbers* highlights the complex historical role of pharmaceuticals in the transformation of disease categories. Greene narrates the expanding definition of the three principal cardiovascular risk factors—hypertension, diabetes, and high cholesterol—each intersecting with the career of a particular pharmaceutical agent. Drawing on documents from corporate archives and contemporary pharmaceutical marketing literature in concert with the clinical literature and the records of researchers, clinicians, and public health advocates, Greene produces a fascinating account of the expansion of the pharmaceutical treatment of chronic disease over the past fifty years. While acknowledging the influence of pharmaceutical marketing on physicians, Greene avoids demonizing drug companies. Rather, his provocative and comprehensive analysis sheds light on the increasing presence of the subjectively healthy but highly medicated individual in the American medical landscape, suggesting how historical analysis can help to address the problems inherent in the program of pharmaceutical prevention.

## Book Information

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"Greene provides suggestions on how to address some of the problems inherent in medical prevention." (Choice)"Shows how the process of defining disease 'illustrates the porous relationship between the science and the marketing of health care.'" (Nina C. Ayub Chronicle of Higher Education)"A gripping story... Greene warns us in his superb book that things are not always as they are claimed." (Howard Spiro Yale Journal for Humanities in Medicine)"This is, I believe, one of the best, and most significant, books published recently on the development of medical practice and the pharmaceutical industry in the USA in the second half of the twentieth century." (Judy Slinn Social History of Medicine)"Greene focuses on the question of how public health priorities became closely aligned with the pharmaceutical industry's marketing practices... Offers a nuanced description of the development of 'therapeutics of risk reduction' with multiple lines of influence, subtle power shifts, and gains and losses for patients and physicians." (Arthur Daemrich Chemical Heritage)"Greene describes the relationship between advances in treatment, the incentives of manufacturers, and the effect on the public of increased attention to prevention... The risk-benefit trade-offs of the quantitative approach are complex, and Greene's historical revelations are timely." (Kevin A. Schulman, M.D. New England Journal of Medicine)"The interaction between medical science and industry has been fruitfully explored by several excellent historians... but Greene's intricate narratives extend their work." (Marcia Meldrum Isis)"I heartily recommend this book." (Toine Pieters Medical History)"By the end of Prescribing by Numbers, one realizes it is an excellent book to think with. Greene uses his case studies to juxtapose the therapeutics of risk with more contemporary health dilemmas." (Gregory J. Higby Pharmacy in History)"Greene's nuanced and lucid research yields new insight into the mechanisms that linked specific medications to the management of particular chronic diseases in the postwar era." (Cynthia A. Connolly, PhD, RN Nursing History Review)"An insightful, engrossing exploration of how our notions of 'disease' have evolvedâ with profound implications for understanding the health care of today and tomorrow." (Jerry Avorn, M.D, Professor of Medicine, Harvard Medical School, author of Powerful Medicines: The Benefits, Risks, and Costs of Prescription Drugs)"What is remarkable about this book is not just the grace and assurance of Greene's writing, but the way Greene combines an insider's view of medical practice and pharmaceutical marketing with much broader social currents. It is an extraordinarily impressive work of scholarship." (Carl Elliott, M.D., Ph.D., University of Minnesota

Center for Bioethics, author of *Better than Well: American Medicine Meets the American Dream*) "Greene's historical account of our brave new world of drug-driven risk reduction is troubling and calls for some response. Both the scholarly depth and balanced tone of *Prescribing by Numbers* suggests that rather than simply rooting out bad actors and unethical practices, we must grapple with the very values and structural forces that are central to medical care and health today." (Robert Aronowitz, M.D., History and Sociology of Science Department, University of Pennsylvania)

The second half of the twentieth century witnessed the emergence of a new model of chronic disease—diagnosed on the basis of numerical deviations rather than symptoms and treated on a preventive basis before any overt signs of illness developed—that arose in concert with a set of safe, effective, and highly marketable prescription drugs. Physician-historian Jeremy A. Greene examines the mechanisms by which drugs and chronic disease categories define one another within medical research, clinical practice, and pharmaceutical marketing, and he explores how this interaction has profoundly altered the experience, politics, ethics, and economy of health in late-twentieth-century America. His provocative analysis sheds light on the increasing presence of the subjectively healthy but highly medicated individual in the American medical landscape, suggesting how historical perspective can help to address the problems inherent in the program of pharmaceutical prevention. "Greene describes the relationship between advances in treatment, the incentives of manufacturers, and the effect on the public of increased attention to prevention... The risk-benefit trade-offs of the quantitative approach are complex, and Greene's historical revelations are timely." • *New England Journal of Medicine* "One of the best, and most significant, books published recently on the development of medical practice and the pharmaceutical industry in the U.S. in the second half of the twentieth century." • *Social History of Medicine* "Greene focuses on the question of how public health priorities became closely aligned with the pharmaceutical industry's marketing practices... [and] offers a nuanced description of the development of 'therapeutics of risk reduction' with multiple lines of influence, subtle power shifts, and gains and losses for patients and physicians." • *Chemical Heritage* "A gripping story... Greene warns us in his superb book that things are not always as they are claimed." • *Yale Journal for Humanities in Medicine* Jeremy A. Greene is a fellow in the Department of Social Medicine at Harvard Medical School and a resident in the Department of Medicine at Brigham and Women's Hospital.

In 1957 the Framingham Study identified the main risk factors of coronary heart disease. High blood pressure and high cholesterol were later joined by diabetes as the three main physiological variants

believed to be mechanistically connected to heart disease. Reduce your blood pressure, your cholesterol level and your blood sugar, and you are less likely to suffer from a stroke or a coronary artery disease. Prescribing by Numbers presents selected episodes in the emergence of these three principal cardiovascular risk factors and the careers of three pharmaceutical products whose fates have been inseparable from the conditions they treated. The narratives of these three prescription drugs--Diuril, Orinase, and Mevacor--overlap to provide a unique perspective on the growth of asymptomatic disease categories and the role of the pharmaceutical industry in their emergence. Diuril represented the first palatable pill for hypertension, and although its history is less well known than the saga of antibiotics, the dramatic emergence of antipsychotic drugs, or the cultural hand-wringing surrounding the minor tranquilizers, the influence of this drug on clinical practice was equally profound. Hypertension became a different disease after Diuril. By making antihypertensive therapy a sweet pill to swallow, Diuril lowered the threshold for the prescription and consumption of hypertensive medications, enlarged the population of potential hypertensive patients in both clinical trials and clinical practice, and contributed to the consolidation of a single threshold for the definition of hypertension. In addition to its significance as a profitable consumer good, Diuril as a therapeutic agent prompted new ways of thinking about hypertension and created the possibility of long-term randomized trials in symptomatic subjects. It is equally true that Diuril, itself the result of a combination of research and marketing, became a different drug after it encountered hypertension. Diuril was first conceived as a diuretic, and it did not have any connection to hypertension until it had left Merck's research laboratories. Diuril's marketers recognized the importance of scientific symposia and journal publications as a way to introduce larger numbers of physicians to novel medications. In the case of Diuril, clinical research was incorporated into the marketing arena. Popular magazine articles, company newsletters, sales force deployment and gift trophies (the "Diuril Man") also became standard ploys in the marketing strategy. The Kefauver Commission's Senate hearings, formed to investigate the promotional misconduct and commercial corruption of the industry, were a first warning that marketing tactics could backfire and tarnish the public image of pharmaceutical companies. Before Orinase, the first oral antidiabetic introduced in 1957, insulin was the principal therapy to treat diabetes. Life under insulin required a swift and total indoctrination into a demanding lifestyle with meticulous labor practices of calorie calculation and insulin self-administration: taking care of one's diabetic self was a full-time job. Although it worked only in certain types of diabetes, Orinase's introduction expanded total market by bringing under medical care diabetics who formerly were not treated. The screening and treatment of "hidden patients" became an important priority of public health policy; as detection efforts shifted to earlier

stages and milder forms of diabetes, the number of the estimated "undetected" grew rather than shrank. Like Diuril, Orinase influenced the definition of disease. It catalyzed a shift in the basic conception of chronic disease from a model of inexorable degeneration to a model of surveillance and early detection. However, the fabric of therapeutic consensus was torn open by the results of the NIH-funded University Group Diabetes Project Study, which suggested that Orinase, then taken by hundreds of thousands of patients, might have severely harmful effects. Those in charge of the study had to wrestle with an entirely new kind of ethical question in the context of clinical trials--namely, how much evidence of the harm of a drug is required to halt a study. The public debate about Orinase and the UGDP trial lasted more than a decade and came to involve a set of congressional hearings, an FBI investigation, and a court ruling challenged all the way up to the US Supreme Court, without coming to a clear-cut conclusion. It was a prelude to the mix of politics, science, and industry interests, mediated by litigation, that characterizes our modern healthcare era. The story of cholesterol in the 1970s and 1980s recounts the failure of a category of risk reduction to impose itself in the absence of an appealing intervention. The first cholesterol-lowering agent, introduced and tested on hapless patients, involved hair loss, cataracts, and severe diarrhea: in retrospect, it is evident that the drug, a granular solution with the smell of rotten fish, should never had gone on the market in the first place. For more than a decade, the development of new drugs was tainted by the memory of its abject failure. The low-fat, low cholesterol diet became the favorite of the supporters of cholesterol as a public health concern, even though some researchers denounced it as "diet fads and quackery". Although Americans learned to "know their cholesterol level", and some even became familiar with low-density lipoprotein or "bad" cholesterol, they were for the most part loath to follow the prescription to "change dietary behavior now to avoid future problems", and public campaigning had only mixed results. Under some definitions, and as a result of the cholesterol-rich "American diet", up to 90 percent of the US population could be defined to have higher than ideal cholesterol. All changed, however, with the introduction of Merck's Mevacor, the first of a class of drugs now known as the statins. Mevacor's success helped Merck become, for many years, the largest and most profitable pharmaceutical company in the world. Although the ideal level of cholesterol remains a matter of debate, there is no such thing as excessively low LDL cholesterol level. By the end of the 1990s, it had become a commonplace occurrence for cardiologists to suggest, only half jokingly, that statins should be included along with fluoride as a general additive to the nation's drinking water supply. A series of conclusions emerge from this book. The first is that pharmaceuticals have become central agents in the definition of disease categories. Neither drugs nor drugs marketers can single-handedly define disease, though: the process

increasingly involves patients, physicians, families, consumer groups, insurance companies, diagnostic technologies, expert committees, regulatory bodies, and the material basis of pathology itself. It is, to use the author's word, an overdetermined process, which illustrates the porous relationship between the science and the business of healthcare. But the pharmaceutical industry played a central and dynamic role in the definition of these categories of illness, as is illustrated by the careers of the three pharmaceutical products whose fate has become inseparable from the conditions they treated. A second conclusion relates to the definition of diseases in terms of numerical thresholds, informed by large-scale trials and shaped by guidelines and expert committees. A central feature of current conceptions of health and illness is that a person is no longer required to notice symptoms or even manifest visible signs of pathology to receive a diagnosis. As a result of evidence-based medicine, the everyday practicing physician gradually came to adopt numerical thresholds (on blood pressure, blood cholesterol, blood sugar) as a principal basis for diagnostic and therapeutic decision making. Patients and healthy people alike are encouraged to "know their numbers" and to monitor them to prevent the apparition of pathologies. These changes in the process of disease definition have created a system that is at once more egalitarian than the physician-controlled process of the early twentieth century and more exposed to the movements of the marketplace. Moving the thresholds to include a larger group of people in the prepathological or pathological categories has become a key strategy in the pharmaceutical companies' efforts to expand market size. Third, correlative to the definition of "diseases without symptoms" and the practice of "prescription by numbers" has been the emergence of a logic of risk reduction. We now treat as diseases loose categories that themselves have never been connected to symptoms, entities such as mild hypertension, elevated cholesterol, and mild diabetes. These are physiological markers with only probabilistic connections to other conditions that do bear symptoms, such as stroke, myocardial infarction, and frank diabetes. The language of risk and morbidity probability, first introduced by the life insurance industry, has become a central concern of public health, and prescriptions for chronic noninfectious diseases and their precursor states now dominate the American pharmaceutical industry's domestic income. The pharmacotherapy of risk is now even expanding into other Framingham risk factors earlier found resistant to drug therapy, such as obesity and cigarette smoking. And the image of the overfed, underexercised American consumer who takes a statin with his cheeseburger has swiftly become something of a cultural cliché.

Prescribing by Numbers is authoritative and erudite, yet reflective and philosophical. First, the author has a firm grounding in the social sciences. He makes use of several strands of research, including the social studies of science, the sociology of the medical profession, the

anthropology of pharmaceuticals, the marketing tools of business studies, and the ethical questionings of philosophy. The author refers in the endnotes to famous social scientists such as Max Weber, Marcel Mauss, Claude Levi-Strauss, Georges Canguilhem, and Michel Foucault. At times, the study raises issues similar to the ones addressed by Foucault in *Discipline and Punish*; but Jeremy Greene does without the obfuscating rhetoric preferred by the French philosopher, and he sticks to the methods and objectives of historiography. *For Prescribing by Numbers* is, first and foremost, a contribution to the social history of contemporary medicine. The author had access to various corporate archives of pharmaceutical companies and public administration files, including recent documents released under the Freedom of Information Act. His ethnographic text analysis of letters addressed to the Food and Drug Administration by patients and physicians worried by the alleged effects of Orinase is both illuminating and path-breaking, as it incorporates the (often sought-after but seldom reflected) patient's view in medical history. He is even able to unearth from the archives a case of public manipulation, as several letters written by "concerned friends" of patients suffering from diabetes were copied verbatim from a public-relations memo of a pharmaceutical company. As the author makes it clear, this book attempts "neither apology nor attack". The conclusions are both morally balanced and intellectually provocative. This is a thought-provoking book of therapeutic breadth and historical depth that will change the reader's thinking about disease, public health, private interests, and normality itself.

Etienne's 5 star review is excellent, I can't add anything to that. In fact, this book will be read and understood only by people like Etienne, it is specialized. The author is extremely intelligent and well educated and writes very well. This is an important book and anyone capable of reading it should. I did research in health care economics but my understanding of medicine falls a bit short when it comes to a book like this. The book begins with a wonderful quote from Sir William Osler, the father of modern medicine, "The way to live the longest is to acquire a chronic disease and take good care of it." Books and other information on health care here: [mwir-improvinghealth.blogspot.com](http://mwir-improvinghealth.blogspot.com). I create and maintain educational websites, Midwest Independent Research.

The author, a physician and historian, weaves together a vast array of useful medical/pharmaceutical information with fine-grained historical analysis. This is absolutely first-rate social commentary on the history of pharmaceutical development and the changing notion of disease. It should be of especial use and value to those who work in bioethics, health care law, medical sociology and anthropology, and pharmaceutical marketing.



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