BOOK REVIEWS

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Medicine In The Thrall Of The Culture Of Drugs

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PHARMAGEDDON
By David Healy
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302 pp.; $39.95

"Medicine as we know it is at death's door," David Healy writes part way through *Pharmageddon*. It is a central theme running through the book by this professor and psychiatrist, working within the National Health Service in North Wales, United Kingdom. The practice of medicine should, he believes, require knowing patients as whole persons, preferably over many years. Instead, he says, medicine is becoming fractured, evolving into a series of problem-based short office visits that make use of guidelines to make medical decisions. Pharmaceutical giants play a huge role in this shift, having moved far beyond discovering new drugs to trying to shape how patients are diagnosed and treated.

Healy's view that pharmaceutical companies are overly influencing medicine comes as no surprise, as the author is one the world's most widely published critics of pharmaceutical hegemony. (The same view has preoccupied my own work in bioethics and health policy.) In *Pharmageddon*, Healy makes full use of Welsh storytelling skills to weave the tale of how the pharmaceutical giants have come to shape patients' personal relationships with their bodies and with their physicians. Citing many studies by others as well as recounting his own experiences, Healy educates readers about the ways in which major pharmaceutical companies have influenced diagnostic categories and clinical guidelines so that physicians—and millions more patients—believe in certain disorders or in new "at-risk" situations that require the use of a drug.[1] In my view, Healy's book is the most powerful and deeply thought of a new crop of books on pharmaceuticals and medicine.[2–4]

One of Healy's case studies of how pharmaceutical companies have conjured up new diagnoses concerns manic depression. Up until the 1990s, the condition, as then diagnosed, was a rare one that affected only ten people in a million. Healy describes the reengineering marketing campaign by Abbott Laboratories to replace the term "manic depression" with the existing phrase "bipolar disorder," which, according to Abbott, affects up to 50,000 people per million. Disease awareness campaigns followed, suggesting that bipolar disorder might be the cause of other problems as well, such as anxiety and depression, and inviting people to self-diagnose.

Marketing achieved the ultimate success: Bipolar became a fashionable disorder. Healy describes how marketers organized conferences to develop guidelines for diagnosing the disorder, ones with a strong basis in clinical trials run by pharmaceutical companies, to prove the benefits that suited their marketing goals. In ten short years, what had been for decades a rare disorder treated by specialists became a broadly constructed mental condition without, Healy contends, solid evidence either that the condition existed or that the drugs prescribed for it were effective.

Healy details several other examples and emphasizes the downside risks. Prescription drugs have become a leading cause of illness, hospitalization, and death.[2] Abbott is at it again now, promoting medication to help with "low T"—lowered testosterone—which, of course, affects any middle-aged man who is ten years older than he was a decade earlier (http://www.isitlowt.com).

Before the 1970s, Healy contends, researchers in major pharmaceutical companies carried out in-depth, observational investigations, just as their academic counterparts did, on how diseases worked and what compounds might have the right mechanism of action. Spectacular discoveries, major clinical advances, and huge profits resulted. Then a new generation of company executives bent on selling more drugs for still more profits changed to having research programs develop new products around clinical targets identified by marketing departments.

Healy contends that the number of breakthrough compounds dropped dramatically. Since then, about fifty out of every sixty "new drugs" marketed have offered few or no advantages over previous ones to offset their risks of harm.[5] Today, Healy contends, the Food and Drug Administration in the United States and the European Medicines Agency, the overarching regulatory agency for twenty-seven nations in the European Union, approve drugs without real evidence that they are better for patients, and they might be worse.

In the United States in the early 1960s, reformers thought requiring randomized clinical trials would lead to superior new drugs. Using case illustrations, however, Healy describes how pharmaceutical companies shape randomized clinical trials to get the results they need for marketing. As a result, physicians who believe that randomized clinical trials mean that new drugs have proven benefits—and could be prescribed with confidence—are being misled. In a quartet of chapters, Healy describes how the big pharmaceutical companies make marginally different drugs look better

than they are.

First, giant pharmaceutical companies do their random sampling for clinical trials from patient populations that exclude those most likely to experience adverse reactions. They also lower the threshold for demonstrating that a new product is better than an inert substance by eliminating subjects who have a strong response to a placebo. Companies use high doses and short trials to maximize evidence of benefit, even though higher doses are more likely to produce harmful side effects weeks after data collection ends. These high, more dangerous dosages then go into the drug's label and into clinical guidelines.

Physicians are impressed by large trials, but companies do them primarily to prove that small benefits are statistically significant. It is not that the Food and Drug Administration is complicit in this. Rather, the agency works within rules and practices that have been set up with a good deal of influence from the pharmaceutical companies and lobbyists.

Second, pharmaceutical companies have repeatedly hidden, denied, or trivialized harmful side effects. Healy has some harrowing examples based on his own experiences as an expert on psychotropic drugs. He was among the first to note that Paxil increased suicidal thoughts in young patients, and he recounts how he began investigations revealing that clinical trials showing high rates of suicide were hidden by GlaxoSmithKline, the maker of the drug, including miscoding suicidal children as "noncompliant." Healy describes his critical role in the lawsuit by Eliot Spitzer, then attorney general of New York, against GlaxoSmithKline for "fraudulent interference with the practice of medicine."

Third, pharmaceutical companies have long kept academic investigators under contract to prevent them from publishing negative results so that prescribing physicians could get a full picture of harms as well as benefits.[6] Healy describes how, since the 1980s, companies have retained teams of skilled science writers and editors to craft articles for medical journals. He estimates that 90 percent of the articles on new drugs in medical journals are ghost managed, and other independent investigators agree.

In his twenty-seven pages of references to supporting studies, Healy cites recent studies that document how the published medical knowledge read and trusted by doctors is seriously biased.[7] Correcting biased medical science takes years, while billions of dollars are racked up by pharmaceutical companies in the meantime. These actions reflect not conspiracy but rational economic behavior by executives who are seeking good returns on their investments.

There you have it: trivial but "significant" benefits from drugs; undertested and underreported risks of harm; ghost-managed articles, reviews, and editorials; and $57 billion spent on marketing to get doctors to prescribe the resulting drugs.[8] The weight of the evidence leads Healy to recommend that patients would be better off if fewer drugs required prescriptions. Of course, ads would endlessly tell patients why they needed to take a certain drug, but then they do that already. However, patients might be more self-protective instead of uncritically trusting their physicians and basking in the benefits of the placebo effect.[9] And the role of physicians would change from using their expertise and authority to prescribe to looking out for harmful side effects from the drugs that their patients decided to take.

Today medical leaders think having evidence-based medicine will rationally rein in costs, but Healy writes that the giant pharmaceutical companies know better because they control how the evidence is constructed and gets into guidelines. Pharmaceutical companies "are prepared to conceal trials or adverse events that might pose problems for their marketing, ghostwrite such trials as are published, and aggressively counter attempts by doctors to describe problems that arise in the course of therapy." Furthermore, physicians are known to report only a small fraction of harmful side effects once drugs come into broad use, compromising the evidence that could be built up in post-marketing drug surveillance.

Healy sees tragic results for society and the economy. More workers think they are "sick." Long use of drugs for prevention or chronic management heightens people's anxieties and alters their bodies or minds in ways not sufficiently understood. "Treating raised cholesterol levels and other 'number disorders'...when medical necessity doesn't call for it is more likely to lead to a decrease in American productivity... an expense that is crippling American industry," Healy asserts.

In *Pharmageddon*, Healy offers a fresh insight that new strategies to develop "personalized medicine" and raise costs to new levels (for instance, by figuring out ways to repatent drugs going off patent) are undermining universal health care in Europe and elsewhere, often with little evidence of real clinical gain. For the most part, he writes, looking for cures is out for pharmaceutical companies because that would end sales. Researching and developing drugs for cancers and HIV/AIDS are largely paid for by taxpayers and donor foundations for specific diseases but then priced at levels that threaten the commitment of nations to affordable universal health care. Increasingly, countries and insurance companies conclude that the modest benefits do not warrant the staggering prices charged and decide not to cover them for patients. However, this leads to two-tier access for patients willing to pay privately.

If people want to understand how the way they think about their bodies as a bundle of risks to be managed by drugs came about, why the workforce is getting "sicker," why the major pharmaceutical companies are banking on further overdiagnosis and overtreatment,[4,10] and why this is undermining universal health care, they should read this book. Then, readers should go on to discuss its implications in classrooms and policy circles. ■

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NOTES

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Queries

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