Book Reviews

The $800 Million Pill: The Truth Behind the Cost of New Drugs, by Merrill Goozner, 269 pp, hardback, $24.95, ISBN 0520239458, Berkeley, Calif., University of California Press, 2004.

If one of my students had submitted this book as a dissertation, he might have gotten failing marks for research, analysis, and possibly integrity.

Merrill Goozner attempts to discredit the widely quoted $802 million figure for average research and development costs of drugs marketed for the first time (i.e., new molecular entities or NMEs). Goozner's analysis is so misguided that his book actually contradicts his own thesis!

Goozner mistrusts the $800-million figure, even though the Office of Technology Assessment independently validated the study's methodology. He introduces this figure for *capitalized* costs to readers on page 3, but doesn't tell them that the study abstract also reported *out-of-pocket* costs of $403 million. The reader is not informed that these figures include costs for both successful drugs and the failures preceding them.

These omissions are significant, since Goozner attempts to discredit the capitalized $800 million figure, which includes failures, with out-of-pocket research and development (R&D) estimates of $150-200 million for four successful drugs: Epogen, Viracept, Agenerase, and Herceptin. Readers, of course, end up comparing $150-200 million in out-of-pocket, successful drug R&D to the nonequivalent capitalized $800-million figure that includes failures.

A back-of-the-envelope approximation of Goozner's out-of-pocket estimates, with failures added, can be made by dividing his figures by 0.3. This is the fraction of potential new drugs that enter clinical testing and stay there long enough to enter the most expensive part of development: Phase III. This is roughly the halfway point in terms of R&D costs. Thus, Goozner's estimates, with failures included, are probably around $500-$667 million, consistent with, if not higher than, the proper out-of-pocket comparator of $403 million.

Unaware that he has presented data that contradict his own thesis, Goozner cites a study by the Global Alliance for TB Drug Development *projecting* what it *might* cost to develop a new, more effective anti-tuberculosis drug, including failures. Goozner embraces their out-of-pocket estimate of $115-$240 million without noting that their clinical protocol calls for only six studies and 1,368 patients. The average new drug in the mid-1990s required 68 studies and 4,237 patients. Goozner's readers, unaware of this discrepancy, are led to make another inappropriate comparison. Tripling the number of patients used by Global Alliance would have roughly doubled their costs to $230-$480, supporting the $403 million figure once again.

Goozner cites the estimates of drug development costs by Public Citizen, an advocacy group founded by Ralph Nader. Goozner, however, in still another fallacious comparison, cites Public Citizen's figure for all new drugs ($108 million out-of-pocket, including failures), rather than their $227-million estimate for NMEs. Although this is about half of the $403 million out-of-pocket costs, Goonzer's readers believe the discrepancy to be much greater. They are comparing the $108 million out-of-pocket that Goozner erroneously cites to the $800 million in capitalized costs.

Goozner notes that Ernst and Young found fault with the Public Citizen's methodology, as I did. But Goozner discounts this prestigious accounting firm's analysis. After pulling the wrong figures from the Public Citizen study, he somehow feels knowledgeable enough to challenge the whole idea of capitalizing drug development costs, a standard accounting practice. Does Goozner really believe that there is no cost involved in sinking millions of dollars into a development program of 14 or more years before receiving a cent in return?

Some of Goozner's mistakes are downright embarrassing, coming as they do from an award-winning journalist. "The basic guidelines for approval have not changed much since 1962," he claims on page 253. "Subsequent changes have shortened the time it takes to get new drugs to market."

In fact, the time it takes to get new drugs to market has increased steadily since 1962, owing to the "regulatory creep" associated with the 1962 Kefauver-Harris amendments. Development times, stable at about 4.5 years prior to the amendments, rose to 8.1 years in the late 1960s, and to 11.6 years in the 1970s, 14.1 years in the 1980s, and 14.2 years in the 1990s. Goozner has confused the time that it takes to get new drugs to market–the total development time–with the time it takes the Food and Drug Administration (FDA) to review studies mandated by the regulations (approval times). In spite of the one-year decrease in approval times due to 1992 legislation, it takes drugs longer to get to market than ever before.

Regulatory impact on drug development times is no secret. Congress passed the Waxman-Hatch Patent Restoration Act in 1984 to give manufacturers back some of the patent time lost because of "regulatory review time," which averaged about 86 percent of total drug development time. Might this high temporal regulatory burden contribute to today's pharmaceutical prices? Goozner never considers this possibility, since he erroneously believes that development times, especially the size of the regulatory component, are on the wane.

Most readers will not have the analytical or historical background to

recognize Goozner's errors, only a few of which can be detailed here. Perhaps they will perceive Goozner's bias when he refers to industry scientists as "private expropriators," and their university equivalents as "public-spirited" (p. 79).

When Goozner recommends that the National Institutes of Health (NIH) "conduct clinical trials that compare existing medicines" (p. 251), readers may recall that he characterized the same studies, when undertaken post-approval by pharmaceutical firms, as wasteful marketing expenses.

In summary, Goozner's book is a "me-too" industry-basher based on serious errors, oversights, and omissions. Goozner may have some relevant points, but my confidence in his accuracy was shaken by his frequent misleading comparisons and the gravity of his mistakes. He would be well advised to have someone who is knowledgeable in drug development look over his future manuscripts and give him some constructive feedback.

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On The Take: How America's Complicity with Big Business Can Endanger Your Health, by Jerome P. Kassirer, M.D., 251 pp, hardback, $28, ISBN 0-19-517684-7, New York, N.Y., Oxford University Press, 2004.

Aimed at a wide audience from physicians to their patients, administrators in health services, legislators, and others, this book is a staggering exposé of financial conflicts in medicine and its consequences for both cost and health. The tone is even-tempered, and many conclusions are formulated by questions for the reader. Fact dense, academically referenced, well indexed, *On The Take* is, nevertheless, easy to read. A former editor-in-chief of the *New England Journal of Medicine,* Dr. Kassirer is a consummate insider with an all-encompassing view of medicine, concentrating here on bribery and other influences on medical practice perpetrated by Big Pharma. In this review, that term will include producers of medical devices and tests as well as drugs. Dr. Kassirer does not use the term, but names specific companies and other organizations wherever possible, as well as individuals.

From pens and pads to personal digital assistants (PDAs) and meals, cruises, airline miles, and fake consulting arrangements, Dr. Kassirer wrote that Big Pharma has caused financial conflicts in many physicians and others willing to be "on the take." Many of the consulting arrangements are to give talks, ostensibly based on good medical science, that actually overpromote a product. Much of this is shown to occur at continuing medical education (CME) courses and symposia sponsored by Big Pharma in which gifts are freely dispensed, reprints of journal articles favorable to products are handed out, and financial ties of the "consultants" giving talks are minimized or concealed. Dozens of actual examples are given.

Trying not to alienate most of the medical profession, Dr. Kassirer wrote that most physicians are basically ethical and went into the profession for nonfinancial as well as financial reasons. Reductions in income with increased workloads due to inadequate compensation from health maintenance organizations (HMOs) and Medicare were given as some of the reasons so many physicians have looked outside normal practice for income. He did not take the step, obvious to many in AAPS, of advising physicians to stop participating in Medicare or HMOs.[1,2,3] Some examples are given of physicians who actually boast about services rendered for Big Pharma.

Academic researchers are shown to be tainted as well. By being encouraged by their universities to obtain contracts with overhead from Big Pharma, they must do research that helps in product development, which may not involve a clinically useful new discovery. Such contracts may have provisions that delay, prevent, or pollute the publication of results. When a product possibility from a government grant is seen, federal legislation passed 20 years ago allows the researcher to patent discoveries, form a company, and do clinical trials on his own potential product. While this may have led to valuable results, the potential for bias at every step due to financial conflict is clearly laid out. The time required may also detract from teaching, serving patients, or bias-free participation on committees.

Journals fare little better at avoiding financial conflicts. Even the prominent *Journal of the American Medical Association, New England Journal of Medicine,* and *Annals of Internal Medicine,* according to Dr. Kassirer, are not beyond the pervasive Big Pharma advertising. Papers that may have been ghost-written by Big Pharma on clinical trials with selectively favorable results are published, often with misleading presentation of data.[4] Editors and peer reviewers may have ties to Big Pharma. Editorials and comments in medical journals may be written by authors with financial conflicts of interest. Revealing such conflicts is mostly on the honor system at present.

Clinical guidelines for physicians are promulgated by committees whose members often have close ties to Big Pharma. The products included in formularies of HMOs, Medicare, and other insurers are influenced by Big Pharma through physician consultants. The legendary lobbying efforts of Big Pharma are mentioned. Dr. Kassirer did not seem to address the degree of influence of Big Pharma on the Food and Drug Administration (FDA), as others have done.[5]

Far from quitting with the devastating description of how bad things are, he goes on to make 10 specific suggestions for reform, and seven more proposals for discussion, while being very realistic about their likelihood of success in eliminating certain conflicts without federal action. He lists many desirable changes: accepting no gifts at all from Big Pharma; boycotting meetings and symposia (including CME) sponsored by Big Pharma; mandating disclosure for all financial ties; and selection of journal editors, officers of medical societies, and leaders of medical schools who have no financial conflicts. Dr. Kassirer is sure that such individuals exist. He suggests that the Institute of Medicine of the National Institutes of Health draft principles and guidelines for avoiding all types of financial conflicts, not just in research grants.

On the downside, he dropped a few hints that he considers many major classes of drugs, including antihypertensives and antihyperlipidemics, to be more beneficial than they actually are[6] and alternative practices in general to be of little worth.[7] These are very minor blemishes on one of the great exposés of all time, the *Unsafe at*

Any Speed of the medical madness in the United States today.

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[1] Huntoon LR. Medicare: incompetence-based bureaucracy. *J Am Phys Surg* 2004;9:102-103.
[2] Paul R. A free-market approach to medical privacy. *J Am Phys Surg* 2004;9:18-20.
[3] Pavey C, Leithart PW, Quinlan D, Jordan WD, Caine CW, Orient JM. Fighting to preserve private medicine: the role of AAPS. *J Am Phys Surg* 2003;8:19-25.
[4] Kauffman JM. Bias in recent papers on diets and drugs in peer-reviewed medical journals. *J Am Phys Surg* 2004;9:11-14.
[5] Angell M. *The Truth About the Drug Companies. How They Deceive Us and What to Do About It.* New York, N.Y.: Random House; 2004.
[6] Kauffman JM. Drugging cardiovascular disease. *J Am Phys Surg* 2004;9:98-99.
[7] Kauffman JM. Alternative medicine: watching the watchdogs at Quackwatch. Website review. *J Sci Exploration* 2002;16:312-337.

Miracle Cure–How to Solve America's Health Care Crisis, and Why Canada Isn't the Answer, by Sally C. Pipes, 219 pp, softback, ISBN 0-93688-92-1 (Pacific Research Institute), ISBN 0-88974-212-5 (Fraser Institute), San Francisco, Calif., Pacific Research Institute, 2004.

This may well be the best book detailing what ails both the American and Canadian medical systems. Sally Pipes, president and chief executive officer of the Pacific Research Institute, is a Canadian who has written an insightful book in a very accessible style, with the mainstream audience in mind.

From the outset the author clearly states that both systems are plagued with problems, which have been brought to light by the motion picture industry. U.S. consumer frustration is depicted by the movie, *As Good As It Gets*, and that of Canadians by *The Barbarian Invasions*.

What sets this book apart from many others in the genre is the author's ability to diagnose the disease that afflicts both countries: "dysfunctional government policies and regulations." In other words, the disease comes from the virus of socialism, which has infected both sides of the border. If that is the case, it follows that the cure is not to inoculate with more of the virus, but to infuse a strong dose of the principles of liberty.

Unlike the American news media, the book exposes the fallacies of the Canadian system. Such exposure is likely to dampen anyone's enthusiasm for a single-payer system.

The book is in two parts. The first discusses the U.S. system; the second, the Canadian. Each considers affordability, access, and quality. While "supporting the three basic human health care needs," the reader is reminded that the goal is to recommend "practical and achievable changes." That is to say, her recommendations for change are actually possible, though not necessarily ideal.

The examples in the first part show how "Washington policy makers are bipolar when it comes to health policy." In other words, Washington has long advocated policies that encourage the growth of medical care, and then tried to impede growth.

For example, "in the 1960s, government planners projected a physician shortage and proceeded to pump billions of dollars into medical schools." Three decades later, "[i]n the Balanced Budget Act of 1997, Congress devoted taxpayer money to pay hospitals to reduce the number of physicians they train." All students of free markets will readily recognize this foot-on-the-gas, foot-on-the-brake conundrum as another example of government's inability to garner the information required to allocate scarce resources rationally. Additional mistakes–involving the tax code, employer-based health insurance, managed care, litigation, and pharmaceuticals–are succinctly and aptly described.

Important economic principles–such as opportunity, costs, price discrimination, and fixed and marginal costs–are described with such clarity that even a reader untutored in economics can readily comprehend them.

The second part of the book indicts the Canadian medical system for failing to pass the litmus test of providing access, affordability, and quality. Access is hindered by government-engineered queuing; affordability is an unconscionable travesty when all costs including opportunity costs are factored in; and quality is as described by a Canadian doctor, who said that "Canada has some of the best medicine the 1970s can provide."

Pipes agrees with the advocates of the single-payer system for correctly pointing out that Canadian doctors are not second-guessed by managed-care companies. But, what advocates fail to mention is that Canadian doctors "are constrained not by proscriptive regulations, but by lack of resources."

She points out that proponents of single-payer shamelessly transfer the blame for the failed Canadian system onto the United States. "As incredible as it may sound, some defenders of the Canadian system blame the United States for raising the expectations of the Canadians."

Dr. Alfons Pomp, a laparoscopic surgeon, described another irrationality of the Canadian system: "You bring money in. The patient is a source of revenue (in the US), whereas in Canada, the patient is a source of expense. So it's to the hospital's benefit to reduce costs [by] doing the least amount of operations as possible, as paradoxical as that seems." American doctors will recognize this flawed incentive structure from their experience with managed care, which places doctors at financial risk for treating the sick. In brief, the differences between both systems may be more imagined than substantive.

Sally Pipes concludes by stating, "for all the vaunted differences between the health care systems in the United States and Canada, they both suffer symptoms of the same disease–the disease of central control. The cure is to open both systems to competition and consumer choice."

Her book may be the best antidote for those shortsighted Americans addicted to a revamped managed-care or single-payer system. It may also serve as the impetus to jettison the failed bromides on both sides of the border, in order to pave the way to restoration of a genuine free-market system.

All legislators, physicians, and patients interested in comparing the two systems should read this book, and realize that when analyzed this way, they may share more similarities than differences.

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How to Talk to a Liberal (If You Must), by Ann Coulter, 344 pp, $26.95, ISBN 1-4000-5418-4, New York, N.Y., Crown Forum, 2004.

Ann Coulter, a syndicated columnist and the legal correspondent for *Human Events*, is one of today's most effective conservative pundits, though she identifies herself as a "middle-of-the-road moderate."

Her book is a delightful series of vignettes, largely taken from her columns, in which she exposes liberal ideology and the liberal mentality. Her many topics

include "9/11" and the "War Against Terror," the "Nanny State," gun control, the "Crusade Against Capitalism" by *The New York Times,* the "Robert C. Byrd Bridge to Poverty," and the Elian Gonzalez case ("the Left's Last Stand for Communism"). Her chapter on "The Battle Flag" (the Confederate flag) is a poignant discussion of the issues faced by the Confederacy, as well as a fascinating look at the culture of the South, which alone is worth the price of the book.

Coulter observes that we live in a Nanny State that takes care of us from cradle to grave, and that steals half our income. She would eliminate the departments of Health and Human Services, Education, Commerce, Agriculture, Housing and Urban Development, and Transportation; the National Endowment for the Arts; and the National Endowment for the Humanities. In addition, she would replace the progressive income tax with a flat tax.

About half our citizens strongly believe they have the right to bear arms. Even though victims in this country use guns about a million times a year against predators, liberals believe guns don't make people any safer. But if we had a world without guns, we would need a world without violence, and this is out of the question, Coulter asserts, because "the world is half male and testosterone causes homicide." She notes that if the courts interpreted the Second Amendment the way they interpret the First Amendment, we would have the right to bear nuclear arms by now.

Coulter's favorite newspaper is the "Treason Times" (*The New York Times*) with its liberal columnist Maureen Dowd and its star reporter Jayson Blair. Its style is "inimitable Stalinist," it promotes "bald-faced lies," and it has become "…America's leading spokesman for the deposed Baathist regime in Iraq."

Senator Robert C. Byrd (D-WV) has built a series of shrines to himself, paid for by taxpayers. Coulter lists several: the Robert C. Byrd Highway, the Robert C. Byrd Locks and Dam, the Robert C. Byrd Institute, the Robert C. Byrd Life Long Learning Center, the Robert C. Byrd Honors Scholarship Program, the Robert C. Byrd Green Bank Telescope, and about 11 more, including a courthouse, a health sciences center, a technical center, a federal building, a street, an office complex, and a library. Coulter concludes that nearly every slab of concrete in the state is named after Bob Byrd, but West Virginians in need are crying out for even more federal projects named after the senator. She worries that he can't rest as long as there may still be a toilet without his name on it.

Her most insightful observations describe liberals and the liberal mentality. For starters, liberals are morally and intellectually superior, good-looking, witty, compassionate, and always right–"Bob Byrd, Jerry Nadler, Al Franken, and Hillary Clinton rolled into one adorable bunch." They are absolutely convinced that there is one set of rules for them, but a completely different set of rules for you and everyone else. They openly admit to being philanderers, draft dodgers, liars, weasels, and cowards. They take a dim view of the family, deem fathers positively malignant, and glamorize single motherhood.

Liberals can win only by cheating or by using force. They refuse to argue: they will change the topic, interrupt, filibuster, heckle, shout down conservative speakers, use physical intimidation, unplug reporters' microphones, and trash and burn student newspapers. They are the "loony left," the "know-nothing crowd," and "fatuous idiots," who thrive on ignorance. If they knew any facts, or cared about ideas, they would cease being liberals, Coulter writes.

Liberals hate the wealthy and they hate America. Their favorite country is the late USSR. They can't understand the advantages of free markets, or the disastrous effects of central planning. They believe the real business of government is redistributing income.

They use their control of the media to lie to us. They don't understand that a lie is something that is intentionally not true. Every day they create a new narrative that destroys the past as it occurred. All their phony policy statements are the opposite of what they really believe. "Be nice to people" means "raise taxes on the productive."

Liberals are against waste–they tell us to conserve from their Gulfstream private jets. Coulter's answer is that we should make cars and airplanes that run on hot air and run a pipeline from the Capitol.

Finally, it is conservatives' obligation to surrender whenever liberals bully them. Otherwise liberal lips quiver, they start crying, and they claim you've injured them cruelly.

Arguing with a liberal is hopeless, she says. But Coulter offers 10 rules to help: (1) don't surrender up front; (2) don't be defensive; (3) outrage the enemy; (4) never apologize; (5) never compliment a Democrat, since compliments always are returned with insults, and it's not worth the time trying to find something nice to say; (6) never show graciousness, since any kindness will be used against you; (7) never flatter a Democrat; (8) don't succumb to liberal bribery, since Faustian bargains are a bad deal; (9) be ready to have your career destroyed if you have any secrets; and finally, (10) encourage liberals in transition–they might get killed before they can move to the other side.

The author accurately characterizes modern liberalism in an entertaining style. But she doesn't explain why liberalism has been able to survive the collapse of socialism (the most conspicuous failure in history), nor does she advise what we might do to fight it.

Men cannot abolish the laws of nature, nor can superstition replace reasoning and science. Liberalism (socialism), one of the most disastrous sets of ideas ever conceived, is at war with civilization. Instead of achieving human happiness and welfare, it has immeasurably increased the suffering of humanity and destroyed millions of lives. It is a utopian illusion based on a false religious faith. This is why rational argument with a liberal can never be effective.

How to Talk to a Liberal documents the tragic result of our system of government-controlled public schools. Promotion of liberalism's ideas over many decades has dangerously weakened our cultural values. We could correct this by insisting that our young citizens and students, who are not yet committed to the religion of liberalism, be taught to think and reason.

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Let Them Eat Prozac: The Unhealthy Relationship Between the Pharmaceutical Industry and Depression, by David Healy, M.D., F.R.C.Psych., 351 pp. hardback, $25, ISBN 0814736696, New York Univ., N.Y., N.Y.U. Press, 2004.

In *Let Them Eat Prozac*, former secretary of the British Association for Psychopharmacology, Dr. David Healy, has produced a watershed critique of Prozac and that whole class of antidepressants now known to the world as SSRIs (selective serotonin reuptake inhibitors).

Dr. Healy lays out a succession of questionable clinical trials, unreported (or under-reported) anomalies and risks, digressions from standard methodology, and misleading marketing ploys that promoted a new genre of drugs supposedly targeting not only depression, per se, but a panoply of nonrelated phenomena–general anxiety disorder (a.k.a. social phobias), panic disorder, obsessive-compulsive disorder, obesity, and even "pain syndromes."

The author details how early trials indicated that fluoxetine (the primary compound in Prozac) might have no antidepressant advantages. He cites a succession of experts who, from the beginning, offered little confidence in fluoxetine as an antidepressant. Among them were H. Y. Meltzer, a clinical researcher who "found little or no effect on depression," and German regulators who, in May 1984 communicated to Eli Lilly's American counterparts: "Considering the benefit and the risk, we think this preparation totally unsuitable for the treatment of depression."

It took drug development veteran Irwin Slater to get the product moving again–for obesity. Dr. Healy indicates that, if a drug is seen to have transfer value to other medical conditions, then it becomes a "cash cow" to fund other research projects–while lining the pockets of manufacturers and shareholders.

When Paxil was licensed in the United States and Britain, Dr. Healy writes that among the supposed advantages of *selective* serotonin reuptake inhibitors was the implied capability to target *specific* chemicals in the brain. But "[c]linicians were misled," he states, "if they thought 'selective' meant that these drugs acted on only one brain site." Like so many others, that term turned out to be a semantic gimmick.

Dr. Healy reveals that data from various clinical trials, beginning early on, showed numerous incidences of self-harm, "explosive episodes," and suicidal behaviors–too many, he suggests, to be coincidental. Such actions were between 1.5 and 3.2 times higher in the under-18 age group taking Seroxat (paroxetine) as opposed to a placebo.

Like all of his books, *Let Them Eat Prozac* is extensively footnoted and meticulously researched. Yet, it remains fast-paced and readable. One doesn't require a medical degree to comprehend it, nor does it bog down the reader in jargon.

The author provides background information on the emergence of antidepressants and explains how clinical trials have "morphed" into highly targeted sales pitches, incurring legal battles–followed by grudging admissions from certain pharmaceutical companies that vital information was concealed or obscured.

Dr. Healy's case against Prozac (and other SSRIs) rests largely on the industry's failure to establish cause and effect. That, in turn, he says, is because psychopharmaceutical companies increasingly have strayed from the scientific method, as government funding of medical and pharmacological research dwindled in the 1970s. This had a particularly negative impact on independent clinical trials, he writes, and marketing/public relations (PR) firms were called in to fill the void. The strategy employed by these PR agents has been to *create a demand* for products, thereby generating a slush fund for research.

One of the more devious means of accomplishing this task entails "molding public opinion" via public "educational" or "awareness" campaigns. These serve in reality as advertisements for illnesses, says Dr. Healy, many of which are misrepresented. He writes how "patient [activist] groups…are the perfect conduits for generating views among the 'informed' general public, such as the idea that depression is known to be a chemical imbalance in the brain." He describes how conferences are held for marketers and product and brand managers to teach "how to successfully create targeted patient education campaigns, establish expertise in disease areas and increase company profile."

One concept produced from these campaigns was that Prozac has weight-reducing properties. This notion "helped Prozac to hit the road running in 1989," writes Dr. Healy. Another PR-generated assumption, which directly affected primary-care clinicians, was "the idea that behind every case of anxiety lay a case of depression."

Anti-anxiety drugs (technically, benzodiazepines like Valium) were known, of course, to lead to dependency, but Prozac, in particular, was pronounced free of that disadvantage–thereby implying a causal link between anxiety and depression–*even though no such link had been established*.

In the sloppy-science department, Dr. Healy reveals that Prozac was assessed for negative reactions among depressives compared to *other antidepressants*, but ***not*** for *total numbers* of side-effects with persons *who had never taken a* ***different*** *antidepressant*. Additionally, Prozac was almost exclusively tested among hospitalized depressives, but ***not*** among *non-hospitalized* depressives, which turns out to be the bulk of those to whom it was eventually prescribed.

It is the *mild* depressives, says Dr. Healy, who typically are seen by primary-care physicians, and the pre-treatment rate for suicide among *that* group was a surprising *flat zero* per 100,000 patients.[1] So when the sudden impulse to take one's life among mildly depressed persons on Prozac shot way up, the psychiatric and pharmaceutical community was left clueless.

Dr. Healy also discusses the self-serving methods of pharmaceutical companies involved in clinical trials for SSRIs. He quotes the US Food and Drug Administration's Paul Leber:

> How do we interpret…two positive results in the context of several more studies that fail to demonstrate that effect?…The sponsor could just do studies until the cows come home until he gets two of them that are statistically significant by chance alone, walks them out and says he has met the criteria.

Dr. Healy is a master at nailing finer points often missed by laypersons; for example, that two positive studies don't "mean the drug works for depression in two studies. It means there are two studies in which the drug can be shown to have an effect in depression–[i.e.,] can be shown to do *something*. Whether it is a good idea to take any of these drugs is not addressed."

In another key point, he refers to the *intensity* of aberrant behaviors under antidepressant drugs being something new. "Nobody had ever seen anything like it," says Dr. Healy. ***"A certain something happens in 60 percent of patients."***

Sadly, while debate rages in the United States and United Kingdom over the possible culpability of SSRIs in highly publicized incidences of violent aggression and suicide, the question of the role of impulse control vis-à-vis these new "brain stressors," as Dr. Healy refers to SSRIs, apparently has not been one that researchers are anxious to pursue.

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REFERENCE

[1] Healy D. *Let Them Eat Prozac*. New York, N.Y.: NYU Press; 2004:100, citing Simon GE, Von Dorff M. Suicide mortality among patients treated for depression in an insured population. *Am J Epidemiol* 1998;147:155-160.