Book Review

Conflicts of interest and the future of medicine: The United States, France and Japan

Marc A. Rodwin
Oxford University Press, New York, 2011, 392pp., $29.95(01), ISBN13: 978-0199755486, ISBN10: 0199755485

Journal of Public Health Policy (2011) **32**, 391–398. doi:10.1057/jphp.2011.19

Too little attention has been given to conflicts of interest, even as they overcome our most basic medical commitment: to care for those who need it. As they constitute a crisis of credibility for the medical profession, conflicts of interests can no longer be ignored. We cannot mask our failure to develop clearer thinking about conflicts of interest.

Marc Rodwin, a professor of law at Suffolk University, provides us a huge book, *Conflicts of Interest and the Future of Medicine*, in which he examines the situation in France, the United States, and Japan. For each country, he presents a long history of the organization of medical practice – beginning in the Middle Ages for France. This precedes a description of the interplay among organized medicine, the market, and the state. The last chapter has two parts: a summary of strategies 'to cope' with conflicts of interest; and comments on the role of professionalism. Encyclopedic, but for this reader, the book was frustrating!

Amazingly, Rodwin ignores the credibility crisis. Fewer and fewer patients, and even fewer physicians, trust today's evidence-based medicine. Witness the epidemic of 'alternative medicines', an oxymoron. To me, the cause is clear: the pharmaceutical industry and too many doctors present benefits while masking risks. They resort to misleading sensationalism, rather than presenting the relevant information for a balanced picture.

A high impact factor journal, for example, recently reported that consumption of fruit lowered by 22 per cent the risk of fatal ischemic heart disease.[1] What was not said was that to avoid one death, 500 people would have to eat eight portions (80 g each) of fruits and vegetables daily for 8.4 years – more like a chimpanzee's diet. Yet, in

the same study 24 per cent of the participants were smokers, the leading avoidable cause of both heart disease and cancer. Here we have more sensationalism than science.

The benfluorex (Médiator*) scandal in France revealed thousands of deaths, plus tens of thousands of patients with new valvular heart disease. Benfluorex, related to fenfluramine (Redux*), had escaped the worldwide withdrawal in 1997 of that family of drugs. In Italy and Spain, survival on the market was short. However, despite specific French pharmacovigilance reports starting in 1999, articles in the independent drug bulletin, *Prescrire*, and other warnings, France withdrew the drug only in 2009. Then more than a year passed before France issued a warning to patients and health-care professionals that urged screening for valvular heart disease in all who had received benfluorex.

Why, for 12 years, were French doctors allowed to prescribe benfluorex? In 2006, the Haute Autorité de Santé (HAS) approved renewal of reimbursement by the National Health Insurance Fund. Misuse, severe adverse effects, and links to a family of banned drugs – all described in the working papers – vanished from the final evaluation report from the Transparency [*sic*] Committee of HAS.

In Rodwin's book, I can hardly find the patients. He seems to have missed the principal consequence of conflicts of interest. Doctors cannot do their jobs properly when the patients' interests no longer come first. Patients will be harmed.

Conflicts of Interest: Interplay at Three Levels – Doctors, Regulatory Agencies, and Industry

Doctors are the first level, and they display both *cupidity* and *ignorance*. For *cupidity*, The *New York Times*[2] revealed an Abbott executive's e-mail celebrating a day in August 2008, 'the biggest day he remembered hearing about'. On that single day, Mark Midei inserted 30 Abbott cardiac stents. Two days later, an Abbott sales representative paid for a US$2,000 barbecue dinner at Midei's home. People do not need all the stents and other procedures they receive. Unneeded procedures still carry the same risks. Among patients receiving implantable cardioverter-defibrillators, for example, more than one in five do not meet evidence-based criteria for implantation.[3]

For *ignorance*, the ASTRAL (Angioplasty and Stent for Renal Artery Lesions) trial reveals that evidence is more important than hope. Despite inadequate assessment, dilating and stenting renal arteries has spread like wildfire since the 1980s. As many as 45 000 patients per year receive the procedure in the United States. Only in 2009 did patients learn that these vascular procedures provide no benefit over drug treatments. They had been at risk of serious complications (23 per 400 patients, including two deaths and three amputations).[4] Doctors used stents where there was little evidence of benefit and no evaluation of harm.

In the United States, the Food and Drug Administration (FDA) has strengthened an independent review and approval process for medical devices. In contrast, the Afssaps, the French FDA, has pledged not to conduct evaluations and has close ties to industry. These links are evident in a book on medical devices given to medical practitioners by Medtronic, a device maker. The preface is written by Afssaps' chief executive officer. Another of the book's authors is director of regulatory affairs at Medtronic, and a third directs evaluation of medical devices at the Afssaps.[5]

Ignorance is magnified by *pride*. Doctors should confess that in many cases they cannot cure. They often fail to take the time to care. Pride can also lead to drama. In one horrible development in France, premature babies were damaged or died as implementation of evidence crept far too slowly into clinical practice. An influential senior clinician attacked critical evidence about risks associated with prescribing corticosteroids, largely because the research was done by a competing team of researchers.

Initial treatment for localized prostate cancer, for which there are no conclusive comparative studies, depends on whom the patient sees – a urologist or a radiation oncologist. These specialists have invested in costly equipment that offers only marginal benefit. In contrast, men seen by primary care physicians are more likely to be managed with *watchful waiting*. (Fifty-eight of those who consulted a general practitioner after seeing a urologist benefited from watchful waiting versus 7 per cent who only saw the urologist.[6])

Regulatory agencies and their experts constitute the second level in conflicts of interest. *Benchmarking* is a simple method to find conflicts of interests far more efficiently than disclosure. One can compare decisions, presumably based on similar information, by the HAS in

France and the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom. NICE rejected reimbursement for vinflunine, a fluorinated Vinca alkaloid, whereas the HAS allowed it.[7] (The US FDA did not approve it.) For Alzheimer's disease, the HAS promoted a new paradigm in 2007: the 'structuring role of the drugs in patient care'. It rated donepezil an 'important benefit for the patient', the highest score possible. NICE, on the other hand, warned against the lack of proven effect on relevant outcomes and the presence of adverse effects, restricting donepezil's use to clinical trials. What conflicts of interest explain these regulatory lapses?

Freedom of information rules are not in place. Europe and regulatory agencies make great efforts to conceal information from the public. *Prescrire* tried to obtain the scientific analysis of rimonabant from the European Medicines Agency (EMEA). The EMEA refused the first request. In response to a second request and following a long delay, the EMEA sent an expurgated document, where only two pages out of 68 could be read.[8] Whom does this practice protect? Surely not the patients.

Industry constitutes the third level of conflict of interest. Public Citizen, a US NGO, observed that 'While the defense industry used to be the biggest defrauder of the federal government under the False Claims Act (FCA), a law enacted in 1863 to prevent military contractor fraud, the pharmaceutical industry has greatly overtaken the defense industry'. Settlements under the law for criminal and civil monetary penalties reached a total of $20 billion in penalties between 1991 and 2010; three out of four of the settlements and penalties occurred in the past 5 years.[9]

The pharmaceutical industry spends endlessly on 'education' (sales representatives and gifts), but that is only the tip of the iceberg. At present, libel laws are being used by industry to gag those who offer independent information. In 2006, the Laegemiddel Industri Foreningen (Danish Pharmaceutical Industry Association) sued researchers, four of whom worked for the Nordic Cochrane Centre.[10] In 2007, in France, AstraZeneca sued a regional National Health Service unit for libel because it had told physicians that rosuvastatine had no proven effect on either stroke or heart attack, and moreover that adverse renal effects had been seen. In 2011, Atsellas Pharma sued *Prescrire* for libel for scientific information it published about tacrolimus, a drug sufficiently dangerous to carry a 'black box warning' in the United

States. (These warnings that appear on package inserts for prescription drugs, which may cause serious adverse effects, do not exist in France).

Wealthy corporate plaintiffs who use Strategic Lawsuits against Public Participation do not care about the judgments handed down by courts. The plaintiff always wins. His goals are to (a) impoverish the already poor defendant with lawyers' fees; (b) intimidate others who might speak out; (c) create a platform for their paid key opinion leaders, who may also sit on official assessment committees.

Strategies: Rodwin presents six strategies, for 'coping with conflicts of interest'; plus a chapter on professionalism. To me, the term *coping* seems like rearranging the deckchairs on the Titanic. I find it unacceptable to 'cope' with conflicts of interest. This is war; a cause not amenable to 'coping'.

No doubt, laws can help. But they must be clear, implemented with investigative powers and adequate penalties, and regularly updated. Nevertheless, they may be ineffective. Laws may increase our awareness, but are no guarantee that justice will be done. Laws and regulations neither prevented fraud nor assured fairness in the financial industry. The Sarbanes–Oxley Act of 2002, governing accounting practices in the United States, did not prevent the Enron and Andersen Consulting (now Accenture) scandals. Laws and policies may, in fact, give a false sense of security.

Professionalism can be summarized easily: loyalty to the patient. The simplest and most effective initiative is 'No free lunch'.[11] In February 2010, *Emergency Medicine Australasia* announced that it had 'stopped all drug advertising forthwith'[12] and called on similar publications to do the same. It is easy to avoid conflicts of interest where there is the will to do so.

Evidence-based medicine is still a dream. In France, at least 10 per cent of doctors practice *alternative medicine*, some exclusively. Afssaps assiduously issued pharmacovigilance warnings following a mix-up of two homeopathic products, each containing no more than water and sugar, which differed only in the labels. Yet Afssaps failed, for more than a decade, as I described above, to withdraw benfluorex.[13]

Frightening graphs, alarming and tricky statistics, sometimes called disease mongering, turn otherwise robust people into hypochondriacs. They crave pills, surgery, and behavioral constraints. Healthy Skepticism, an international membership association coordinated by Peter

Mansfield, aims to improve health by reducing harm caused by misleading health information.[14] Wisely, No Free Lunch and Healthy Skepticism are merging.

Consumer groups must act to protect the public interest, proactively educating themselves and recruiting their own experts. Life is about interests. Lobbies, neither clever nor honest, do protect their interests. Patients must organize themselves similarly and protect their interests. Worryingly, more and more groups now receive industry funds. Many countries allow drug and device companies to communicate directly with patients about their products. Class actions lawsuits, as used in the United States, may foster consumer protection; but sadly, they are almost impossible to pursue in France (and this is probably not a matter of chance).

A more comprehensive arsenal of tools or laws, as is available in the United States, is needed, but only as a start. Law *per se* does not change society. Laws arise from collective consciousness. If collective consciousness does not change, the law will not change the society. The legal arsenal begins with laws such as:

(a) The Freedom of Information Act in the US.
(b) The False Claim Act (1863) and the Lloyd-La Follette Act (1912).
(c) Freedom of speech and opinion, as protected in the Article 19 of the Universal Declaration of Human Rights: Everyone has the right to freedom of opinion and expression.

In many European countries at present, independent experts and doctors who highlight problems in the health service are facing more and more severe and organized attacks.[15] According to Einstein, 'the world is a dangerous place to live; not because of the people who are evil, but because of the people who don't do anything'. In some parts of the world, whistle-blowers efficiently protect the people.[16] Thus, they are attacked.[17] They need protection.

C*orruption* – a euphemism for conflicts of interest – can be found everywhere. In the United States, the government prosecutes corruption, whereas in many European countries, such as France, government hands out reprimands. Is there a stronger will to fight unacceptable behavior in the United States? As far from perfect as the United States may be, it remains a great example for more concerted pursuit of corruption, based on democracy and freedom.

Before closing the book, I must mention the last thing, the index. I did not find any of the following: *benchmarking, lobby, key opinion leader, disease mongering, and whistle-blowing*.

Editors' Note

We asked Alain Braillon to review Professor Rodwin's topical book, because in France, Dr Braillon has been at the center of a national controversy. The French Ministry of Health removed him from a post as a hospital-based senior consultant in public health (a tenured position), overturning a vote by the National Statutory Committee to retain him. His heartfelt essay may say more about his experiences than about Professor Rodwin's book.

References

1. Crowe, F.L. *et al* (2011) Fruit and vegetable intake and mortality from ischaemic heart disease: Results from the European Prospective Investigation into Cancer and Nutrition (EPIC) – Heart study. *European Heart Journal*, advance online publication 18 January, doi:10.1093/eurheartj/ehq465.
2. Gardiner, H. (2010) Doctor faces suits over cardiac stents. *The New York Times* 5 December: A15, http://www.nytimes.com/2010/12/06/health/06stent.html, accessed 16 March 2011.
3. Al-Khatib, S.M. *et al* (2011) Non-evidence-based ICD implantations in the United States. *Journal of the American Medical Association* 305(1): 43–49.
4. ASTRAL Investigators *et al* (2009) Revascularization versus medical therapy for renal-artery stenosis. *The New England Journal of Medicine* 361(20): 1953–1962.
5. Braillon, A. (2009) Medical devices and the approval processes: United States vs France. *Archives of Internal Medicine* 170(22): 2040–2041.
6. Jang, T.L. *et al* (2010) Physician visits prior to treatment for clinically localized prostate cancer. *Archives of Internal Medicine* 170(5): 440–450.
7. National Institute for Health and Clinical Excellence. (2011) Transitional cell carcinoma of the urothelial tract – Vinflunine: Final appraisal determination. 7 March, http://guidance.nice.org.uk/TA/Wave23/13/FAD, accessed 16 March 2011.
8. Editorial. (2009) L'Agence européenne du médicament censure les données de pharmacovigilance. *Rev Prescrire* 29(309): 536, http://www.prescrire.org/editoriaux/EDI33693.pdf, accessed 16 March 2011.
9. Almashat, S., Preston, C., Waterman, T. and Wolfe, S. (2010) Rapidly increasing criminal and civil monetary penalties against the pharmaceutical industry: 1991 to 2010. 16 December, http://www.citizen.org/hrg1924, accessed 16 March 2011.
10. Gornall, J. (2009) Industry attack on academics. *British Medical Journal*: 338–b736.
11. Goodman, B. (n.d.) Corporation for non-promotion-based medicine. About us, http://www.nofreelunch.org/aboutus.htm, accessed 16 March 2011.
12. Jelinek, G.A. and Brown, A.F. (2011) A stand against drug company advertising. *Emergency Medicine Australasia* 23(1): 4–6.
13. Braillon, A. (2010) Homoeopathic remedies and drug-regulatory authorities. *Lancet* 375(9711): 279–280.

14. Mansfield, P. (n.d.) Introduction to Healthy Skepticism Inc, http://www.healthyskepticism.org, accessed 16 March 2011.
15. Jordan, A. (2011) Silence is not always golden. Medical Independent 10 February: 10–4, http://www.medicalindependent.ie/page.aspx?title=silence_is_not_always_golden, accessed 16 March 2011.
16. Braillon, A. (2011) Challenging special interest groups: Whistleblowers may help. Help them! *Psychotherapy Psychosomatics* 80(2): 116–117.
17. Braillon, A. and Dubois, G. (2010) Whistleblowing and the abuse of libel law: A view from France. *HealthWatch Newsletter*, issue 79, p. 3, 7, http://braillon.net/alain/healthwatch_oct10.pdf, accessed 16 March 2011.

Alain Braillon
Gres, 27 rue Voiture, 80000 Amiens, France