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## THE RELIABILITY OF OUR MEDICAL KNOWLEDGE AS A PRODUCT OF INDUSTRY RELATIONSHIPS

*John Abramson\**

Comparing Americans' life expectancy and medical expenditures to those of the other industrialized countries hardly leads to the conclusion that we receive the best medical care in the world. Far from it. But the argument is legitimately made that Americans receive more medical treatments and procedures—like joint replacements, cataract surgeries, cardiac procedures, and the like—that improve our quality but not necessarily the length of our lives. To promote more meaningful comparisons between citizens of different countries, the World Health Organization created a more dimensional index of overall health known as Healthy Adjusted Life Expectancy (“HALE”). Calculated as the average number of healthy years of life experienced by each nation's sample population, this index represents the number of years that a country's citizens can expect to live in good health.<sup>1</sup> For example, if a citizen of one nation lives to be eighty-six, but has chronic renal failure for the last six years of life, compromising his quality of life by fifty percent, then his years of healthy life would be eighty-six minus half of six, or eighty-three.

Figure 1 shows the relationship between HALE and per person medical expenditures for the twenty-two wealthiest Organisation of Economic Co-operation and Development (“OECD”) countries. Those with the most effective and efficient healthcare systems are located in the upper left quadrant, where healthy life expectancy is greatest and per

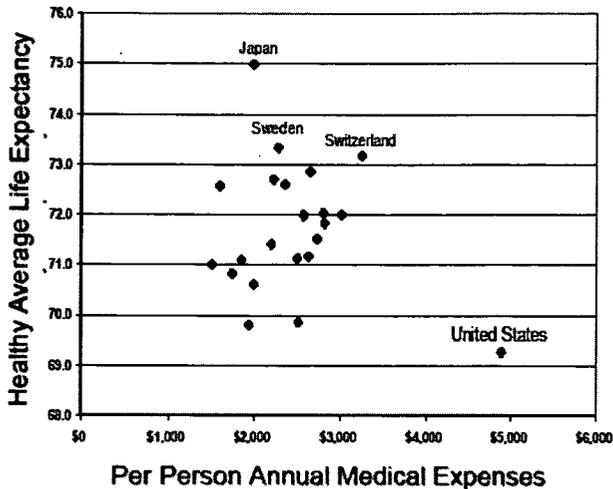
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\* Clinical Instructor at Harvard Medical School and author of *Overdosed America*. I would like to thank Hofstra University President Stuart Rabinowitz, Dean Aaron Twerski, and Professors Robert Wild, Janet Dolgin and Joel Weintraub, for hosting this important conference, providing us with the opportunity to examine the pharmaceutical industry's relationship to the “scientific evidence” that informs our medical care.

1. See WORLD HEALTH ORG., THE WORLD HEALTH REPORT 2003: SHAPING THE FUTURE 21 (2003), available at [http://www.who.int/whr/2003/en/whr03\\_en.pdf](http://www.who.int/whr/2003/en/whr03_en.pdf).

FIGURE 1

### Healthy Average Life Expectancy and Per Person Medical Expenses in 22 OECD Countries



person medical costs are lowest. Japan is a clear outlier here. At the other end of the spectrum, the lower right quadrant is where the countries with the least effective and most costly healthcare are located. Figure 1 shows that despite spending twice as much as the other industrialized countries on healthcare, Americans live the shortest amount of time in good health—averaging 2.5 years less than the citizens of the other countries.<sup>2</sup>

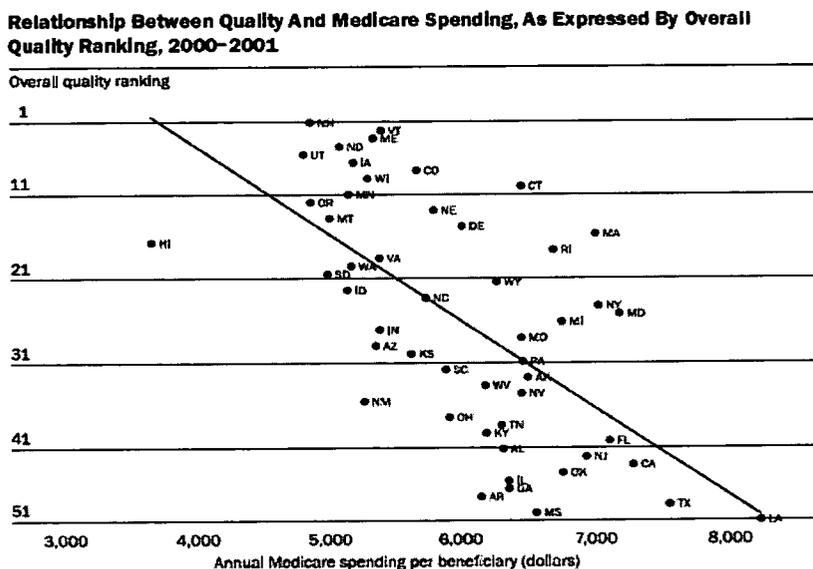
Comparisons within the United States present an equally disturbing picture. Figure 2 shows the relationship between the quality of medical care for Medicare patients and per person costs on a state-by-state basis.<sup>3</sup> The quality measures used in this study are based on widely accepted and non-controversial indicators, such as the percentage of patients

2. See *id.* at 166-69, 178-81; see also *OECD Health at a Glance—How France Compares*, OECD OBSERVER POL'Y BRIEF, Oct. 2003, at 1, available at <http://www.oecd.org/dataoecd/58/13/16073264.pdf> (detailing how France compares with other countries and finding that “health spending in France is relatively high in comparison with the . . . average”).

3. Katherine Baicker & Amitabh Chandra, *Medicare Spending, the Physician Workforce, and Beneficiaries' Quality of Care*, HEALTH AFF., Apr. 7, 2004, at W4-187 & exhibit 1, <http://content.healthaffairs.org/cgi/reprint/hlthaff.w4.184v1>.

admitted to the emergency room with pneumonia who receive an antibiotic within the first eight hours of arrival, and the percentage of patients admitted to the hospital with a myocardial infarction who are given an aspirin. States are ranked by the quality of their medical care with the best state ranked number 1, and the worst state ranked number 51 (Puerto Rico is counted as a state). Intuitively, we expect a positive correlation between money spent on healthcare and the quality of care, or that the slope of the line plotting this relationship would go from the lower left quadrant of the graph to the upper right. But the slope of the line is exactly the opposite: the greater the per capita expenditure on Medicare patients within a state, the *lower* the quality of care.<sup>4</sup>

FIGURE 2



**SOURCES:** Medicare claims data; and S.F. Jencks et al., "Change in the Quality of Care Delivered to Medicare Beneficiaries, 1998-1999 to 2000-2001," *Journal of the American Medical Association* 289, no. 3 (2003): 305-312.  
**NOTE:** For quality ranking, smaller values equal higher quality.

Researchers from Dartmouth Medical School's Center for the Evaluative Clinical Sciences looked at the variations in medical spending in the 306 Medicare regions around the country. They found that patients living in the highest spending regions received sixty percent more care than patients living in the lowest spending region, and these

4. *Id.*

differences were not explained by age, sex or disease burden.<sup>5</sup> They then looked at how patients with three distinct disease entities—first heart attack, first broken hip, and initial diagnosis of cancer of the colon—fared according to the level of spending in their Medicare region.<sup>6</sup> It turns out that patients in the higher spending regions had no better access to care, no greater satisfaction with care, no better quality of care, and actually had a higher mortality rate.<sup>7</sup> Based on this data, later researchers determined that if all Medicare patients with these three diseases received the quality of care provided in the best performing quarter of Medicare regions, we would not only save 8400 lives a year, but also \$900 million a year—better health outcomes for significantly less money.<sup>8</sup> The results of the original study were published in two very dense articles in the *Annals of Internal Medicine*.<sup>9</sup> Dr. Elliot Fisher, the lead author of this study, summarized the findings in an op-ed piece published in the *New York Times*:

Our study suggests that perhaps a third of medical spending is now devoted to services that don't appear to improve health or the quality of care—and may make things worse.<sup>10</sup>

In 2006, the United States will spend approximately \$2.2 trillion on healthcare.<sup>11</sup> In other words, we are wasting about \$700 billion a year on medical care that is either unnecessary or harmful—that is more than one and a half times the entire budget of the U.S. Defense Department, including the cost of the war in Iraq.<sup>12</sup>

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5. Elliott S. Fisher et al., *The Implications of Regional Variations in Medicare Spending, Part 1: The Content, Quality, and Accessibility of Care*, 138 ANNALS INTERNAL MED. 273, 284-86 (2003) [hereinafter Fisher et al., *Part 1*].

6. *Id.* at 273-77.

7. *See id.* at 283-85; Elliott S. Fisher et al., *The Implications of Regional Variations in Medicare Spending, Part 2: Health Outcomes and Satisfaction with Care*, 138 ANNALS INTERNAL MED. 288, 291-92 & fig.1 (2003) [hereinafter Fisher et al., *Part 2*].

8. Cathy Schoen et al., *U.S. Health System Performance: A National Scorecard*, HEALTH AFF., Sept. 20, 2006, at W469, <http://content.healthaffairs.org/cgi/reprint/25/6/w457?ck=nck>.

9. *See supra* notes 5-7.

10. Elliott S. Fisher, Op-Ed, *More Medicine Is Not Better Medicine*, N.Y. TIMES, Dec. 1, 2003, at A23.

11. C. Eugene Steuerle, Senior Fellow, The Urban Inst., Economic Challenges Facing Middle Class Families, Testimony Before the Comm. on Ways and Means 2 (Jan. 31, 2007).

12. *See* Press Release, U.S. Dep't of Defense, Fiscal 2006 Department of Defense Budget is Released (Feb. 7, 2005), available at <http://www.defenselink.mil/releases/2005/nr20050207-2066.html> (requesting "\$419.3 billion in discretionary budget authority for the Department of Defense").

Authors from the Commonwealth Fund recently published a score card on American medicine in *Health Affairs*, the premier American health policy journal.<sup>13</sup> This study established reasonably attainable benchmarks for healthcare quality, access, equity, and outcomes. According to these measures of reasonably attainable levels of performance, an optimal score of 100 in each of these areas was actually being achieved, for international comparisons, by the average of the three best countries, or, for comparisons within the United States, the best ten percent of states. Overall, American healthcare earned a score of sixty-six,<sup>14</sup> otherwise known as a straight “D”. Some examples of comparisons solidify the point: the infant mortality rate in the United States is 7.0 per 100,000 births, while the benchmark is 2.7; sixty year-old men in the United States have a 2.1 year shorter life expectancy than the international benchmark, and sixty year-old American women live 2.9 years less; the efficiency of our healthcare—how much health we get for the money we spend—earned a fifty-one, or a straight “F”.<sup>15</sup> In other words, we are wasting enormous amounts of public and private resources on suboptimal medical care.

It is important to understand that this overview of American healthcare is not just the view of an unhappy radical minority. The first chapter of the recently published book *Redefining Healthcare*, by Professors Michael E. Porter of Harvard Business School and Elizabeth Olmsted Teisberg of the University of Virginia, presents a very similar snapshot of American healthcare.<sup>16</sup>

The obvious question is: How can so many dedicated, well-meaning health professionals and policy makers proceed with healthcare as usual when the totality of their effort is so wasteful and ineffective? The answer is that the source of these problems lies deep beneath the surface of what appears to be a reasonably functioning healthcare system. Above the surface we see the more than \$4 billion in advertising that floods our airwaves, newspapers, and sporting events,<sup>17</sup> hawking prescription drugs directly to American consumers—among industrialized countries, such direct-to-consumer advertising is allowed

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13. See Schoen et al., *supra* note 8.

14. *Id.* at W472-73.

15. *Id.* at W473.

16. See MICHAEL E. PORTER & ELIZABETH OLMSTED TEISBERG, *REDEFINING HEALTH CARE: CREATING VALUE-BASED COMPETITION ON RESULTS* 17-32 (2006).

17. See U.S. GOV'T ACCOUNTABILITY OFFICE, *PRESCRIPTION DRUGS: IMPROVEMENTS NEEDED IN FDA'S OVERSIGHT OF DIRECT-TO-CONSUMER ADVERTISING* 12 (2006).

only in the United States and New Zealand.<sup>18</sup> Doctors and other healthcare providers are also the targets of intense marketing. There is one drug representative for every five office-based doctors.<sup>19</sup> Sixty percent or more of doctors' continuing medical education is funded by the medical industries.<sup>20</sup> Countless free lunches, educational dinners, ballpoint pens, clocks, sticky pads, and other promotional gifts, are constant reminders of drug companies' relentless intrusion into the practice of medicine. And a growing army of lobbyists representing the Pharmaceutical Research and Manufacturers of America ("PhRMA") and the medical industry to "educate" our senators and congressman show up in Washington each year—one lobbyist for every member of Congress in 2004, two in 2005, and now reportedly three.<sup>21</sup>

But the "core lesion," as we say in medicine, remains hidden in plain sight: The fundamental role of medical knowledge in our society has been quietly but radically transformed over the past twenty-five or thirty years from a public good into a private commodity, produced for its potential commercial value rather than its potential to improve Americans' health. Since the late 1970s, the medical research enterprise has been almost completely privatized. At least seventy percent of clinical trials are now commercially sponsored.<sup>22</sup> And the fundamental purpose for which this research is done is consistent with the primary fiduciary responsibility of the pharmaceutical and other medical industries—to maximize their return on research investment for their shareholders and investors.

There are two perspectives from which the "knowledge" that informs doctors' decisions can be viewed. It can be considered from an idealist or Platonic perspective, as a small bit of scientifically proven absolute truth. For the most part, this is the perspective that doctors are taught, and for which they are held responsible when they practice the "evidence-based medicine" that reflects the scientific research published

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18. *Id.* at 8.

19. Scott Hensley, *As Drug-Sales Teams Multiply, Doctors Start to Tune Them Out*, WALL ST. J., June 13, 2003, at A1.

20. Arnold S. Relman, Letter in Reply, *Industry Sponsorship of Continuing Medical Education*, 290 JAMA 1149, 1150 (2003) (arguing that over sixty percent "of the total amount spent on [continuing medical education] came from industry").

21. Interview with Sam Brunelli, President, Team Builders International, Washington, DC., in Avon, Colo. (Nov. 18, 2007).

22. Michelle M. Mello et al., *Academic Medical Centers' Standards for Clinical-Trial Agreements with Industry*, 352 NEW ENG. J. MED. 2202, 2202 (2005).

in the medical journals.<sup>23</sup> Alternatively, medical knowledge can be regarded from the sociological perspective, asking what the criteria are by which doctors determine whether to accept a particular piece of new information as legitimate,<sup>24</sup> and why doctors consider the scientific evidence about these particular issues instead of others.

A landmark article published in 1982 in the journal *Science* pointed out the transition: "Scientists who [ten] years ago would have snubbed their academic noses at industrial money now eagerly seek it out."<sup>25</sup> The transformation gained momentum when President Reagan came to office in 1980, inheriting a weak economy and bringing with him a mandate to downsize government. One of his first actions was to downsize the funding at the National Institutes of Health for clinical trials.<sup>26</sup> To fill this void, the pharmaceutical industry increased expenditures on research and development six-fold between 1977 and 1990.<sup>27</sup> There is nothing inherently wrong with this transition to commercial funding of clinical trials. Private enterprise is the engine that drives much of the ingenuity in our economy. The drug companies invest in research with the goal of developing socially useful products in order to maximize their profits. The problem is not with the entrepreneurial incentives of capitalism, but with the academic and regulatory context in which this transition has unfolded and continues to unfold. Just as the need for adequate government and academic oversight of commercially-funded "scientific evidence" being purveyed as "medical knowledge" was increasing, the effectiveness of that oversight was being eroded by the growing influence of the drug and other medical industries.

During the 1980s, the proportion of funding for clinical trials coming from commercial sources grew significantly. Even so, not much changed in the quality of our medical literature between 1980 and 1991 because, until 1991, about eighty percent of these commercially-funded trials were still performed in universities, where academic researchers continued to play a major role in designing the research, analyzing the

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23. See Evidence-Based Med. Working Group, *Evidence-Based Medicine: A New Approach to Teaching the Practice of Medicine*, 268 JAMA 2420, 2420 (1992).

24. SUSAN HAACK, EVIDENCE AND INQUIRY: TOWARDS RECONSTRUCTION IN EPISTEMOLOGY 136-38 (1993).

25. Barbara J. Culliton, *The Academic-Industrial Complex*, 216 SCIENCE 960, 960 (1982).

26. See *Reagan's Science Budget: Cries of Pain*, THE ECONOMIST, Feb. 13, 1982, at 79-80.

27. JOHN ABRAMSON, OVERDOSED AMERICA: THE BROKEN PROMISE OF AMERICAN MEDICINE 94 (2004).

data, and overseeing publication of the results.<sup>28</sup> But this changed radically in the following decade. By 2000, only forty-one percent of commercially funded clinical trials were conducted in universities—the rest outside of academic environments by for-profit contract research organizations (“CROs”).<sup>29</sup> And by 2004 this number had dwindled to twenty-six percent.<sup>30</sup>

There is nothing inherently unethical about the pharmaceutical industry contracting with private research companies to do their studies. Again, the efficiency of the marketplace is at work. The for-profit research companies can conduct studies more quickly, with less red tape and less overhead than academic medical centers. But this transition radically changed the locus of control of medical research: Responsibility for research design, data analysis, and publication shifted from academic researchers and institutions to the commercial sponsors of the research. This left many of the authors of the papers that became accepted as scientific evidence without free access to their own data.<sup>31</sup> And medical journal editors and peer reviewers only have access to the manuscripts submitted to them, not to the research protocols (to verify whether the manuscript accurately reflects the original outcome measures and other pre-specified details) or to the raw data (to verify that the conclusions drawn are supported by the actual results).

The dialectic of the commercialization did not stop there. The next step was that the major advertising agencies began buying up these CROs.<sup>32</sup> Again, there is nothing unethical here. This is perfectly logical because the primary purpose for which commercially-sponsored medical research is undertaken is to maximize product sales, and there is no one better to oversee the process of creating the “knowledge” to best support sales than the real specialists—the advertisers.

The bottom line is that the scientific evidence appearing in even our most trusted medical journals is now heavily biased to support commercial sponsors’ products. A study published in the *Journal of the American Medical Association* (“JAMA”), titled *Empirical Evidence for*

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28. See Thomas Bodenheimer, *Uneasy Alliance: Clinical Investigators and the Pharmaceutical Industry*, 342 NEW ENG. J. MED. 1539, 1540 (2000). By 2004, this number had dwindled to twenty-six percent. See Robert Steinbrook, *Gag Clauses in Clinical-Trial Agreements*, 352 NEW ENG. J. MED. 2160, 2161 (2005).

29. See *id.*

30. Steinbrook, *supra* note 21, at 2161-62.

31. See Bodenheimer, *supra* note 28, at 1541-42.

32. See Melody Petersen, *Madison Ave. Has Growing Role in the Business of Drug Research*, N.Y. TIMES, Nov. 22, 2002, at A1.

*Selective Reporting of Outcomes and Randomized Trials*, found significant disparities between the outcome measures identified in the original protocols and the articles that purportedly presented the results.<sup>33</sup> Overall, fifty percent of efficacy measures and sixty-five percent of harm measures that were identified in protocols were reported incompletely in the published reports of the clinical trials.<sup>34</sup> The article concludes:

The reporting of trial outcomes is not only frequently incomplete but also biased and inconsistent with protocols. Published articles, as well as reviews that incorporate them, may therefore be unreliable and overestimate the benefits of an intervention.<sup>35</sup>

Another study published in *JAMA* looked at the highest quality clinical trials, the ones that are accepted into the Cochrane reviews,<sup>36</sup> and found that when a study is commercially funded the odds are 5.3 times greater that it will conclude that the sponsor's drug is the treatment of choice than when a study of exactly the same drug is non-commercially funded.<sup>37</sup> So, doctors are being implored to practice evidence-based medicine in the new privatized research enterprise, more than 3.2 times as often they are being implored to practice "infomercial-based" medicine.

Therein lies an enormous and rapidly growing problem—going back to the sociological perspective of knowledge, doctors have been well trained to accept the conclusions of these articles at face value. An article that appeared on the front page of the *New York Times Science Times* section last May quoted the current editor of the *Lancet* and the former editor of the *British Medical Journal*, saying that medical "[j]ournals have devolved into information-laundering operations for the

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33. An-Wen Chan et al., *Empirical Evidence for Selective Reporting of Outcomes in Randomized Trials*, 291 *JAMA* 2457, 2457 (2004).

34. *Id.* at 2461, tbl.3 & fig.3.

35. *Id.* at 2457.

36. The Cochrane Library "consists of a regularly updated collection of evidence-based medicine databases, including The Cochrane Database of Systematic Reviews." The Cochrane Collaboration, <http://cochrane.org/reviews/clibintro.htm> (last visited Mar. 2, 2007). Cochrane reviews "are based on the best available information about healthcare interventions. They explore the evidence for and against the effectiveness and appropriateness of treatments (medications, surgery, education, etc.) in specific circumstances." *Id.*

37. Bodil Als-Nielsen et al., *Association of Funding and Conclusions in Randomized Drug Trials*, 290 *JAMA* 921, 924-25 & tbl.3 (2003).

pharmaceutical industry.”<sup>38</sup> This is an ethical, scientific and political crisis that we can no longer afford to ignore—because of its cost in terms of dollars and, even more important, its cost in terms of our health.

When one discusses the ethics of biomedical research and the law, one must understand that the fundamental ethical problem here is that the primary goal of the medical research enterprise itself is not to optimize America’s health, but rather, to fulfill pharmaceutical industry executives’ primary—and fiduciary—responsibility: to maximize return on research investment for shareholders. But entrepreneurial incentives driving medical research need not necessarily be a bad system, as long as there are adequate regulatory and oversight mechanisms in place to ensure both the accuracy and epidemiological balance of commercially sponsored medical research. However, just as the process of medical knowledge creation and dissemination was being privatized, the academic institutions’, medical journals’, and FDA’s ability to provide independent oversight to maintain the integrity of our medical knowledge has been weakened by growing dependence on drug and other medical industry revenues.

As a result of the Prescription Drug User Fee Agreement, (“PDUFA”),<sup>39</sup> the division of the FDA that approves new drugs and oversees drug safety, the Center for Drug Evaluation and Research, is now more than half-funded by the drug industry.<sup>40</sup> Academic medical centers rely upon industry sponsorship for seventy-nine percent of clinical trials they conduct.<sup>41</sup> And the medical journals are in the untenable position of having to trust the veracity of commercially-sponsored studies without having the access or the resources necessary to evaluate whether submitted manuscripts accurately reflect the results of studies. Dr. Drummond Rennie, Deputy Editor of *JAMA*, told the *Wall Street Journal*: “Science depends on trust . . . . You can’t have a policeman in every lab.”<sup>42</sup>

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38. Lawrence K. Altman, *For Science’s Gatekeepers, A Credibility Gap*, N.Y. TIMES, May 2, 2006, at F1.

39. Prescription Drug User Fee Act of 1992, Pub. L. No. 102-571, 106 Stat. 4491 (codified as amended at 21 U.S.C. § 379g note (2000)).

40. U.S. GEN. ACCOUNTING OFFICE, EFFECT OF USER FEES ON DRUG APPROVAL TIMES, WITHDRAWALS, AND OTHER AGENCY ACTIVITIES 8, 9 fig.1 (2002).

41. Mello et al., *supra* note 22, at 2204.

42. Anna Wilde Mathews, *Worrisome Ailment in Medicine: Misleading Journal Articles*, WALL ST. J., May 10, 2005, at A1.

And finally, academic researchers are no longer protected from commercial pressure, as described in a joint statement by thirteen editors of the world's leading medical journals:

Investigators may have little or no input into trial design, no access to the raw data, and limited participation in data interpretation. These terms are draconian for self-respecting scientists, but many have accepted them because they know that if they do not, the sponsor will find someone else who will.<sup>43</sup>

So we have a big problem, and thus the title of this Article: *The Reliability of Our Medical Knowledge as a Product of Industry Relationships*. What are the criteria of reliability? First, are the research results presented in respected, peer reviewed journals consistent with the pre-specified outcome measures of benefit and harm identified in the original research designs and based upon an unbiased analysis of the data?

Let us examine Merck's large post-approval study ("VIGOR") of its former blockbuster arthritis drug Vioxx, comparing the actual data that Merck submitted to the FDA to the results of the VIGOR trial that were published in the *New England Journal of Medicine* ("NEJM") in November of 2000.<sup>44</sup> The research design led to a skewed sample of patients in the study, hardly representative of the general population of people who would be using Vioxx. Fifty-five percent of the people in the study were taking steroids concurrently with an anti-inflammatory drug, which accentuates gastrointestinal ("GI") problems.<sup>45</sup> In addition, only four percent of people included in the study had a history of cardiovascular disease that would make them candidates for prophylactic aspirin, whereas in the general population twenty percent or more of takers of non-steroid anti-inflammatory drugs ("NSAIDs") have a history of cardiovascular problems.<sup>46</sup> As a result, the potential of this study to determine the potential of Vioxx to increase in the risk of cardiovascular harm was minimized in the study population.

Nonetheless, were the results of the VIGOR trial presented in a fair and balanced way in this article? Even though the reduction in serious

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43. Frank Davidoff et al., Editorial, *Sponsorship, Authorship, and Accountability*, 345 NEW ENG. J. MED. 825, 825 (2001).

44. See Claire Bombardier et al., *Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis*, 343 NEW ENG. J. MED. 1520 (2000).

45. See *id.* at 1523.

46. *Id.*

GI complications experienced by the patients taking Vioxx instead of naproxen was actually overshadowed by the increased number of serious cardiovascular complications, the *NEJM* article failed to report the cardiovascular complications—just a post hoc subset of cardiovascular complications, myocardial infarctions.<sup>47</sup>

So even the most disciplined doctors, carefully reading our most prestigious medical journal, could not have known that there were more cardiovascular problems caused by Vioxx than serious GI problems prevented by Vioxx. Nor could they have known that the VIGOR study really showed that, overall, Vioxx caused significantly more serious adverse events than did naproxen.<sup>48</sup> Moreover, the data for heart attacks, presented instead of cardiovascular complications in toto, were reported incompletely. In December 2005, the editors of *NEJM* wrote an “Expression of Concern” stating that three of the heart attacks that occurred among people taking Vioxx had not been included in the November 2000 article even though the Merck-employed authors of the article knew about these three heart attacks at latest by July 2000—a full four and a half months before the *NEJM* article was published.<sup>49</sup> Of the thirteen authors of this article, eleven were non-Merck employees, and two were Merck employees. The eleven non-Merck employees, including the lead author, responded to the editors’ Expression of Concern, writing that the three heart attacks were not “known to [them] during the review process.”<sup>50</sup> In other words, these eleven authors including the lead author, were not provided unfettered access to the data from the study that was published under their names in *NEJM*. And still unexplained is why the *NEJM* editors waited nearly four years after becoming aware of this to inform their readers that omission of the three heart attacks led to readers being falsely reassured that the increased rate of heart attacks experienced by people taking Vioxx instead of naproxen did not extend to people without a previous history of cardiovascular disease.<sup>51</sup>

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47. *Id.*

48. QIAN LI, STATISTICAL REVIEWER BRIEFING DOCUMENT FOR THE ADVISORY COMMITTEE 5-15 (2000), available at [http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b2\\_04\\_stats.pdf](http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b2_04_stats.pdf).

49. Gregory D. Curfman et al., Editorial, *Expression of Concern: Bombardier et al.*, “Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis,” *N Engl J Med* 2000;343:1520-8, 353 NEW ENG. J. MED. 2813, 2813 (2005).

50. Claire Bombardier et al., Correspondence, *Response to Expression of Concern Regarding VIGOR Study*, 354 NEW ENG. J. MED. 1196, 1196-98 (2006).

51. “The editors first became aware of the additional myocardial infarctions in 2001 when updated data were made public by the Food and Drug Administration.” *Expression of Concern*,

The second criterion of the reliability is whether or not the results are published at all, and therefore available to doctors, purchasers of healthcare, and policy makers. The classic example here is the safety and efficacy of antidepressants in the treatment of depressed children and adolescents. In the scientific literature there were six articles, all showing these drugs to be safe and effective. Clinicians had good reason to believe that treatment of depressed children and adolescents with the new antidepressants was evidence-based care. What they did not know is that there were not six, but fifteen studies of the safety and efficacy of these drugs in children and adolescents that had been completed. The other nine studies had shown that the drugs were neither effective nor safe—that they doubled the rate of suicidal thoughts and behaviors. In fact, even among the six positive studies that were published, the claims in three “were not confirmed after independent analysis by the regulatory agencies.”<sup>52</sup>

And finally, the third criterion of reliability—does the research enterprise reasonably reflect the implied goals of improving health and addressing the epidemiological challenges of the population? This is where our research is really failing. Health is primarily determined by how and where we live our lives. A study by researchers from the Robert Wood Johnson Foundation shows that forty percent of our health is determined by behavioral patterns, fifteen percent by social circumstances, and five percent by environment.<sup>53</sup> The Institute of Medicine has observed that seventy percent of preventable deaths in the United States are due to behavior and environmental factors.<sup>54</sup> And yet

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*supra* note 50, at 2813. The *NEJM* editors stated that they “believed that these were late events that were not known to the authors in time to be included in the article published in the *Journal* on November 23, 2000.” *Id.* However, it makes little difference to prescribing doctors or their patients exactly when the authors knew of the additional three heart attacks; the editors’ primary concern should have been that care being rendered by doctors trusting the *NEJM* was based on false information and should have been corrected as soon as possible—regardless of why the information was false.

52. *Antidepressant Medications in Children and Adolescents*, THERAPEUTICS LETTER (Therapeutics Initiative, Vancouver, B.C.), Apr./May/June 2004, available at <http://www.ti.ubc.ca/PDF/52.pdf> (discussing the controversy surrounding the fifteen randomized studies, of which only six were published).

53. J. Michael McGinnis et al., *The Case for More Active Policy Attention to Health Promotion*, 21 HEALTH AFF. 78, 78-83 (2002).

54. INST. OF MED. OF THE NAT’L ACADS., *THE FUTURE OF THE PUBLIC’S HEALTH IN THE 21ST CENTURY* 21 (2003).

we focus ninety-five percent of our time and money on biomedical interventions, not epidemiologically balanced interventions.<sup>55</sup>

The misdirection of our research agenda is being driven by the drug companies, which now sponsor at least seventy percent of clinical research, directing their studies to the areas that have the greatest potential to maximize return on investments. At best—without fraud, misrepresentation, or selective publication of positive studies—our medical knowledge grows toward corporate profits the way that plants grow toward sunlight, and not in the direction that would best improve the health of our population.

I think most would agree that the primary mission of American healthcare ought to be to optimize Americans' health as efficiently as possible, while maintaining reasonable individual freedoms. I continue to hope that the medical profession can explore better ways to harness the engine of private enterprise to serve our shared commitment to achieve a more effective and efficient healthcare system.

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55. McGinnis et al., *supra* note 52, at 78.