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WHY MEDICAL RESEARCH NEWS CAN'T BE TRUSTED

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"Publish or perish" has long been the mantra for medical researchers and physicians on the faculty of medical schools – and with good reason. Frequent publications can play a crucial role in obtaining grants, a top position in industry, or academic advancement and tenure. Because of increasing competition in all these areas, the pressure to publish, particularly in very prestigious journals, is greater today than ever before. But how is the relative stature or reputation of a journal determined?

Doctors and others looking for more information on a specific article, author or topic usually search PubMed, the National Library of Medicine's free online database of citations and abstracts from 5,400 biomedical journals here and in 80 other countries. Papers published in these journals often help to increase an author's recognition and status.

Embase is another large database that contains over 23 million indexed biomedical references from more than 7,500 medical journals but requires a subscription. Journals not indexed by either of these are less likely to have valuable content. There are now up to 20,000 print journals in addition to a growing number of others available only on the Internet. The leading ones have a large backlog of articles that can fill up the next four issues, which can pose problems when different groups are working on the same project. Priority is crucial, since the authors of the earliest publication tend to get the most subsequent citations, as well as credit and awards for being first.

Lengthy lags between submission, acceptance and publication are not unusual for the most desirable journals, not only because of space constraints, but also the time consumed in the peer review process by two or more authorities and editorial revisions that must then be approved by all authors. In some instances, co-authors may disagree with each other, a reviewer's criticisms or an editor's revisions. These and other communication snags can lead to lengthy correspondence back and forth for months before there is agreement between all involved and publication can be scheduled. Since it can take over a year for an article to appear, many scientific journals now release those deemed to be particularly important on their websites well in advance of their print versions to provide this protection. In contrast, a paper might be published in the next or following issue of a less sought-after journal where the editor is the only judge and there is no peer review. Letters dealing with a recent article must be received within a few weeks after they appear, so that they are timely and can be published promptly if accepted. Such correspondence is not subjected to peer review, but if multiple responses to a specific article are accepted, they are often referred to the original authors for comments and rebuttals, and all will appear together in a subsequent issue, which could be several months later.

Deteriorating Quality Due To Drug Company Deceit And Fiscal Forces

There are numerous differences in the procedures involved in having an article accepted and published in a medical or scientific publication as opposed to the lay media. Contributors to popular magazines are paid for their articles and freelance writers often shop around to find the highest bidder. Prior to publication, there is apt to be a great deal of publicity about what it contains, including selected excerpts designed to attract attention. Medical journals do not compensate authors, and before an article is even considered, require a written statement that it has not been submitted elsewhere. Once it is accepted, journals can impose severe restrictions on what authors can say publicly about its contents before it is published. Any violation of these rules can lead to severe penalties. The journal owns the article and not only collects all the income from sales of reprints, but also charges authors for additional copies. It is preferable to have an article accepted by a publication that has the best reputation for reaching the largest audience likely to be interested in your work. How a journal's reputation is determined, and particularly its ranking with respect to its competition is extremely important, not because it reflects the quality of content, but rather a huge difference in income that can amount to millions.

Unfortunately, like many other facets of modern medicine, the prime purpose of many journals now is to make more money, and there is little doubt that their profits can be astronomical, especially for the most prestigious. **Reed Elsevier has an annual income over $7 billion just**

from the reprints sold by its 2,000 medical and scientific journals. While it is generally believed that journals derive most of their profits from advertising and subscriptions, **more than half the income for JAMA and *The Lancet* comes from reprint sales to the pharmaceutical industry.** NEJM does not release financial statements but its total revenues are estimated to be as high as $100 million/year. A drug company might pay over $1 million for reprints of just one study it funded, since distributing an article to a physician from the *New England Journal of Medicine* (NEJM), *Journal of the American Medical Association* (JAMA) or *The Lancet* has the semblance of being educational rather than promotional. As it is not likely to be read in its entirely, drug representatives can put a spin on it or emphasize certain portions. Such a presentation is much more credible compared to discussing a company's biased literature simply because it has the journal's seal of approval. Unlike advertisements, which most doctors discount as being self-serving, a large clinical trial published in a major journal that is distributed worldwide can attract global media coverage. This is usually facilitated by simultaneous press releases from an experienced but expensive public relations firm, as well as the journal itself, which is anxious to increase its importance and influence.

A positive drug trial is worth thousands of pages of advertising to a pharmaceutical company since it increases sales, stock prices and stature. Such studies are also prized by publications that profit from selling reprints, frequent advertisements for the products, and widespread exposure that enhances its reputation. Drug companies are not required to publish or even report negative or dubious studies, and in some instances, have been able to twist their findings so that they appear favorable. In other cases, the design of the study or how the results are reported guarantees its success. Some of the techniques commonly used include: Conducting a trial of the drug against another known to be inferior, a trial comparing the drug against too low a dose of a competitive drug to imply that it is more effective, a trial that makes the drug appear less toxic by comparing it against too high a dose of its competitor, trials that are too small to show differences from drugs already approved for the same indication, having multiple endpoints for a trial but only publishing results from those that have good results, conducting multicenter trials and publishing results from only centers that are favorable, analyzing subgroups based on age, ethnicity or other demographic criterion and excluding results that don't support your claims.

As noted in previous Newsletters, a common strategy is to utilize deceptive statistics, such as relative rather than absolute risk reduction, or the number of patients needed to treat for one to receive any benefit. For example, your doctor tells you there is a new statin drug, and that if you take it every day for the next five years it will significantly "reduce your risk" of having a heart

attack. This is based on the company's advertisements stating that people taking this drug for five years had 34% fewer heart attacks than controls on a placebo. **Thus, the relative risk reduction is 34%.** Sounds attractive since it suggests that you will reduce the likelihood of a heart attack by more than a third. What you are not told is that over five years, 2.7% of patients taking the drug had heart attacks compared to 4.1% for the placebo group, which is an **absolute risk reduction of only 1.4%.** Nor would you know that the same study also showed that **if this drug is taken by 71 people for five years, it will prevent only one person from having a heart attack, but it is not known if that person will be you.** That is obviously much less appealing, but as Harry Truman advised, "If you can't convince them, confuse them."

Mark Twain noted, "There are three kinds of lies: lies, damned lies and statistics." Statistics are like expert witnesses–they will testify for either side, and drug companies have become adept at getting both statistics and experts to support the claims of studies they have sponsored. A review of all the 56 trials of non-steroidal anti-inflammatory drugs that were funded by pharmaceutical companies revealed that in every case, the sponsor's drug was better or as good as any competitive product. Although all studies must be registered, drug companies are not required to publish those with negative results. In one analysis of FDA registered studies, almost a third were not published. Those that were had favorable results in 95 percent of cases because the presentation frequently emphasized certain positive end points and discarded others. When the FDA reviewed all the data, only 51% were considered positive. This is a particular problem with respect to granting approval for psychotropic drugs, which is based on subjective criteria such as how patients respond to carefully worded questions about efficacy and side effects and the personal opinion of the investigators. Since the latter are selected and funded by the drug's manufacturer, it is not surprising that these views are biased. As emphasized in prior Newsletters, most antidepressant trials show such minuscule improvement over placebos, that new drugs are now compared with an existing antidepressant, since demonstrating that it is just as effective and safe will suffice.

Problems With Journal Rankings, The Integrity of Editors And Peer Review

Since the most highly regarded journals are likely to sell more reprints and advertising, editors and publishers are constantly searching for ways to increase the reputation of their products. The current method for measuring the prestige of a journal is by its "impact factor", often abbreviated IF. Most doctors have never heard of IF despite the fact that it influences their opinion of a journal's authenticity and therefore its contents. A journal's IF represents the average number of citations received per paper during the two preceding years. For example, if a journal has an impact factor of 3 in

2009, then its papers published in 2008 and 2007 received an average of 3 citations based on the following formula: A = the number of times all articles published in 2008 and 2007 were cited by indexed journals during 2009. B = the total number of citable articles published by that journal in 2008 and 2007. The 2009 impact factor is derived by dividing A by B. The 2010 impact factor rankings for the top six general medical journals are: 1.NEJM (47.05), 2.Lancet (30.758), 3.JAMA (28.899) 4.Ann int Med (16.225) 5.BMJ (13.66) 6.PLOS med (13.05). At the bottom of this list of 40 is Intern Med Journal with an impact factor of 1.786.

The impact factor approach for rating medical journals, which began in 1988, has obvious flaws, since it does not necessarily reflect overall quality. A review paper might receive thousands of citations during a two-year period, whereas others would attract only a handful. Therefore editors and publishers prefer comprehensive reviews, and may even commission them, especially from authors who are apt to cite previous papers published in the same journal. There are other tricks of the trade. Although editorials are not included when calculating the total number of articles, their references to articles that have appeared in that journal help to increase the impact factor. To protest against this, a specialty journal with an impact factor of 0.66 published an editorial in 2007 that cited all of its articles from 2005 and 2006, which more than doubled its IF to 1.44. An even bolder illustration was a 2008 journal article describing a specific methodologic technique, which instructed all readers to refer to it as the gold standard when discussing any aspect of this topic. This paper was cited over 6,600 times and while the second highest article had only 28 citations, the journal's impact factor skyrocketed from 2.051 in 2008 to 49.926 in 2009. Notice also that these figures are listed not in the nearest whole number or tenths, but in thousandths, which implies a degree of accuracy that is hardly justified.

There are so many other deficiencies that plague current medical publishing practices that it would take several Newsletters to discuss them in detail. Most are relatively recent; since early medical journals had no commercial ties and accepted no advertisements, save for medical texts that might be of interest to their readers. They were published by various city or state medical societies to provide useful information for their memberships. The first medical journal that was not affiliated with any medical society or group was *The Lancet*, which was founded in 1823 by Thomas Wakley, a London surgeon. As he explained, "A lancet can be an arched window to let in the light or it can be a sharp surgical instrument to cut out the dross and I intend to use it in both senses". The purpose of this weekly publication was to instruct, entertain and reform and it was more like a newspaper. At the time, medical education came largely from paying to listen to lectures by prominent physicians. Wakley would attend these, write down the essence of

the presentation, and publish it the following week. Instruction also came from the publication of interesting case histories provided they were well documented. Entertainment was provided by theatrical reviews, biographies of non-medical celebrities, piquant political commentary, news and material from other publications and even a weekly chess column, since crossword puzzles did not appear until the 20th century. But it was reform that *The Lancet* became best known for, particularly with respect to launching campaigns that exposed corruption, quackery and nepotism.

Wakley's outspoken and piercing criticisms of the common practice of using a public office or position of trust for personal gain led to a number of law-suits from physicians and organizations he had named, which only increased his influence and fame. Some examples of these tirades include:

> "We deplore the state of society which allows various sets of mercenary, goose-brained monopolists and charlatans to usurp the highest privileges.... This is the canker-worm which eats into the heart of the medical body."
>
> "The Council of the College of Surgeons remains an irresponsible, unreformed monstrosity in the midst of English institutions – an antediluvian relic of all... that is most despotic and revolting, iniquitous and insulting, on the face of the Earth".

He was especially caustic about what he regarded as quackery. The English Homeopathic Association were "an audacious set of quacks" and its supporters "noodles and knaves, the noodles forming the majority, and the knaves using them as tools". (Noodle at the time referred to a stupid or silly person and a knave was a thief or dishonest and unscrupulous man.) He attacked the constitution of the Royal College of Surgeons, and exposed so many abuses that its members had been unaware of, that a petition to Parliament in 1827 resulted in a return of public money it had granted. He later was elected to Parliament and effectively argued that coroners should not be political appointments of lay people, but rather qualified physicians.

Wakley became a coroner himself and insisted on inquests into anyone who died in police custody, since this was not infrequently due to brutality. He also successfully campaigned against flogging as a punishment and was the coroner when a private in the Army was subjected to 150 lashes of the cat-o'-tails for a disciplinary offense and died a month later. According to Army doctors, death was due to "serious cardiac and pulmonary mischief", and, under direct orders from the regiment's Colonel, had stated on the certificate that "cause of death was in no way connected with the corporal punishment." Before burial, the presiding vicar expressed his contrary

opinion to Wakley, who issued a warrant for an inquest. Evidence was given by Army surgeons, the hospital physician and orderlies, but also by independent experts, who made it quite clear that the flogging and subsequent death were causally related. The jury concurred, and added a strongly worded rider expressing their "horror and disgust that the law of the land provided that the revolting punishment of flogging should be permitted upon British soldiers". Flogging as a form of punishment was later abolished. His last campaigns against adulteration of foods and impurities in the water supply were also successful in bringing about much needed reforms. Like his successors and other early editors, Wakley was a physician well versed in literature and the arts, who insisted that journal contents were accurate and had the power and authority to insure this.

Contrast this with today's medical journals, whose editors often have little or no editorial experience. As Richard Smith, former editor of the *British Journal of Medicine* noted, "Most editors of the world's more than 10,000 biomedical journals have received no training. One day you're a professor of cardiology; the next you're editing a journal.... For an editor with no training in cardiology to become a cardiologist overnight would be unthinkable, but it's routine the other way round". Smith, who worked at the BMJ for 25 years, spent the first 12 as assistant editor, and followed a long line of distinguished predecessors who also honed their skills through years of apprenticeship. Other British journals similarly appointed chief editors who came up through the ranks, in contrast to many in America, where the criteria can be vague and may not require any experience. Some editors abuse their position to promote themselves, and although this can be difficult to prove, some have been caught, including a few in London. An especially egregious example occurred several years ago, when there was international media coverage of two physicians who were able to transplant an ectopic pregnancy through the cervix that resulted in the natural birth of a healthy baby. This was a remarkable achievement that had eluded doctors for years but there was no reason to doubt its accuracy, since the first author, Malcolm Pearce, was a senior lecturer at St George’s Hospital Medical School in London, and a world famous expert on ultrasonography in obstetrics. His co-author was Geoffrey Chamberlain, president of the Royal College of Obstetricians and Gynecologists, professor and head of the department at St George’s, and editor of the *British Journal of Obstetrics and Gynecology* that published the article. Pearce was an assistant editor, and the same issue contained a randomized controlled trial by Pearce, Chamberlain and others, in which 191 women with recurrent miscarriages were successfully treated with human chorionic gonadotrophin.

A young doctor at St. George's, who was suspicious about the authenticity of both articles, since it seemed strange that nobody else at the hospital was

aware of these studies. He instigated an investigation, which revealed that the ectopic pregnancy patient did not exist and that none of the patients in the alleged randomized trial could be found. Among other prior Pearce studies, three others also proved to be fraudulent, two of which had been published in the *BMJ*. All of these papers were subsequently retracted, Pearce was fired from the hospital, and Chamberlain resigned from all his prestigious positions. When asked why he agreed to be a coauthor, he said "I rubber stamped this paper out of politeness and because he asked me to as head of the department." This was not an uncommon practice at the time, since including a distinguished co-author, who was usually listed last, made the paper more prestigious. In his defense, Chamberlain argued that even rigorous peer review would not necessarily detect outright fraud. "This paper was peer reviewed twice, both medically and statistically. It never occurred to the referees that the whole thing might be a lie."

One of the best examples of editorial self-promotion was Sir Cyril Burt, who was elected President of the British Psychological Society in 1942 and was later knighted for his contributions to the measurement of intelligence and psychological testing. He believed that personality characteristics determined what diseases people were likely to develop and that specific temperaments were associated with a 20-fold increase in certain malignancies. He suggested that there was no real connection between smoking per se and cancer of the lung, because individuals attracted to cigarettes were going to get lung cancer eventually because of their personalities. He pointed out that many who never smoked or had a family history died from cancer of the lung and others who were heavy smokers lived long lives with no evidence of the disease. He also believed that intelligence, as measured by IQ testing, was inherited and that blacks had significantly lower IQs. Burt was also the editor of the *British Journal of Statistical Psychology* for many years, during which he published 63 articles expounding on these theories; altered the work of others without permission; published a letter he wrote under a pseudonym; and also wrote a response under a pseudonym to discredit a colleague. None of this was discovered until his personal property became available after his death. While many of his publications have been discredited, they are still often cited or referred to as being accurate.

To prevent such abuses, most journals require peer review approval prior to publication, and some now insist that each individual listed as an author or co-author of a paper must explain exactly how they contributed to it. Peer review consists of submitting a paper to two or more individuals with expertise in the topic being discussed and/or the ability to determine the accuracy and relevance of conclusions based on statistical data. Peer reviewers, who usually receive no compensation for their efforts, are arbitrarily selected, and may or may not be aware of the authors, or their

affiliated institutions, both of which can influence decisions, and often simply skim through the material. Many authorities feel that the peer review process is seriously flawed, and BMJ editor Richard Smith, explains why in his book *The Trouble With Medical Journals*, a scathing exposé of this and other deficiencies. In one study, twelve papers emanating from esteemed institutions like Harvard and Yale that had been published in prestigious psychology journals were retyped, but the authors, titles and sources were changed. Thus, instead of coming from Harvard, something very unsophisticated was substituted, such as East Montana Institute for the Improvement of Human Potential. **The identical paper was then resubmitted to the same journal that had previously published it. Only three journals detected this, and in seven of the eight other submissions, the duplicate manuscript was rejected.**

Smith also described a study in which his staff inserted eight obvious errors into a 600-word paper and sent it to 400 reviewers. Of the 300 responses received, "nobody spotted more than five of the errors; a median number spotted was two, and 20% didn't spot any." Peer review is easily abused, since the reviewer is granted anonymity. In some cases, ideas are stolen and the response is deliberately delayed so the reviewer can publish it first in another journal. In other instances, where the identity of a rival can be determined, the response can be unduly critical, whereas a friend's paper or one that supports the reviewer's own work is quickly approved and praised. Richard Horton, editor of *The Lancet* summarized the situation as follows:

> The mistake, of course, is to have thought that peer review was any more than a **crude means of discovering the acceptability — not the validity — of a new finding.** Editors and scientists alike insist on the pivotal importance of peer review. We portray peer review to the public as a quasi-sacred process that helps to make science our most objective truth teller. But we know that **the system of peer review is biased, unjust, unaccountable, incomplete, easily fixed, often insulting, usually ignorant, occasionally foolish, and frequently wrong.**

Pharmaceutical Fraud, Conflicts of Interest And John Ioannidis

Having served as the chief editor of a peer reviewed journal published by John Wiley in the U.K., as an associate editor of several peer reviewed journals, as well as a reviewer for the British Medical Journal and other prestigious publications, I can testify to the accuracy of this assessment. Others with far more experience also agree and place the blame squarely on the pharmaceutical industry as the major cause of our current problems. In her book, *The Truth About Drug Companies*, Dr. Marcia Angell, wrote:

> This industry uses its wealth and power to co-opt every institution that might stand in its way, including the U.S. Congress, the Food and Drug Administration, academic medical centers and the medical profession itself.
>
> **It is simply no longer possible to believe much of the clinical research that is published, or to rely on the judgment of trusted physicians or authoritative medical guidelines.** I take no pleasure in this conclusion, which I reached slowly and reluctantly over my **two decades as an editor of *The New England Journal of Medicine.***

Angell succeeded Dr. Jerome Kassirer as NEJM editor-in-chief after he was fired by the Massachusetts Medical Society, **which had purchased the publication in 1921 for a dollar**. As she wrote in her first editorial

> Most observers were baffled by the decision, since the *Journa*l was obviously flourishing under Kassirer's superb leadership. In a joint announcement on July 25, Kassirer and Jack T. Evjy, president of the society, referred only to **'honest differences of opinion between Dr. Kassirer and the Medical Society over administrative and publishing issues.'**
>
> It is no secret that the other Journal editors and I were dismayed by the society's decision to let Kassirer go, and that we shared many of his concerns about the use of the *Journal's* name to promote other products. The society's action precipitated a crisis unique in the *Journal's* 187-year history. There was even talk of a mass resignation by the editors, an event from which the *Journal* might never have recovered.

What she was referring to was Kassirer's objection to the society's ambitious plans to repackage the Journal' s content for consumers and entering into joint arrangements ("cobranding") with various information-based commercial enterprises. As editor-in-chief, he strongly opposed the use of the Journal's name to promote products for which he and his staff had no responsibility, since such activities threatened the Journal's credibility. Angell accepted his post only after the society agreed it would have no authority over content or editorial policy and that any use of the name, logo, and content of the *New England Journal of Medicine*, in print or any other form, including consumer versions would be subject to her approval.

In his 2005 book, *On the Take: How Medicine's Complicity with Big Business Can Endanger Your Health*, Kassirer also indicted profit driven pharmaceutical manufacturers as the source of publishing and other current problems. Emphasis is devoted to how financial conflicts of interest occur when drug companies promote products at Continuing Medical Education courses they sponsor. These are frequently held at lavish resorts, where gifts are freely dispensed and reprints of favorable journal articles are distributed. For many of the registrants, these events are often a paid weekend vacation for them and their families, since there is ample time off for golf, tennis or sightseeing. The medical education lectures given by paid

"consultants" are primarily promotional pitches, and their financial arrangements with the company are rarely revealed or are minimized. There are also hordes of drug company representatives that call on doctors to provide free samples, literature and a variety of presents and perks, like theater and sporting event tickets and lunches for the office staff. **Drug companies spend over $30,000.00 per year on each U.S. physician** to promote and market their products. As Kassirer notes "the billion-dollar onslaught of industry money has deflected many physicians' moral compasses and directly impacted the everyday care we receive from the doctors and institutions we trust most."

Dr. Arnold Relman, who preceded Kassirer as NEJM editor-in chief, has weighed in on this in *A Second Opinion: Rescuing America's Health Care*, in which he proposes some remedies. In *Patents, profits & American medicine: conflicts of interest in the testing & marketing of new drugs*, a paper that he co-authored with Angell, he has also denounced drug company influences on the practice of medicine. Since then, the concerns of all these distinguished individuals have been vividly confirmed by concealed company documents that were obtained during the course of litigation. Last year, a suit in which Vioxx was alleged to have caused a heart attack, revealed that Merck had paid an undisclosed sum to Elsevier to publish several volumes of The *Australasian Journal of Bone and Joint Medicine*, by its Exerpta Medica "strategic medical communications" division. Although it had the appearance of a peer reviewed journal, it contained only reprinted or summarized articles, most of which dealt with the benefits of Merck products. Four of the 21 articles featured in the first issue referred to Fosamax, Merck's osteoporosis drug, and in the second issue, 9 of the 29 articles promoted Fosamax and 12 praised Vioxx. There were few advertisements save for these two drugs, but there was no indication that Merck had sponsored the journal, which had no website and was not even listed in Index Medicus or any database. Merck described it as a "complimentary publication", denied claims that any articles had been ghost written by Merck, and that all had been reprinted from peer-reviewed medical journals. However, Elsevier subsequently conceded that these were "sponsored article compilation publications, on behalf of pharmaceutical clients, that were made to look like journals and lacked the proper disclosures." They also acknowledged that this "was an unacceptable practice" and that they had five additional bogus journals in other specialties under the Excerpta Medica imprint. Elsevier sold Excerpta Medica to Omnicon two months ago for an undisclosed sum.

Internal company communications obtained in other lawsuits and via the Freedom of Information Act reveal that ghostwriting is rampant. There are over 10,000 lawsuits related to Wyeth's Prempro hormone replacement product, which has been shown to increase women's risk of breast cancer,

stroke, and dementia. After reviewing more than 1500 documents not previously available, it was discovered that Wyeth had not only fabricated evidence supporting Prempro's safety, but also paid a ghostwriting agency to plant vast amounts of these misrepresentations in various forms in places where they would be most effective. DesignWrite, the company they hired, boasted that, for over 12 years they have "planned, created, and/or managed hundreds of advisory boards, a thousand abstracts and posters, 500 clinical papers, over 10,000 speakers' bureau programs, over 200 satellite symposia, 60 international programs, dozens of websites, and a broad array of ancillary printed and electronic materials."

GlaxoSmithKline's shell company, CASPPER (Case Study Publications for Peer Review), hired prominent professors and researchers to take credit for papers written by company consultants, who mimicked the fake author's writing style. Impressive data to support the positive results being reported were also created, and CASPPER would then be responsible for placing each article in a pertinent and prestigious journal. The internal records indicate that the company had budgeted for 50 such articles in 2000, the year they spent over $92 million in an ad campaign to promote social anxiety disorder, and became the first drug approved for this controversial condition. It was also clear that the company was concerned about significant side effects, including suicide, in one in five patients after starting Paxil that were minimized or not reported. Because of mounting evidence that children and teenagers were at particular risk the U.K. banned the use of Paxil for anyone under the age of 18. There was no mention of this in the ghostwriting articles published in five journals between 2000 and 2002, including the *American Journal of Psychiatry* and the *Journal of the American Academy of Child and Adolescent Psychiatry*, both of which have high impact factors.

With respect to the Vioxx lawsuit, Merck also concealed safety information. The lead author of a report published in the *Annals of Internal Medicine* in 2003 explained, "Merck designed the trial, paid for the trial, ran the trial. Merck came to me after the study was completed and said, 'We want your help to work on the paper.' The initial paper was written at Merck, and then it was sent to me for editing. Basically, I went with the cardiovascular data that was presented to me." In 2000, when NEJM published the VIGOR study to show its superiority over similar drugs with respect to GI side effects, the high incidence of heart attacks was glossed over. There were numerous concerns raised with the editor, Jeff Drazen, but the journal was selling thousands of reprints and these were ignored, including complaints by the FDA and AMA. And even though Merck was forced to withdraw the drug in September 2004 because of 60,000 deaths, Drazen waited until December 2005 to publish an expression of concern about the validity of the study. It is

estimated that NEJM took in $1 million for reprints during this five-year period, and they were publicly rebuked in several prominent journals.

Many editors of leading journals are now between a rock and a hard place, as they have to decide between publishing a trivial drug sponsored study or supplement that can bring in $800,000 or more, or find some other funding to avoid laying off staff. The 2003 Vioxx Annals article had been rejected twice by 2 other journals as not being novel, but this is not unusual. The top publications NEJM, Lancet, BMJ, JAMA have rejection rates of 90 to 95% so the article keeps getting resubmitted down the pecking order until it is accepted. As Drummond Rennie, deputy JAMA editor wrote, **"There seems to be no study too fragmented, no hypothesis too trivial, no literature citation too biased or too egotistical, no design too warped, no methodology too bungled, no presentation of results too inaccurate, too obscure, and too contradictory, no analysis too self serving, no argument too circular, no conclusions too trifling or too unjustified, and no grammar and syntax too offensive for a paper to end up in print."** In short here is no article that cannot be published, which is why there is so much garbage out there that cannot be believed.

Ninety percent of the published medical information that doctors rely on is flawed according to Dr. John Ioannidis. Few have been able to dispute the meticulous investigations that led him to this disappointing conclusion. The son of two Greek physician- researchers, he decided to follow in their footsteps, and worked with illustrious scientists at several U.S. institutions, including Johns Hopkins and the National Institutes of Health, where he also held positions. Ioannidis was astonished by the number of drugs and tests hailed as breakthroughs that were subsequently banned because of safety concerns or lack of efficacy. Hormone replacement therapy and antidepressants are two examples, and even the inventor of the PSA prostate cancer test now agrees it is worthless, stating, "I never dreamed that my discovery four decades ago would lead to such a profit-driven public health disaster." He noted that the annual bill for PSA screening is at least $3 billion, with much of it paid for by Medicare, and "As I've been trying to make clear for many years now, **PSA testing can't detect prostate cancer** and, more important, it can't distinguish between the two types of prostate cancer -- the one that will kill you and the one that won't."

The public is also confused by articles claiming staying out of the sun as much as possible increases cancer risks; drinking lots of water during intense exercise can be fatal; taking fish oil, exercising, and doing puzzles doesn’t really help prevent Alzheimer’s disease as generally believed; and peer reviewed studies that come to opposite conclusions about whether cell phones cause cancer, sleeping more than eight hours is dangerous or

healthy, taking aspirin every day is more likely to save your life or cut it short, and if angioplasty works better than pills to unclog heart arteries.

Ioannidis, who was considered a child prodigy because of his mathematical prowess, discovered that erroneous conclusions were often due to what questions researchers asked, how they set up the studies, which patients were recruited; what was measured; what end points were selected; how the data was analyzed; how the results were prevented; and how particular studies came to be published in specific medical journals. It is not surprising that he discovered that this was mostly due to drug company manipulation of data and an obsession with attracting funding that would provide profits. Newer no longer means better, and recently approved drugs are mostly "me too" copies of preexisting ones that have lost their patent protection. There is much more that could be said about Ionnadis' research findings, which have been published in prestigious journals and are attracting increased international attention because they cannot be contested, and we will revisit this at a later date because of space constraints.

They support my view that the deterioration in medical care and the quality of medical publishing is largely due to the relentless pursuit of profit, not only by the pharmaceutical industry, but physicians and everyone involved in the delivery of health care. Pasteur, Cannon and Selye were motivated by curiosity and the desire to find the truth rather than financial gain, but "Art for Art's sake" is dead. This is true not only in medicine, but professions like law, music and motion pictures, where making money is now the main goal. In thinking about all of this as it relates to medical journals, I could not help but be reminded of Ivan Illich's statement that "The medical establishment has become a major threat to health", Thoreau's "Men have become the tools of their tools", and a Jeep Cherokee ad that similarly warns, "The things we make, make us." Hope may be on the horizon — so stay tuned!

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