

Assessing 'Real Science': Poor Studies, Industry Ties Taking Toll

By Janyce Hamilton

Far too often, scientific studies — subsequently printed in dental journals — are poor^{1,2} or influenced by product manufacturers.³⁻⁶ This misconduct is not limited to industry-funded researchers. Some individual and academic researchers also play loosely with the facts.^{7,8} Government research is subject to mechanisms of supervision⁹ or oversight.^{9,10} But in the case of oversight, who is watching the watchdog? Worse, dentists are making clinical decisions and product recommendations based on these studies because they either don't know how to evaluate a study's scientific merit, or are not privy to the industry ties or other motivations influencing its authors. Regardless of the funding source, if a manuscript is well-written, it is virtually impossible to detect fraudulent data within its pages. Whistleblowers¹¹ and confessions then become the only hope.

This report looks at what constitutes "real science" and at some of the conflicts of interest in dental research and publishing. It seeks answers to the following questions:

■ How are dentists doing at evaluating the scientific merit of studies they read?

■ Can they trust the information about the products recommended in articles?

■ Do pharmaceutical as well as materials, devices, and equipment companies have too much control over how their studies are designed and whether unfavorable findings are published at all?

Searches via MEDLINE, Google, and the ADA Library were combined with interviews to identify the issues around good vs. poor research and the conflicts of interest affecting dentistry and medicine. One interviewee preferred to remain anonymous.

Included are tips for health care professionals to better dissect data, weed out weak studies, and assess whether a research-industry relationship exists in a published study.

Plaguing the health of real science are problems that show no signs of de-

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creasing. As suggestions for safeguards have emerged in medicine, organized dentistry is finding its footing as sentry of research-industry ethics.

What Is and Is Not Real Science?

It's hard enough for a doctor of dental surgery or medicine to decipher if real science is behind a study, let alone to know the competence and integrity of its lead author. Imagine what the public goes through when they hear the latest dental scare on the news.

With the Internet and nonpeer-reviewed magazines disseminating what appears to be "solid evidence" on the dangers of amalgam restorations, for example, the public starts getting more than a little anxious. Policymakers, even congressional representatives¹² — "scientific illiterates"¹³ untrained in evaluating real science from junk studies — pass a law, such as California's Proposition 65. Before you know it, dental offices are passing out Dental Materials Fact Sheets to all patients like they are invitations to a party.¹⁴

Meanwhile, in several other countries, the U.S. science exonerating amalgam risks is deemed an insufficient contribution to the body of evidence. Health Canada — the equivalent of the U.S. Food and Drug Administration — for example, recommends that amalgam not be placed or removed during pregnancy and that parents consider amalgam alternatives in children.¹⁵ In fact, the contraindications to using amalgam are listed by some manufacturers abroad on amalgam package inserts.

And that's just amalgam.

Meanwhile, periodicals such as the journal *Fluoride* look and read every bit as professionally as the big peer-reviewed dental journals. "A publication that has the tone and trappings of science, but is so fundamentally and demonstrably flawed as to lack any serious claim to credibility"¹³ is the definition of junk science, according to Marjorie K. Jeffcoat, DMD, editor of the *Journal of the American Dental Association*. Unfamiliar dental terms such as "fluoroporosis" and "toxic fluorification" may tip off savvy readers of a publication's anti-fluoridation agenda. Groups that oppose fluoride, such as the Fluoride Action Network¹⁶ of Burlington, Vt., put articles on the front page of their web sites from well-known newspapers or magazines that seemingly indict fluoride. Take, for example, the headline "Weak Link on Fluoride and Cancer Is Backed" in the *New York Times* in April of

1990.^{16,17} It's a good example of don't believe everything you read. The article seized upon unauthorized data released from a Public Health Service National Toxicology Program investigation and reported *inconclusive findings* of a weak association between high fluoride consumption and osteosarcomas in male rats.¹⁸ Fluoride Action Network displays the *Times* article on its web site as if it were the final verdict in the trial of fluoride's carcinogenicity. This tactic of overgeneralization is another hallmark of junk science, according to *JADA's* Jeffcoat, who defines overgeneralization as "when association is confused with causation."¹⁹

The Fluoride Action Network's web site fails to mention — even at this writing in the year 2004 — that the National Toxicology Program subsequently found that the supposed link between high amounts of fluoride and cancer in male rats was deemed inconclusive.²⁰ Nowhere in the "scientific references" lists of these organizations are the 1991 Public Health Service report,²¹ the 1993 National Research Council literature review,²² the 1999 Centers for Disease Control and Prevention article,²³ or the 2000 National Cancer Institute cancer fact sheet on fluoridated water.²⁴ Any of those references lay to rest the debate that "credible evidence" has proven fluoridated water causes cancer in humans.

So much for fluoride and "real science."

Caries research confusion is divided much as the country is split between two political parties. In 2003, why did the American Academy of Pediatric Dentists accept a \$1 million grant from Coca-Cola to its foundation? Dentists have long pointed to the equation of "sugar + acid = bad news" in dentistry. It is not uncommon for soft drink companies to get cash-strapped schools to sign exclusive pouring-rights contracts. For every bottle of product sold, the schools get money back, which allegedly motivates schools to provide easy student access to pop machines. In 2000, ADA passed a resolution stating its position as being opposed to such contracts. An ADA spokesperson commented that the science suggests excessive consumption of sugar, such as through soda pop, can harm teeth. A National Institutes of Health systematic review²⁵ supports the philosophy of limiting sugar. But what if the consumption isn't excessive, and it is the consumer who is at fault for overindulging?

"There's no science to bash soft drinks; that's just old-school simplistic thinking. Why has permanent dentition caries declined as sugar consumption and school-age chil-

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Table 1

Seven Elements Required in Any Good Clinical Trial.*

1. A clear statement of the objective based on sound scientific rationale, and a description of how the methods of analysis were selected.
2. A design that permits a valid comparison with a control to provide a quantitative assessment of the therapeutic effect. The study design should be described in detail (e.g., duration of treatment periods; whether the treatments were parallel, sequential, or crossover; how the sample size was determined).
3. A method of selection of subjects that provides adequate assurance that they have the disease or condition being studied.
4. A method of assigning subjects to treatment and control groups that minimizes bias and is intended to ensure comparability of the groups with respect to pertinent variables such as age, sex, severity of disease, duration of disease, and use of drugs or therapy other than the one being tested. The study should describe how subjects were assigned to groups. This is normally accomplished through randomization.
5. Adequate measures must be taken to minimize bias on the part of the subjects, observers, and data analysts. This is normally accomplished through blinding.
6. The methods of assessment of subjects' response should be well-defined and reliable.
7. The analysis of the results of the study are adequate to assess the effects of the drug.

*Source: Adapted from various Food and Drug Administration publications.²⁷⁻³⁰

dren's access to vending machines has increased consistently since 1968?" asks AAPD's past president, professor of pediatric dentistry at Ohio State University, and interim editor-in-chief of the *Journal of Dentistry for Children*, Paul S. Casamassimo, DDS, MS.²⁶ Casamassimo counters that the peanut butter sandwich on wheat bread in a child's lunch bag may be more cariogenic than the can of pop from the school vending machine that will be washed away by saliva. He let his own offspring eat candy during their childhood, and today as adults their permanent dentition remains cavity-free.

"I see the AAPD as Robin Hood, taking from the rich (Coca-Cola) to fund the poor (AAPD research) to learn about complex caries-carbohydrate comorbidities to help kids," he said. "Science is changing, but dentists are holding onto old beliefs."

He urges skeptical dentists to read about the conflicting data on sugar and tooth decay in the 2003 World Health Organization review "Diet, Nutrition, and the Prevention of Oral Diseases."

Web sites such as www.dentalwatch.org and www.junkscience.com point out some of the more typical methodologies that organizations and individuals use to give their research findings the stamp of credibility. Visiting web

Table 2

NIDCR's Division of Population and Health Promotion Sciences Good Quality Research Attributes.*

1. It is ethical and incorporates principles of respect for people (obtains appropriate informed consent), beneficence (does no harm, maximizes benefits, minimizes possible harm); and justice (fairness in distribution of benefits and burdens of research).
2. It adheres to all applicable federal and local regulations and guidelines for clinical research.
3. It is appropriately designed to answer questions that are of clinical importance to patients, consumers, and practitioners.
4. It has a sound biologic rationale.
5. It has appropriate statistical power to detect clinically meaningful results.
6. If it is a clinical trial, it is randomized with patients and clinicians appropriately masked to treatment procedures and outcomes.
7. If it is a clinical trial, it is of appropriate length to demonstrate a clinically meaningful result.
8. The population being studied is representative of those who are affected by the disease or condition being investigated.
9. The results can be generalized to the population at risk for the disease and not just to a very select sample of people.
10. The statistical methods are appropriate for the design of the study.
11. The investigator appropriately discloses any financial support for the study and any financial interests that he or she may have in any products or drugs that are involved in the research.
12. It is published in a highly respected peer-reviewed scientific journal.

*Source: Bruce L. Pihlstrom, DDS, MS, Division of Population and Health Promotion Sciences NIDCR.



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sites such as these can be useful in developing and maintaining a critical eye for discerning credible scientific studies.

Studies published in peer-reviewed journals have a better chance of being well-designed, with the results being valid, said Kenneth Burrell, DDS, senior director of ADA's Council on Scientific Affairs. "However," Burrell, cautioned, "readers should always look at any article with a critical eye, since even well-respected, peer-reviewed journals occasionally can publish questionable studies." Burrell provided a "checklist" of what he looks for when assessing a clinical trial in **Table 1**.²⁷⁻³⁰

A clinical trial is one type of research. Bruce L. Pihlstrom, DDS, MS, acting director, Division of Population and Health Promotion Sciences of the National Institute of Dental and Craniofacial Research, had his own list of attributes of good quality clinical research, shown in **Table 2**.

To be safe, dentists should never change what they prescribe or how they treat patients based on a single study.

How Well Are Dentists Assimilating Dental Data?

"Dentists aren't doing very well in general at evaluating studies and assimilating all the data published yearly in the journals on each clinical dental topic," Michael G. Newman, DDS, admitted. Editor of the *Journal of Evidence-Based Dental Practice*, adjunct professor at the University of California at Los Angeles School of Dentistry, and past president of American Academy of Periodontology, Newman said poor dentists are twisting in the wind trying to get the information they need from the thousands of research reports published each year.

"The classic scenario illustrating the problem is when the patient comes to the dentist with a clinical question," Newman said. "For example, 'What do you think about bleaching safety, doctor?' 'I don't know, I'll have to get back to you.' He goes to the Internet with the question and up comes 17,000 articles."

All dentists base their decisions on evidence, but the evidence they use isn't always valid and can't always be generalized. What Newman's journal does is publish reviews on clinical dental questions. An evidence-based assessment involves evaluating whether a study is scientifically sound and if the results can be generalized. See **Box**, this page, for examples of evidence-based dental web sites.

ADA supports the evidence-based dentistry concept,^{31,32} as does NIDCR.³³

"But from the practitioner's perspective," Burrell said, "evidence-based dentistry isn't there yet." Supporting his opinion, Burrell cited that, at this writing, only 72 clinical questions have been answered using evidence-based criteria out of thousands that need to be answered.

World Wide Web Examples of Evidence-Based Dentistry Information*

1. Journal of Evidence-Based Dental Practice

<http://www.us.elsevierhealth.com/product.jsp?isbn=15323382>

2. University of Michigan Dental Library

<http://www.lib.umich.edu/hw/dent/clinical/eb.html>

3. Centre for Evidence-Based Dentistry

<http://216.239.41.104/search?q=cache:q7BGFbdNB7sJ:www.ihs.ox.ac.uk/cebdl/+8hl=en&ie=UTF-8>

4. The Cochrane Library

<http://www.update-software.com/cochrane/>

5. The National Library for Health

<http://www.nelh.nhs.uk/>

*Nos. 4 and 5 are evidence-based medicine sites with dental articles.

Because they help to cull out what might be fraudulent, systematic reviews are desirable for good research. Burrell said ADA can play a role in evaluating the quality of systematic reviews, and summarizing and publishing condensed versions of such reviews along with its findings on the review. "Some reviews are known to be better than others."

ADA members are being surveyed in 2004 to learn which clinical questions clinicians want answered. For all groups conducting systematic reviews, ADA is holding a symposium in August to determine what clinical questions they want answered, and to gauge interest in conducting reviews to answer these questions and determine funding sources for such a cooperative project.

In the meantime, high schools and universities should teach critical thinking as part of the fabric of education in science. "By the time a student begins his or her dental education, it's almost too late," Burrell said. But applying evidence-based dentistry principles through the dental training process is a good way to foster critical thinking.

"Real science" tables and checklists are fine for some. But when Harold Slavkin, DDS, dean of University of Southern California's School of Dentistry, sits down with his dental journals (9,000 dental articles are published worldwide each year), he is able to recognize the real stuff. He looks for the gold standard — results derived from peer-reviewed multicenter, randomized, prospective clinical trials supported by funding that is without real or perceived conflict of interest. According to Slavkin, former director of NIDCR and current member of the Institute of Medicine's Clinical Research Roundtable, "Although the importance of research in dental and medical education has long been recognized, education

of the practicing clinical community about the clinical research process has not received sufficient attention. We must do a better job in education and training to best advance an understanding of the ethical, regulatory, and legal issues of clinical research.”

Reading and interpreting real science also requires professional education and training. “Molecular dentistry, the human genome project, and proteomics have opened vast opportunities for translation of basic science discoveries to the chairside and bedside through clinical research. Training at the National Institutes of Health as well as several major research-intensive universities now offer MS and PhD education and training in the principles and applications of clinical research,” Slavkin said. “The bar has been raised.”

Besides evidence-based decision-making and roundtables, helping to raise the bar of quality research is Consolidated Standards of Reporting Trials. CONSORT (<http://www.consort-statement.org/>) consists of a checklist and flow diagram for investigators and editors to use to assess quality criteria and standardize reporting when they write and edit trials so that results can be “interpreted both readily and accurately.”³⁴ The failure to use a process such as CONSORT in the past has resulted in some reports omitting information critical for evaluating a study’s conclusion, according to Burrell. A study of published trials in journals before and after use of CONSORT tools found that the clarity of reporting improved by 22 percent.^{35,36} This “help” has been embraced abroad¹ and by U.S. medical and health journals. In dentistry, the *British Dental Journal* and the *Journal of the Canadian Dental Association* have signed on to these tenets.

Always a sentry of research quality, ADA is pushing itself further. Coming from ADA are new guidelines for clinical trial reporting called Standardized Clinical Trial Protocol. A draft of the protocol indicates it will be used to help ADA evaluate clinical studies, including whether there may be financial conflicts of interest.

Industry-Funded Research: A Conflict of Interest?

Are industry ties nourishing or poisoning medicodental research? The popular media and health professions literature are sounding the alarm bells that they are.³⁷⁻⁴⁰ Yet, many argue that industry — from a small dental lab supply

company to a giant pharmaceutical maker — have more to lose if they are caught altering records or eliminating data. Their researchers must be just as vigilant as academic, government, and independent researchers in using credible methodology and keeping clean records. Reputation and goodwill take years to build, and companies don’t take risking them lightly. Should fraudulent practices such as bribes or falsification of documents be uncovered, the wrath of boards of directors and shareholders and big fines are likely. Jail time is also a possibility — and a strong deterrent.

Dentistry has been flying under the radar when it comes to unethical conflicts of interest for researchers, authors, and lecturers in contrast to the attention paid these topics in medicine. But what’s happening in medicine may foretell dentistry’s pending predicament.

Following are the good, the bad, and the ugly in medicine’s uneasy alliances with industry.

The good. Fantastic drugs, devices, and machinery that have clearly improved clinical practice were borne by industry-funded research fueled by the for-profit motive⁴¹: gene chips; new technologies to design and more quickly produce vaccines and antibodies against cancer and even viruses or bacteria released for hostile purposes; and more recently, synthetic high-density lipoprotein to flush clogged arteries.⁴² In fact, this is how nearly all drugs

are “discovered” today.

“Without industry funding, we would have no new products,” Newman said. They have so much money at stake that he believes their regulatory departments comply very carefully and try harder than “the little guy” who doesn’t have the funding for well-conducted studies.

In fact, the FDA approves only 1 of 5,000 screened compounds.⁴³ The growing complexity and increased length of trials required by the FDA means that researching, developing and introducing a new drug costs on average \$802 million in 2000 dollars.⁴⁴

According to the 2003 industry profile provided by the Pharmaceutical Research Manufacturers of America, U.S. pharmaceutical companies spend more each year on pharmaceutical research and development (\$32 billion in 2002) than the total NIH operating budget — an amount that has more than tripled from 1990.⁴⁵ NIDCR’s slice of the NIH pie is thin, only 1.58 percent of the total budget, according to Slavkin. This may not sound great, but NIDCR offers more

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KENNETH BURRELL, DDS



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funding now than five years ago, he said.

Government and academic researchers are increasingly being lured away from their traditional funding sources and toward industry financiers. Maryka H. Bhattacharyya, PhD, is a senior biochemist at Argonne National Laboratory, Argonne, Ill. Her life's research has been the effects of cadmium on bone loss. While she hasn't looked at bone density loss in the jaws, data analyzed from NHANES III show that postmenopausal women with osteoporosis have double the risk for tooth loss compared with those who don't have the disease.⁴⁶ Since 1980, Bhattacharyya has received \$12 million in federal funding. Today at age 60, however, Bhattacharyya is in a predicament. Her last five grant proposals to NIH have been turned down. She is discovering that while federal health sciences funding has increased in recent years, in this postgenomic era, the funding trends have moved toward large-center grants that fund multidisciplinary research teams. A researcher just out of school makes perhaps 20 percent to 40 percent more in a biotech industry than one hired by a national laboratory, Bhattacharyya estimated. "As an older researcher, I would not benefit so much (salary wise) from switching to industrial research. Plus, I would have a hard time finding such a position." Her husband, also a scientist, left a national laboratory and formed his own business to continue researching on contract. Bhattacharyya has two patents but never made money from them. So today, she must keep her funding options open, or be jobless. Industry, once viewed as guys in black hats, are today being viewed more as "partners in research" with academia and government, Bhattacharyya reported. As such, for the first time in her career, she applied for funding for a three-year study from Research Management Group, through a program 100 percent funded by Philip Morris Co. The company is interested in the effects of cadmium on calcium loss in human bone because it is present in tobacco leaves.

She wondered just how her colleagues would react to her pursuit of Philip Morris research. "I mentioned it to several of my colleagues, and they were either being funded by (Philip Morris), or were also applying for it."

Bhattacharyya's first choice is doing federally funded research on a basic science question that interests her. But at this point, she welcomes the opportunity to research questions tied to the health effects of a marketable product —

Industry, once viewed as guys in black hats, are today being viewed more as "partners in research" with academia and government.

namely, cigarettes. After all, there is that chance that her research would lead to reduced cadmium in cigarettes to lessen potential osteoporosis risks, should such related risks be discovered.

"I feel no pressure to 'get certain results' that will be favorable to Philip Morris' interests regarding hazards associated with smoking cigarettes. I would not change the design of my experiments to get certain results," Bhattacharyya said.

Part of her comfort level comes from the safeguard Philip Morris put up of having a separate management group run their external research program, she said.

But are they really separate?

The bad. Drug and material safety trials used to be done at academic medical centers but are increasingly done at private "separate" research centers. "Their only income comes from drug companies that contract with them to do these clinical drug trials, so they really have no independence from the drug companies," said Thomas Bodenheimer, MD, MPH. He practices part-time at a low-income California clinic on Valencia Street in San Francisco. Besides being known as a clinical professor at the University of California at San Francisco School of Medicine, Bodenheimer has gained a reputation as a national correspondent for

the *New England Journal of Medicine*. He lectures on the extent of pharmaceutical industry influence on the design of clinical trials, and how often studies with negative outcomes are suppressed.

How widespread are industry ties in research and publishing? The February 2002 *Journal of the American Medical Association*, reported that "90 percent of authors of clinical practice guidelines received research funding from, or acted as consultants to, a drug company." Are these authors at fault for such uneasy alliances? They may not be. More than half reported that there was no formal procedure for reporting these relationships to the publication or their affiliated institution. The thinking goes like this: "If there are no rules on it, it must be OK."

A 2002 editorial in the *Lancet* bemoaned that independent U.S. medical journals are publishing biased articles: "Industry may have delivered a fatal blow to a laudable enterprise: The bias that industry has injected effectively demolished the foundation upon which public and professional trust had been built."⁴⁷

Bodenheimer is not alone. There's a courageous cadre of

health care and allied professionals, including the former editor of the *New England Journal of Medicine*, who oppose practices that bring medicine into disrepute. They are concerned that the situation is out of hand, and speak out in lectures and articles.

The response seems to be more of a ripple than a roar.

Research on research integrity sparse. An exhaustive review in 2000, "Assessing the Integrity of Publicly Funded Research," sponsored by the NIH Office on Research Integrity and other organizations, confirms that research on research integrity is relatively sparse in medicine. In dentistry, it's almost nonexistent.

A 2003 systematic review looked at eight articles that studied industry-sponsored research results in a total of 1,140 studies. The finding was that the association between study outcomes that favored industry and studies that are industry-sponsored is statistically significant (Mantel-Haenszel odds ratio, 3.60; 95 percent Confidence Interval, 2.63-4.91).⁴⁰ There was no statistically significant difference between studies that were randomized controlled trials and those that were not. This is not conclusive proof that negative findings on products are squelched by researchers, however. Other factors, such as publication bias, can favor studies that have positive results, regardless of funding source.⁴⁸

While it is unfair to pick on industry as the poster child of research misconduct, researchers and authors with industry ties do their share. To be fair, it is important to remember that some university faculty members who want to get tenure may be tempted to fudge data. Some federal or Indian Health Service employees who want to be promoted to a supervisory position could be thinking about plagiarizing. If problems such as these are not acknowledged and better managed by health care leaders — especially when it involves drugs — how can we expect people to continue to volunteer for clinical studies?⁴⁹

The ugly. A survey of more than a thousand postdoctoral fellows about ethical matters related to biomedical research and publishing showed revealing findings on misconduct. Twenty-seven percent said they were willing to select or omit data to increase the chances of getting a grant funded; 15 percent would select or omit data to make publication of their work more likely or benefit their career.⁵⁰ Surprisingly, having taken a course on research ethics had no bearing on stated willingness to fabricate data.

"An error of omission is viewed less harshly than the error of commission," said a Midwest cardiac interventional radiologist who preferred to remain unnamed.

Fortunately, documented science, medical, and dental researcher misconduct is rare.⁵¹ But still, preventive strategies and good supervision of researchers is advised by Jane Steinberg, a research integrity officer at the National Institute of Mental Health. Steinberg advises organizations doing research to "inoculate staff against the temptation to find a 'better' way to run the study midstream."⁵¹

"Human nature cannot be legislated," the radiology physician commented. This same physician explained that he is approached frequently with offers of free trips to destinations such as Las Vegas and other substantial perks. Although he refuses most of them, he said it would be easy to get a company to pay the tab for a fantasy vacation. "I can turn in my airfare and other receipts with no questions asked."

Meanwhile, if this radiology physician wants to invest in stock in the company that makes a product upon which he is doing academic medical research, his teaching university allows this. Harvard Medical School does too.^{52,53} If that same company continues to fund grants for the radiology physician to do studies of their

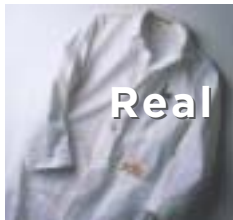
product, as well as lavish dinners and golf, this is allowable too. He continues to reinvest his earnings in the company, and around it goes.

Why do we assume a medical researcher is more immune to financial influence than any other person? Why are there not certain conflicts that are not allowed in health research?

One reason for the status quo is that universities don't want to lose prestigious physicians to other institutions with less stringent conflict-of-interest policies, so they don't crack down. In one study of the top 100 institutions receiving the most funding from the NIH, most of these institutions' policies on conflict of interest lacked specificity about which kinds of relationships with industry are permitted and which kind are prohibited.⁵⁴ The NIH Office of Extramural Research also reports finding "diffuse policy on and vague statements in conflict of interest policies" in its study of more than 100 policies representing a mix of public and private academic institutions, public and private research institutions, hospitals, and large and small for-profit organizations.⁵⁵ But public scrutiny of these ties is increasing⁵⁴ If nothing is done by institutions, organizations, or govern-

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ment, research standards in the United States could erode further. “Doing something” would include more than having a clear, specific conflict of interest policy — it would mean having an additional policy on management strategies to mitigate or eliminate each type of conflict of interest.^{56,57} For example, when does stock need to be sold? When does a new principal investigator need to be named for the study? Does a researcher need to resign from a post before the study will be published? Granted, none of these rules would undo fraud already committed at the research stage. Yet, having policies and procedures at, say, the publishing stage, culls out unethical activities. The potential for author embarrassment could serve to discourage those prone to sleazy practices from submitting their manuscripts, and encourage researchers with twinges of ordinary human greed to ignore temptations to shortcut and “keep it clean.”

Publication Problems and Their Prevention in Medicodental Journals

Accuracy alone is a challenge. By the time research makes it into a journal, the resulting article may be the one in four published articles whose abstract does not necessarily accurately reflect what’s in the article.⁵⁸ One investigator claims providing authors with instructions for abstracts

doesn’t adequately eliminate abstract deficiencies, but having journal editors assume this responsibility does.⁵⁹ Meanwhile, there are some who call for industry ties to a study’s author to appear in the “methods” section of the published reports to increase the chances that these conflicts of interest will make it to the MEDLINE abstracts.

Burrell thinks it is unnecessary for industry sponsorship to be in the abstract as long as it is obvious in another area of the paper. “Somewhere in the article it should be revealed,” he said. Bhattacharyya says that’s a great idea. (The *Journal of the California Dental Association* requires authors to disclose any affiliations with a company that has direct financial interest in subject matter discussed within the article. These are printed in a “disclosures” or “acknowledgments” section.)

Bodenheimer, in a recent *New England Journal of Medicine* article, explained that the pharmaceutical industry’s partnerships with commercial research companies to create clinical drug trials is a slick business enterprise on more than one front. Staff writers and independent ghostwriters for these companies are purported to create articles the marketing people tell them to write. The company then convinces academic scientists and physicians to willingly sign on as the “authors” of studies. Why would they do so? Little or no work on their part, and all the recognition in a publish-or-perish environment.

How to tell if a study is funded by industry. If you are reading a journal that has conflict of interest sunshine policies, there are tip-offs that a study is linked with a manufacturer. For instance, a statement in the article says the study is funded by the company or that the researchers received a grant from the company. Or perhaps at least one of the co-authors of the study is affiliated with “a middleman” — a medical education or research firm. This information may be found in the acknowledgements or author biography section of an article.

A journal that fails to reveal industry-funding information should not be relied upon as a sole source of educational information since all the facts are not revealed. It is ill-advised for a practitioner to make any clinical decision without all the facts.

In a study linked with manufacturers, it may be harder for the researchers to be 100 percent financially independent from that product’s makers and marketers. This does not mean one should devalue the insights provided by the study. “Companies can support studies to find out if their products work or not. What is important are that safeguards are in place to prevent misconduct,” Burrell said.

Organized dentistry and medicine must continue pursuing these issues through talking about them in workshops, publishing articles on conflict-of-interest issues, and updat-

There is Nothing ‘Potential’ About a Conflict of Interest

By Marcia Angell, MD*
Editor-in-Chief, *New England Journal of Medicine*

A financial conflict of interest, I believe, is any financial association that would cause an investigator to prefer one outcome of his research to another. Let me give you an example. If an investigator is comparing drug A with drug B and owns a large amount of stock in the company that makes drug A, he will prefer to find that drug A is better than drug B. That is a conflict of interest.

Note that it’s a function of the situation, not the investigator’s response to it. If the investigator then finds that drug B is better, he may swallow his disappointment and report the facts objectively — or he may not. Thus, there is nothing “potential” about a conflict of interest. Either it exists or it doesn’t. What is potential is whether a conflict leads to bad research.

*Excerpt from a speech delivered at the HHS Conference on Financial Conflicts of Interest, Aug. 16, 2000.

ing their policies to self-police, or government watchdogs may further intervene with legislation.

Currently, it is not possible to assess the degree to which a researcher-industry relationship is problematic, so scrutiny of study design is advised. Research has found that some companies have been known to design studies in a way that favors their products.⁴¹ To brush up on the methods some companies may use to produce desired results, worthwhile reading is an article by Bero and Rennie that catalogues some of these methods.⁶⁰

Even industry-sponsored placebo-controlled trials for a new drug for persistent asthma (a life-threatening and debilitating disease) has suffered from numerous and serious ethical flaws.⁶¹ If that's how industry treats asthma, what's to say they won't be more bold on claims, and lax on research and reporting standards, when it comes to periodontal disease?

The suggestions provided in the first half of this article provide several suggestions for how to prevent being duped by poor research.

Industry-supported and -sponsored research in dental journals. "Industry-supported research can be superb in every way," Slavkin said. "Major pharmaceutical companies very often sponsor outstanding clinical studies. The devil is in the details."

The details hidden from view may or may not reflect ethical abuses. If dentistry continues to shine more light on such details, it will spare its reputation from going through the meat grinder of public opinion.

According to John Kanca, III, DMD, editor-in-chief of the *Journal of Esthetic Dentistry*, "Abuse invites regulation."⁶² Kanca is one dentist who is unhappy that air abrasion is used to diagnose caries in stained pits and fissures without "definable data to establish an epidemiological basis." Yet, where are the systematic reviews proving either effectiveness and safety or just the opposite? They haven't been done yet, and that's the challenge.

As a result, dentists' individual skills and experience on this and other clinical issues will continue to be valued as much as any study. Most of the time, dentists conservatively implement trial and error in treating their patients with newer products and ideas to make incremental improvements by themselves. By the time the research-publication lag has caught up with them, they already know what works for their patients.

As a guardian of the profession, ADA's Principles of Ethics and Code of Professional Conduct calls on dentists to disclose to readers (of articles) and participants (in seminars) any "monetary or special interest the dentists may have with a company whose products are promoted or endorsed in the presentation."⁶³ Of course, a lawyer could advise a researcher how to work around not "promoting" or "endorsing" the product they are researching. Regardless, this is a noble effort by the profession's leading organization to light a pathway for those in the dark on this issue.

JADA reveals conflict of interests — such as sources of research support and industry affiliations — with a disclaimer in a "prominent and accented position" in the article.⁶³

Research of health care literature may clear up whether problems result if these affiliations are not specifically included in journal articles' "methods" sections. In theory, placement in the "methods" section would increase the odds that this information makes it to MEDLINE, which usually only includes article abstracts. Yet we live in a world where some researchers are not scrupulous enough to access the full text and instead cite research results by reading abstracts only. This makes it clear that the responsibility for ethical values rests with the individual as much as it does within the policies of organizations, academia, government, and publications.

What about when a dental education company hired by the dental equipment manufacturer (much like pharmaceutical companies hire research companies) uses ghostwriters to say what the equipment company wants? Medical education company affiliations are often perceived to be "separate," even though their funding depends on keeping their equipment manufacturer client happy. More research is needed into whether any influence actually results when these subcontractors — independent entities on paper — are hired by industry to do research, writing, and education.

Slavkin, Burrell and Jeffcoat contend that the threat of harsh penalties that could result from fraudulent research and authorship practices is a big deterrent. So while attorneys are helping their clients parse what they can get away with, dental researchers need to be reminded that fraud can qualify as a criminal act, and that medical researchers have landed in jail for this.

Lisbeth Maxwell, editorial director of JADA, had this comment: "I truly hope none of our authors has succumbed to this

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Real Science

temptation — but if any have, they are in the minority. I have found dentists to be scrupulous.” JADA’s policy to instruct its authors to adhere to the 2001 Uniform Requirements for Manuscripts Submitted to Biomedical Journals helps it to zero in on affiliations that require a closer look.⁶⁴

Summary

Preliminary research is still done by academic researchers. The expense of designing and conducting a good clinical trial by today’s standards (i.e., a multicenter randomized controlled trial) has resulted in academic institutions not being able to afford to conduct such studies. Therefore, research on dental products and drugs is often funded by the companies that have the potential to profit off their success. This is a trend, and there is good that comes from this. With plentiful funding, for instance, a study’s sample size may be larger and the equipment used may be cutting edge compared with what could be mustered by a lone university researcher assisted part-time by two dental student interns.

Stories of industry hijinks such as controlling study design, storing the data and refusing to release it to the study’s researchers, writing the manuscript and then only allowing portions of the results to be reported, continue to make the news. Whether factual or fictional, these stories are fueling the conspiracy theories of compromised research integrity.

Research shows financial backing from a company introduces a conflict of interest in a study because the arrangement may reduce the independence of the investigators. Subconsciously, a researcher may feel an allegiance to the funding source. Meanwhile, a contracted research or education company doesn’t want to upset its clients, or it would go out of business in a competitive market. Thus, they may be consciously designing the study as directed by the companies, for the purpose of finding the findings desired. These biases on the part of the researchers cannot be used to vilify industry funders. To be fair, they are researcher issues.

Companies are not alone in doing pretesting in internal pilot investigations before a full-blown study to avoid wasting money on trials that are unsuccessful at producing desired results. Because of this, there is evidence that negative findings on drugs, devices, products, and machinery are less frequently published. Are disclosure laws on study results needed to protect the public? If a telemarketer can be fined \$10,000 for interrupting someone on the do-not-call list who is watching TV, shouldn’t a research team be fined something for halting studies “not going well,” and for subsequently failing to mention the dangerous side effects found with the product if used under certain circumstances?

To quiet the controversy, perhaps leaders in industry,

academia, government, and publications need to create clearly written researcher and author policies with defined do’s and don’ts. Additional articles on managing research and publication conflicts of interest are welcome in the dental literature. Combined with the recent move in organized dentistry to request that researchers follow certain clinical protocol, this would bode well for the profession. They would serve as evidence that dentistry is a health profession that has a working compass that continues to point toward justice. It will take discipline to use self-determination to follow the ethical road becoming less traveled.

Ideally, studies of all funding source types will try to utilize researchers employed by dental schools to control the design, implementation, data analysis and publication. Whether industry scientists, commercial research companies, academic, government, or individual researchers are at the helm, publication editors should hold their manuscripts to strict methods CONSORT standards.

Dentists should seek to learn more about evidence-based dentistry, and heed the advice from ADA Council on Science reports on what is clinically trustworthy.

Conclusion

Is real science endangered?

While industry ties and weak studies are perceived by some to be taking a toll on dental research, Burrell does not seem worried. He said that he uses skepticism to protect against poor science. “A healthy attitude might be that all research is guilty until proven innocent. It doesn’t matter if it’s from industry, academia, government, or an individual.”

“The ADA knows that fraud exists in research and publications,” Burrell said. “We are on it, and we’re doing something about it to protect you.”

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