Epidemiological Research, Interest Groups, and the Review Process

COLIN L. SOSKOLNE

INTRODUCTION

THE scientific review process has evolved on the premise that "two heads are better than one." Its application in epidemiology, as in any other endeavor, is essential for maintaining standards which are fundamental to the advancement of the science. In principle, the guidance of peers is sought to ensure that new evidence, or a new perspective on old evidence, is added to traditional scientific evidence in accord with "the scientific method." In recent years, however, the practical application of the review process has caused ethical concerns to be raised, particularly when the interpretation of the science requires an artistic component as well. A delicate balance can be involved in judging whether or not a piece of research conforms with "the scientific method." It is the purpose of this paper to highlight instances where the review process has been shown to have been imperfect and to recommend the development of safeguards to help advance epidemiology as a science.

THE REVIEW PROCESS

Peer review is usually invoked at three distinct stages: first, in developing a research proposal; second, while work is in progress, as in a site review or through the scrutiny of preliminary findings; third, at the time of manuscript submission for publication. The latter can occur both internal to the establishment conducting the research when obtaining publication clearances, and externally at the publishing journal's discretion. A fourth stage of review can be imposed, however, in the form of a "consultant review."

Input from colleagues at the design stage in developing a research proposal can take a number of forms. Depending on the nature of the institution supporting the research, the form that the review process may take can range from informal comment provided by colleagues to the more

formal calling of "protocol parliaments" which provide a structured forum for collegial inputs. Such feedback and interaction ensure that the proposal both meets the needs of the institution in which the research is to be conducted and maximizes its potential for funding. In essence, discussions among the institution's own researchers or representatives and the primary investigator help ensure successful research.

The second stage at which review is often mandatory occurs while work is in progress, by means of a "site review" or through the presentation of preliminary findings. The purpose of a review at this time might be to provide the investigators with recommendations for additional or more directed analyses of their data in order to achieve the study objectives.

Some research establishments may require the "internal clearance" of a manuscript prior to journal submission for publication. The reasons for this can be many, including: (1) the altruistic concern that the submission be maximally successful; (2) informational, so that ramifications of the research findings about to be submitted for publication can be assessed with sufficient advance notice to allow the institution time to prepare its response to anticipated questions, or (3) political; anecdotes exist concerning incidents where institutions have attempted to delay or block the submission of manuscripts at this stage. It is here that some institutions seek pre-publication review from respected senior scientists, usually academicians, and the fourth stage of review can then be invoked.

THE CRITIQUE, INTEREST GROUPS, AND THE EPIDEMIOLOGIST

By the nature of epidemiologic training, skills at critiquing population-based studies are sharpened. This sharpness is misguided in those instances when only a narrow view of a piece of research, the report of which is under review, is considered, without placing any of the limitations found in some perspective. Such instances may arise when groups having a vested interest in the reported findings arising from the research call on so-called "consultant epidemiologists" to critique a manuscript.

Often motivated by controversy, institutions such as governments, corporations and unions can solicit, with their substantial financial resources, external consultants mandated to critique completed work. Where a research study's findings are neither controversial, nor potentially damaging to institutional interests, external consultant reviews may be less likely. The epidemiologist's compliance with and motivation for a biased approach to the "consultant review" process forms the substance of this paper. Examples are used to heighten awareness among epidemiologists assuming this

role as to how their expertise may be used, and of the potential for misuse of their science. The paper concludes with the outline of a set of narrowly focused guidelines proposed for epidemiologists serving as consultants, and stresses the need for a code of ethical conduct embracing all of epidemiologic endeavor in the interests of epidemiology as a progressive science.

PREVIOUS REFERENCE TO THE PROBLEM

At the Sixteenth Annual Meeting of the Society for Epidemiologic Research (SER) which took place in Winnipeg, Manitoba, Canada, over the period June 15–17, 1983, the then president of the SER, Dr. Paul D. Stolley, presented in his plenary session remarks an impelling paper entitled "Faith, Evidence, and the Epidemiologist" (1). Dr. Stolley was critical of epidemiologists who criticize or dismiss important epidemiologic findings because of real or imagined minor flaws. He argued for greater reliance on the whole body of actual scientific evidence in settling controversies rather than leaning towards faith at such times.

Scientific controversy involving epidemiologists over the past decade was described by Dr. Stolley as being characterized by an inability (or an unwillingness) on the part of epidemiologists to synthesize available data coming from all fields that bear on the problem at hand; instead, they place extraordinary importance on small defects in study designs. As an example, he cited studies on the relation of toxic shock syndrome to the use of highly absorbent tampons. A group of investigators, either acting independently or hired by the company, began a kind of "witch-hunt" for alleged bias and confounding in order to challenge these findings. "Biases that may be only postulated are somehow given a reality before their actual existence is even demonstrated . . ." (1).

Dr. Stolley was not suggesting that results should *not* be scrutinized and challenged, but rather that this should be done with a sense of social responsibility. There is a decided conceptual difference between posing a test to challenge an hypothesis and applying the test. "An hypothesis does not fail a test just because it is speculated that it will. A group of case-control studies, for example, are not invalid because certain biases that might have occurred are postulated" (1). In fact, it may be that some severe biases misled the investigator; but merely raising these possibilities does not necessarily destroy the validity of the study.

Epidemiologic studies which incorporate in their design scientific methods to reveal the quality of the investigation are more likely to be recommended for funding and less likely to experience negative reviews ultimately. The assessment of data quality (such as reliability and/or validity) and the evaluation of potential biases are particularly important methodologies in observational studies so common in epidemiology (2). When a reviewer can evaluate the underlying scientific quality of the evidence presented, the results of an investigation are more defensible. Where circumstances have not permitted the researcher to include those methods fundamental to a scientific evaluation of underlying data quality, the discussion section of a manuscript might well reflect this fact.

In Samuel S. Epstein's book, *The Politics of Cancer* (3), published in 1978, numerous examples are described which reflect on the role of scientific experts employed by industry "to advocate its position in professional journals," and thereby delay or prevent effective government regulations. The examples cited include occupational exposure to asbestos, vinyl chloride, bischlormethylether, saccharin and other chemicals then recently accepted as being carcinogenic. Those epidemiologists who adopt speculative allegations in an advocacy role have become known generally as "apologists." The examples cited by Epstein are by no means exhaustive. Further examples of interest groups other than industry can be found which employ such approaches, and some of these are addressed below.

THE RESPONSE OF OTHER SCIENTIFIC DISCIPLINES

Over the past year, the journal *Science* has carried a number of editorials on the subject of peer review. In one of these, William D. Carey appealed to the integrity of scientists in the application of their knowledge in the area of nuclear weapons (4). He appealed to the values of scientists by stating that "in our time, when science is being employed most conspicuously as an adjunct of politics and strategic national purposes, a vacuum of internal values tends to be invaded by prevailing external values."

Perhaps the question of nuclear weapons development is too emotive a concept at this time; however, I would suggest that the analogous values in terms of ethical conduct on the part of scientists are called into question at the consultant review level as well. For it is at this stage that the ramifications of the research under review can be most influenced by group interests. At this level, the scientist who makes recommendations based on or weighted by faith or intuition, must be distinguished from the scientist who makes recommendations based on scientific evidence alone. It is at this juncture that the question of ethical conduct arises.

In a news item appearing in the February 10, 1984, issue of *Science*, the

American Association for the Advancement of Science's (AAAS) fall 1983 meeting is reported, at which more than 20 AAAS-affiliated societies had gathered, for the first time, to look at professional ethics programs (5). They exchanged experiences and materials describing codes of ethics and case review procedures within their organizations. A number of societies either already had established or were in the process of establishing a code of ethics for their membership. For example, a statement of ethical behavior was being developed for microbiologists in all fields of endeavor, including aspects of how the society should respond to violations of its ethical code. The American Chemical Society had published "The Chemist's Creed", and had recently issued a third edition of professional employment guidelines. Milton Lunch, general counsel for the National Society of Professional Engineers, presented a film entitled "The Truesteel Affair," sponsored by the Association of Professional Engineers of Ontario, Canada. The film examines an ethical dilemma in which a structural engineer was ordered by his employer, the owner of a construction company, to compromise quality control concerns in delivering an urgent order. How do epidemiologists respond when called upon to serve as consultants and, through the carrot of financial support, are directed to critique or "kill" a scientific manuscript?

Some societies have established procedures for reviewing individual cases (5). William Middleton, chair of the ethics task force of the Institute for Electrical and Electronics Engineers, said that his group reviews individual cases which raise questions about actions by employers or others which might conflict with the professional standards of the Society. The American Psychological Association adjudicates about 70 cases a year involving complaints of unethical conduct by its members. Joan Berman, administrative assistant in the American Psychological Association (APA) ethics office, said that the decisions on these cases are confidential, but in situations where a member is expelled from the APA, a notice is mailed to the membership regarding the action. Affiliated state associations and examining boards also may be notified if this is determined to be necessary in order to protect the public (5). The American Psychiatric Association, the American Society for Pharmaceutical Therapeutics, and the Society on Aggression Research, among numerous others, have been developing ethical codes of conduct, education programs, and case review procedures. The AAAS maintains a committee on scientific freedom and responsibility which maintains liaison with the professional societies.

A RESOLVABLE CONTROVERSY?

In a report in the April 24, 1984, issue of *Science*, Eliot Marshall drew attention to the "backstage maneuverings that went on at the National Cancer Institute (NCI) and among the chemical companies in early 1981" in reviewing the legal case of Melvin Reuber, who had found chemicals carcinogenic when other researchers did not (6). Reuber had been reprimanded by his employers in 1981 for preemptively claiming, in various circles, the superiority of his own analysis and resultant manuscript over that officially submitted by the NCI for publication. The potential weakness in Reuber's approach was that his papers were not peer reviewed (6). With regard to several chemicals, Reuber had analyzed the pathological data on his own time and had written up his findings outside the formal review system. Reuber had tried to submit his personal work to NCI reviewers for clearance, but he is reported to have claimed that he was told not to do so (6). Attention was drawn through this case to the relationship between the chemical companies and the government.

If Reuber, in fact, had been blocked at each turn, he well may have had no conscionable alternative but to resort to avenues inconsistent with traditional peer review. I suggest, however, that if a code of conduct were in place which provided appropriately effective and objective channels for lodging grievances, this would have been the preferable route under such circumstances. Indeed, in support of the peer review process, Eliot Marshall concluded that whatever the outcome of the Reuber trial, it would illustrate some of the pitfalls of mixing politics with toxicology. It also may reinforce the traditional methods of review and discipline by peers in the scientific agencies, methods that were by-passed with disastrous results in the Melvin Reuber case (6). This controversy serves as an example of the need for codes of conduct to protect both the researcher and the funding institution or agency, be it government, corporate, union, foundation or private.

The Reuber issue serves also to open the question of any detectable tendency to give preferential consideration to publishing findings generally conforming with prevailing policy and norms. Constraints such as these clearly would act against the progress of science. New evidence and the methods by which such evidence had been obtained ought to be published in those instances where the journal review process elects to elevate a finding beyond any controversial internal review. In this way, the findings are exposed to a broader, more extensive review and to an open discourse.

INDUSTRIAL FUNDING OF UNIVERSITY-BASED RESEARCH

For the purposes of this paper, the examples cited are not intended to be exhaustive. Cursory reference only is made to a series of articles and reports that have appeared in *Science* over the past few years which deal with industrial funding of University-based research in general (7–14). To sum up this trend, an article by Clayson and Halpern in the September, 1983 issue of the *Journal of Public Health Policy* (15) states that the "industrial connection" is encouraged by tax breaks, government seed money for joint ventures, long-term contracts in basic and applied science, and institutionalized consultantships. However, while most academics consider themselves honest enough to resist overt manipulation, the article points out that industry tactics can be very subtle. Corporations are "buying into basic laboratory science, toxicology, epidemiology and other areas of public health. . . They 'lease scholars.' These new generations of students, lured by the ample fellowships, new programs and large research grants, will rarely think twice about the social and political implications of their fascinating scientific work" (15).

To exemplify industry's offensive against the regulation of health and safety hazards through their use of academics to downplay or deny the seriousness of alleged hazards, Clayson and Halpern cite the analysis of Marvin Schneiderman and his former colleagues at the NCI, which showed a link between the chemical revolution of the 1950s and the 10% increase in cancer incidence over the last decade. The authors reported that the petrochemical industry immediately hired its own consultants to deny the validity of the data and Schneiderman's conclusions (15). If, in fact, the consultants took on the project to do just that, then, I suggest, they may have been behaving unethically. Epstein (3) cites numerous analogous examples.

The paper in the *Journal of Public Health Policy* (15) goes on to describe the work of reputable epidemiologists in the United States and elsewhere relating to cotton dust, where poorly designed industry-financed studies were used to deny the well-accepted correlation between dust exposures and chronic lung disease in textile workers. Instead, cigarette-smoking was blamed. The consultant epidemiologist's role in this controversy exists at the stage of interpreting the available body of scientific evidence. Clayson and Halpern (15) argue that the art of victim-blaming has been raised to the level of science through the questionable use of multiple regression techniques. Through such techniques, blame can not only be quantified,

but the onus of correcting the problem of occupational disease is thereby shifted from employers to workers. By finding consultant epidemiologists who will generate disagreement within the scientific community concerning basic facts about a disease, interest group lobbyists are able to maintain the status quo indefinitely; disagreement among scientists "sustains and interacts with the ongoing public controversy over the problem and its appropriate solutions" (16).

Clayson and Halpern also stress, as even more disturbing in its implications, the attempt to develop a method of genetic screening to detect "hypersusceptible" workers. Although none of the tests for genetic screening or monitoring meet established scientific criteria for routine use in an occupational setting, they are being utilized in some industries. The financing of genetic research by industry promises a big payoff, since weeding out "genetically defective" workers would reduce future potential corporate liability. This is cheaper than putting in costly engineering controls to prevent disease, and may even be a way to replace redundant workers by automation, the article indicates (15). I suggest that epidemiologists consider their professional role in applying such screening techniques and the resultant credibility that the epidemiologist's direct or indirect association adds to them.

A motivation for encouraging epidemiologists to develop a code of ethical conduct stems from the personal experience of the author, which is mentioned as a final example. My doctoral dissertation (17) had been supported by a large corporation. Toward the end of that piece of work, elements within the corporation employed a team of highly respected epidemiologists associated with universities to critique that work. The critique contained little balance, mentioning virtually none of the strengths of the study, mainly listing postulated weaknesses with no overall summary within an epidemiological context. The reviewers singled out innovative methodological approaches for criticism. However, they did show that the positive findings of the study held up by more conventional methods. Unfortunately, the technical detail of their review was such that their support of a positive finding was not recognized by management. The consultants did recommend further review jointly with the investigators, but the corporation chose to ignore this single recommendation. If the purpose of the consultant review was to identify pitfalls prior to the finalization of the work, such a critique may have been constructive. If, however, elements within the corporation commissioned this review to cast doubt on the scientific merit of the dissertation, then I submit that the review may have

been inappropriate. But, if the consultant epidemiologists had queried the motivation for the request, they may well have produced a more balanced and effective review.

On the basis of the Clayson and Halpern analysis, the examples mentioned, and personal experience, I agree with the recommendation of Clayson and Halpern when they state that academically-based professionals must work to establish within their universities a code of ethical conduct and public accountability to expose and correct any conflict of interest resulting from industrial (and, indeed, any special interest group's) financing of research (15). In particular, the foregoing suggests the need for a formal code of ethical conduct applied to epidemiologists in a general public health framework. "Scientists must push for safeguards, including financial disclosure, established guidelines for adequate epidemiologic research design, requirements for peer review, and publication of all research results undertaken by faculty, regardless of the funding source; and accountability to the worker cohorts and unions with whose cooperation research is done, to assure prompt and comprehensible feedback of results" (15).

In further support of this recommendation, a recent article by Baram (18) examines the future course for the corporate management of health risks. Baram, generally promoting the concept of corporate risk assessment, indicates that "no panaceas are at hand for corporate health professionals" (including epidemiologists) who need to infuse the decision-making process with a strong sense of "personal and professional ethics." This perception underscores the need to provide epidemiologists with a code of ethical conduct which could assist them in applying such "personal and professional ethics" in the execution of their responsibilities; this is particularly true of those assuming roles on corporate risk assessment boards.

CONCLUSIONS AND RECOMMENDATIONS

In conclusion, there is clear concern about the scientist's ability to adhere to unwritten ethical codes of conduct in the pursuit of truth. The various scientific disciplines whose societies have joined forces to examine professional ethics should be joined by the discipline of epidemiology. Perhaps the International Epidemiological Association, or perhaps national societies of epidemiologists such as the SER and the American College of Epidemiology (ACE), should consider their possible involvement with the professional societies' ethics group of the American Association for the Advancement of Science (AAAS). Such involvement could assist in ensuring that

epidemiologists, as health professionals, have an appropriate code of ethical conduct, including procedures for dealing with enforcement and grievance.

As far back as 1950, Pigman and Carmichael (19) suggested "an ethical code for scientists," recognizing the "big business" nature inherent in modern science. Prior to the second World War, the relatively few scientists in existence had cultivated a code of professional tradition and ethics largely in unwritten form. This unwritten code is "the foundation of the scientific method in many of its aspects . . . The effect of disregard for scientific traditions" can have a profoundly negative effect on the advancement of science (19). Epidemiology is a relatively new and important science, and there is no doubt about the special interests of growing numbers of groups in specific types of research and in the interpretation of evidence generated therefrom. The potential for conflict-of-interest situations is great and, directly or indirectly, the epidemiologist is involved. In addition, with the expanding number of practicing epidemiologists, the opportunity for infringements of unwritten codes grows; in the absence of disciplinary procedures to defend the integrity of the profession and to protect its professional standards, the advancement of epidemiology as a science is threatened.

Since the late 1970s, affiliated societies and academies of the AAAS have seen fit to work jointly in developing codes of ethical conduct specific to their branches of scientific endeavor. The AAAS itself addresses ethical problems related to science and technology that cut across disciplinary lines. Each affiliated society or academy of science acts independently in its own specialist field or geographical area (20). Epidemiology, like other branches of science, has its own special requirements in terms of a code of ethical conduct for its members. From my perception in North America, the ACE is the most appropriate body to take a leadership role in formalizing such a code, enforcing it, and providing channels for grievance.

A set of guidelines for epidemiologists serving as consultants should include the following three points: (1) an awareness of the use to which a critique will be put, identifying both the strengths and weaknesses of the study under review. One way that Webster's Dictionary (21) defines "critique" is as "an act of criticizing"; to criticize is "to consider the merits and demerits of and judge accordingly." It is this definition of critique that I suggest epidemiologists embrace in a code of conduct; (2) the basis and possible direction of any bias that may be postulated should be explored as part of any critique; and (3) a definitive summary of the critique should be provided within a general epidemiological perspective, relating the critique

to the results of the study under review. The summary ought to be written so as to assist not only epidemiology professionals, but also business managers who may be the initiators of consultant reviews and on whose shoulders rests the responsibility of translating scientific recommendations into practical action.

It is suggested that failing the adoption of a set of guidelines for consultant epidemiologists as part of a broader code of ethical conduct for epidemiologists in general, a disservice to epidemiology as a science could result. Such a disservice could arise in at least two ways: (1) methodologic innovation will be discouraged for fear of providing sponsors with ammunition which could be used to attack or defend future findings; and (2) the credibility of epidemiologists may be diminished if opinions favored by an interest group are seen to be purchasable.

As a start, instructors of epidemiology should teach students not only to identify the limitations of a study, but also to assess the study's strengths within an epidemiologic context. This action could be instituted immediately, and is suggested as being appropriate and useful pending the adoption of a code of ethical conduct for epidemiologists.

It is imperative in the pursuit of truth that Dr. Stolley's points made at the SER meeting in 1983 be carried forward into action. The action that I propose is that epidemiologists set in order that component of their house dealing with ethical codes of conduct through their respective societies worldwide.

Acknowledgments: Colleagues are thanked for editorial comments which have added significantly to the author's desired balance through the various drafts of this manuscript. Ms. Gail Cameron typed the manuscript which is based on a paper presented under the same title at the Tenth Scientific Meeting of the International Epidemiological Association at the University of British Columbia, Vancouver, Canada, August 19–25, 1984. Mr. Michael Libman edited the final manuscript.

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