Guidelines for the Ethical Re-analysis and Re-interpretation of Another's Research

The following guidelines were adopted by the governing council of the International Society for Environmental Epidemiology in May 2009. From time to time the Society reviews its guidelines. We welcome comments, which should be sent to the designated member of the Society's Ethics and Philosophy Committee at raymond.neutra@gmail.com.

ISEE endorses the following ethics guidelines with regard to the re-analysis and re-interpretation of epidemiological studies. The guidelines address the duties of original investigators, the sponsors of re-analysis and re-interpretation, and the researchers who carry it out. The rights and interests of these parties, research subjects/participants, and the community at large need to be protected. We highlight the issues that each of these parties need to consider. (See Neutra R, Cohen A, Fletcher T, Michaels D, Richter E, Soskolne C. Epidemiology 2006;17 (3): 335-338 for a discussion of the background to these guidelines.)

Re-analysis and re-interpretation occur when a person other than the original investigator obtains an epidemiological dataset and conducts analyses to evaluate the quality, reliability or validity of the dataset, its methods, its results, or the conclusions reported by the original investigator(s). Re-analysis of another's data to explore an unrelated hypothesis which the original author was not interested in pursuing also raises ethical issues, but is not the focus of these guidelines.

Rationale

Epidemiological studies play a central role in policies and regulations of government and international agencies designed to protect public health. Epidemiological studies are also important in the legal arena, assisting in the determination of the cause of an individual's illness or injury, or quite frequently of injury to a class of individuals, such as a community. Controversy in the public health sciences has more often been resolved through replication than through re-analysis of existing data. However, re-analysis and re-interpretation are becoming increasingly common. Since the results and interpretation of epidemiological studies can have significant implications for stakeholders' interests or ideological commitments, it is not surprising that parties whose policy preferences are challenged by the "facts" revealed by a study could be highly motivated to demand the opportunity to closely examine the data from such a study. They may hope to find results more to their liking or at the minimum to "manufacture doubt" about the original results so as to make them seem less useable for the formation of policy.

Just as one example of regulation associated with re-analyses, under US law, for study data meeting certain conditions around their use in decision-making and the nature of the matter under consideration, investigators must provide the raw data from federally-funded studies in response to requests under the Freedom of Information Act. [i] The rationale for this provision, originally passed by the US Congress in 1998, was to enable parties affected by government regulation to examine (and presumably challenge) the data used in developing these regulations. However, in the US there are no equivalent legal requirements for access to raw data of studies that have been paid for with private funding, whether or not they are used in regulatory

proceedings, which does open the question of equality of use of available data. For this reason, most re-analyses to date have been performed on publicly-supported studies.

This new environment for re-analyses of data in the US creates new technical and ethical responsibilities for original investigators, those who are tasked with funding and overseeing a re-analysis and re-interpretation, and the re-analyzers and re-interpreters themselves. This situation has prompted the development of the following guidelines. We do recognize that some of these guidelines may not be relevant in countries without such regulation, or with different context and regulations. This may require further development of these guidelines if ethically problematic issues arise from applying them in such countries.

We have organized them according to the stakeholders whose legitimate interests are being protected.

Protecting the Public's Interest in Valid Information

1) Data from epidemiological studies should be available for properly organized and competent re-analysis and re-interpretation, regardless of whether the study was funded by public monies or by groups with particular interests or ideologies.
2) The original authors have a responsibility to cooperate with, and facilitate, properly organized and competent (as indicated below) re-analysis and re-interpretation of their data.
3) The original authors also have a duty to advocate for proper organization and competence in re-analysis/re-interpretation of their data, as specified in these guidelines.
4) A process should be created that leaves the re-analyst free of any conflicting interests or at least declaring them publically.
5) An independent advisory structure for the re-analysis and re-interpretation should be established that can correct unintended bias in the analysis and in the scientific and public re-interpretations, and assure that the persons chosen to do the re-analysis and re-interpretation are professionally competent to do so. All human beings are prone to have biases that they do not recognize in themselves. The best way to correct for this is to invite advisors with opposing biases based on their public statements or publications to comment on each stage of the process. When funding is available, this advisory process may be quite formal and extensive. However, even when re-analysis is done without special funding, an independent advisory structure, albeit less extensive and perhaps with pro-bono participation, should still be implemented.
6) There should be agreement in advance among the original investigators and re-analysts as to which hypotheses will be explored, and on the extent to which different patterns of evidence would support or not support each of the different hypotheses and why. This may take the form of a formal analytic plan for the re-analysis.
7) Procedures should be established that afford equal opportunity for stakeholders and their scientific advisors on various sides of the issue to comment for the public record on the re-analysis and re-interpretation.
8) The process of re-analysis should assure in advance that the results of the re-analysis and re-interpretation will be widely available regardless of the outcome.

9) The re-analysis and re-interpretation should be published in a way that respectfully clarifies the factual grounds, the scientific claims, the inferential assumptions that warrant those claims and the reasons behind any differences in interpretation.

10) All stakeholders should resist political or other pressures to deviate from these guidelines.

11) Normally, notwithstanding the above guidelines, the re-analyst should recognize that what is being requested essentially constitutes a secondary data analysis. As such, the re-analyst should be required to prepare a formal research proposal including the goals, rationale, hypothesis to be tested and methods of his/her intended re-analysis. This should, like any research proposal, then be submitted to two levels of review:
    a) Scientific peer review; and
    b) Institutional Review Board (or, a human subjects protection review committee) review through a *bona fide* institution to ensure the protection of the original subjects.

    A proposal prepared in this more formal way would also facilitate the work of the independent advisory structure indicated under point #5 above.

Protecting the Rights of Study Participants

12) All appropriate and necessary measures should be taken to ensure that the confidentiality and privacy of participants in the original study be preserved throughout the re-analysis, including scrupulous adherence to agreements that may have been undertaken between the original investigators and participants or between the original investigators and providers of data.

13) When appropriate and in the case of publicly funded research in the United States, informed consent should mention the possibility of re-analysis by persons other than the original researchers.

Protecting the Interests of the Original and Re-Analyzing Authors

14) Rights of data ownership and access to data should be explicitly stated and agreed to in advance by all parties to the re-analysis. In particular, care should be taken to ensure that the original study data not be used for purposes beyond the agreed scope of the re-analysis.

15) Activities should be avoided that obfuscate the facts, harass epidemiologists who have presented unwelcome results, or intimidate future investigators from working in this area.

16) The re-analysts should work to ensure open communication, and fair and respectful dealings with the original investigators. They should create an environment of collegial yet critical truth finding, and provide the original researchers the opportunity to comment on the rationale and methods chosen for re-analysis before it takes place, as well as on the interpretation of the results of any new analysis. If there are differences in interpretation, all parties should respectfully explain the reasons for these differences in written form so that third parties can fairly draw their own conclusions.

17) The re-analysts should acknowledge where appropriate the role of the original investigators in the development of the original methods and instruments and in the collection of the data.

18) The re-analysis process should guarantee the ability of the original authors to publish their work within a reasonable time before any re-analysis and re-interpretation is published.

19) If the re-analysis has dedicated funding, a reasonable budget should be established to facilitate the involvement of the original investigators.

Institutional Changes to Facilitate Proper Re-Analysis/Reinterpretation

The ability to find, access, interpret and re-analyze data according to these guidelines would be facilitated by changes which go beyond the ability of individual researchers to implement. We make three suggestions that ISEE is willing to help realize.

(a) Adequate documentation of data and methods is critical to the conduct of valid scientific research. The sponsors of research should, therefore, provide funds to pay for maintaining adequate documentation of the entire project, including coding manuals and programs used in analysis.

(b) It is in the public interest that certain key research data and their documentation continue to be available for additional scientific research that may be needed, perhaps even far into the future. Government agencies and other funders should work with the research community to develop guidelines for deciding which data to preserve, how and where to preserve them, how the data sets would be indexed, and how and by whom they may be accessed. Approaches to implementing these systems should be broadly consistent with the above guidelines. ISEE stands ready to advise in the development of such systems.

(c) These guidelines could be useful to ISEE members approached by stakeholders who request that a re-analysis of another's work be carried out. In this situation, these guidelines could be incorporated into the contract for the work to be conducted. These guidelines could also help ISEE members whose work is to be re-analyzed in that cooperation beyond what is mandated by the law[1] could be contingent on an agreement to adopt all of these guidelines.

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[i] United States Office of Management and Budget, Uniform Administrative Requirements for Grants and Agreements with Institutions of Higher Education, Hospitals, and Other Non-Profit Organizations. Circular A-110, Sept. 30, 1999. Available at: http://www.whitehouse.gov/omb/circulars/a110/a110.html.