

## Invited Commentary

### Invited Commentary: Driving for Further Evolution

**Robert A. Hiatt\***

\* Correspondence to Dr. Robert A. Hiatt, Department of Epidemiology and Biostatistics, School of Medicine, University of California, San Francisco, 550 16th Street, 2nd Floor, Box 0560, San Francisco, CA 94158 (e-mail: robert.hiatt@ucsf.edu).

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The concept of translational cancer epidemiology has evolved since its early beginnings in 1937 with the establishment of the National Cancer Institute. Conceptual models of cancer control research have also evolved over the last 30 years, to the point where we now have 4 stages of translational research (T0–T4). The current review by Lam et al. (*Am J Epidemiol.* 2015;181(7):451–458) covers cancer epidemiology research supported by the National Cancer Institute and a selected sample of the cancer epidemiology literature. It suggests that most cancer epidemiology in the last 10 years has been in pure discovery research. Current “drivers” of cancer epidemiology research, including new technologies, team science multilevel research, and knowledge integration, are not strongly represented in the review. However, the use of epidemiology in the latter stages of translation may not have been captured by the scope of this review. The closer epidemiologists get to advanced stages of translation, the more likely they are to work with investigators in other disciplines in other sectors of society. An argument can be made that regardless of whether this kind of research is not happening or was just missed by the current review, the field of cancer epidemiology can expand its scope and further evolve towards more effective applications in population health.

cancer; epidemiology; systematic reviews; translational science

Abbreviation: NCI, National Cancer Institute.

Conceptual models and views of how cancer epidemiology research moves from pure discovery to application have a long history. Over the last 20 years, there have evolved increasingly descriptive models of the dynamic process of cancer research and the role of epidemiology in that process. In this issue of the *Journal*, Lam et al. (1) report on a systematic review of the cancer research currently being funded by the National Cancer Institute (NCI). In their review, Lam et al. attempted to assess the current practice among cancer epidemiologists within the framework of translational research introduced by Khoury et al. (2) about 7 years ago. The review suggested that most such research is focused on etiological investigation, or so-called T0 research. Lam et al. found that very little of it is performed in the T2–T4 range, which is related to the dissemination and implementation of epidemiologic findings. The review gives one an opportunity to consider whether a survey of grants funded by the NCI and a literature search strategy focused on publications using strictly cancer epidemiology terms gets to the heart of the issue.

One can go back to 1937, when Congress established the NCI as the first of what later became the National Institutes of Health. The legislative language actually introduced the precursor of what we today call “translational research,” with the charge that NCI investigators would conduct intramural research and support extramural research and cancer control or “the useful application of their results” (3, p. 958). Before that, although there had been some classic epidemiologic studies, research was hardly an issue. Cancer was usually a fatal disease, and there wasn’t much known about how to prevent or treat it (4). “Cancer control,” a term first introduced in 1913, was primarily an educational activity focused on the early detection of cervical cancer—the most prevalent female cancer at the time—and early efforts at registering cancer patients (surveillance) (3).

It was Greenwald and Cullen in 1985 (5) who actually made cancer control a research enterprise, and it was largely based on the discipline of epidemiology. They conceptualized 5 phases of research: hypothesis generation, methods

development, controlled intervention trials, studies in defined populations, and demonstration projects. This linear conceptualization of the phases of cancer research provided a framework that allowed investigators to understand the translational nature of the process, from the pure discovery of etiological factors to intervention trials and finally to large “demonstration” or implementation projects. It incorporated the concept of translation, but the words “translational research” were not then part of the biomedical vocabulary.

In the late 1990s, when Drs. Barbara Rimer and Robert Hiatt were establishing the new Division of Cancer Control and Population Sciences at the NCI, they took this concept a step further. Building on the Greenwald-Cullen model and also the work of a Canadian advisory board, they created a dynamic model of cancer control with epidemiology and behavioral sciences as critical disciplines. This model combined fundamental or discovery research with intervention research and surveillance, all connected with knowledge synthesis activities (systematic reviews, meta-analysis) in a continuous feedback process. The last step was the dissemination and implementation of effective interventions and policy changes to reduce the population burden of cancer (3). The term “translational research” was still not a common part of the biomedical vocabulary, but it was in the wings. This model was iterated through further collaborations with Canadian colleagues and leaders in the field (6) and became the conceptual foundation for many of the NCI’s efforts in building infrastructure for epidemiology and other cancer population sciences, with the development of large consortia, expanded surveillance and methodologies, and transdisciplinary centers focused on major cancer control challenges (7). In 2005, Dr. Elias Zerhouni, then the director of the National Institutes of Health, introduced the Clinical and Translational Science Awards, and translational science was fully launched (8).

In recent years, substantial advances in how we think of cancer research in human populations have been made by Khoury et al. (2, 9–13). Now, based on this earlier work and on a broad consensus on the current “drivers” of cancer epidemiology research (12, 13), research groups at the NCI and the Centers for Disease Control and Prevention have further parsed the work of cancer epidemiologists on the road to application. The current paper by Lam et al. (1) goes beyond the earlier descriptive and conceptual efforts and tries to put some meat on the bones. Just exactly how much research in each of the phases is being done? The question is whether the results of such an analysis can help to realign the kinds of research being funded by the NCI or the focus of investigators in the field.

Lam et al. conducted a thorough systematic review of funding from the Division of Cancer Control and Population Sciences and the Division of Cancer Prevention at the NCI, as well as a selected sample of the cancer epidemiology literature for 3 years: 2000, 2005, and 2010 (1). The “drivers” used to categorize this research were derived from a consensus meeting of a large number of investigators in the field (12). Specifically, they are: 1) collaboration and team science, 2) emerging technologies, 3) multilevel approaches, and 4) knowledge integration. Lam et al.’s findings provide a perspective on how well the field has done during the first decade of the 21st century in translational research or, if you will, in actually carrying out the intent of Congress in 1937 in

usefully “applying the results” of publicly funded research. We learn from their review that we may not be doing so well.

The authors found that most of the cancer epidemiology carried out over the last decade was T0-heavy, comprising mostly etiological discovery research, and that there were relatively few examples of T2–T4 research. This implies that cancer epidemiologists are not paying sufficient attention to the potentially more applied aspects of their work, or perhaps that the T0–T4 categorization makes too fine a separation between more advanced types of research or translational research and does not weight their impact properly (14). The review found that cancer epidemiology is not generally being done with teams, is not using new technologies beyond genome-wide association studies, makes limited use of multilevel approaches, and has not really used knowledge synthesis techniques to its advantage. Lam et al. further conclude that consortia seem to be more successful at incorporating the features identified as “drivers” than single-institution-based studies (1). The fact that team and multilevel science can frequently be carried out at 1 institution, if the study design is not driven entirely by the need for a large sample size, seems to have been missed. Nevertheless, one might ask, What is going on here? Was something missed in Lam et al.’s review, or are cancer epidemiologists not directing the field towards application?

A review focused on cancer epidemiology research funded by the NCI’s Division of Cancer Control and Population Sciences or Division of Cancer Prevention probably does capture the large majority of such research being carried out in the United States. The review was appropriately extended to cover those NCI programs beyond the epidemiology and genetics program (into the behavioral, applied research, and surveillance programs) to pick up epidemiologic studies likely to focus on more advanced stages of translation. Lam et al. acknowledged that by excluding research funded by the Department of Defense, the Centers for Disease Control and Prevention, individual states, and private foundations, they may have missed some relevant work, but what was missed by this limitation is a matter of speculation. Thus, for what the authors set out to do, this review was probably reasonably accurate in reflecting what the NCI is supporting in the various stages of translational research. So the interesting question now is what really happens to epidemiologic findings, whether in cancer or other disease-specific fields, when the research moves beyond the T2 phase along the “research continuum.” (1, p. 457).

It seems to me that as more epidemiologists engage in later forms of translational research (i.e., T2–T4), the more likely it will be that this research will involve other disciplines, perspectives, funding agencies, and societal sectors. As epidemiologic knowledge is translated into practice, applications become less “epidemiologic” in nature (in the classic sense of risk factor identification) and require the use of methods that take into account the complex-systems nature of many of our most important population health problems. For example, epidemiologic findings that relate obesity to cancer risk (or to diabetes and cardiovascular disease), when translated along the continuum, may wind up in health policy applications. These efforts are frequently not directed by epidemiologists, although epidemiologists are a key part of the team. Epidemiologic

studies of early cancer detection may lead to guideline changes and government reimbursement decisions that are outside of the domain of epidemiology and its journals per se. Similar examples could be selected from the application of genetic studies, when they lead to testing strategies and policy decisions, or from the use of epidemiologic studies with geographic information system technologies, when they are applied to urban development strategies. In this type of translational research, epidemiologists must be more involved in the appropriate interpretation and application of their results, not just assume that policy decisions will be “informed by epidemiologic findings” (1, p. 457).

This kind of translation is a good thing, but it is unlikely to be funded directly by the NCI or picked up in a search of the cancer epidemiology literature that uses search terms like “retrospective,” “genome-wide association studies,” or “random effects model.” How much of this occurs is an empirical question that requires more inquiry, but it may be misleading to leave the impression that epidemiologic knowledge is not finding its way into applications outside of NCI funding circles.

An example of epidemiologic research being translated into these latter stages of application comes from the work of trainees in the Robert Wood Johnson Health and Society Scholars program (<http://www.healthandsocietyscholars.org>). This program has supported training in interdisciplinary population health research for the last decade, with a distinct orientation toward understanding the underlying mechanisms of health and disease from genetics to social determinants, as well as the applications of this understanding to policy change. The scholars come from many backgrounds, including epidemiology, sociology, psychology, economics, medicine, demography, basic science, ecology, and anthropology. The resulting research often uses epidemiologic methods, some in cancer epidemiology, but the product is no longer purely epidemiologic in nature. Rather, it has integrated epidemiologic perspectives and methods in a transdisciplinary way to reach solutions to problems that would be unexpected in epidemiology alone. Knowing that these kinds of scientific approaches are being pursued suggests that there may be other ways to assess the success of the translation of cancer epidemiology research that go beyond that which can be documented by the kind of search conducted by Lam et al.

This is the territory along the research continuum where “knowledge integration” comes into play, in the sense of epidemiologic knowledge being integrated into other sectors of society where it is intended to have an impact (15) rather than in the sense of knowledge synthesis (e.g., systematic reviews) (16). It may well be territory in which epidemiologists could and should make more of a contribution. Who better than epidemiologists can interpret and apply epidemiologic findings in their most effective way?

So, although a good argument can be made for why epidemiology is the key discipline in translational research (14), it is important for epidemiologists to become comfortable bringing their skills into larger collaborative endeavors, where transdisciplinary approaches will require them to bring epidemiologic knowledge and perspectives to the table, listen to other views, and work collaboratively to solve the important population health problems of the day. The review by Lam et al. (1) contributes considerably to our understanding of

the current focus of cancer research and provides some evidence on where further research is needed. The message is that we can expand what we do in translational cancer epidemiology and more deeply explore the nature of epidemiologic contributions to applications in population health. As translational activity moves closer to application in policy and practice, epidemiologists must adopt more of a collaborative role. Translation requires interdisciplinary collaboration in these teams, and epidemiologists must be willing to hold our knowledge lightly and listen and learn from others to facilitate useful application of our findings.

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UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, California; and Department of Epidemiology and Biostatistics, School of Medicine, University of California, San Francisco, San Francisco, California.

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