Invited Commentary


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In this issue of the Journal, an expert panel offers 7 recommendations on how population studies supported by National Heart, Lung, and Blood Institute contracts might be strategically transformed (Am J Epidemiol. 2015; 181(6):363–368). The Institute and its external advisors seemingly established this panel of epidemiologists and nonepidemiologists primarily to find ways to save research costs. Although the working group’s recommendations offer reasonable approaches, we believe that, even in tough fiscal times, the main drivers of cardiovascular epidemiologic research must remain 1) scientific questions that are important and 2) study designs to match these. Although cardiovascular epidemiology admittedly is often redundant and needs to be more efficient, undue focus on administrative efficiency and cost savings will not necessarily guarantee cutting-edge population research.

Abbreviations: NHLBI, National Heart, Lung, Blood Institute; NIH, National Institutes of Health.

There have been many remarkable achievements in cardiovascular epidemiology. Large cohort studies have been the workhorse of our field, permitting the identification of risk factors that could be targeted by population-based and individual-level approaches to help reduce cardiovascular morbidity and mortality. Indeed, a substantial portion of the remarkable decline in cardiovascular mortality rates over the past 4 decades is attributable to the ability of epidemiologists to identify the root etiological causes of the cardiovascular disease epidemic.

Those successes rightfully prompt questions about “what’s next” for cardiovascular epidemiology. Are there still undiscovered risk factors that are strong enough to be useful in cardiovascular risk prediction or that could be targeted for intervention? How do we identify the most important remaining questions for epidemiologic research in the next few decades? How many cohorts do we need in an era of limited research funding, and how can they be more efficiently utilized to answer the key research questions in the near future?

In this issue of the Journal, Roger et al. (1) describe the recommendations of a working group charged by the National Heart, Lung, and Blood Institute (NHLBI) to primarily address questions about efficiency. As principal investigators in some of the NHLBI contract-supported cohort studies, we do not have major arguments with the recommendations themselves. However, we do offer a few additional comments on the future of cardiovascular epidemiologic research.

First, it is striking to compare this specific NHLBI report to some reports of past NHLBI panels/task forces on cardiovascular epidemiology. For example, the 1994 NHLBI report of the Task Force on Research in Epidemiology and Prevention of Cardiovascular Diseases outlined dozens of research questions that were important for the field (2). In contrast, it seems that the NHLBI gave the current task force a much narrower charge, and the result is a document that focuses primarily on process issues (including data-collection processes) and not on the research priorities facing the field. Roger et al. recognize this constraint with their first recommendation that “[t]he NHLBI should convene a scientific forum to anticipate the major scientific questions and methodological needs in epidemiology and population science over the next 10–20 years” (1, p. 364). We totally agree and urge the NHLBI to continue to stimulate identification of important research questions regarding the leading cause of death in the United States and not just focus on process and efficiency.
In this context, in-person scientific workshops might be the best way to promote active dialogue because many researchers seem disinclined to blog about these issues on the NHLBI’s digital forum (3), as evidenced by the limited number of commentaries on this online forum. Of specific interest may be Dr. Lewis Kuller’s comments already posted on the report by the committee (4). One striking comment from Dr. Kuller that is worth pausing and reflecting upon is, “The recommendations suggest epidemiology as a data collection science, which it is not.”

The committee’s first recommendation implies a belief that important questions about the etiology and prevention of cardiovascular disease remain, and we agree. Although the omics era of epidemiology still has had limited success in improving clinical risk prediction and prevention, these approaches are suggesting new etiological pathways and potential targets for drug therapy. To address contemporary etiologic questions and those that arise in the future, some large epidemiologic projects certainly must be maintained.

Second, we support the recommendation by Roger et al. of a synergistic and collaborative approach to epidemiologic cohort studies, not just within NHLBI but across the constituent institutes of the National Institutes of Health (NIH). The NIH should seek to maximize the yield from existing cohort studies, perhaps by facilitating the blending of newer initiatives with established cohort studies. In this context, one of the active debates (including in the pages of this Journal) has been about the optimal approaches to address key epidemiologic questions in the present millennium. Arguments favoring a more centralized approach that involves very large samples of the population (such as the UK Biobank (5)) have been made. These discussions have been met with strong rebuttals by some epidemiologists (6–8) who argue for an approach that preserves exiting cohorts with a population-based sampling design. We submit that well-phenotyped cohorts could serve as population health laboratories to validate/replicate findings from very large data sets; that is, they are complementary approaches to epidemiologic research. One example of such an effort is the Cardiovascular Disease Research Using Linked Bespoke Studies and Electronic Records (CALIBER) program in the United Kingdom (9), which attempts to link studies with the electronic health records of the constituent participants to answer key research questions in cardiovascular medicine. The notion of forming cohort consortia is well established in genetic research, such as the Cohorts on Heart and Aging-Related Research in Genetic Epidemiology (CHARGE) consortium (10). An extension of such trans-cohort consortial collaborations to the nongenetic domain is welcome (recommendation 6 by Roger et al.). Such discussions may be aided and informed by previous efforts in cancer epidemiology to promote consortial efforts (11).

Third, we submit that any discussion on the transformation of cohort studies must include representation of the key stakeholders—the investigators, the funding agencies, the highly trained staff, and the participants (who altruistically gift their time, data, and biosamples for the advancement of science). An open dialogue with cohort participants is essential to understand and manage expectations and responsibilities, as well as to transition cohorts to quasi-online cohorts via newer ways of electronic monitoring. Of note, some of these densely phenotyped cohorts are reaching the prime age for delayed degenerative diseases of the heart, lungs, and brain, and their continued follow-up would represent a unique scientific opportunity to relate the cumulative observations gathered over the life course on these persons to the risk of late-life disease outcomes.

Fourth, at the very heart of the debate about the future of cardiovascular-focused cohort studies is one of resource constraints within the NIH in general and within the NHLBI in particular (as a natural corollary of the former). We believe that the funding of public health research merits a greater national discussion, including revisiting the cuts in public health funding at times of economic hardships, an argument made recently by Lang and Rayner (12). In parallel, it is critical to formulate a flexible funding structure for cohort studies that is not solely reliant on the federal government but also incorporates additional support from donors, private foundations, and industry (13) consistent with a changing landscape for funding science in the United States. Furthermore, the cohorts themselves could work collaboratively to identify process efficiencies, cost-cutting strategies, and prioritization approaches that can maximize the scientific yield for the dollars invested. Such a discussion would seem worthwhile as part of both the scientific forum and the cohort consortium efforts advocated by Roger et al. (1). Additionally, the existing cross-cohort consortial arrangements remain largely self-driven and self-funded efforts by the cohort investigators. Conceptualizing the funding mechanisms for supporting the cohort consortium would be fundamental to its long-term sustainability. In any case, studies should be designed not just to be efficient and inexpensive, but rather to effectively address important scientific questions.

Fifth, we would like to draw specific attention to the recent shift in focus of the NHLBI towards more investigator-initiated grant applications and the prevalent notion that contracts (such as those that fund cohort studies) might not offer the best return on dollars invested. Although certainly a reevaluation of the funding of cohort studies relative to the return on investments seems appropriate, it is critical to note that investigator-initiated R01 grant applications are in jeopardy of being well received in study sections/peer-review panels in the absence of a commitment from the NHLBI (or other NIH institute) to maintain a certain level of funding for the follow-up of the parent cohorts. This is partly due to the inherent lack of hypothesis-driven research in infrastructure grant applications that might adversely affect their scores upon peer review, a point underscored by Roger et al. (under recommendation 7). Our own recent experience suggests that scientific review panels also may be critical of the prospective components of hypothesis-driven research when there is limited statistical power within the proposed duration (typically 4 years) of the grant applications (in the absence of some kind of assurance that follow-up of these cohorts will likely happen beyond the duration of a submitted grant application). A greater discussion of these issues is warranted within the scientific community and the NIH.

Sixth, underlying the committee’s seventh recommendation are NHLBI questions about the potential return on investment from large population studies. These questions seem to have partly motivated recent NHLBI cuts in funding of their contract-supported cohorts. It therefore is worth looking critically at some of the implicit assumptions made about
the return on investment from science in general and epidemiology in particular. Return-on-investment evaluations are challenged by numerous issues (14, 15), including but not limited to the choice of the appropriate set of metrics that can truly assess attribution and contribution of cohort studies in a quantitative, scalable, and comparative way; the need for factoring in the time lag between research and health benefits; the question of how to formulate suitable metrics for valuing health benefits and research costs; and the question of how to evaluate societal benefits on a global scale. In this context, the recently launched Science and Technology for America’s Reinvestment: Measuring the Effect of Research on Innovation, Competitiveness and Science (STAR METRICS) program might offer some insights into how to estimate the influence of federal investments on science, society, the workforce, and the economy. Until such time that such robust assessment accrues, we believe that the jury is out about the true return on investments from epidemiologic cohort studies.

In summary, we greatly appreciate the step taken by the NHLBI and by the expert panel in beginning a complex dialogue that likely will help define the future of cohort studies in the United States. We offer the above constructive comments as a prelude to greater discussions and debates that will certainly ensue as result of the expert panel recommendations.

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