

CORRESPONDENCE



NIH Report Card

TO THE EDITOR: Nathan and Wilson (Nov. 6 issue)¹ discuss the position of the National Institutes of Health (NIH) with respect to clinical research. The NIH is biased toward basic science and is prejudiced by the idea that clinical research is best performed in a university setting by means of prospective trials. However, many clinical questions cannot be addressed in this way, especially when the goal is to determine which established techniques are most effective in an era of cost containment. Doctors with access to the numbers of patients needed for both retrospective and prospective studies of outcomes are frequently not based at a university. These doctors are alienated from the research infrastructure and are inexperienced with grants, institutional review boards, and research budgets. In the past, they self-funded the publication of their results, but funding for this effort is drying up. The NIH needs to establish a mechanism to fund studies that address many of the everyday questions we face for which the evidence is meager.

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1. Nathan DG, Wilson JD. Clinical research and the NIH — a report card. *N Engl J Med* 2003;349:1860-5.

TO THE EDITOR: Nathan and Wilson conclude from their analysis of a cohort of first-time NIH-funded clinical and nonclinical investigators that there was a “substantial decrease” in both categories in the number of researchers who reapplied for funding and “in particular, a large decrease in the number of clinical investigators (81 percent).” Their data do not support these conclusions.

Although the authors make interpretation needlessly difficult by conflating “investigators” and “applicants” with “applications,” it appears (from their

discussion and Table 2) that nearly 233 (a few applied for more than one grant) of the 255 recipients of NIH clinical grants in 1996 reapplied for funding, 49 through a type 2 renewal mechanism and 184 through a new application. This reapplication rate of approximately 91 percent is gratifying. Also encouraging is the success rate: 112 of 233 applicants (48 percent) received an award. In the non-clinical comparison cohort of 884 applicants, there were 965 type 1 and type 2 reapplications, but because of multiple applications the number of individual investigators who reapplied cannot be determined. Nonetheless, in neither cohort was there a substantial decrease in the number of investigators who reapplied, nor was there an alarming (81 percent) loss to the system of first-time clinical investigators. Because the data do not indicate whether all the type 1 reapplications from the clinical-research cohort could be considered “clinical-research” applications, one cannot determine what fraction of this cohort may have been lost to clinical research at the time of a first reapplication.

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Although the production and retention of clinical investigators, especially physician-scientists, must be a priority for academic medical centers and the NIH, this article offers no insight into the environmental factors that play a crucial role in determining the fate of freshly minted clinical investigators in academic medicine. An understanding of these factors is crucial to the formulation of sound educational and funding policy.

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THE AUTHORS REPLY: Drs. Schneider and Korn have a right to be testy. In our article we state that there was “a substantial decrease in the number of researchers in all categories who applied for grants after receiving a first-time grant.” This statement is erroneous. The words “renewal” or “type 2” should have been included before the word “grants.” We apologize for the confusion. The point is that only 19 percent of the successful first-time clinical-research applicants submitted renewal grants, as opposed to 41 percent of the basic investigators. We worry that this might represent abandonment of clinical research in favor of no research or basic re-

search by successful first-time clinical-research awardees, and we call on the NIH to follow the cohorts carefully. We admit that the sample we describe is very small, and much more evidence needs to be gathered before storm flags are flown.

As for their second point, our article was not intended to deal with the environment, about which much has been written. Instead, it describes the recent NIH response to the environment. But we are glad to see that the Association of American Medical Colleges agrees that academic health centers share responsibility for the unfavorable status of clinical research. That is a big step forward since 1995, when the NIH was often a singular depository of blame for the problem.

Dr. Kaufman is correct in pointing out that practicing physicians are in a perfect position to provide valuable data on outcomes. Indeed, very large group practices, such as Kaiser, are prominent recipients of NIH clinical-research grants. If sufficient numbers of practices could be brought together in a high-quality trials and outcomes system, we believe that the NIH would respond very favorably.

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Prognostic Value of Myeloperoxidase in Patients with Chest Pain

TO THE EDITOR: Brennan et al. (Oct. 23 issue)¹ report an intriguing study of myeloperoxidase in the evaluation of patients with acute chest pain. However, the use of a test for clinical prediction also requires decisions about the sensitivity and specificity

of any selected cutoff point.² The only information of this type provided in the article is the evaluation of the creatine kinase MB isoform (CK-MB), C-reactive protein, and myeloperoxidase for the prediction of major cardiac events within 30 days in patients with

Table 1. Sensitivities, Specificities, and Likelihood Ratios for the Prediction of Major Cardiac Events at 30 Days.

Test	Major Cardiac Event at 30 Days			
	Sensitivity	Specificity	Positive Likelihood Ratio	Negative Likelihood Ratio
Creatine kinase MB isoform	0.424	0.947	8.0000	0.61
C-reactive protein	0.317	0.689	1.0193	0.99
Myeloperoxidase	0.657	0.607	1.6718	0.57