Nomenclature in Translational Research

Reply

Steven H. Woolf


http://jama.ama-assn.org/cgi/content/full/299/18/2149-a
In Reply: In response to Dr Falk and colleagues, as a non-specialist I cannot comment on the merits of any particular screening mechanism or the coronary artery calcium score vs the Framingham Risk Score as a better predictor of coronary artery disease. However, I take issue with their statement that “the proposed Texas legislation incorporates what we consider to be the most accepted part of the SHAPE guidelines.” Accepted by whom and under what circumstances? Are they conceding that the guidelines as a whole have not been accepted as professional consensus through the peer review process? Most importantly, should legislators determine which aspects of guidelines should be mandated and which should not?

What is missing from their letter is a compelling reason why the legislature should be involved. For example, is there evidence that insurers are refusing to cover the specific tests for the early detection of cardiovascular disease (CSHB No. 1438)? Texas State Legislature. http://www.legis.state.tx.us/tlodocs/80R/billtext/pdf/HB01438H.pdf. Accessed March 7, 2008.

Financial Disclosures: Dr Naghavi is chair of the Society for Heart Attack Prevention and Eradication (SHAPE), and Drs Falk and Shah are members of the board of directors of SHAPE; they reported receiving no compensation for these roles. Dr Naghavi reported being a shareholder of Volcano Corporation and Endothelix and president of American Heart Technologies. Dr Falk reported being a shareholder of Endothelix and a scientific advisor to BG Medicine and Boston Scientific. Dr Shah reported being a scientific advisor to Roche, BG Medicine, Kowa Pharmaceuticals, Revologix, Cardiovasx, and BioInvent.


To the Editor: In his Commentary, Dr Woolf identified a critical problem in the field of translational research—lack of clarity in nomenclature. Vague language conflates very different types of research and fosters definitional creep as researchers struggle to ensure that their own work falls under this umbrella. We agree that the terms T1 and T2 lack inherent meaning and should be replaced with ones that are more descriptive.

We suggest that T1 be replaced with the term preclinical research. We define this as research designed to yield a tool or an intervention related to screening, risk assessment, prevention, diagnosis, treatment, or rehabilitation that will be suitable for clinical evaluation within 10 years. Long-term preclinical translational research would have a time frame of 5 to 10 years. Short-term preclinical translational research would be less than 5 years. Basic research that has an anticipated time frame beyond 10 years would not be considered preclinical translational research.

Nomenclature in Translational Research

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We suggest that T2 be replaced with the term applied clinical research. We define this as research designed to determine how to best adapt, implement, or disseminate clinical findings among clinicians, patients, organizations, or communities. Applied clinical research would include studies with results applicable to improving the health of patients or populations within 5 years. Subcategories of applied clinical research would include clinician-, patient-, organizational-, and community-focused depending on whether the primary thrust of the research is on clinician or patient behavior, office or health systems organizational change, or community empowerment and health. The onus would be on researchers to demonstrate in their funding applications that their research could be feasibly translated into practice within the designated time periods.

Use of these explicit and descriptive terms and time frames should improve public understanding of translational research, increase transparency in funding decisions, and foster genuine collaboration not only between basic and clinical researchers, but also between clinical researchers, health services researchers, community physicians, patients, and communities.

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To the Editor: In his Commentary, Dr Woolf commented on the confusion arising from using the term translational research to describe both T1 (moving research findings from “bench to bedside”) and T2 (the translation of results from clinical studies into everyday clinical practice and health decision making) and the need for greater emphasis on T2. We agree with both points.

A unique aspect of the parliamentary mandate for the Canadian Institutes of Health Research is the direction to focus on promoting what is termed knowledge translation. Although this is essentially T2, the definition is more inclusive: “Knowledge translation is a dynamic and iterative process that includes synthesis, dissemination, exchange and ethically sound application of knowledge to improve the health of Canadians, provide more effective health services and products and strengthen the health care system.” In this view, translational research ends with the development and testing of the clinical application and does not include its widespread promotion, whereas the knowledge translation process is about identifying solutions to clinical, health services, and population health problems and facilitating their widespread application.

Knowledge translation is further divided into 2 main categories: end of grant knowledge translation and integrated knowledge translation. With end of grant knowledge translation, researchers develop and implement a plan for making potential users of the knowledge gained from the project aware of the findings. Integrated knowledge translation is a different way of doing research that meaningfully engages knowledge users in the research process, including determining the research question. It is about collaborative, action-oriented, participatory research and involves 2-way interactions between researchers and knowledge users (eg, clinicians, health system administrators and managers, policy makers, patients, or the public). By helping set the research question and being involved in the research process, the knowledge users are predisposed to applying the results when they become available.

We believe that increasing emphasis on and making more funding opportunities available for integrated knowledge translation has provided a vehicle to move research into practice and policy that is in line with Woolf’s call for a greater commitment from funding agencies to strike a balance between T1 and T2 funding. While the Canadian Institutes of Health Research continues to be committed to fund excellence through investigator-driven discovery research (including T1), it is increasingly providing funding for integrated knowledge translation. It is also encouraging researchers to think about the impact of their research and to translate it to appropriate knowledge users to improve health and provide more effective health care delivery.

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In Reply: Among the suggestions in my Commentary was to replace the vague label “translational research” with more descriptive terms that better differentiate T1 from T2, and I commend both letters for beginning to examine the options. The terms suggested by Dr Fiscella and colleagues—preclinical research and applied clinical research—are useful to consider but may be inadequate to clear up the confusion. Whether or not applied clinical research was meant to include conventional drug and device trials, those who
conduct such studies are likely to assume that their work falls under this category. Conversely, public health and health services researchers might be confused to see the term applied to their work.

Furthermore, using “clinical” in both terms perpetuates the tendency of the medical profession to view health research through the clinician’s lens alone. Fiscella et al do include “organizational- and community-focused” research within their definition of applied clinical research, but labeling health interventions outside the clinic as “clinical” research may be a forced fit. Pros and cons exist with other potential terms such as knowledge translation—the term discussed by Dr Graham and Ms Tetroe—but all of them are an improvement over the ambiguity of T2.

Graham and Tetroe call attention to the excellent work of the Canadian Institutes of Health Research. Canadian investigators and institutions have played a leadership role not only in writing about the need for researchers to align their work with the information needs of end users but also in making real commitments in programs and funding to facilitate T2 as a nation. The United States would do well to follow the Canadian example.

T1 is among a group of clinical research movements that are attracting attention and resources but are ultimately unhelpful to patients without T2. Recently, politicians and industry have announced plans to channel millions of dollars per year into research on “comparative effectiveness” and “personalized medicine” while keeping funding for health services research threadbare. Popular research initiatives address worthy questions: whether a treatment can be produced (T1), whether it improves health (evidence-based medicine), which treatment is best (comparative effectiveness), and which is best for an individual patient (personalized medicine). But the answers remain academic if the patient cannot obtain or use the intervention. Overcoming such obstacles so that the products of research benefit all those in need is itself a crucial research priority.

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CORRECTIONS

Incorrect Data: In the Perspectives on Care at the Close of Life article titled “Managing an Acute Pain Crisis in a Patient With Advanced Cancer: ‘This Is As Much of a Crisis as a Code’” published in the March 26, 2008, issue of JAMA (2008;299[12]:1457-1467), an incorrect dose ratio appeared in Table 2. The hydromorphone-to-methadone ratio for less than 330 mg/24 hours of hydromorphone that read “16.1” should have been “1.6:1.”

Incorrect Legend: In the Special Communication entitled “How to Interpret a Genome-wide Association Study” published in the March 19, 2008, issue of JAMA (2008;299[11]:1335-1344), an integral word was omitted from the Figure 3 legend. The sentence that read, “Genome-wide association studies assume no a priori hypotheses about candidate genes or regions that might be associated with disease; rather, they test single-nucleotide polymorphisms (SNPs) throughout the genome for possible evidence of genetic susceptibility” should have read, “Genome-wide association studies assume no a priori hypotheses about candidate genes or regions that might be associated with disease; rather, they test single-nucleotide polymorphisms (SNPs) throughout the genome for possible evidence of genetic susceptibility.”

Unreported Research Funding: In the Research Letter titled “Exhaled Carbon Monoxide With Waterpipe Use in US Students,” published in the January 2, 2008, issue of JAMA (2008;299[1]:36-38), the Financial Disclosures should have included the following: Dr Hammond reports that she has received research funding for studies on environmental tobacco smoke from the National Institutes of Health and from the Flight Attendants Medical Research Institute. However, none of these grants were used to support the study reported in this Research Letter.