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The Meaning of Translational Research and Why It Matters

Steven H. Woolf, MD, MPH

TRANSLATIONAL RESEARCH MEANS DIFFERENT THINGS to different people, but it seems important to almost everyone. The National Institutes of Health (NIH) has made translational research a priority, forming centers of translational research at its institutes and launching the Clinical and Translational Science Award (CTSA) program in 2006. With 24 CTSA-funded academic centers already established, other universities are transforming themselves to compete for upcoming CTSA grants. By 2012, the NIH expects to fund 60 such centers with a budget of \$500 million per year.¹ Besides academic centers, foundations, industry, disease-related organizations, and individual hospitals and health systems have also established translational research programs and at least 2 journals (*Translational Medicine* and the *Journal of Translational Medicine*) are devoted to the topic. By some accounts, translational research has become a centerpiece of the European Commission's €6 billion budget for health-related research, and the United Kingdom has invested £450 million over 5 years to establish translational research centers.²

What exactly is translational research? For many, the term refers to the “bench-to-bedside” enterprise of harnessing knowledge from basic sciences to produce new drugs, devices, and treatment options for patients. For this area of research—the interface between basic science and clinical medicine—the end point is the production of a promising new treatment that can be used clinically or commercialized (“brought to market”). This enterprise is vital, and has been characterized as follows: “effective translation of the new knowledge, mechanisms, and techniques generated by advances in basic science research into new approaches for prevention, diagnosis, and treatment of disease is essential for improving health.”³

For others—especially health services researchers and public health investigators whose studies focus on health care and health as the primary outcome—translational research refers to translating research into practice; ie, ensuring that new treatments and research knowledge actually reach the patients or populations for whom they are intended and are implemented correctly. The production of a new drug, an end point for “bench-to-bedside” translational research, is

only the starting point for this second area of research. According to McGlynn et al,⁴ US patients receive only half of recommended services. The second area of translational research seeks to close that gap and improve quality by improving access, reorganizing and coordinating systems of care, helping clinicians and patients to change behaviors and make more informed choices, providing reminders and point-of-care decision support tools, and strengthening the patient-clinician relationship.

The distinction between these 2 definitions of translational research was articulated by the Institute of Medicine's Clinical Research Roundtable,⁵ which described 2 “translational blocks” in the clinical research enterprise and which some now label as T1 and T2. The first roadblock (T1) was described by the roundtable as “the transfer of new understandings of disease mechanisms gained in the laboratory into the development of new methods for diagnosis, therapy, and prevention and their first testing in humans.” The roundtable described the second roadblock (T2) as “the translation of results from clinical studies into everyday clinical practice and health decision making.”

Referring to T1 and T2 by the same name—translational research—has become a source of some confusion.⁶ The 2 spheres are alike in name only. Their goals, settings, study designs, and investigators differ. T1 research requires mastery of molecular biology, genetics, and other basic sciences; appropriately trained clinical scientists working in strong laboratories and with cutting-edge technology; and a supportive infrastructure within the institution—all elements the CTSA seeks to nurture.

In contrast, the “laboratory” for T2 research is the community and ambulatory care settings, where population-based interventions and practice-based research networks⁷ bring the results of T1 research to the public. T2 requires different research skills: mastery of the “implementation science”⁸ of fielding and evaluating interventions in real-world settings and of the disciplines that inform the design of those interventions, such as clinical epidemiology and evidence synthesis, communication theory, behavioral science, public policy, financing, organizational theory, sys-

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tem redesign, informatics, and mixed methods/qualitative research. T1 and T2 face different challenges. T1 struggles more with biological and technological mysteries, trial recruitment, and regulatory concerns. T2 struggles more with human behavior and organizational inertia, infrastructure and resource constraints, and the messiness of proving the effectiveness of “moving targets” under conditions that investigators cannot fully control.^{9,10}

Both T1 and T2 research are vital, but T1 seems to overshadow T2 in the United States.⁶ Most individuals have T1 in mind when they use the term translational research and T1 attracts more funding. According to Moses et al,¹¹ the \$22.1 billion NIH budget for 2002 included \$9.1 billion for “applied and development research” (\$13.0 billion for basic research) but only \$787 million for health services research. The NIH maintains an active program in “dissemination” research,¹² but across all funding sources in 2002—federal and foundations—spending on health services research represented only 1.5% of biomedical research funding.¹¹ National Institutes of Health leaders and the CTSA program advocate both T1 and T2, but the focus is on T1. The CTSA program does encourage “community engagement,” but whether this entails T2 is often unclear. Rather than promoting the efferent process of exporting research findings to the community and facilitating their implementation in practice, CTSA often portrays community engagement as an afferent process for researchers; ie, a way to “foster collaborative research partnerships and enhance public trust in clinical and translational research, facilitating the recruitment of research participants from the community.”¹³

Arguably, the federal responsibility for T2 research lies not with the NIH but with the Agency for Healthcare Research and Quality (AHRQ). According to its recent report to Congress, “the ultimate goal [of AHRQ] is research translation—that is, making sure that findings from AHRQ research are widely disseminated and ready to be used in everyday health care decisionmaking.”¹⁴ But Congress allocates AHRQ only approximately \$300 million per year for this work: just over 1% of the NIH budget. AHRQ does what it can—in 1999 and 2000 it issued 27 Translating Research into Practice (TRIP) grants,¹⁵ and it has also sponsored TRIP conferences—but funding for TRIP later declined as congressional earmarks began carving out much of AHRQ’s budget for specific topics (eg, patient safety, information technology). In 2000, AHRQ spent \$7 million (3% of its budget) on TRIP studies,¹⁶ but by 2004 it spent only \$2 million (1%).¹⁷

The T2 research community is still defining itself, both in name and in scope. Being named TRIP, T2, or even translational research is unsatisfactory to many in the discipline, but no consensus has coalesced around alternative terms (eg, dissemination, health services, knowledge translation/transfer, implementation, or quality improvement research). The scope of T2 research is also unclear. The roundtable model⁵ portrays T2 as one step—the translation of new

knowledge into clinical practice—but the process is rarely that simple.^{8,18} Westfall et al¹⁹ redrew the model to include a third step (T3), practice-based research,⁷ which is often necessary before distilled knowledge (eg, systematic reviews, guidelines) can be implemented in practice.

Even this expanded model is incomplete because it sees knowledge implementation only through the eyes of physicians, but practitioners other than health care professionals also translate research into practice. Science informs choices about health habits (eg, diet, smoking), environmental policy, injury prevention, parenting, healthy workplaces and schools, population health campaigns, and other interventions outside the clinic. The “practitioners” who apply evidence in these settings include patients, public health administrators, employers, school officials, regulators, product designers, the food industry, and other consumers of evidence. Trials that test the implementation of evidence in these settings can be just as vital as similar T2 work in clinical settings.²⁰

How attention and resources are apportioned to T1 and T2 matters because, for many diseases, T2 could save more lives than T1. The “bench-to-bedside” T1 enterprise occasionally yields breakthroughs that markedly improve the prognosis for a disease,^{21,22} but most new drugs and interventions produced by T1 only marginally improve efficacy. These incremental advances are certainly welcome, but patients might benefit even more—and more patients might benefit—if the health care system performed better in delivering existing treatments than in producing new ones. For example, greater fidelity in administering aspirin to eligible patients might prevent more strokes than developing more potent antiplatelet agents.²³ At a time when experts warn of the fragmented health care system and of a widening “chasm”²⁴ in access, quality, and disparities, interventions to close these gaps—the work of T2—may do more to decrease morbidity and mortality than a new imaging device or class of drugs.

Public interest therefore requires T2 to come out from under the shadow of T1. It needs a new name; translational research is now too vague a term for T2 (or T1) and not using the same label for both endeavors would help to reduce confusion. More than a new name, however, T2 needs new recognition and emphasis. Policy makers and the academic research community must come to a clearer understanding of the distinction between inventing treatments and getting them used in practice. Those who fund research must weigh carefully the relative capacity of each research sphere to improve health and economic outcomes and should fund each endeavor accordingly. Disproportion has consequences,²⁵ and the current policy of spending 1.5% of research dollars on health services research¹¹ is probably costing lives.

Moreover, adequate investment in T2 research is vital to fully salvage investments in T1 research. Bringing a drug to market without knowing how to bring it to patients un-

dermines its larger purpose and can only diminish its profitability for investors.

A consequence of a stronger commitment to T2, especially outside clinical settings, is to expand the boundaries of basic science beyond the bench research that T1 typically showcases. Successful health interventions in hospitals, homes, and statehouses require the translation of other “basic sciences”—such as epidemiology, behavioral science, psychology, communication, cognition, social marketing, economics, political science—not only the translation of biotechnological insights and novel therapies. These disciplines deserve their place not only in definitions of basic science but also in funding priorities. Poverty matters as much as proteomics in understanding disease.

Discovering better ways to ensure that patients receive the care they need—safely, compassionately, and when they need it—is not easy and poses formidable methodologic challenges. Scientific discoveries and spectacular new devices are more fascinating to the public and more lucrative for industry. The betterment of health, however, should dictate priorities in health research. Funders should strike a balance between areas of research—T1 vs T2, clinical vs population-based research—and emphasize each endeavor in proportion to its ability to improve health.

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