

# Practice-Based Research—“Blue Highways” on the NIH Roadmap

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On the old highway maps of America, the main routes were red and the back roads blue. Now even the colors are changing. But in those brevities just before dawn and a little after dusk—times neither day nor night—the old roads return to the sky some of its color. Then, in truth, they carry a mysterious cast of blue, and it's that time when the pull of the blue highway is strongest, when the open road is a beckoning, a strangeness, a place where a man can lose himself.

William Least Heat-Moon, *Blue Highways*<sup>1</sup>

U S ROUTE 34 DROPS OUT OF THE ROCKIES LIKE SO many spring-fed creeks. Passing through the front-range sprawl of bedroom communities and suburbs, it narrows to 2 lanes and begins its trek across the Great Plains. In its heyday it was a bustling highway with countless travelers on their way to vacation in the cool Colorado Mountains. Now it lies still, a “blue highway,” heat rising in waves off the pavement, dotted with small, dusty farming communities. A brochure for a nearby town boasts, “Just an hour from I-70.”

But do not be fooled. The communities through which it runs are active, vital centers of business and agriculture. A lot of life happens in these communities, and a lot of health care is delivered. This blue highway connects hundreds of small, vital communities to the roaring interstate system, linking people, commerce, and ideas across our vast country. Even though most Americans may not live in rural towns, the majority live in communities far removed from the academic tertiary medical centers where most federally funded research is conducted, and it is not only distance that separates these two worlds.

The National Institutes of Health (NIH) spends billions of dollars annually on biomedical research. Most of this money is spent on basic research that aims to understand how living organisms work. A relatively smaller amount is spent on clinical studies involving people. A new initiative, the NIH Roadmap, has focused increased attention on the need to “translate” basic research more quickly into human studies and then, hopefully, into tests and treatments that can improve clinical practice for the benefit of patients.<sup>2</sup> The NIH Roadmap may benefit from “blue highway” research that connects the major academic science labo-

ratories to the physicians and patients in primary care offices across the United States.

Inventing a new medicine or treatment is only the starting point for improving the health of an individual patient. The magnitude and nature of the work required to translate findings from human medical research into valid and effective clinical practice, as depicted in the current NIH research pipeline diagrams,<sup>3</sup> have been underestimated. Frequently, years or even decades are required for laboratory discoveries to reach clinical practice. It takes an estimated average of 17 years for only 14% of new scientific discoveries to enter day-to-day clinical practice.<sup>4</sup> McGlynn et al<sup>5</sup> reported that Americans only receive 50% of the recommended preventive, acute, and long-term health care. For example, just over 50% of eligible Americans have received appropriate colorectal cancer screening.<sup>6</sup> While the beneficial effect of  $\beta$ -blockers in acute myocardial infarction was established 25 years ago,  $\beta$ -blockers are widely underused and there is still wide variation in their use.<sup>7</sup>

Myriad detours, speed traps, roadblocks, and potholes limit the movement of treatments from bench to practice. They include the limited external validity of randomized controlled trials, the diverse nature of ambulatory primary care practice, the difference between efficacy and effectiveness, the paucity of successful collaborative efforts between academic researchers and community physicians and patients, and the failure of the academic research enterprise to address needs identified by the community.<sup>8</sup>

The vast majority of patients receive medical care in the ambulatory primary care setting, yet the majority of clinical research occurs in the academic clinical setting.<sup>9,10</sup> Clinical research studies, with their tight inclusion and exclusion criteria, create an artificial sample of patients who are not representative of the majority of those who present to primary care offices across the United States. Because treatment recommendations and disease management guidelines are often based on evidence from a relatively small num-

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ber of large tertiary care centers, their applicability to the everyday practice of medicine may be limited.

What is efficacious in randomized clinical trials is not always effective in the real world of day-to-day practice. The treatment effect and benefit-to-harm ratio reported in randomized trials are often not found in clinical practice. Graham et al<sup>11</sup> reported that patient-specific factors greatly affect physicians' treatment of heart failure and pointed out that imprecise definitions, reliance on single measures, and organizational factors limit the validity of heart failure treatment guidelines. O'Connor et al<sup>12</sup> reported that the evidence-based clinical practice guideline on upper respiratory tract infections was generally unhelpful because only 13% of patients with upper respiratory symptoms were actually eligible for adherence to guideline care. Katz<sup>13</sup> found that guidelines for treating unstable angina likely do not decrease unnecessary hospitalizations and might actually increase admission to limited intensive care unit beds. After initial widespread use of tissue plasminogen activator for acute ischemic stroke, several studies reported significant deviation from national treatment recommendations leading to unacceptably high complication rates.<sup>14</sup> Physicians and care teams involved in randomized trials are often the best in their discipline and the clinical skills they possess may not be available in all communities.

Frequently, the major questions that need to be answered to close the gaps between scientific discovery and widespread use in primary care are not prioritized by funders or undertaken by academic researchers. For example, many studies have involved hypertension, and hypertension treatment guidelines are routinely updated and distributed. Yet, fundamental questions about how to implement these recommendations in primary care remain unresolved. What is the incremental benefit to lowering blood pressure an additional 10 mm Hg by adding another medicine? What are the additional risks? Patients want to know if the benefit is worth the costs of taking yet another pill.

The Family Practice Inquiries Network has begun soliciting clinical questions from practicing physicians with the intent to find practical, relevant answers to these questions.<sup>15</sup> Arising from the everyday clinical practice of medicine in primary care offices, these questions address common issues that seek to bridge the gap between recommended care and actual care. Unfortunately, these questions are infrequently addressed by academic and industry trials, which focus their attention and resources on discovering new medicines and treatments. This network may be an important source for clinical questions for future funding initiatives.

Essential elements in the NIH Roadmap and the research pipeline are the translational steps: translation of basic science laboratory work in animals into an understanding of basic human medical chemistry and physiology and translation of basic human chemistry and physiology into improved diagnostic tests, medicines, and treatments for use

in clinical practice. The final crucial step in clinical care is the delivery of recommended care to the right patient at the right time, resulting in improvement in that patient's health. While the standard NIH Roadmap includes 2 translational steps from bench to bedside to practice, an additional research "laboratory" and another essential translational step involves research in ambulatory clinical practices (FIGURE). This additional laboratory and third translational step seek to solve the problems encountered by primary care physicians as they attempt to incorporate new discoveries into clinical practice. The lower portion of the Figure depicts these additional steps and how the development of a medicine or treatment is just the beginning of the work necessary to improve an individual patient's medical care.

Missing from the NIH Roadmap are the blue highways that form a 2-way connection between the interstates of academic scientific discoveries and the patients receiving care in the ambulatory practice. Without translation to ambulatory practice, individual patient care will not change. The improvements in care outlined in the Institute of Medicine report *Crossing the Quality Chasm*<sup>16</sup> require significantly more research in the ambulatory setting than is currently funded.

A potential solution to these problems is the expansion of practice-based research, which is grounded in, informed by, and intended to improve practice. Practice-based research occurs in the office, where most patients receive most of their care most of the time and may be the essential link between bench discoveries, bedside efficacy, and everyday clinical effectiveness. Practice-based research and practice-based research-networks (PBRNs) may help because they can (1) identify the problems that arise in daily practice that create the gap between recommended care and actual care; (2) demonstrate whether treatments with proven efficacy are truly effective and sustainable when provided in the real-world setting of ambulatory care; and (3) provide the "laboratory" for testing system improvements in primary care to maximize the number of patients who benefit from medical discovery. Practice-based research may be the blue highway between the academic interstate of basic and clinical research and the tree-lined streets where the majority of Americans live and obtain medical care.

Practice-based research has a long and robust history in the United States and throughout the world but receives limited attention from mainstream academic clinical research laboratories and the NIH.<sup>17</sup> The Agency for Healthcare Research and Quality has been a leader in funding PBRNs, and now more than 100 networks are actively conducting practice-based research across the United States.<sup>18,19</sup> Other federal funding agencies and national foundations have begun targeting PBRNs for specific research funding, but the total dollar amount available is inadequate for the breadth and depth of the research necessary to reduce the gap in quality ambulatory care. The NIH Roadmap includes practice-based research and clinical

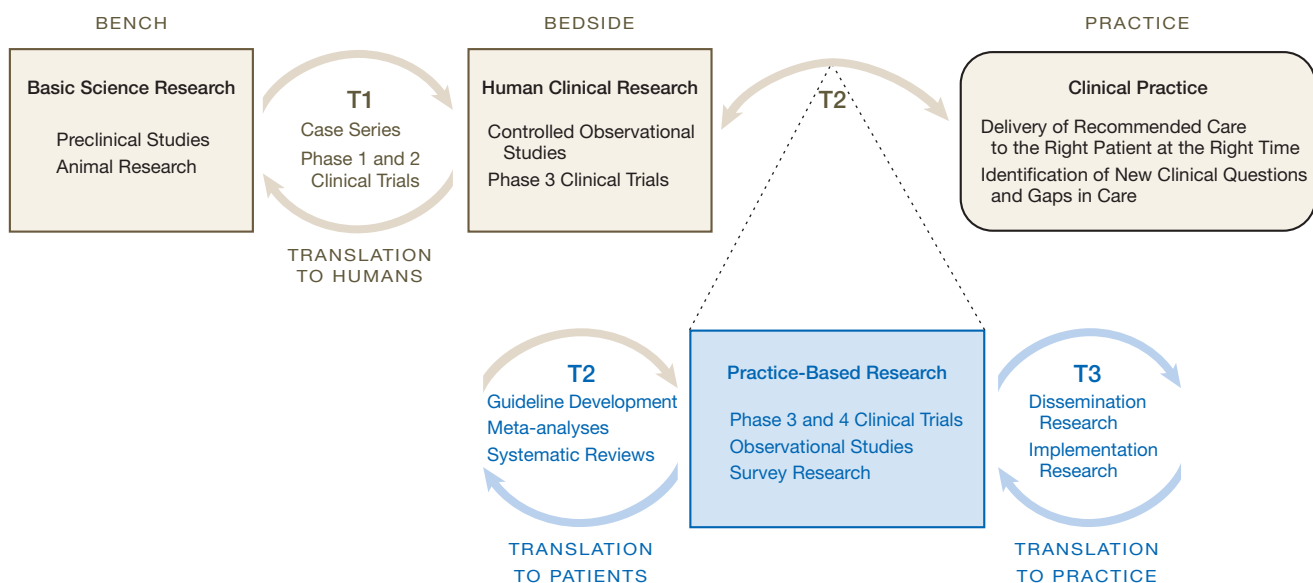
research networks as part of its plan to reengineer the clinical research enterprise,<sup>3</sup> and research networks are an important component of the Clinical and Translational Science Awards (CTSAs). Specifically, practice-based research fits well with the vision of the NIH Roadmap to “develop new partnerships of research with organized patient communities, community-based health care providers . . . who care for sufficiently large groups of patients interested in working with researchers to quickly develop, test and deliver new interventions.”<sup>2</sup> However, the role for networks envisioned by the Roadmap initiative is largely a recruitment vehicle for clinical trials.

While practice-based research may provide an appropriate setting for randomized controlled trials, such trials do not take full advantage of the strength of practice-based research. The benefit of practice-based research goes beyond the simple notion of access to large numbers of patients. Practice-based research also provides the laboratory for observational studies, physician and patient surveys, secondary data analysis, and qualitative research. Well positioned to conduct translational research, practice-based research is not synonymous with translational research. Practice-based research may be the best setting for studying the process of care and the manner in which diseases are diagnosed, treatments initiated, and chronic conditions managed.<sup>20</sup> It is in practice-based research where effectiveness can be measured,<sup>21</sup> where new clinical questions may arise,<sup>15</sup> where

readiness to change and adopt new treatments can be studied and addressed,<sup>22</sup> where patient knowledge and preferences are encountered and managed,<sup>23</sup> and where the interface between patients and their physicians can be explored and medical care improved.<sup>24</sup> Practice-based research is the final common pathway for improving individual patient care and outcomes.

Academic institutions can play an important role in collaborating with community clinicians and their patients through PBRNs. The NIH Roadmap initiatives offer the opportunity for academic researchers to partner with communities and PBRNs for clinical translational research. The specific requirement of the CTSA program to engage communities and carry translational research into clinical practice is recognition of the need and opportunity for practice-based research. The 12 academic health centers that received first-round CTSA implementation awards describe strong collaborations with community partners—clinicians, practices, and organizations.<sup>25</sup> Appreciating the potential of PBRNs as a rich laboratory for describing the phenomena of the patient-physician encounter, introducing innovative practice improvements, and providing access to patients for new discovery will ultimately lead to higher-quality medical care. Practice-based research networks exist throughout the United States in nearly every state and have affiliations with numerous academic medical institutions. Specialty-based clinical researchers as well as health services

**Figure.** “Blue Highways” on the NIH Roadmap



The current National Institutes of Health (NIH) Roadmap for Medical Research includes 2 major research laboratories (bench and bedside) and 2 translational steps (T1 and T2). Historically, moving new medical discoveries into clinical practice (T2) has been haphazard, occurring largely through continuing medical education programs, pharmaceutical detailing, and guideline development. Proposed expansion of the NIH Roadmap (blue) includes an additional research laboratory (Practice-based Research) and translational step (T3) to improve incorporation of research discoveries into day-to-day clinical care. The research roadmap is a continuum, with overlap between sites of research and translational steps. The figure includes examples of the types of research common in each research laboratory and translational step. This map is not exhaustive; other important types of research that might be included are community-based participatory research, public health research, and health policy analysis.

researchers and primary care researchers will find enthusiastic collaborators along the blue highways of practice-based research, perhaps in your own institution.

Without the blue highways of practice-based research, an important concern is that the NIH Roadmap will focus its research in academic tertiary and quaternary care centers. Biomedical discoveries may not be successfully translated past the academic medical center, and the unanswered questions of day-to-day clinical practice may never be addressed by the scientific community. The 2-way interface between basic science laboratory and clinical practice must be reimagined and strengthened. The best new treatments will achieve little if they never reach the patients for whom they were developed. The physicians engaged in practice-based research are eager to conduct research that will help bring those discoveries to their patients. However, practice-based research is more than a conduit to patients. Practice-based research provides the laboratory that will help generate new knowledge and bridge the chasm between recommended care and improved health. Practice-based research is not the only needed expansion of the NIH Roadmap. Community-based participatory research, public health research, and health policy analysis are essential research endeavors that require continued support and expanded NIH funding.

Just as “blue highway” has entered the American travel lexicon, “practice-based research” should enter the mainstream medical research vocabulary and become a strong component of the NIH Roadmap and the CTSA program. Practice-based research is a crucial scientific step, the blue highway, between the great medical advances of the next 25 years and the millions of Americans who want to live a long and healthy life.

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