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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*[1]

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US 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.[2] The NIH Roadmap may benefit from "blue highway" research that connects the major academic science laboratories 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,[3] 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.[4] McGlynn et al[5] 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.[6] While the beneficial effect of β-blockers in acute myocardial infarction was established 25 years ago, β-blockers are widely underused and there is still wide variation in their use.[7]

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.[8]

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.[9,10] 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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