Considerations for Diabetes Translational Research in Real-World Settings

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"NIDDK's mission is to conduct and support research on diseases such as diabetes in order to increase knowledge to improve the public's health. NIDDK's goals will not be completely achieved until the knowledge gained from the research it supports is translated and fully applied."

—Allen Spiegel, MD, Director, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), 27 September 2002 (1).

Tremendous advances have occurred in diabetes research over the past decade. Landmark clinical trials such as the Diabetes Control and Complications Trial (DCCT) and U.K. Prospective Diabetes Study (UKPDS) have demonstrated that tight glycemic and blood pressure control reduce the rate of complications (2–4). More recently the Diabetes Prevention Program (DPP) showed that lifestyle interventions incorporating healthy diets and exercise, as well as treatment with the drug metformin, delay or prevent the development of diabetes in people with impaired glucose tolerance (5). Armed with such knowledge, health care providers and public health professionals have the potential to prevent morbidity and enhance quality of life in a cost-effective manner (6).

Unfortunately, little of this potential has been realized. Numerous studies in a variety of settings indicate that real-world diabetes care frequently does not adhere to evidence-based practice standards for glycemic, blood pressure, and lipid levels and for providing recommended processes of care such as the Diabetes Quality Improvement Project indicators (7,8). The challenges of adhering to recommendations regarding diet, physical activity, medications, and other medical care are formidable. A complex array of social, financial, behavioral, and organizational barriers impede the application of high-quality diabetes care. These multifactorial barriers can be daunting, but significant advances have occurred in learning how to translate research findings from the clinical research setting into real-world practice.

In September 2002 the Diabetes Mellitus Interagency Coordinating Committee, which was created by Congress by Public Law 93-354 and comprises representatives from federal departments and agencies whose programs are relevant to diabetes and its complications in the U.S., held a meeting that highlighted the accomplishments, key issues, and potential of diabetes translational research. In this commentary, we describe diabetes translational research and identify priority translational research areas (Table 1). We also discuss challenges of moving diabetes translational research forward. As Dr. Spiegel notes, the work of NIDDK and other federal agencies is not complete until research findings are widely applied in the real world.

Diabetes translational research and prior lessons learned

Translation occurs in two continuous phases (9). The first is "bench to bedside," i.e., from laboratory research to clinical research application. For example, hypoglycemic treatments such as insulin, sulfonylureas, and biguanides were discovered in the laboratory and then tested in clinical trials such as the DCCT and UKPDS. The second translational phase is from the clinical research setting to real-world practice (10). Often clinical trials include highly selected populations with particularly intensive treatment protocols conducted by expert multidisciplinary research teams. The challenge is determining how to translate findings from an ideal setting to the frequently less-than-optimal situations that face typical clinicians, who care for diverse communities with finite resources and face many competing demands. This commentary concentrates on the second translational phase, from clinical research to real-world practice. In particular, we focus on diabetes translational research, the investigative work that informs one of how to take knowledge from clinical research environments and successfully apply or adapt these findings to real-world environments. It is also important to note that observational studies of real-world

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Abbreviations: DCCT, Diabetes Control and Complications Trial; DPP, Diabetes Prevention Program; NIDDK, National Institute of Diabetes and Digestive and Kidney Diseases; UKPDS, U.K. Prospective Diabetes Study.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Key diabetes translational issues in real-world settings*

Descriptions and prior lessons learned
- Translation occurs in two continuous phases. The first is "bench to bedside," from laboratory research to clinical research. The second phase goes beyond the clinical research bedside to the community at large.
- Many barriers to adoption of new science into clinical care at the community level exist.
- Diabetes translational issues are diverse and complicated, involving quality of care, outcomes, access to care, and costs across the multiple intervention levels of patients, including children and older individuals, providers, centers, health care systems, and society.
- Behavior is influenced by a combination of multilevel forces: predisposing, enabling, and reinforcing factors.
- No single best practice is appropriate for all patients and practitioners. Tailoring to patients and customizing to settings is necessary.
- Real-world translation requires flexibility to deal with pragmatic issues such as provider time constraints, reimbursement, and system problems.
- Rigorous nonrandomized study designs including quasi-experimental, time-series, and observational studies are frequently most appropriate.

Priority areas for much-needed diabetes translation
- External validity issues and applicability of programs and results to different settings.
- Identifying and understanding barriers and facilitators to translating research into practice.
- Moving from an acute-care paradigm to a multifaceted chronic-care model that is population-based as well as patient-centered.
- Vulnerable, understudied populations—older persons, minority populations, children/adolescents, and people at risk for diabetes, including the overweight and obese.
- Diabetes translational interventions.
- Sustainability of organizational interventions.
- Community-based participatory translational efforts involving researchers, community members, and governmental/private agencies.
- Economic studies of translation, including cost-effectiveness analysis.
- Public health and public policy efforts.

practices and examination of natural experiments in clinical care can help identify best practices and innovative programs worthy of translation, but that is beyond the scope of this article.

Many barriers exist to hinder the adoption of new science into clinical care (11). These barriers include behavioral impediments, cultural misunderstanding, poor diffusion of knowledge, underutilization of information technology, inefficient organization of care, financial disincentives, lack of insurance, and ineffective public policies. These roadblocks occur at the level of the patient, provider, health care organization, community, and society. They span multiple human developmental stages, from childhood and adolescence to adulthood and older age. Diabetes translational problems are diverse and complicated, involving such issues as access to care, quality of care, outcomes improvement, and cost (12).

No single best practice is appropriate for all patients, clinicians, or settings. The specific barriers for a given diabetes translational problem must be identified and addressed in translational research. Translation requires the flexibility to deal with real-world issues, such as patient diversity, provider time constraints, reimbursement limitations, history and politics of an organization, and system problems. General principles are useful, but they must be adapted to specific circumstances. In essence, people, communities, organizations, and cultures are richly diverse and complex. It is a given that barriers to translation go beyond any one disciplinary vantage point; therefore, inherently multidisciplinary expertise is required for success. Behavioral scientists, organizational theorists, health services researchers, epidemiologists, economists, sociologists, psychologists, anthropologists, political scientists, medical informatics experts, biostatisticians, community experts, patients, nurses, social workers, and clinicians are just some of the people whose expertise and experience are necessary to tackle diabetes translational issues successfully.

While the challenge is enormous, significant advances have been made in diabetes translational research (13). Recent reviews summarize the effectiveness of disease and case management for people with diabetes (14), changing provider behavior (15), diabetes self-management (16–18), diabetes prevention (19), and behavioral interventions (20). Important progress in translational research has influenced practice in areas such as patient empowerment interventions (21,22), nurse-implemented disease management (23), use of planned, proactive population-based quality improvement interventions (24), and to some extent in addressing health disparities.

Priority areas for diabetes translation

While impressive lessons have been learned about how to improve diabetes translation, the stark national figures documenting suboptimal diabetes care demonstrate that much more needs to be understood regarding how to implement and sustain evidence-based diabetes care in the real world.

We highlight several priority areas for diabetes translational research. While many important research areas exist, we believe the ones outlined below are fundamental and thus have particular importance.

1. Attention to external validity and the applicability of programs and results in different settings. Traditionally many researchers, grant-review study sections, and funding agencies have stressed the importance of internal validity—that the results of a study are valid within the particular study population. The result is that the randomized controlled trial, often of narrowly defined populations with intensive interventions difficult to replicate in the real world, has been hailed as the gold standard of research designs. External validity, the applicability of the study to other populations and settings, has received less attention. This results in a major gap in our understanding of how to implement and sustain ideal diabetes care in the real world (25).

The primary focus in diabetes translational research, as in any research, should be selecting important research questions. The appropriate methods then follow from the questions, and in fact, a variety of rigorously performed research techniques and evaluation designs can in-

crease the study's validity in diverse settings. For example, if the question is whether a culturally sensitive case-management system works among people with diabetes in the Latino community, then a randomized controlled trial with liberal entry criteria might be ideal. If the target Latino community generally thought that a randomized controlled trial of the system was unethical or inappropriate, then a rigorous quasi-experimental approach, a time-series design, or an observational study might be most suitable (26).

2. Identifying and understanding barriers and facilitators to diabetes translation in different settings. A rich variety of barriers and facilitators exist among different patients and locales. Behavior at the individual and group levels is influenced by a combination of factors that predispose, enable, and reinforce a behavior (27). Each of these leverage points might be addressed to maximize the chance of successful translation. These mediators include behavioral factors, such as self-efficacy and social support, as well as environmental factors, such as organizational structure and community support. We need to better understand the mechanisms by which these mediators work and how they can be enhanced individually and in combination. Multiple research methods can be used to determine the root causes of the barriers and facilitators. For example, to determine what key factors should be considered in designing a culturally sensitive case-management system for Latino patients with diabetes, qualitative methods or surveys might supply the most useful information (28,29).

3. Moving from an acute-care paradigm to a multifaceted chronic-care model that is population-based, proactive, and patient-centered. Increasingly clinicians and health care planners are realizing that viewing and caring for diabetes as an acute, episodic illness akin to short-term and curable infectious diseases is ineffective. Chronic-care and disease-management models have emerged that emphasize improving active patient self-management and empowerment, decision support for providers, clinic efficiency, information systems, organizational leadership, and a population-based community health perspective (30). Each component of these chronic-care models requires more research to determine how to optimize it for real-world translational efforts (31). In addition, the summative, holistic effects of complex systems change need further investigation. The Institute of Medicine highlights that a poorly organized health care delivery system is one of the root causes of inadequate quality of care in the U.S. (32).

4. Particularly vulnerable, understudied populations. These groups include the increasing number of older patients with diabetes, who often have multiple competing comorbid conditions and limited resources (33); minority populations, for whom cultural issues may be relevant; socially and economically disadvantaged groups; and patients at very high risk for developing diabetes, including overweight and sedentary obese children, adolescents, and adults (34).

5. Diabetes translational interventions. Ideally intervention research builds upon previous work identifying and understanding barriers to translation and mediators of translation. However, it is not enough to identify relationships between factors and outcomes in observational work; this does not demonstrate that those factors can be successfully addressed or modified. Translational intervention research tests programs and should document whether patient outcomes improve in the real world. Given the diversity of practice settings and patient populations, more intervention research is urgently needed and is one of the highest priorities.

6. Sustainability of organizational interventions. Most intervention studies are designed and funded to determine whether the program works in the short term. Much less is known about how to sustain an intervention once the intensity and excitement of the study are over (35). Developing the organizational, financial, attitudinal, and cultural supports and grant mechanisms for sustaining gains at the individual patient level and program level is a ripe area for real-world translational research.

7. Community-based participatory translational efforts involving partnerships among researchers, community members, and governmental/private agencies. Community members often have the best sense of what the key barriers to translation are in their local settings and what types of interventions are most likely to succeed. In addition, if improvement is to be significant and sustainable, then involvement and buy-in must ultimately happen at the grass-roots level. Thus, community-based participatory research holds significant promise for translating research into practice (36,37).

8. Economic studies of translation, including cost-effectiveness analysis. The real world has finite resources with many worthy competing demands. The benefits and costs of diabetes translational efforts need to be rigorously assessed if we are to make wise societal decisions regarding resource allocation. Economic studies, including cost-effectiveness analysis, would supply important information to decision makers (38).

9. Public health and public policy efforts. The field of smoking cessation has demonstrated how strong, creative public health and public policy initiatives can change harmful behavior, prevent morbidity, and save health care expenditures on an enormous scale (39). The National Diabetes Education Program, a partnership of the National Institutes of Health, Centers for Disease Control and Prevention, and more than 200 public and private organizations, has helped increase public awareness and understanding of diabetes (40). However, many public health areas relevant to diabetes have been relatively underexplored and understudied, including availability and acceptability of healthy foods in our schools (41), promotion of incentives and environments for exercising (42), insurance coverage for diabetes (43), and cardiovascular risk factor modification in patients with diabetes.

Challenges of moving diabetes translational research forward

Addressing these diabetes translational issues effectively will require change on the part of researchers, policy makers, funding organizations, grant-review committees, and journal editorial boards. For example, if the best and most important diabetes translational work is to be funded, then it is essential to ensure that grant-review study sections have the relevant expertise in behavioral sciences, organizational theory, epidemiology, statistics, applied health services research, clinical medicine, economics, public policy, and multimethod research, as well as the ability to determine the most appropriate research methodologies given the study question and study pop-

ulation. Attempts at change on the part of any one of the key players impacting diabetes translational efforts without support from the others will fail (9). In addition, it is vital that institutional review boards safeguard potential and actual research subjects while maintaining the public's access to studies they might wish to participate in (9,44,45).

Diabetes translational research is an exciting area, the outcomes of which can prevent much morbidity and suffering. Translational challenges are complex, multilevel, and multifactorial, reflecting the diverse nature of real-world patients, health systems, and communities. Ultimately the solutions will require multipronged approaches that address the patient, provider, health care system, public health, and public policy. More research along these various fronts is necessary if we are to realize the potential of landmark trials such as the DCCT, UKPDS, and DPP and prevent the enormous aggregate burden of diabetes on our society.

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