

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 Mel-

litus 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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Received for publication 19 May 2003 and accepted in revised form 10 June 2003.

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.

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

<p>Descriptions and prior lessons learned</p> <ul style="list-style-type: none"> • 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. <p>Priority areas for much-needed diabetes translation</p> <ul style="list-style-type: none"> • 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.
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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 trans-

lational 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 improve-

ment 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 multi-pronged 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.

References

1. Spiegel A: Opening remarks. *Diabetes Mellitus Interagency Coordinating Committee Translation Conference*. Washington, D.C., 27 September 2002
2. The Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 329:977–986, 1993
3. UK Prospective Diabetes Study Group: Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 352:837–853, 1998
4. UK Prospective Diabetes Study Group: Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. *BMJ* 317:713–720, 1998
5. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM, Diabetes Prevention Program Research Group: Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 346:393–403, 2002
6. Narayan KM, Gregg EW, Fagot-Campagna A, Engelgau MM, Vinicor F: Diabetes: a common, growing, serious, costly, and potentially preventable public health problem. *Diabetes Res Clin Pract* 50 (Suppl. 2):S77–S84, 2000
7. Saaddine JB, Engelgau MM, Beckles GL, Gregg EW, Thompson TJ, Narayan KM: A diabetes report card for the United States: quality of care in the 1990s. *Ann Intern Med* 136:565–574, 2002
8. Fleming BB, Greenfield S, Engelgau MM, Pogach LM, Clauser SB, Parrott MA: The Diabetes Quality Improvement Project: moving science into health policy to gain an edge on the diabetes epidemic. *Diabetes Care* 24:1815–1820, 2001
9. Sung NS, Crowley WF Jr., Genel M, Salber P, Sandy L, Sherwood LM, Johnson SB, Catanese V, Tilson H, Getz K, Larson EL, Scheinberg D, Reece EA, Slavkin H, Dobs A, Grebb J, Martinez RA, Korn A, Rimoin D: Central challenges facing the national clinical research enterprise. *JAMA* 289:1278–1287, 2003
10. Narayan KM, Gregg EW, Engelgau MM, Moore B, Thompson TJ, Williamson DF, Vinicor F: Translation research for chronic disease: the case of diabetes. *Diabetes Care* 23:1794–1798, 2000
11. Hiss RG: The concept of diabetes translation: addressing barriers to widespread adoption of new science into clinical care. *Diabetes Care* 24:1293–1296, 2001
12. The CDC Diabetes Cost-effectiveness Group: Cost-effectiveness of intensive glycemic control, intensified hypertension control, and serum cholesterol level reduction, for type 2 diabetes. *JAMA* 287: 2542–2551, 2002
13. Clark CM Jr., Chin MH, Davis SN, Fisher E, Hiss RG, Marrero DG, Walker EA, Wylie-Rosett J: Incorporating the results of diabetes research into clinical practice: celebrating twenty-five years of Diabetes Research and Training Center translation research. *Diabetes Care* 24:2134–2142, 2001
14. Norris SL, Nichols PJ, Caspersen CJ, Glasgow RE, Engelgau MM, Jack L, Isham G, Snyder SR, Carande-Kulis VB: The effectiveness of disease and case management for people with diabetes: a systematic review. *Am J Prev Med* 22 (Suppl. 1):15–38, 2002
15. Renders CM, Valk GD, Griffin SJ, Wagner EH, Eijk Van JT, Assendelft WJ: Interventions to improve the management of diabetes in primary care, outpatient, and community settings: a systematic review. *Diabetes Care* 24:1821–1833, 2001
16. Norris SL, Nichols PJ, Caspersen CJ, Glasgow RE, Engelgau MM, Jack L, Snyder SR, Carande-Kulis VB, Isham G: Increasing diabetes self-management education in community settings: a systematic review. *Am J Prev Med* 22 (Suppl. 1):39–66, 2002
17. Norris SL, Lau J, Smith SJ, Schmid CH, Engelgau MM: Self-management education for adults with type 2 diabetes: a meta-analysis of the effect on glycemic control. *Diabetes Care* 25:1159–1171, 2002
18. Norris SL, Engelgau MM, Narayan KM: Effectiveness of self-management training in type 2 diabetes: a systematic review of randomized controlled trials. *Diabetes Care* 24:561–587, 2001
19. Fisher EB, Walker EA, Bostrom A, Fischhoff B, Haire-Joshu D, Johnson SB: Behavioral science research in the prevention of diabetes: status and opportunities. *Diabetes Care* 25:599–606, 2002
20. Wing RR, Goldstein MG, Acton KJ, Birch LL, Jakicic JM, Sallis JF Jr., Smith-West D, Jeffery RW, Surwit RS: Behavioral science research in diabetes: lifestyle changes related to obesity, eating behavior, and physical activity. *Diabetes Care* 24:117–123, 2001
21. Anderson B, Funnell M: *The Art of Empowerment: Stories and Strategies for Diabetes Educators*. Alexandria, VA, American Diabetes Association, 2000
22. Glasgow RE, Toobert DJ, Hampson SE, Strycker LA: Implementation, generalization and long-term results of the “choosing well” diabetes self-management intervention. *Patient Educ Couns* 48: 115–112, 2002
23. Aubert RE, Herman WH, Waters J, Moore W, Sutton D, Peterson BL, Bailey CM, Koplan JP: Nurse case management to improve glycemic control in diabetic patients in a health maintenance organization: a randomized, controlled trial. *Ann Intern Med* 129:605–612, 1998
24. Wagner EH, Glasgow RE, Davis C, Bonomi AE, Provost L, McCulloch D, Carver P, Sixta C: Quality improvement in chronic illness care: a collaborative approach. *Jt Comm J Qual Improvement* 27: 63–80, 2001
25. Green LW: From research to “best practices” in other settings and populations. *Am J Health Behavior* 25:165–178, 2001
26. Cook TD, Campbell DT: *Quasi-experimentation: Design & Analysis Issues for Field Settings*. Chicago: Rand McNally College Publishing Company, 1979:
27. Green LW, Kreuter MW: *Health Promotion Planning: An Educational and Ecological Approach*. Mountain View, CA, Mayfield Publishing Company, 1999
28. Creswell JW: *Qualitative Inquiry and Research Design: Choosing Among Five Traditions*. Thousand Oaks, CA, Sage Publications, 1998
29. Aday LA: *Designing and Conducting Health Surveys*. San Francisco, Jossey-Bass Publishers, 1989
30. Wagner EH, Austin BT, Von Korff M: Organizing care for patients with chronic illness. *Milbank Q* 74:511–544, 1996
31. Glasgow RE, Hiss RG, Anderson RM, Friedman NM, Hayward RA, Marrero DG, Taylor CB, Vinicor F: Report of the health

- care delivery work group: behavioral research related to the establishment of a chronic disease model for diabetes care. *Diabetes Care* 24:124–130, 2001
32. Institute of Medicine Committee on Quality of Health Care in America: *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, D.C., National Academy Press, 2001
 33. Chin MH, Polonsky TS, Thomas VD, Nerney MP: Developing a conceptual framework for understanding illness and attitudes in older, urban African Americans with diabetes. *Diabetes Educator* 26: 439–449, 2000
 34. Burnet D, Plaut A, Courtney R, Chin MH: Preventing type 2 diabetes in minority youth: a practical model and empirical evidence. *Diab Educ* 28:779–795, 2002
 35. Boothroyd P, Green LW, Hertzman C, Lynam J, McIntosh J, et al: Tools for sustainability: Iteration and implementation. In *Ecological Public Health: From Vision to Practice*. Chu C, Simpson R, Eds. Toronto, Centre for Health Promotion, University of Toronto, 1994, pp. 111–121
 36. Israel BA, Schulz AJ, Parker EA, Becker AB: Review of community-based research: assessing partnership approaches to improve public health. *Annu Rev Public Health* 19:173–202, 1998
 37. Minkler M, Wallerstein N: *Community-Based Participatory Research in Health*. San Francisco, Jossey-Bass, 2003
 38. *Cost-effectiveness in Health and Medicine*. Gold MR, Siegel JE, Russell LB, Weinstein MC, Eds. New York, Oxford University Press, 1996
 39. Siegel M, Mowery PD, Pechacek TP, Strauss WJ, Schooley MW, Merritt RK, Novotny TE, Giovino GA, Eriksen MP: Trends in adult cigarette smoking in California compared with the rest of the United States, 1978–1994. *Am J Public Health* 90:372–379, 2000
 40. National Diabetes Education Program: <http://ndep.nih.gov/index.html>. Accessed 20 March 2003
 41. Critser G: *Fat Land: How Americans Became the Fattest People in the World*. New York, Houghton Mifflin, 2003
 42. Marcus BH, Dubbert PM, Forsyth LH, McKenzie TL, Stone EJ, Dunn AL, Blair SN: Physical activity behavior change: issues in adoption and maintenance. *Health Psychology* 19 (Suppl. 1):32–41, 2000
 43. Eisenberg JM, Power EJ: Transforming insurance coverage into quality health care: voltage drops from potential to delivered quality. *JAMA* 284:2100–2107, 2000
 44. Newgard CD, Lewis RJ: The paradox of human subjects protection in research: some thoughts on and experiences with the Federalwide Assurance Program. *Acad Emerg Med* 9:1426–1429, 2002
 45. Hirshon JM, Krugman SD, Witting MD, Furuno JP, Limcangco R, Perisse AR, Rasch EK: Variability in institutional review board assessment of minimal-risk research. *Acad Emerg Med* 9:1417–1420, 2002