



**Testimony
Before the
Subcommittee on Health
Committee on Energy and Commerce
United States House of Representatives**

**Testimony for hearing entitled,
“The Battle Against Diabetes: Progress Made;
Challenges Unmet”**

Statement of

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**For Release on Delivery
Expected at 10:00 a.m.
July 1, 2010**

Mr. Chairman and Members of the Committee: I am Judith Fradkin, Director of the Division of Diabetes, Endocrinology, and Metabolic Diseases of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Our Institute has primary responsibility for diabetes research at the National Institutes of Health (NIH), an agency of the U.S. Department of Health and Human Services (HHS).

On behalf of the NIDDK and the other Institutes and Centers of the NIH, I am pleased to report that we are vigorously pursuing research on diabetes and its complications. Through collaborative and coordinated research, we are gaining important insights into the molecular mechanisms underlying disease, identifying and testing promising therapies to prevent and treat the disease and its complications, and striving for a cure. In these efforts, we are fortunate to often partner with other HHS agencies, such as the Centers for Disease Control and Prevention (CDC) and the Indian Health Service (IHS), and other non-federal diabetes organizations.

ADVANCES FROM DIABETES RESEARCH

This year marks the NIDDK's 60th anniversary of conducting and supporting research to combat debilitating diseases within its mission, including diabetes. Diabetes is characterized by the body's inability to produce and/or respond appropriately to insulin, a hormone that is necessary for the body to absorb and use glucose, or sugar, as a cellular fuel. The most common forms of the disease are type 1 diabetes, in which the body loses its ability to produce insulin; and type 2 diabetes, which is due to a combination of insulin resistance and insufficient insulin production. Women can also develop gestational diabetes, a risk factor for type 2 diabetes, during pregnancy. Rarer forms of diabetes also exist.

To appreciate the tremendous progress that has been achieved in recent decades, we can look back at how diabetes was treated in 1950, at the inception of the Institute. Sixty years ago, patients monitored their blood glucose levels with urine tests, which recognized high but not dangerously low glucose levels and reflected hours-old, not current, glucose levels. People with type 1 diabetes relied on painful injections of animal-derived insulin. People with type 2 diabetes had few treatment options: injections of insulin or drugs that stimulated insulin release from the beta cells of the pancreas. Both of these therapies had associated risks. No proven

strategies existed to prevent disease complications, such as blindness, heart disease, kidney disease, and nerve damage.

Insights gained from NIDDK and NIH-supported research over the past 60 years have contributed to a knowledge base leading to improvements in survival and quality of life for people with diabetes. Doctors now use simple blood tests to diagnose diabetes and to assess long-term blood glucose control. People at high risk for type 2 diabetes can prevent or delay disease onset by losing a modest amount of weight through dietary changes and moderate exercise. People with type 1 diabetes can reduce their risk for complications by intensively controlling blood glucose levels. Doctors can prescribe new classes of oral drugs and combinations of drugs to treat people with type 2 diabetes. Patients can use new technologies, such as insulin pumps and continuous glucose monitors, to manage their diabetes. As a result of these past accomplishments, people with diabetes are living longer and healthier lives than ever before. I am pleased to provide you with a few specific examples of how NIH-supported research has contributed to these tremendous improvements in the health and quality of life of people with diabetes.

RESULTS OF MAJOR CLINICAL TRIALS AND TRANSLATING THOSE RESULTS TO IMPROVE PUBLIC HEALTH

One approach to combat the diabetes epidemic in the U.S. is to prevent the disease. A landmark clinical trial studying type 2 diabetes prevention was spearheaded by the NIDDK. The Diabetes Prevention Program (DPP) clinical trial showed that people with pre-diabetes—defined as having blood glucose levels that are higher than normal but not yet high enough to be diagnosed as diabetes—can dramatically reduce their risk of developing type 2 diabetes through lifestyle changes that achieve modest weight loss or through treatment with the drug metformin, although the metformin intervention was much less effective than the lifestyle intervention.¹ The interventions worked in all ethnic and racial groups studied, in both men and women, and in women with a history of gestational diabetes. Research now shows that, after a 10-year period of following DPP participants, the interventions result in long-term benefits: people still had a

¹ Knowler WC, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 346:393-403, 2002.

lower risk of developing type 2 diabetes and those who made lifestyle changes also had reduced cardiovascular risk despite taking fewer drugs to control their heart disease risk factors.²

Building on these critically important results, the NIDDK supports research to translate DPP findings to improve public health and benefit the approximately 57 million Americans with pre-diabetes.³ One successful research effort utilizes local YMCAs for delivering a group-based DPP lifestyle intervention. A pilot study showed that this group-based approach reduces costs to deliver the intervention, while achieving similar levels of weight loss in participants;⁴ a larger trial is ongoing. The impressive findings of this pilot study serve as the basis for a new partnership established earlier this year among the UnitedHealth Group, the National YMCA, and the CDC to offer a diabetes prevention program in sixteen U.S. cities, with plans for a national roll out over the next couple of years.

Another way that the DPP results are being translated to the public and health care providers is through the National Diabetes Education Program (NDEP), which is a partnership between the NIDDK and the CDC. The NDEP developed the “Small Steps. Big Rewards. Prevent Type 2 Diabetes” education campaign to disseminate the DPP results. The NIDDK and its collaborators remain dedicated to building on the tremendous successes to date in order to take advantage of new and emerging opportunities to expand type 2 diabetes prevention efforts.

Another NIDDK-led clinical trial has changed the face of type 1 diabetes management. The Diabetes Control and Complications Trial (DCCT), and its follow-on, the Epidemiology of Diabetes Interventions and Complications (EDIC) study, conclusively demonstrated that early and intensive blood glucose control prevented or delayed the debilitating complications of type 1 diabetes involving the heart, eyes, kidneys, and nerves.⁵ These impressive findings have revolutionized the management of type 1 diabetes, as physicians now recommend that people control their disease as early and intensively as possible. Intensive treatment is being translated

² Diabetes Prevention Program Research Group, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. *Lancet* 374:1677-86, 2009.

³ CDC. National diabetes fact sheet: general information and national estimates on diabetes in the United States, 2007. Atlanta, GA: U.S. Department of Health and Human Services, CDC, 2008.

⁴ Ackermann RT, et al. Translating the Diabetes Prevention Program into the community. The DEPLOY Pilot Study. *Am J Prev Med*. 35: 357-63, 2008.

⁵ 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; Nathan DM, Cleary PA, Backlund JY, et al. Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group. Intensive diabetes treatment and cardiovascular disease in type 1 diabetes mellitus. *N Engl J Med* 353: 2643-2653, 2005.

into improved health, as researchers recently reported that the outlook for people with longstanding type 1 diabetes has greatly improved in the past 20 years.⁶

The NIDDK-supported United Kingdom Prospective Diabetes Study showed that people with type 2 diabetes also benefit from improved glucose control early in the course of the disease with respect to reducing rates of disease complications.⁷ However, in people with long standing type 2 diabetes who also are at high risk for heart disease, more intensive blood glucose control than is currently recommended by treatment guidelines can be dangerous, as demonstrated in the ACCORD clinical trial, which is led by the National Heart, Lung, and Blood Institute.⁸ The trial found that lowering blood pressure to normal levels did not significantly reduce the risk of cardiovascular events overall, although it may reduce the risk of stroke. In the lipid trial, combination therapy of a statin and a fibrate appeared to be safe, but did not lower the risk of heart attack, stroke, or death from heart disease more than statins alone. The ACCORD findings indicate that people who have longstanding type 2 diabetes and are at high risk for a cardiovascular event and are well controlled as per current recommendations do not need to be treated more intensively to reduce heart attacks, strokes, and other cardiovascular events. Thus, the patients can be spared from unnecessary additional medications. These key results from type 2 diabetes clinical trials suggest that, rather than a one-size-fits-all approach, recommendations for treating people with type 2 diabetes can be personalized.

Further insights into the management of type 2 diabetes are expected to emerge from the NIDDK-led Look AHEAD (Action for Health in Diabetes) clinical trial, which is examining the health effects of a lifestyle intervention designed to achieve and maintain weight loss over the long term in over 5,000 overweight and obese adults with type 2 diabetes. Encouraging results are already emerging. After following participants for 1 year, researchers found that people in the intensive lifestyle arm showed improved diabetes, blood pressure, and lipid control, with

⁶ DCCT/EDIC Research Group, et al. Modern-day clinical course of type 1 diabetes mellitus after 30 years' duration: the diabetes control and complications trial/epidemiology of diabetes interventions and complications and Pittsburgh epidemiology of diabetes complications experience (1983-2005). *Arch Intern Med* 169:1307-16, 2009.

⁷ Holman RR, et al. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med* 359:1577-89, 2008.

⁸ Action to Control Cardiovascular Risk in Diabetes Study Group, et al. Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* 358: 2545-49, 2009; ACCORD Study Group, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med* 362:1575-85, 2010; ACCORD Study Group, et al. Effects of combination lipid therapy in type 2 diabetes mellitus. *N Engl J Med* 362: 1563-74, 2010.

reduced medication use and costs.⁹ After 4 years, researchers observed a sustained effect of the lifestyle intervention on weight loss, as well as improved glucose control with reduced medication use.¹⁰ Participants continue to be followed to assess longer-term outcomes. These are just a few examples of the NIH-supported clinical trials that have provided unprecedented insights into diabetes prevention and management.

DISPROPORTIONATE IMPACT ON MINORITY POPULATIONS

Type 2 diabetes occurs more frequently among racial and ethnic minority groups in the U.S., including American Indians, African Americans, Hispanic/Latino Americans, and Asians/Pacific Islanders.¹¹ Because of this disparity, the NIH has included large numbers of minority participants in its type 2 diabetes studies. For example, nearly half of the DPP participants were from minority groups, and the interventions worked in all groups. Those results are being translated in culturally appropriate ways through the NDEP and other translational research efforts.

Type 2 diabetes is an emerging health problem in youth, particularly minority youth, being driven by the obesity epidemic. The NIH and its partners are tackling this issue on many fronts. For example, just this week, researchers announced results from the NIDDK-led HEALTHY clinical trial, which examined whether a middle-school based intervention could lower risk factors for type 2 diabetes. The study was conducted in schools with a high enrollment of minority children and youth from low-income families. The intervention was found to lower the obesity rate in students at highest risk for type 2 diabetes—those who started out overweight or obese in sixth grade. However, schools that implemented the program did not differ from comparison schools in the study's primary outcome—the prevalence of overweight and obesity combined—which had declined by 4 percent in both the intervention and control schools by the end of the 3-year study.¹² These results are important for informing future school-based efforts to reduce overweight and obesity in children.

⁹ Redmon JB, et al. Effect of the look AHEAD study intervention on medication use and related cost to treat cardiovascular disease risk factors in individuals with type 2 diabetes. *Diabetes Care* 33: 1153-8, 2010.

¹⁰ The Look AHEAD Study: Design of the Lifestyle Intervention and Four-Year Weight Losses. Presented at the American Diabetes Association 69th Scientific Sessions, June 2009. Publication in press, *Archives Int Medicine*.

¹¹ CDC. National diabetes fact sheet: general information and national estimates on diabetes in the United States, 2007. Atlanta, GA: U.S. Department of Health and Human Services, CDC, 2008.

¹² Presented at the American Diabetes Association 70th Annual Sessions, June 2010.

Another school-based effort is the Diabetes Education in Tribal Schools (DETS) Project, on which NIDDK and IHS partner. The DETS Project is a K-12 curriculum focused on increasing American Indian/Alaska Native students' understanding of health, diabetes, and maintaining life in balance; understanding and application of scientific and community knowledge; and interest in science and health professions. The NIDDK is currently building on the success of the DETS Project to develop a K-12 curriculum for African American and Hispanic students.

For children who already have type 2 diabetes, the NIDDK supports the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) clinical trial at centers around the country to test three different treatment regimens. A large percentage of children who are enrolled in this study are from minority groups disproportionately burdened with type 2 diabetes. Through TODAY and other studies, the NIDDK hopes to ameliorate type 2 diabetes and its complications in this most vulnerable population.

Gestational diabetes mellitus (GDM) also disproportionately affects minority groups. Although this form of diabetes generally goes away after the baby is born, it leaves both mother and child at increased risk for developing type 2 diabetes. Important insights about GDM have emerged from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, which is led by NIH's *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). The HAPO study showed that the higher a pregnant woman's blood glucose is, the higher her risk of pregnancy complications—whether or not her blood glucose reached the level at which GDM was diagnosed at the time of the study.¹³ The effect is significant enough that a recent panel of experts has recommended changing the diagnostic criteria for GDM to be less stringent, such that under the proposed new guidelines, the prevalence of GDM will more than double.¹⁴ The good news is that the DPP showed that a healthy diet and exercise can help prevent later type 2 diabetes in women who have had GDM. For this reason, the NDEP, in collaboration with the NIH Office of Research on Women's Health, recently expanded its

¹³ HAPO Study Cooperative Research Group, et al. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med* 358: 1991-2002, 2008.

¹⁴ International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 33: 676-82, 2010.

educational campaign for women with a history of GDM to raise awareness of the health risks for these women and their offspring.

CURRENT RESEARCH

The NIDDK and other NIH Institutes and Centers are supporting a wide range of diabetes research efforts that are having a far reaching impact. For example, the NIH supports research to improve diabetes treatment strategies, to help patients achieve blood glucose control associated with reduced rates of complications and to reduce the burden of diabetes self-care. NIH-supported research contributed to the development of continuous glucose monitoring technologies, which reveal dynamic changes in blood glucose levels by assessing glucose levels hundreds of times per day and displaying trends. The NIH is committed to capitalizing on this technology and supports research on “artificial pancreas” technology to “close the loop” and link insulin delivery to continuous glucose measurements. This technology has the potential to benefit people with both forms of diabetes.

The NIDDK also supports research on cell replacement therapy for people with diabetes, which could potentially restore the body’s ability to produce sufficient levels of insulin and properly control blood glucose levels. The NIDDK-led Beta Cell Biology Consortium is making significant progress in understanding beta cell biology and development toward the goal of generating unlimited supplies of beta cells in the laboratory for transplantation, or promoting growth of new beta cells in the pancreas. Because impaired function of the beta cell is central to both type 1 and type 2 diabetes, this research can inform treatment strategies for people with both forms of the disease.

Although the DPP identified effective strategies to prevent or delay type 2 diabetes, disease prevention remains a major goal of type 1 diabetes research. The NIDDK-led Type 1 Diabetes TrialNet is tackling this goal by conducting prevention trials, including a trial testing whether oral insulin could prevent the disease in people who have high levels of antibodies to insulin (a pre-clinical marker of disease). TrialNet plans to launch a second prevention trial with an agent proven to slow beta cell loss in new onset type 1 diabetes. An NICHD-led clinical trial, called TRIGR (Trial to Reduce the Incidence of Type 1 Diabetes in the Genetically at Risk), is determining whether weaning newborns at risk for type 1 diabetes to extensively-hydrolyzed

formula, as compared to standard cow's milk formula, will reduce the risk of developing type 1 diabetes.

Diabetes has a strong genetic basis that is modified by environmental factors. The last few years have seen unprecedented discoveries in diabetes genetics research. Recent research has identified over 40 genes or genetic regions associated with type 1 diabetes,¹⁵ and 38 associated with type 2 diabetes.¹⁶ The NIDDK is now supporting research to pinpoint the exact genes involved and to understand their function in health and disease. New insights about the genetic underpinnings of diabetes can inform new strategies for prevention or treatment, and even on a personalized or customized basis.

With respect to environmental factors, The Environmental Determinants of Diabetes in the Young (TEDDY) study has recently completed recruitment of over 8,000 newborns at high genetic risk for type 1 diabetes and is now following them to age 15 to identify environmental triggers of disease. Identification of a dietary or infectious cause of type 1 diabetes could have an enormously positive impact on public health through a diet change or vaccine for disease prevention, for example. Importantly, TEDDY may also contribute to understanding the development of celiac disease, which is an autoimmune disease primarily affecting the gastrointestinal tract. Some genes confer susceptibility to both celiac disease and type 1 diabetes, and many people have both diseases. Thus, TEDDY may benefit not only people with, or at-risk for, type 1 diabetes, but also people with celiac disease and other autoimmune diseases.

New insights about diabetes in youth are stemming from the SEARCH for Diabetes in Youth study, which is supported by CDC and NIDDK. SEARCH is defining the incidence and prevalence of diabetes in youth, which is important for informing public health efforts. Because of SEARCH, for the first time we now can estimate how many children in the U.S. have diabetes, and we will be able to see how the rates are changing over time. This knowledge could help to explain the findings from HEALTHY showing that overweight and obesity rates seemed to fall in both the intervention and control schools; SEARCH could help us determine if this trend is also being seen on a broader level.

¹⁵ Barrett JC, et al. Genome-wide association study and meta-analysis find that over 40 loci affect risk of type 1 diabetes. *Nature Genetics* 41: 703–707, 2009.

¹⁶ Personal communication; unpublished data.

Another high impact program conducted jointly by NIH and CDC is improving standardization of hemoglobin A1c (HbA1c), which is a measurement that provides information on a person's average blood glucose levels for the past 2-3 months. This program has been important for translation of the good glucose control proven so beneficial in DCCT and other trials nationwide. I am pleased to testify today with Dr. Ann Albright, Director of the CDC Division of Diabetes Translation, because our agencies work so effectively together on efforts to combat diabetes, such as on this standardization program, the SEARCH study, the NDEP, and several other efforts.

COORDINATING RESEARCH ACROSS THE GOVERNMENT

Diabetes research is effectively coordinated throughout the government toward a common goal of improving health. One important venue for coordination is the statutory Diabetes Mellitus Interagency Coordinating Committee (DMICC), which is chaired by the NIDDK and includes other components of NIH and other HHS and federal agencies that support diabetes-related activities. The DMICC facilitates cooperation, communication, and collaboration on diabetes among these government entities. DMICC meetings help members identify emerging issues and opportunities and develop ways in which different government components can work together and build upon each other's expertise and resources. This approach helps ensure that federal diabetes activities are coordinated and not duplicated, and also stimulates collaborations.

The DMICC, with leadership by the NIDDK, has undertaken a diabetes research strategic planning process to help guide the federal investment in diabetes research. The draft Plan is currently posted on the NIDDK website and is expected to be finalized later this summer. The Plan was developed as a collaborative effort across federal agencies and with input from the external research and patient advocacy communities. The Plan will guide the NIH, other federal agencies, and the investigative and lay communities in our pursuit of a common goal of conquering diabetes.

FUTURE DIRECTIONS FOR RESEARCH

As the NIDDK reflects on the past 60 years of supporting and conducting research on diabetes, it is clear that the scientific progress achieved during that time period has been remarkable. People with the disease are living longer and healthier lives than they did a few short decades ago. However, diabetes still places an enormous personal and economic toll on our country, so it is critically important to continue the pursuit of research to make further improvements in patients' health and quality of life.

For example, it is critical to link glucose monitoring to insulin delivery to create an artificial pancreas, which can help people with diabetes achieve blood glucose control associated with reduced complications, as well as alleviate the everyday burden of self-care. Now that we are collecting thousands of samples through the TEDDY study, researchers can use new and emerging technologies to analyze those samples and identify an environmental trigger of type 1 diabetes. We must break the link between diabetes and its complications, and prevent the disproportionate burden that heart disease places on people with the disease. With the availability of many new medicines for type 2 diabetes, comparative effectiveness research can help inform doctor's decisions about what medicines to prescribe for their patients at different stages of disease to achieve the best health outcomes. Research can identify new strategies to help people maintain weight loss that is needed to prevent or delay development of type 2 diabetes.

Vital to these and other research efforts is the continued vigorous support of basic, pre-clinical, and clinical research, including research to address disparities in minority populations disproportionately burdened by diabetes. We will also continue to develop educational materials to disseminate new research findings to patients, their families, and health care providers. Strategic planning, including the new Diabetes Research Strategic Plan, will continue to guide future research directions. The NIH will remain steadfast in our goal to support and conduct research that can continue to improve the health of people with and at risk for diabetes.

In closing, thank you Mr. Chairman and members of the Committee for the opportunity to share with you a few highlights of NIH-supported diabetes research efforts. I am pleased to answer any questions you may have.

**U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Institute of Diabetes and Digestive and Kidney Diseases
Biographical Sketch
Judith E. Fradkin, M.D.**

Dr. Judith E. Fradkin became the Director of the Division of Diabetes, Endocrinology, and Metabolic Diseases (DEMD) at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH) in 2000. She had previously served as the Deputy Director of the Division, Chief of the Endocrinology and Metabolic Diseases Programs Branch, Acting Chief of the Diabetes Research Programs Branch, and Director of the Cystic Fibrosis Research Program within the Division.

Dr. Fradkin graduated magna cum laude from Harvard College, received her medical degree from the University of California at San Francisco, and completed her internship and residency in internal medicine at Harvard's Beth Israel Hospital in Boston. She came to NIDDK as a clinical associate in 1979 after an endocrinology fellowship at Yale University. Dr. Fradkin is board-certified in Internal Medicine and in Endocrinology and Metabolism.

In her 31-year career at NIDDK, Dr. Fradkin has created or directed a diverse array of high-impact clinical and basic research programs, including multi-centered clinical trials to evaluate new approaches to prevent and treat diabetes and its complications, scientific consortia to define the genetic and environmental triggers of diabetes, and diabetes research centers. She is responsible for a major series of diabetes initiatives focused on beta cell development and function, improved glucose control through development of continuous glucose monitors and an artificial pancreas, and research on obesity, insulin action, and animal models of diabetes.

Under Dr. Fradkin's leadership of DEMD, major new clinical research networks have been created to conduct trials for prevention or delay of progression of type 1 diabetes, prevention of development of risk factors for type 2 diabetes in children, and comparison of treatment approaches to type 2 diabetes in children, and the landmark Diabetes Prevention Program clinical trial was successfully completed.

Dr. Fradkin serves as Chair of the Diabetes Mellitus Interagency Coordinating Committee, which is charged with facilitating collaboration on diabetes among Federal entities.

She also serves the on the Executive Committee providing leadership for the National Diabetes Education Program.

In addition to her oversight of major biomedical research programs, she has served as an endocrinology consultant at the National Naval Medical Center in Bethesda, Maryland, since 1984.

The recipient of numerous NIH and Public Health Service awards, Dr. Fradkin is also the 2003 recipient of the American Medical Association's Dr. Nathan Davis Award for outstanding public service in the advancement of public health.