Diabetes Mellitus Interagency Coordinating Committee

Fiscal Year 2002 | Annual Report

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INTRODUCTION

In accordance with Section 429 of the National Diabetes Mellitus Research and Education Act, the Diabetes Mellitus Interagency Coordinating Committee (DMICC) prepares an annual summary report of its activities as well as other Federal research activities in the field of diabetes. It is submitted to the Secretary, Department of Health and Human Services (DHHS), and the Director of the National Institutes of Health (NIH). This is the annual report of the DMICC for Fiscal Year (FY) 2002.

LEGISLATIVE MANDATE

The DMICC was authorized by Public Law 93-354 and established in fall 1974; subsequent legislation modified some of the charges to the Committee. The legislative authority of the Committee is presented in Appendix A. The charge to the DMICC is to coordinate the research activities of the NIH and other Federal agencies relating to diabetes mellitus and its complications and to contribute to the adequacy and technical soundness of these activities by providing a forum for communication and exchange of information.

The Committee includes representatives from Federal agencies whose programs are relevant to diabetes mellitus and its complications. The chairman, designated by the Director, NIH, is the Director, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). In FY 2002, the DMICC membership included representatives of 32 Federal organizations. A roster of Committee members as of the close of the fiscal year is included as Appendix B.

ACTIVITIES OF THE DMICC

The DMICC facilitates cooperation, communication, and collaboration among agencies that conduct or support diabetes-related activities. These activities may range from support for biomedical research to direct provision of health care services. The DMICC provides both a forum for initiating interactions and a mechanism for tracking progress.

ACTIVITIES OF MEMBER ORGANIZATIONS

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Agency for Healthcare Research and Quality (AHRQ)

The Agency for Healthcare Research and Quality continues to be involved in a broad range of activities related to improving the quality of health care, reducing its costs, improving patient safety, decreasing medical errors, and broadening access to essential services related to diabetes. These activities include the support of research and collaborations with others in the public and private sectors to improve outcomes for those with diabetes and to prevent the condition across the population.

Current Activities

The Agency is funding and involved with a large number of studies related to diabetes. A new initiative this past year should have major implications for efforts to improve the quality of diabetes care. Under a partnership with the Health Resources and Services Administration, AHRQ funded two studies to assess the impacts of the Health Disparities Collaboratives. Hundreds of Community Health Centers have been involved in the diabetes collaboratives, a learning process built on the Institute for Healthcare Improvement's methods for improving care and outcomes and the Chronic Illness Model. The Agency also has numerous ongoing studies related to diabetes. Under the TRIP II (Translating Research Into Practice II) and EXCEED (Excellence Centers to Eliminate Ethnic/Racial Disparities) initiatives, researchers are examining why disparities exist in the care and outcomes of minorities with diabetes and what can be done to reduce or eliminate them. Projects include an examination of the association between diabetes education programs and quality of care indicators in the Indian Health Service; implementation of successful managed care models of diabetes care in underserved populations; a community-based participatory research study aimed to improve processes of care for elderly African American diabetics; an evaluation of the impact of point of service testing of hemoglobin A1c on care and outcomes; and the development and evaluation of a culturally sensitive multimedia education program aimed at increasing diabetes-related knowledge, self-efficacy, and self-care for African Americans and Latino populations. Other studies that are being funded include an assessment of diabetes care in community health centers, the effects of Navajo interpreters on diabetes outcomes, the effectiveness of an automated telephone disease management system for English- and Spanish-speaking patients, and an evaluation of the impact of changes in managed care policy towards reimbursement for glucose self-monitoring on utilization and outcomes.

Staff at AHRQ are also involved in a number of intramural studies of diabetes. Investigators are using data from the Medical Expenditure Panel Survey (MEPS) to develop national estimates for medical visits, individual expenditures, and sources of payment for people with diabetes. Another study is identifying factors associated with multiple hospitalizations of diabetics using Healthcare Cost and Utilization Project data.

AHRQ continues to work with individuals and organizations to ensure that the evidence-base is being employed. The Agency recently launched an initiative to strengthen partnerships with stakeholders across the health care spectrum. Under a partnership with the American College of Physicians–American Society of Internal Medicine, the Agency will be involved with broad efforts to improve the quality of care for type 2 diabetes. The Agency also continues its involvement with the National Diabetes Quality Improvement Alliance (formerly called the Diabetes Quality Improvement Project (DQIP)), an effort to develop uniform, core measures of diabetes performance that allow benchmarking across organizations and identify opportunities for improvement among health plans and providers. Reporting on DQIP measures is now required of managed care organizations by CMS and results will be madepublicly available.

Future Activities

Much of the work mentioned above will continue during the next fiscal year. It is expected that additional work will be funded under the Agency's program announcements (PAs) and Request for Applications (RFAs). Priorities with particular pertinence to diabetes include translating research into practice, patient-centered care, patient safety and medical errors, and the relationship between systems factors and quality.

Center for Scientific Review (CSR)

The Center for Scientific Review is a center within NIH, where a majority of investigator-initiated applications in diabetes and obesity areas are reviewed. The mechanisms of application support are the investigator-initiated individual project applications (R01s), High Risk/High Impact Pilot grant applications (R21s), Small Business Innovation Research Applications or Technology Transfer (SBIR/STTR), and Individual Fellowship Applications: Predoctoral (F31 and F30), Postdoctoral (F32), and Senior Fellowships (F33).

Under the above research support application mechanisms, pertinent areas that are covered fall into two main categories: Basic and Clinical Translational Research. Areas include: Beta Cell Biology, Islet and Pancreas Transplantation, Insulin Action, Insulin Resistance, Pathogenesis of Type 1 and Type 2 Diabetes, and also study of pathogenesis of obesity. These studies invoke molecular genetic, metabolic (which includes nutritional intervention), cell biological, and histochemical approaches.

These applications are reviewed in several Integrated Review Groups (IRGs) within which individual subcommittees (study sections) are located. Each of these sub-committees has definite expertise to review specific areas relevant to diabetes and obesity. Thus, the mission of CSR to activities of DMICC is central and pivotal through help in maintaining the quality of diabetes and obesity research in the nation. The knowledge gained through these NIH-supported projects will help control/treat type 1 diabetes and type 2 diabetes and obesity, in areas of the world where these diseases are prevalent.

Centers for Disease Control and Prevention (CDC)

The mission of CDC is to eliminate the preventable burden of diabetes through leadership, research, programs, and policies that translate science into practice. CDC's National Diabetes Program conducts health promotion and disease prevention activities to improve the health of people with, or at risk for, diabetes. CDC's Diabetes Program is a multifaceted, science-driven public health program that monitors the extent of the diabetes program in the United States through surveillance; translates research findings into clinical and public health practice; conducts state-based diabetes prevention and control programs; and provides information to increase public awareness about how to prevent and control diabetes. The Division of Diabetes Translation at CDC has these major components: Define the Diabetes Burden - Public Health Surveillance; Conduct Applied Translational Research; Develop/Maintain National and State-based Diabetes Prevention and Control Programs; and Support for the National Diabetes Education Program.

Current Activities

National Public Health Initiative on Diabetes and Women's Health. Obtained the support of three major organizations—American Diabetes Association (ADA), American Public Health Association (APHA), Association of State and Territorial Health Officials (ASTHO); formed a Task Force that proposed recommendations for needed strategies, policies, surveillance, and research to improve the lives of women across the life stages who are diagnosed with, or at risk for, diabetes; prepared an interim report that outlines proposed recommendations; and in August 2002, with a national symposium, selected recommendations that are of highest priority to improve the lives of women who are diagnosed or at risk for diabetes.

Office of Management and Budget (OMB) Review. Coordinated a cross-divisional response to an extensive 5-month OMB audit using the Performance Assessment Rating Tool.

Secretary's Prevention Initiative. Prepared a diabetes component of this Initiative that includes proposed new funding to support pilot projects for primary prevention of type 2 diabetes.

Primary Prevention of Type 2 Diabetes. Developed programmatic and scientific strategies to focus on the population at highest risk for type 2 diabetes—the sixteen million with "prediabetes"; co-authored four publications on primary prevention of type 2 diabetes; initiated primary prevention pilot project with Health Resources and Services Administration (HRSA) and the Community Health Centers (CHC) through the National Diabetes Collaborative.

Management Information System. Completed a Diabetes Management Information System (that began in 1999) for Diabetes Prevention and Control Programs to effectively address limited access to information, non-standardized reporting, limited accountability, and cumbersome paper trails; as of June 28, 2002, all State programs went online; designed with the ongoing involvement and support of State program staffs to enable them to share information on diabetes and related programs through a central Internet interface.

Worksite Initiatives. Produced the National Diabetes Education Program Diabetes Worksite Kit in April 2002 as a Web-based interactive application at diabetesatwork.org, in collaboration with the Washington Business Group on Health.

Project DIRECT National Forum. Held in April 2002 in Raleigh, NC, to share lessons learned from Project DIRECT (Diabetes Intervention Reaching and Educating Communities Together) with interested community and public health program planners; attended by more than 133 people from 18 States, one U.S. territory, and the District of Columbia, who represented diabetes control programs (DCPs), community health centers, REACH 2010 programs, community-based organizations, residents of the Southeast Raleigh community, faith-based organizations, county and State health departments, and CDC's Division of Diabetes Translation.

US-Mexico Border Diabetes Prevention and Control Project. Collaborated with border health offices, the Mexico Ministry, DCPs in California, New Mexico, Arizona, and Texas; almost completed (86%) the prevalence household survey with 3,960 interviews having occurred in the United States and Mexico; scheduled to be finished by October 1, 2002; developed a communication plan and project Web site and established site selection and clinic criteria (Intervention Committee); actively engaged in developing a major component of the project—its intervention; the committee is using a collaboration to gather input from all partners to develop the intervention.

Community Health Workers and Promotores de Salud Integrated Projects. The purpose of this project is to help reduce the burden of diabetes by creating vital links between health care providers (and/or systems) and communities in culturally meaningful and linguistically appropriate ways by involving the unique skills of community health workers (CHW) and promotores de salud in collaboration with health care teams; conducted a preliminary search for diabetes-related programs and literature and the National Diabetes Prevention Center is compiling these resources into an accessible format others can use.

National Diabetes Prevention Center (NDPC). NDPC has formed formal working partnerships directly with the following American Indian/Alaska Native organizations—National Indian Council on Aging; American Indian Higher Education Consortium; Association of American Indian Physicians; and Native American Diabetes Program, University of New Mexico; developed an American Indian/Alaska Native Interactive Diabetes Atlas using Geographic Information System mapping technology.

Diabetes Forecasting Models. Developed forecasting models to provide projections of the numbers of people with diabetes by age, race, sex, and related cost for the next 50 years and published reports.

Diabetes Translation Research Study: Translation Research Into Action for Diabetes (TRIAD). Completed collection of baseline data on more than 11,000 patients in largest cohort study designed to monitor delivery of efficacious preventive care services and identify modifiable barriers to sub-optimal care; completed protocol of ancillary study on examining the relationship of socioeconomic status as a risk factor for diabetes; completed protocol of ancillary study on examining the relationship of socioeconomic status as a risk factor for diabetes.

Vision Health. Conducted pilot study of prevalence and causes of visual impairment and quality of eye care among people with diabetes in managed care settings; established a research agenda for eye health including partnerships with key nonprofit and voluntary organizations; convened expert panel to examine strategies for eye health.

Surveillance in Minority Populations and Other Surveillance Issues. Convened expert panel to advise us on issues relating to surveillance in minority populations; through University of Arizona, completed a BRFSS in-person household survey in an American Indian population; through NY State Department of Health, conducted Behavioral Risk Factors Surveillance System (BRFSS) in New York Puerto Rican population; final report on Medicaid surveillance project received and will be edited and sent to diabetes control programs; continued to provide technical assistance to Indian Health Service (IHS) on public health surveillance of diabetes in American Indians and Alaska Natives.

Future Activities

Plans for Program Effectiveness: Government Performance and Results Act (GPRA). Achieved three of four of the Division's GPRA measures; developed and introduced several new measures to gauge intermediate impact and to correspond with potential new projects proposed for FY 2004 funding; improvement in documentation of impact will receive attention.

Implemented Program Effectiveness: Measuring Program Performance. Finalized the implementation phase of the division's MIS; implemented strategies to strengthen the evaluation skills of the division's program development officers and the evaluation capacity of the DCPs; introduced a new program assessment approach for the DCPs that is based on the 10 Essential Public Health Services.

The Future is Now for Diabetes Prevention and Control. Plan to expand support for comprehensive State-based DPCPs and reinforce them as the lead venue to implement public health programs in diabetes; establish epidemiology, health services research, and programs in primary prevention for type 2 diabetes that focus on identifying preventive behavioral strategies for people with pre-diabetes.

Centers for Medicare & Medicaid Services (CMS) [formerly HCFA]

Diabetes activities at CMS fell into several broad categories: evaluation of the quality of care provided to Medicare beneficiaries, national and State-level quality improvement projects designed to improve care for Medicare beneficiaries; beneficiary educational campaigns; and research to support quality diabetes care.

Current Activities

The *Doctor's Office Quality Project* is a three-State pilot of an outpatient quality measurement and improvement model for chronic disease care and preventive services that will include diabetes. The project goal is to develop a model for measurement and improvement of quality care for chronic disease and prevention services at the level of the individual physician/medical office. A toolkit of materials and strategies for improvement will be developed to support improvement in diabetes care. The Doctor's Office Quality Project will also explore incentives for improving quality of care, including Continuing Medical Education (CME) provisions, linkages to reduction in malpractice premiums, and public recognition. A focus on reduction of disparities in care has been added to this project. The project will take place in Iowa, New York, and California.

The *National Diabetes Quality Improvement Alliance* is the group that developed the nationally used measure set for diabetes. CMS continues to support and partner with this effort.

The *Quality Improvement Organizations* (one per State) have been working to improve diabetes care in the following areas:

- Annual hemoglobin A1c testing.
- Biennial lipid profile.
- Biennial eye examination.

These will remain a focus as the Quality Improvement Organizations move into their new contract cycle, which ends in 2005.

Culturally and Linguistically Appropriate Services in Managed Care (CLAS). In June of 2002, the Center for Beneficiary Services convened a "CLAS". Best Practices Medicare + Choice plans were invited to share effective strategies for CLAS in their plans. Based on the presentations, a compendium of best practices was compiled. The compendium is available on the web site. The site is http://cms.hhs.gov/healthplans/quality/project 03.asp. The compendium is also available through the Quality Improvement Organizations Net.

Future Activities

Best Practices in Diabetes Conference for Spring 2003. The goal of this conference is to present practices that have been successful in improving diabetes care over the past 4 years with an emphasis on practices that have been aimed at improving disparities in care. The original conference was a kick-off in 1999 and was co-sponsored by the American Diabetes Association and the American Association of Health Plans. The audience will be Medicare + Choice organizations, Quality Improvement Organizations, Medicaid Agencies, and any other organization that is interested in this topic.

2004 Diabetes National Project. Medicare + Choice organizations have the option of conducting either the national diabetes project as defined by CMS or a regional collaborative project of their own choosing. The national project will allow the Medicare + Choice plans the option of focusing on reducing disparities in care as opposed to focusing on the larger diabetic population.

Methods for Increasing Communications With People With Medicare. The Center for Beneficiary Services has an agreement with the National Diabetes Educational Program (NDEP) to promote preventive services for people with Medicare. Currently our promotion efforts include the "Power to Control Diabetes Is in Your Hands" brochures, posters, Community Kits, and Practitioner Kits. We are also preparing a new fact sheet that will advise people with diabetes about the new self-monitoring benefit and the medical nutrition benefit to supplement the Power to Control campaign.

Department of Health and Human Services (DHHS)

DHHS Office of Minority Health

The OMH of the U.S. Department of Health and Human Services (DHHS) was created in December 1985 with a mission to improve the health of racial and ethnic minority populations through the development of health policies and programs to address health disparities and gaps. As called for in its legislative mandate (P.L. 105-392), and consistent with its mission, OMH's role is to improve and protect the health of racial and ethnic minority populations, eliminate the gap in health status between minority groups and the rest of the population, and coordinate across DHHS the development and implementation of policies, programs, and practices that will address health disparities negatively impacting racial and ethnic minority populations. OMH supports research and service demonstration programs, conducts evaluation activities, and depends on its resource center for up-to-date information and information dissemination to inform policy, program, and budgetary decisionmaking regarding health issues, such as diabetes, affecting racial and ethnic populations.

Current Activities

During FY 2002, projects in three OMH-funded programs and one cooperative agreement targeted diabetes as a priority health issue.

OMH's Bilingual/ Bicultural Service Demonstration Grant Program. The purposes of this program are to:

- Improve and expand the capacity for linguistic and cultural competence of health care professionals and para-professionals working with limited-English-proficient (LEP) minority communities, specifically Asian Americans, Pacific Islanders, and Latinos with limited English proficiency.

- Improve the accessibility and utilization of health care services among the LEP minority populations.

Activities vary by project and include utilizing promotores (lay health educators) to conduct education and outreach to the target population; providing diabetes screening in community settings such as churches, schools, and work sites; case management to assist individuals with diabetes; conducting workshops that encourage physical fitness and better nutrition; and developing bilingual health education materials.

These projects also reach health care providers to enhance the quality of care delivered to minorities with LEP through cultural competency training and providing health care facilities with interpreters for LEP patients. These demonstration programs are funded for 3 years. During FY 2002, four projects were in their first year of operation, and five were in their second year. Each project received up to $150,000 per year of funding.

Health Disparities in Minority Health Grant Program. This new program was implemented in FY 2001 with projects funded for 1 or 2 years. This program is intended to demonstrate the merit of using local, small-scale programs to address health problems and issues that affect the health and well-being of local minority populations and to support the elimination of racial and ethnic health disparities. Several of the projects within the Health Disparities in Minority Health Grant Program addressed diabetes prevention education interventions, self-management educational sessions, and access to health care for defined minority populations. In FY 2001, 12 projects were awarded, and in FY 2002, five projects were awarded, ranging between $48,000 and $50,000 per year, respectively.

Community Programs To Improve Minority Health Grant Program. These programs include projects targeting diabetes. In general, the purpose of this program is to improve the health status of targeted minority populations through health promotion and disease risk reduction programs. This program is different from the previous because it fosters the use of a community coalition approach to health promotion and risk reduction as a means of reaching targeted minority populations, especially those at risk or hard to reach. The program is intended to demonstrate the effectiveness of coalitions in carrying out projects that coordinate integrated, community-based, educational screening and outreach services, including linkages for access and treatment to minorities in high-risk, low-income communities, and that address sociocultural and linguistic barriers to health care.

This program supports existing coalitions composed of three discrete organizations—a minority community-based organization, a health care facility, and at least one other entity. Activities of the projects targeting diabetes include seeking to improve the delivery of comprehensive diabetes care in the community through a patient-based care management model, health care provider education, and telemedicine technology; improving access to health care to yield an increased number of persons screened for diabetes among the high-risk population, specifically Hispanics/Latinos; improving the health and well-being of Cherokee women through prevention and early detection of diabetes; providing immigrants, refugees, and other low-income residents with the knowledge, skills, and resources necessary to meet their health care needs relative to vision and diabetes; and increasing awareness and knowledge of diabetes risk factors, prevention strategies, and methods of treatment and control among the target population. These demonstration programs are funded for 3 years. During FY 2002, five projects were in their second year of operation. The projects funded in FY 2001 and FY 2002 ranged between $129,595 and $150,000, respectively.

American Indian Higher Education Consortium Cooperative Agreement. The Centers for Disease Control and Prevention (CDC), the Indian Health Service Diabetes Program, and OMH collaborated on the project, "Honoring Our Health: Tribal Colleges and Communities Working Together to Prevent Diabetes." In FY 2001, CDC provided $748,000 to this project, which is aimed at supporting health and reducing the impact of type 2 diabetes in tribal communities through the involvement of Tribal Colleges and Universities (TCUs). Subcontracts were awarded to 10 TCUs to: 1) develop infrastructure for diabetes education and community mobilization; 2) establish diabetes-related curricula; 3) connect diabetes prevention to land preservation, aquaculture, gardens, and bison restoration; 4) develop diet-related curricula; 5) increase education, awareness, and the opportunity to practice good health behaviors; 6) support community health and wellness centers; 7) foster faculty development in diabetes-related fields; and 8) stimulate capacity building for health-related research.

The 10 TCUs that received funding were:

- Blackfeet Community College, Browning, Montana
- College of Menominee Nation, Keshena, Wisconsin
- Fort Belknap College, Harlem, Montana
- Fort Peck Community College, Poplar, Montana
- Haskell Indian Nations University, Lawrence, Kansas
- Northwest Indian College, Bellingham, Washington
- Sinte Gleska University, Rosebud, South Dakota
- Stone Child College, Billings, Montana
- Turtle Mountain Community College, Belcourt, North Dakota
- United Tribes Technical College, Bismarck, North Dakota

In FY 2002, CDC funds were awarded to fund additional TCU projects, which will be selected through a competitive cycle.

Lastly, the theme of the September/October 2002 issue of the OMH publication, *Closing the Gap*, was diabetes and contained information on the link between diabetes and cardiovascular disease, complications secondary to diabetes, the rise of type 2 diabetes among minority youth, and departmental campaigns targeting "pre-diabetes" for high-risk populations, including Hispanics/Latinos, African Americans, American Indians/Alaska Natives, and Asian Americans and Pacific Islanders. *Closing the Gap* is a free, monthly publication circulated to more than 40,000 public and private community-based organizations, health professionals, State and government representatives, and others. The Office of Minority Health Resource Center provides free information on various health issues, such as diabetes, affecting U.S. minorities, and has up-to-date information, including *Closing the Gap*, on its Web site, www.omhrc.gov.

Future Activities

In FY 2003, OMH will solicit applications for the three grant programs—Bilingual/Bicultural Service Demonstration Grant Program, Community Programs To Improve Minority Health Grant Program, and Health Disparities in Minority Health Grant Program. Funding will be awarded to the new grantee partners and those partners who are entering their second or third year of funding.

DHHS Office of Public Health and Science (OPHS)

The Office of Public Health and Science within the Office of the Secretary serves as the focal point for leadership and coordination in public health and science across the U.S. Department of Health and Human Services provides direction to program offices within OPHS and through the Assistant Secretary for Health provides advice and counsel on public health and science issues to the Secretary. OPHS identifies innovative solutions to public health problems and issues and provides health policy advice to public health and other professionals and information to the public to improve the prevention and treatment of diseases, including diabetes.

Current Activities

Federal Information Resources on Diabetes. The Office of Public Health and Science established and coordinates several Federal information resource centers with toll-free call centers and Internet portals that provide comprehensive and reliable health information about the causes, treatment, and prevention of diabetes. They include the National Health Information Center (healthfinder.gov and 800-336-4797), the National Women's Health Information Center, (4woman.gov and 800-994-woman), the Office of Minority Health Resource Center, (omhrc.gov and 800-444-6472), and nutrition.gov, and fitness.gov. In 2002, nutrition.gov featured an article for the public on its homepage providing information about the causes, treatment, and prevention of diabetes.

Within the OPHS, several offices support programs and initiatives related to diabetes:

The Office of Disease Prevention and Health Promotion (ODPHP) serves as the overall coordinator of the national Healthy People 2010 effort. Diabetes is one of the 28 Healthy People 2010 focus area chapters. The diabetes focus area identifies 17 specific health promotion and disease prevention objectives aimed at achieving the goal of using prevention programs to reduce the disease and economic burden of this illness and to improve the quality of life for all persons who have, or are at risk for, diabetes. In 2002, ODPHP began preparations for a progress review on diabetes. The purpose of the progress review, scheduled for December 18, 2002, is to provide a venue for Federal agencies to report on their progress toward achieving the Healthy People 2010 goals and objectives for diabetes and to integrate new data to update the status of the specific health objectives related to diabetes. ODPHP is coordinating the diabetes progress review, working with the two lead agencies for this focus area—the Centers for Disease Control and Prevention and the National

Institutes of Health. The progress review will provide an opportunity for discussion about implementation challenges, strategies, and best practices. It will identify 1)strategies for overcoming barriers to achieving the diabetes objectives 2) areas requiring additional efforts, and 3) the potential for collaborative diabetes prevention and treatment programs and initiatives with a broad range of stakeholders and partners.

The Office on Women's Health (OWH) programs include a focus on raising awareness and attention to diabetes and women. OWH reviews current scientific knowledge to prevent, reduce, or delay onset, morbidity, and mortality of diabetes and its complications; facilitates (where appropriate) DHHS commitment to the prevention, treatment, control, and cure of diabetes through discussion of programs, partnerships, and plans; and serves as a forum to strengthen partnerships and identify collaborative opportunities to promote diabetes-related activities. OWH supports several contracts that promote diabetes awareness and control in women including a contract awarded to the National Indian Women's Health Resource Center for diabetes, lupus, HIV/-AIDS, and domestic violence for American Indian and Alaska Native communities. In partnership with the Food and Drug Administration's (FDA's) Office of Women's Health, OWH awarded a contract to the Boston University National Center of Excellence in Women's Health to advance research in monitoring glucose levels in diabetics (to determine the difference in long-term diabetes control with blood glucose monitoring via finger stick versus an alternative site). Additionally, OWH has participated in a partnership with the Division of Diabetes Translation of the CDC's Office of Disease Prevention and Health Promotion, to develop an action plan for the "National Public Health Initiative on Diabetes and Women's Health." OWH also partnered with the FDA Office on Women's Health in the "Take Time to Care About Diabetes" initiative. The office works with many Federal agencies and private sector organizations to provide informational materials on diabetes for diabetes awareness events and health fairs across the country. Publications produced by the OWH include fact sheets, 2002 Women's Health Daybooks, and A Lifetime of Good Health, with sections devoted to diabetes.

The President's Council on Physical Fitness and Sports (PCPFS) stresses the health benefits of regular physical activity for all Americans, including people with chronic health conditions such as diabetes. Each November, PCPFS publishes a Web site feature for the American Diabetes Month: "Physical Activity: A Key to Diabetes Control and Prevention," which includes information on physical activity for people with diabetes and links to other health Web sites as well. In March 2002, PCPFS published a feature on the Web on diabetes for the National Diabetes Alert. Also, in March and November 2002, PCPFS distributed talking points on diabetes for the twenty PCPFS Council members for use in their public presentations on the health benefits of physical activity.

The Office of the Surgeon General (OSG) released "The Surgeon General's Call To Action To Prevent and Decrease Overweight and Obesity" in December 2001. This document describes obesity as a risk factor for diabetes. It also provides a series of recommendations to mobilize all sectors of society to work to decrease overweight and obesity, to promote healthy lifestyles, and to decrease the risk of diabetes and other illnesses. The Surgeon General has also made numerous speeches and appearances on diabetes and its prevention. OSG staff work with the leadership of the American Diabetes Association to develop activities to support diabetes awareness, reduction, and prevention. Additionally, OSG staff working with the leadership of the National Institute of Diabetes and Digestive and Kidney Diseases identify ways in which the Surgeon General can help "spread the word" about prevention and treatment of diabetes and its complications.

The Office of Population Affairs (OPA) administers two Federal grant programs, the Title X National Family Planning Program and the Title XX Adolescent Family Life Program. Both are designed to reduce the incidence of unintended pregnancies in the populations they serve. The Adolescent Family Life program funds projects that are designed to prevent teen pregnancy and to provide care and support to pregnant and parenting teens and their families. While most projects do not directly provide clinical services, they refer for screening and treatment, including for diabetes, when indicated. The Title X National Family Planning program funds clinical services related to family planning and reproductive health. Specific laboratory testing, including diabetes testing, are required for the provision of specific methods of contraception, either on site or by referral.

Future Activities

National Diabetes Prevention Campaign. On November 20, 2002, Secretary Thompson launched the first national diabetes prevention campaign in an effort to stem the explosion of diabetes in the United States and to help Americans live longer and healthier lives. This new campaign, "Small Steps, Big Rewards" emphasizes that modest lifestyle changes—including healthier diets and physical activity—can help prevent the onset of type 2 diabetes, the most common form of the disease. The program will be run by the National Diabetes Education Program, which is jointly sponsored by DHHS' National Institutes of Health and the Centers for Disease Control and Prevention.

Diabetes Progress Review. On December 18, 2002, the Office of Disease Prevention and Health Promotion will convene the diabetes progress review for Healthy People 2010. The diabetes progress review will identify 1) strategies for overcoming barriers to achieving the diabetes objectives, 2) areas requiring additional efforts, and 3) the potential for collaborative diabetes prevention and treatment programs and initiatives with a broad range of stakeholders and partners.

Leading Health Indicators. In FY 2003, the U. S. Department of Health and Human Services plans to release the first-ever report on the Leading Health Indicators. The Leading Health Indicators (identified in Healthy People 2010) are a set of 10 high priority public health issues in the United States including physical activity, overweight and obesity, tobacco use, substance abuse, responsible sexual behavior, mental health, injury and violence, environmental quality, immunization, and access to health care. Progress on these indicators helps to measure the health status of our country. Several of these health indicators relate to diabetes prevention and control.

OPHS Consumer Information Resources. New information on diabetes will be included on the various consumer information Web sites supported by OPHS including healthfinder.gov, 4woman.gov, nutrition.gov, and omhrc.gov.

The President's Council on Physical Fitness and Sports, a publication on physical activity for people with chronic health conditions, including diabetes.

Diabetes Town Hall Meeting: A Town Hall meeting on Capitol Hill is planned for the spring of 2003 focusing on women's health and diabetes. The Office on Women's Health will co-lead this program with the FDA's Office on Women's Health and the DHHS Coordinating Committee on Women's Health to highlight DHHS diabetes programs and initiatives. Congressional, government, community leaders, and the general public will be invited to participate in this program.

Women's Health Screening Day. The Office on Women's Health will coordinate a day of free health screenings for women across the country during May 12–16, 2003. Potential screenings will be for diabetes, blood pressure, cholesterol, mammography, BMD, and mental health. The screening day will become a "signature event" for National Women's Health Week. The Federal Planning Team includes OPHS, FDA, Health Resources and Services Administration (HRSA), CDC, and NIH.

Minority Health Grants. In FY 2003, the Office of Minority Health will solicit applications for the three grant programs that include a focus on diabetes—the Bilingual/Bicultural Service Demonstration Grant Program, Community Programs to Improve Minority Health Grant Program, and Health Disparities in Minority Health Grant Program. Funding will be awarded to the new grantee partners as well as continuation for those partners who are entering their second or third year of funding.

A Surgeon General's Report on Prevention is under consideration. This report would include a focus on diabetes.

DHHS Office of the Secretary (OS)

The Office of the Secretary (OS) provides leadership and policy direction on programs and initiatives across the agencies and offices of the U.S. Department of Health and Human Services (DHHS).

Current Activities

Selected diabetes-related initiatives ongoing within the Office of the Secretary include:

- *HealthierUS* is a White House initiative with leadership from DHHS. The aim of HealthierUS is to empower all Americans with the knowledge, motivation, and skills they need to make healthy choices in order to prevent diseases such as diabetes; improve government policies and services to help provide the American people with an environment that supports healthy choices for disease prevention; and to increase collaboration among the Federal Government, States, communities, and the private sector to ensure that the American people receive health services that are effective and efficient including those for diabetes prevention and treatment.
- "*VERB: It's What You Do" a National Youth Media Campaign.* In July 2002, the Secretary of Health launched this national education campaign that aims to promote a healthier lifestyle for "tweens" (children ages 9–13) through physical activity and community involvement while decreasing unhealthy, risky behaviors. The campaign uses mass media, interactive media, partnerships, and community events to increase "tweens'" level of physical activity and positive behaviors in order to promote healthy lifestyles and prevent diseases including diabetes. The Centers for Disease Control and Prevention are managing this campaign that encourages youth to pick a verb, such as run, paint, dance, bowl, and use it as a launching pad to regular physical activity and healthy social behavior.

Food and Drug Administration (FDA)

FDA is charged with approving safe and efficacious agents for public use. This is especially important with regard to therapeutic agents in the treatment of diabetes mellitus.

There has been a growing recognition that diabetes is a vascular disease. In the Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program Guideline, diabetes is recognized as a Coronary Heart Disease risk equivalent. Insulin resistance is the hallmark of type 2 diabetes. Since the approval of the new class of insulin-sensitizing agents, the thiazolidinediones that decrease hyperinsulinemia by alleviating insulin resistance, troglitazone, the prototype, was withdrawn from the market due to liver toxicity. Two newer members of the thiazolidinedione class have since beenapproved: rosiglitazone in May and pioglitazone in July 1999. Numerous clinical trials are now reporting multiple cardiovascular benefits of this class of agents. Recognizing and treating insulin resistance

has been the focus of newer therapeutic agents approved by FDA this current year. Avandamet (rosiglitazone maleate and metformin HCL) was approved in October 2002. Megaglip (glipzide/metformin HCL) was also approved in October 2002. Both were approved either as initial therapy as an adjunct to diet and exercise, or as second-line therapy when a sulfonylurea or metformin do not result in adequate glycemic control in patients with type 2 diabetes. Along a similar line to improve glycemic control, Prandin (repaglinide) was approved for combination therapy use in patients whose hyperglycemia cannot be controlled by monotherapy with any of the following agents: metformin, sulfonylureas, repaglinide, or thiazolidinediones.

Other non-thiazolidinedione peroxisome proliferator-activated receptor (PPAR) dual agonists, active at both alpha and gamma PPAR receptors, are being developed by various pharmaceutical companies. Currently, there are more than a dozen such agents in the various phases of the drug development process. They have been demonstrated to have both glucose-and lipid-lowering activities.

No significantly new insulin formulation or insulin-analog has been approved this year. The use of parenteral insulin to prevent type 1 diabetes through the modulation of anti-islet immune response ("beta-cell rest") did not prove to be efficacious in two independent controlled trials (the Diabetes Prevention Trial– Type 1 Diabetes Study and the European Prediabetes Prevention–Subcutaneous Insulin Trial).

Health Care Financing Administration (HCFA)
See **Centers for Medicare & Medicaid Services (CMS)**

Health Resources and Services Administration (HRSA)

The Health Resources and Services Administration manages several health care systems programs that include diabetes identification, education, prevention or treatment.

Current Activities

Bureau of Primary Health Care. HRSA's Bureau of Primary Health Care (BPHC) established two strategic goals: to move toward the elimination of health disparities and toward a 100 percent access system for all Americans. The Health Disparities Collaboratives, started in FY1999, seek to: (1) generate and document improved health outcomes for underserved populations; (2) transform clinical practice through new models of care; (3) develop infrastructure, expertise, and multi-disciplinary leadership to improve health status; and (4) build strategic partnerships.

The initiative originally focused on diabetes mellitus—to delay or decrease disease complications—by implementing an evidence-and population-based model of care, which relies on knowing which patients have the illness and helps them participate in their own care. It has six basic elements: support of patient self-management, clinical decisions support, delivery system redesign, a clinical information system, organization of health care, and strong partnerships with local government and community organizations.

Activities include:

- 367 health centers participated or are in the year-long diabetes collaboratives. Eighty-eight centers in 1999, 118 centers in 2000, 62 centers in 2001, and 67 centers in 2002 are currently participating in the Diabetes 4 Collaborative.

- After completing the year-long collaborative, health centers continue to receive support to promote the model of care throughout their organizations, bring change to clinics, and measure its impact on the health of underserved patients.

- An orientation and training video and brochure describe the initiative.

- A software program was developed to meet the need for a comprehensive prevention and multiple disease clinical information system.

- Depression screening is included in care of diabetes patients.

- Partnerships with other Federal agencies, State diabetes control programs, and private-sector organizations grow stronger.

Outcomes (through July 2002) include:

- Health centers continue to report on the shared key goal that 90 percent of patients with diabetes will receive two HbA1c tests annually, at least 3 months apart. Starting in 2000, a shared health outcome measure was added to all the diabetes collaboratives requiring them to report on control of glucose levels (average HbA1c) and a self-management support measure. Additional measures focus on prevention of cardiac as well as microvascular complications, the latter including eye, kidney, and lower extremity disease.

- There are over 60,000 persons with diabetes in electronic registries that enable centers to track and manage the health of these patients.

- The average HbA1c has decreased from 9.2 to 8.2 for nearly 24,000 patients in the Diabetes 1 Collaborative.

- The average HbA1c has decreased from 8.77 to 8.06 on more than 32,500 patients in the Diabetes 2 Collaborative.

- The average HbA1c has decreased from 8.63 to 8.03 on more than 8,500 patients in the Diabetes 3 Collaborative.

- Average percentage of patients with two HbA1c tests in 12 months increased from 24% to 39.2% in Diabetes 1, 2, and 3 Collaboratives as they disseminated the care model throughout the organization and the registry size grew.

- 39.6% of patients have documented collaboratively set self-management goals.

Strategic partnerships and infrastructure development includes:

- Nine cluster directors and 10 information systems specialists are employed by the five lead Primary Care Associations.

- Thirty State-based staff provide additional support to the centers.

- National BPHC director of the collaboratives started in April 2000.

- National BPHC Clinical Information Systems Coordinator started in December 2001.

- Primary Care-Public Health partnerships are highlighted as a programmatic success. The partnership with the Centers for Disease Control and Prevention's Division of Diabetes Translation continues to be strengthened.

- 1999: 15 initial partnerships between State health department Diabetes Control Programs (DCP) and health centers working on the diabetes collaborative. $1.3 million direct support to health centers from DCPs.

- 2000: $2.7 million support to health centers.

- 2002: additional 15 partnerships formed between State health departments Diabetes Control Programs.

In 2002 the Agency for Health Research and Quality began assisting with program evaluation strategy.

Maternal and Child Health Bureau. The Maternal and Child Health Bureau (MCHB) administers maternal and child health (MCH) Block Grants to States to support programs that promote the health of all the Nation's mothers and children and ensure Statewide systems of health care for the MCH population. Diabetes screening, education, prevention, and treatment programs may be supported through these grants.

Additional Title V activities, such as MCH research, training, genetic services, and MCH improvement projects, are supported under Special Projects of Regional and National Significance (SPRANS). While these activities may not specifically target diabetes mellitus, core elements of community systems of care serving children with special health care needs are addressed by the Program for Children with Special Health Care Needs. The Healthy Start Initiative to significantly reduce infant mortality in targeted communities also includes services addressing diabetes in mothers and children. In addition, MCHB promotes diabetes detection and care through school-based and school-linked health programs. Finally, the MCH Training Program provides training grants to graduate programs and professional schools to support teaching, research, and service activities that focus on women and children. Its Leadership Education in Adolescent Health (LEAH), public health nutrition, and pediatric nutrition grantee programs include diabetes education, and the Indiana LEAH is nationally recognized for their work in diabetes.

HIV AIDS Bureau. Derangements of glucose metabolism, including both glucose intolerance and frank diabetes, have been associated with the use of highly active antiretroviral therapy to treat HIV infection. As part of comprehensive primary care, Ryan White CARE Act funded clinical programs provide monitoring, treatment, patient education, and nutritional counseling for this complication of HIV treatment. The AIDS Education and Training Centers provide education and training to clinicians regarding this recently described complication and rapidly disseminate information on new treatment strategies as they evolve.

The Office for the Advancement of Telehealth has, at a minimum, 16 active grantees that use Telehealth technologies to provide a range of services to improve the management of diabetic patients. The Office has funded the Marshfield Medical Foundation to work with the Office for the Advancement of Telehealth's other grantees to create technical assistance materials for programs that wish to employ Telehealth technologies in the management of diabetes.

Bureau of Health Professions. The Bureau of Health Professions (BHPr), which provides national leadership in establishing the Nation's health personnel, charges its Division of Health Careers Development to provide technical assistance to community groups to improve the health status of diverse and disadvantaged populations significantly affected by diabetes mellitus.

Office of Rural Health Policy. In FY 2002, the Office of Rural Health Policy had 19 active Rural Health Outreach and 2 Rural Network Development grants. Each grant is awarded for up to 3 years. Currently there are 7 active grants awarded in 2000, 5 awarded in 2001, and 10 awarded in 2002. The awards ranged from approximately $163,000 to $200,000 for FY 2002, each providing a variety of services, which may include the delivery of diabetes health care, treatment, patient education on self-management, and prevention. Projects focusing primarily on diabetes include:

- The Diabetes Prevention and Care Project: a collaborative effort coordinated and overseen by the Chiricahua Community Health Center, Elfrida, Arizona, focuses on the provision of treatment and education about diabetes for at-risk individuals in a predominately Hispanic community (68%).

- The Pinal County Public Health Outreach project in Coolidge, Arizona, enhances health care services delivery including diabetes self-management, education, and prevention.

- The Ajo Community Health Center in Ajo, Arizona, provides diabetes outreach and education programs to reduce the incidence of diabetes among Native Americans (46%), Hispanics (26%), and aging non-Native Americans.

- The Panhandle Area Health Network in Marianna, Florida, provides diabetes screening, education, and support to high poverty, chronically ill residents of the panhandle.

- The Baker County Health Department in MacClenny, Florida, connects chronically ill and medically underserved adults with appropriate health care coverage including diabetes.

- The Rural Health Partnership of North Central Florida in Lake Butler, Florida, provides diabetes education and outreach to decrease morbidity among minority and medically underserved populations.

- The McKinney Community Health Center in Waycross, Georgia, provides care, medications, patient education, and outreach to a population with a high prevalence of chronic diseases, including diabetes in several southeast counties of Georgia.

- The Lowndes County Board of Health in Clyattville, Georgia, includes The Well City Diabetes initiative that targets the reduction of type 2 diabetes occurrence and minimizes the long-term complications for those diagnosed with this disease.

- The East Georgia Health Cooperative, a nine-county network in Louisville, Georgia, created an outcome improvement health plan to treat chronic diseases including diabetes.

- The Moloka'I Heart Health Plan in Kaunakakai, Hawaii, uses the Cardiovascular Risk Clinic model to identify native Hawaiians with high rates of diabetes, obesity, hypertension, cholesterol, and smoking and alcohol consumption.

- The We Care Project, Inc. in Great Bend, Kansas, addresses health disparities among Hispanics diagnosed with hypertension and diabetes by providing access to care that is affordable and culturally and linguistically competent.

- The Salina Cares Health Clinic in Salina, Kansas, is part of a network of organizations that seek to improve health care services for the poor and uninsured in Central Kansas.

- Migrant Health Services in Moorhead, Minnesota, provides health care services and uses lay educators to extend education to a migrant farmworker population, including those diagnosed with diabetes.

- Alcorn State University in Alcorn State, Mississippi, is a Collaborative project that reduces the incidence of diabetic complications by increasing access to and coordination of care and by improving self-management practices.

- The Park County Diabetes Project in Livingston, Montana, seeks to improve knowledge, management, and coordination services for people with diabetes.

- The South East Rural Physician Alliance (SERPA) in Crete, Nebraska, seeks to improve quality care and treatment by training all SERPA members, increasing public awareness of risk factors, and improving patient self-management of the disease.

- The Fit for Life project in Saranac Lake, New York, is a supervised exercise program for at-risk residents for heart disease, diabetes, and obesity.

- The Hertford-Gates Health Department (Network) in Winton, North Carolina, is a multi-level organized network with a community-based approach to care for chronic disease management.

- The Hampton Regional Medical Center in Varnville, South Carolina, seeks to increase patient awareness of the importance of preventive health screenings for diabetes, cancer, and osteoporosis.

- The Rutherford Memorial Hospital in Carthage, Tennessee, provides access to wellness promotion, disease prevention, and screening for conditions such as diabetes, heart disease, cancer, and stroke.

Office of Special Programs. HRSA has been working with the Organ Procurement and Transplantation Network, the national system for matching donated organs with patients on the transplantation waiting list, to facilitate the allocation of pancreatic organs for use in pancreatic islet cell transplants in treating patients with type 1 diabetes mellitus. Five transplant centers are now performing islet cell transplants.

Future Activities

In FY 2003 the Maternal and Child Health Bureau will implement the Healthy Communities Innovation Initiative (HCII), a 20 million dollar effort to improve prevention strategies for diabetes, obesity, and asthma in five communities across the Nation with demonstrated high rates of these conditions. The key features of this initiative include: (1) community control and implementation of comprehensive, evidence-based programs, (2) significant public/private coalitions to develop and drive the implementation of comprehensive evidence-based programs, and |(3) definable health outcome goals and measures for accountability.

HCII will be launched in five geographically defined communities. Based on the principles of innovative integrated service delivery; community/individual commitment to goals and objectives; increased access to preventive, health, education, and social services; and multi-agency and culturally competent, family-centered, community-based services, the initiative is centered around the implementation of prevention programs that may include: (1) nutrition, fitness, and smoking cessation counseling services, (2) community-wide youth fitness programs, (3) expert disease prevention and management education to children, youth, and families, as well as providers, (4) increased availability of walking and bike trails that link schools, work sites, and residential areas, (5) healthy food options in schools, child care, work sites, and aging centers, (6) training for families and providers in identification of conditions and the use of early interventions, (7) youth speakers bureaus for community and provider education, and (8) home modification education and intervention to address potential allergens.

Although the Healthy Communities Innovation Initiative targets two conditions in addition to diabetes, the initiative expects to contribute to the attainment of the goals of the Secretary's Prevention Initiative and the Healthy People 2010 Objectives related to diabetes. These goals include prevention of diabetes, reduction in the overall rate of diabetes, the increase in the proportion of adults who are at a healthy weight, and the reduction in the proportion of children and adolescents who are overweight or obese. In addition, Department of Health and Human Services has developed shared performance measures that will guide and focus the work of all participating agencies. This initiative is designed to achieve the following specific outcomes related to diabetes among target populations in communities and States covered by the program over a five-year period:

- Increase by 25% the use of proven clinical preventive services in the areas of diabetes, obesity, and asthma for both children and adults.

- Increase by 25% the proportion of persons with impaired glucose tolerance (pre-diabetes) who are diagnosed and counseled regarding their risk of diabetes.

- Decrease by 25% the number of people with impaired glucose tolerance (pre-diabetes) who advance to a diagnosis of diabetes.

- Slow the growth of obesity by 20% for both children and adults.

Collaboration among Federal agencies is a required and key component of this initiative. As indicated in the Secretary's Prevention Initiative, agency programs will be operationalized as integrated efforts with joint goals, accountability, and timelines. The announcement of funding will be fully coordinated among agencies, and funding decisions will be based on a joint technical review process involving representatives from all agencies. A coordinated evaluation process will be initiated to assess progress on the joint performance measures on an annual basis.

Indian Health Service (IHS)

The mission of the IHS National Diabetes Program (NDP) is to develop, document, and sustain a public health effort to prevent and control diabetes in American Indian and Alaska Native (AI/AN) people. The agency promotes collaborative strategies for the prevention of diabetes and its complications in the 12 IHS Administrative Service Areas (regions) through coordination of a network of 19 Model Diabetes Programs and 12 Area Diabetes Consultants. They in turn provide resource distribution, program monitoring and evaluation activities, and technical support to 36 Federal hospitals, 63 Federal health centers, 44 Federal health stations, 13 tribal hospitals, 158 tribal health centers, 76 tribal health stations, 34 urban Indian health centers and 170 Alaska village clinics at the local level in the delivery of comprehensive health care to over 1.5 million American Indians and Alaska Natives. The NDP also continues to develop and operate the Special Diabetes Program for Indians grant program with 318 grantees in 35 States. The agency also disseminates current information about all aspects of diabetes surveillance, treatment, education, and prevention.

Diabetes was the most frequently identified health problem in IHS Area tribal consultation workshops for FY 2003 planning. Type 2 diabetes disproportionately affects AI/AN adults who are over 3 times more likely to have diabetes than the general U.S. population. A recent alarming trend is the increase in prevalence of type 2 diabetes in young AI/AN. Over an 11 year period, from 1990–2001, the prevalence of diabetes rose 68% in AI/AN adolescents and young adults. Recent data show that diabetes mortality is 4.3 times higher in the AI/AN population than in the U.S. population. There was a 24 percent increase in the American Indian age-adjusted diabetes-related death rate from 1991–1993 to 2000. There is clear evidence that for Indian people the health disparity related to diabetes is increasing.

Current Activities

Special Diabetes Program for Indians, 1997 Balanced Budget Act & 2001 Consolidated Appropriations Act. In 2002, the IHS National Diabetes Program administered Year 5 of the Special Diabetes Program for Indians of the 1997 Balanced Budget Act and the Consolidated Appropriations Act of 2001. One hundred million dollars per year have been distributed from these funds through 286 non-competitive grants administered at 318 sites throughout Indian country. Over 96% of these funds are distributed through grants to tribes, IHS facilities, and urban Indian centers while 3.8% are withheld for administration of the grant program. Tribal entities are the direct recipients of 81% of the grants, while Federal and urban programs comprise the remainder. The IHS National Diabetes Program works closely with the Tribal Leaders Diabetes Committee to administer this program. The Request for Application (RFA) developed by the IHS NDP this year once again included a Best Practices approach with 14 strategies identified, researched, and compiled for use by applicants. Sixty-seven percent of the grantees have indicated that they devote a significant portion of their funding to primary prevention of diabetes. A Final Report to the Congress summarizing the findings from this program is being prepared for submission on January 1, 2003.

IHS became a Deeming Entity for Diabetes Education Certification. The IHS National Diabetes Program, with agency and tribal leader support, established an Indian Health Diabetes Education Accreditation Program and received notification from the Centers for Medicare & Medicaid (formerly HCFA) that the IHS NDP application to become a deeming entity has been approved (*Federal Register April 2002*). This process allows Indian health diabetes education programs to become certified and thus seek Medicare reimbursement for diabetes education. Thus far seven (programs have applied for and become certified, and two additional new applications are under review.

Obesity Prevention. For 3 years the IHS National Diabetes Program has coordinated an obesity prevention initiative targeting Head Start children (0–5 yrs), families, Head Start staff, and AI communities. Five tribal Head Start pilot sites, in collaboration with their respective community health partners, have developed obesity and diabetes prevention interventions in their local communities. Each Head Start site community action plan includes multifaceted program activities and milestones focusing on healthy eating, physical activity, healthy behavior and community partnerships. The core component of the initiative is to develop and sustain local community partnerships in the implementation of each program's interventions. Each site has fully implemented their respective community plans. The Initiative is presently addressing dissemination activities and sharing promising practices with other Head Start programs.

Medical Nutrition Therapy (MNT) and Diabetes Self-Management Training (DSMT) for Medicare Beneficiaries. IHS NDP is taking an active role in the rapid dissemination of information on the two new Medicare Part B Benefits: Medical Nutrition Therapy (MNT) and Diabetes Self-Management Training (DSMT) for Medicare Beneficiaries that have diabetes and/or kidney disease. We provide technical assistance and consultation to the I/T/U clinicians and medical records and patient billing office staff on putting systems into place for electronic billing, medical records documentation (i.e., MNT PCC+), tracking of claims and reimbursements and implementing systems to determine outcome- and cost-effectiveness of these services. This provides an other opportunity to promote and facilitate the implementation of the new third-party collections opportunities within the I/T/U system.

Joslin Vision Network Teleophthalmology Project. In FY 2002 Congress increased the IHS appropriation by $1.5 million to address evaluating American Indians and Alaska Natives for diabetic retinopathy through a collaborative project with the Joslin Diabetes Center using the Joslin Vision Network (JVN). The JVN is a telemedicine system that uses low-level illumination and no pupil dilation to remotely diagnose diabetic retinopathy. The acquired retinal image is sent electronically to a reading center using existing IHS networks, and an analysis of the level of diabetic retinopathy is returned to the remote site. The IHS has deployed imaging sites at the Phoenix Indian Medical Center (PIMC), Sells PHS Indian Hospital, Tuba City Indian Medical Center, Parker Indian Hospital, Hopi Health Care Center, and the Chief Andrew Isaac Health Center in Fairbanks, Alaska. Certified readers at the IHS/JVN National Reading Center in Phoenix evaluate the images acquired from these sites. Since entering its clinical phase, the program has evaluated more than 1,500 patients who had not currently met the prescribed level of care. Many of these required referral due to a dangerous level of diabetic retinopathy or other ocular pathology. Controlled study of this initial outcome indicates that this telemedicine system can markedly increase the annual diabetic retinopathy examination rate. The most mature deployment site increased its examination rate from 47% to more than 70% in less than 1 year. Ten to fifteen additional sites will be deployed during the next year at locations throughout Indian country. Primary challenges to future site development in remote locations include availability of clinical space and staffing.

Joslin Diabetes Center Partnership. In addition to the Joslin Vision Network, the IHS NDP is partnering with the Joslin Diabetes Center to develop a Web-based system that is based on the case management model that tracks diabetes care and education called the Comprehensive Diabetes Management Program (CDMP). Its components include a Clinical Assessment Module, a Behavioral Assessment Module, and an Education/Reinforcement Module. Health-care professionals on this workgroup comprise clinicians and educators who specialize in diabetes care and education and represent Joslin, IHS, U.S. Department of Defense and the U.S. Department of Veterans Affairs. The CDMP will be integrated with the IHS electronic medical records system database. Beta testing of CDMP is targeted for January 2003.

NIDDK/IHS/TLDC/AIHEC collaboration to Recruit AI/AN Students into Biomedical Science Research and Diabetes Careers. In FY 2001, at the request of tribal leaders serving on the Tribal Leaders Diabetes Committee (TLDC), the IHS and the National Institute of Diabetes and Digestive and Kidney Diseases collaborated on a project to encourage young AI/AN students to consider careers in biomedical research and diabetes. This project also involves the Centers for Disease Control and Prevention (CDC) and the American Indian Higher Education Consortium (AIHEC), which represents the 34 tribal colleges around the country. An RFA was released in spring FY 2002 on this interagency collaborative project designed to increase diabetes knowledge among AI/AN students through a multicultural diabetes-based science education curriculum for grades K–8 and high schools. By engaging AI/AN youth in the biomedical sciences at an early age in a culturally sensitive manner, a goal of increasing the number of American Indian/Alaska Native health science professionals can hopefully be achieved. Eight planning grants, approximately $150,000 each, have been awarded to AIHEC institutions throughout Indian Country.

CDC/IHS Collaboration on Redesign of the National Diabetes Prevention Center. The IHS National Diabetes Program worked closely with the CDC Division of Diabetes Translation (DDT) in FY 2001 to restructure and re-orient the National Diabetes Prevention Center (NDPC) in Gallup, New Mexico, to ensure consistency with the NDPC's original mission to provide diabetes outreach, information, and technical assistance to tribes throughout the U.S. Especially important in this strategic action planning process was a report containing input from eight regional meetings with tribal diabetes prevention workers, conducted in 1999–2000 as a joint effort of CDC and IHS. The Tribal Leaders Diabetes Committee also provided valuable advice and guidance during the strategic planning process—and continues to advise the NDPC on a regular basis.

The National Diabetes Prevention Center's activities planned for FY 2002 and FY 2003 include gathering, connecting, and disseminating information about "what works" in diabetes care and prevention for all American Indian and Alaska Native communities. Presently, the NDPC is working in collaboration with the IHS National Diabetes Program and its partners to develop a variety of user-friendly tools, resources, curricula, and data approaches to assist in diabetes care and prevention efforts; a series of reports about "what works" in information technology, community diabetes care, and prevention planning activities; and educational resources.

IHS NDP continues to collaborate with NDPC on the development and printing of the IHS NDP *Health for Native Life* magazine. This popular publication is developed for members of tribal communities who have diabetes and their family members. The focus is on individuals who have diabetes and the various educational topics around treatment, care, and education and community related support systems and activities. A FY 2002 issue highlighted the results of the Diabetes Prevention Program and the American Indian participants. Distribution is to I/T/U grant programs, facilities, and tribal organizations nationwide.

In addition, the CDC DDT provides diabetes epidemiologic support to the IHS National Diabetes Program with one full-time position and close collaboration on projects of mutual concern.

Clinical Standards, Best Practices & the Diabetes Care and Outcomes Audit. In 2001 the IHS National Diabetes Program updated the IHS Standards of Care for Diabetes (originally published in 1986) to reflect new science and best practices. In 2002 the IHS National Diabetes Program developed 14 Best Practices documents, in part based upon these Standards of Care. The Annual IHS Diabetes Care and Outcomes Audit, a voluntary medical records review of 87 clinical care and public health practices and outcomes, is designed to measure and trend these standards and best practices. The standards, best practices documents, and audit summary results are distributed to providers IHS-wide through a network of regional Area Diabetes Consultants and local Diabetes Coordinators and are used as quality indicators at the local, regional, and national levels to identify specific problems and to determine policy and practice.

Collaboration and Partnership with Other Federal Agencies and Organizations. The IHS NDP Director serves as a member of the newly formed Translation Committee of the Diabetes Prevention Program, an NIH-sponsored study showing that type 2 diabetes can be prevented. The IHS NDP Director also serves as a member of the Steering Committee of the National Diabetes Education Committee, a joint effort of NIH and CDC to promote national awareness about diabetes.

IHS NDP supports the American Diabetes Association's outreach initiative program for American Indian/Alaska Native communities: Strong in Body and Spirit. IHS NDP provides expert guidance related to diabetes program development and modification based on participant evaluation.IHS NDP participates in the American Indian subcommittee of the National Diabetes Education Program. The IHS NDP provides regular representation to the committee and helps with the formulation and distribution of program materials. IHS NDP also participates in the Diabetes in Children and Adolescents Work Group of the National Diabetes Education Program. The IHS NDP contributed to the development of the Diabetes in Schools Guide and will assist in its dissemination to schools serving AI/AN students.

IHS NDP partners with the National Indian Council on Aging on a diabetes monograph series, newsletters for tribal leaders, and development of an electronic automated diabetes audit.

A key partnership has been established with the American Indian Higher Education Consortium Board to help build tribal college and university capacity and infrastructure for diabetes training and program activities in AI/AN communities.

Several IHS Area Diabetes Programs have partnered with CDC's State Diabetes Control Programs (e.g., Montana, Alaska, California, New Mexico) to share skills, resources, and training.

Future Activities

In FY 2003 IHS NDP will develop a Diabetes Collaborative, based on the model used by the Bureau of Primary Health Care at the Health Resources and Services Administration, to address primary prevention of type 2 diabetes in AI/AN.

IHS NDP plans to hold a national diabetes conference in collaboration with the TLDC in Denver, Colorado, December 2002. The conference will feature successful grant programs and results of the Diabetes Prevention Program study.

IHS NDP will conduct further in-depth evaluation, validation studies, and key informant interviews of Special Diabetes Program for Indians grant program activities, as well as dissemination of successful grant program strategies.

IHS NDP will implement and fine-tune culturally acceptable screening approaches for AI/AN communities.

IHS NDP will develop and provide more technical assistance and training (for health professionals, tribal leadership, administrators, paraprofessionals, and patients) and promote increased awareness regarding new diabetes prevention findings through media, booklets, Internet, and other avenues of communication.

IHS NDP will partner with the American Indian/ Alaska Native Boys and Girls Clubs and the National Native American Law Enforcement Association (NNALEA) to promote healthy lifestyles for children and youth aimed at reducing the risk for early on set of diabetes in youth.

IHS NDP will continue to promote data improvement through implementation of an enhanced electronic medical record specific to diabetes to be used IHS-wide, development of an electronic medical records audit, centralized technical support for the Diabetes Management System of the IHS electronic medical record, and ongoing collaboration with and support for a Diabetes Collaboration amongst the Tribal Epidemiology Centers.

IHS NDP will continue to focus efforts on dissemination of information on the Medicare Part B Medical Nutrition Therapy (MNT) and Diabetes Self-Management Training (DSMT) benefits to I/T/U health care facilities. Seeking reimbursement for MNT and DSMT will have far-reaching benefits for tribes and tribal communities by increasing access to diabetes education and nutrition services. Increased access not only benefits those with diabetes and/or pre-dialysis kidney disease, but also expands opportunities for lifestyle interventions for the primary prevention of diabetes and other chronic diseases.

National Center for Complementary and Alternative Medicine (NCCAM)

The mission of the National Center for Complementary and Alternative Medicine is to support rigorous research on complementary and alternative medicine (CAM), to train researchers in CAM, and to disseminate information to the public and professionals on which CAM modalities work, which do not, and why. To achieve its objectives, NCCAM supports basic and clinical research on CAM, awards grants to train researchers in CAM, and sponsors a variety of outreach activities. The diabetes-related projects that NCCAM is currently supporting reflect its commitment to the clinical study of promising CAM substances and modalities.

Current Activities

In FY 2001, NCCAM and its cosponsors, the NIH Office of Dietary Supplements and the National Institute of Diabetes and Digestive and Kidney Diseases, released a Program Announcement (PA), "Chromium as Adjuvant Therapy for Type 2 Diabetes and Impaired Glucose Tolerance." The PA's purpose is to generate applications from researchers interested in conducting (1) basic studies of chromium action on insulin secretory and signaling pathways and (2) clinical studies to assess the safety and efficacy of chromium as an adjuvant treatment of type 2 diabetes and/or impaired glucose tolerance. As a result of this PA, in FY 2002, the Center funded a project that is investigating the biochemical basis for chromium enhancement of insulin action.

Other diabetes-related projects the Center is supporting include basic studies that are examining the mechanisms by which Ginkgo Biloba may accelerate pancreatic function and reduce glucose metabolism, identifying the anti-hyperglycemic constituents of Panax ginseng berry, and studying the synergistic effects between these constituents. NCCAM is also supporting a project devoted to the pre-clinical development of a standardized botanical extract, PMI-5011, which has lowered blood glucose in insulin-deficient and insulin-resistant animals. Another NCCAM-sponsored project is studying the effectiveness and underlying mechanism of the angiogenic agent Picroliv for better management of diabetic wounds, while another project is developing technology to improve the detection of chromium in diabetes patients. Finally, the CAM Research Center for Cardiovascular Diseases is supporting a study that is examining whether Reiki applied to patients with painful diabetic neuropathy, with or without diabetic autonomic neuropathy, can improve the glycemic control and cardiac autonomic function.

NCCAM's intramural research program has established a Diabetes Unit. Its primary research goals are: (1) to develop simple methods for assessing insulin sensitivity and insulin secretion *in vivo*; (2) to evaluate the effects of nutritional supplements on insulin sensitivity; and (3) to understand the molecular mechanisms of insulin action.

In FY 2002, one percent of the NCCAM clearinghouse inquiries were related to diabetes and CAM therapies. The revamped NCCAM Web site provides links to informative fact sheets on diabetes and CAM.

Future Activities

The Chromium as Adjuvant Therapy for Type 2 Diabetes and Impaired Glucose Tolerance PA is still posted on the NCCAM Web site and continues to generate interest from the research community. Further, NCCAM encourages researchers to submit investigator-initiated applications related to diabetes.

National Center for Health Statistics (NCHS), CDC

NCHS's mission, as it relates to diabetes, is to monitor and provide national diabetes statistics in the form of summary health measures and individual level data for research. This information originates from vital records, interview and examination surveys, medical records, and patient encounters (such as, ambulatory care visits).

Current Activities

NCHS released the initial set of data from the 1999-2000 National Health and Nutrition Examination Survey (NHANES). This information provides national estimates of self-reported diabetes, glycemic control, and hypertension control among people with diabetes. Nutritional assessments and anthropometry findings were also released. Resources provided by CDC's Division of Diabetes Translation facilitated the analysis of NHANES data on lower extremity disease risk factors among people with diabetes.

Diabetes information from national vital statistics were disseminated, including diabetes-related mortality, prevalence estimates of maternal diabetes and its risk factors (e.g., maternal weight gain), and health status of infants born to women with diabetes.

The components of the National Health Care Survey continue to obtain information on diabetes-related hospitalizations, doctor office visits, and home health care. Data from these efforts can characterize trends in diabetes pharmacologic therapy and patterns of care for diet and weight counseling and lipid testing.

NCHS continued its collaborative research with multiple academic centers, such as the Johns Hopkins University. Published studies include national assessments of diabetes-attributed mortality, renal function among persons with diabetes, and progress toward achieving the national objectives to reduce the burden of diabetes.

Future Activities

A new U.S. Standard Certificate of Live Birth will be implemented in 2003, and it will include a question that differentiates between pre-pregnancy and gestational diabetes.

With sponsorship by the National Institute of Diabetes and Digestive and Kidney Diseases, the National Health Interview Survey will obtain additional information in 2003 on preventive health care among people with diabetes.

The 2003 edition of the *Health, United States Chartbook on Trends in the Health of Americans,* will include a new section on trends in the burden of diabetes.

National Center for Research Resources (NCRR)

NCRR develops and supports research technologies and shared resources that are critically important to research efforts directed at maintaining and improving the health of our Nation's citizens. NCRR programs also provide support for the career development of clinical and veterinary biomedical investigators. The current NCRR diabetes research portfolio includes approximately 960 basic and clinical research subprojects, a significant increase over the previous year. Selected highlights of NCRR-supported research activities and future plans that relate to diabetes are presented below.

Current Activities

Now in their second year, the 10 NCRR-supported Islet Cell Resource (ICR) centers provide approved transplant programs throughout the country with clinical grade islets to treat patients afflicted with severe type 1 diabetes. A coordinating center has now been established to provide bioinformatics and biostatistical support for laboratory studies at ICRs and clinical programs that use ICR-generated islets nationwide.

The 81 General Clinical Research Centers (GCRCs) and their satellites provide the infrastructure needed by diabetes investigators, who are funded by NIH, private foundations, and corporations to:

- Study normal and abnormal glucose metabolism, diabetic complications, islet and whole pancreatic transplantation, risk factors, epidemiology, genetics, and pharmaceutical interventions.
- Investigate the pathologic consequences of diabetes using high-intensity MRI.
- Develop novel treatments using continuous glucose sensors and insulin pumps.
- Determine the role of race and ethnicity, gender, age, pregnancy, and patient education in diabetes prevention and treatment.

Three Science Education Partnership Awards (SEPAs), which are designed to improve life science literacy, focus on diabetes and disseminate information about risk factors and prevention through local science museums, schools, churches, and community groups.

The NIH Clinical Loan Repayment Program enables talented physicians to continue their clinical research. NCRR sponsors three such individuals engaged in diabetes research.

The WICELL Research Institute received an NCRR grant to expand and distribute human embryonic stem cells, which may lead to new methods by which islet cells can routinely be generated for subsequent transplantation into diabetic patients.

NCRR co-sponsored the International Congress of the Immunology of Diabetes Society and the annual meeting of the Western Region Islet Study Group.

Researchers continue to develop a computational metabolic model that can be used to characterize metabolic function in a single patient with a simple clinical protocol.

Investigators are characterizing a transgenic mouse that may be useful as a model for changes that occur in the heart of diabetics.

The Shared Instrumentation Grant program provided funds for mass spectrometers, flow cytometers, phosphoimagers, and DNA sequencers to support diabetes research.

Investigators at six NCRR-supported Research Centers in Minority Institutions (RCMIs) are studying neuropathy in young Puerto Rican diabetics, expression of biochemical markers for type I diabetes, and health disparities among minority populations, particularly along the U.S. and Mexican border.

The Clinical Research Education and Career Development Awards at Meharry Medical College and the University of Puerto Rico support diabetes research and training.

The Biomedical Research Infrastructure Network and the Centers of Biomedical Research Excellence, part of the Institutional Development Enhancement Award program, support diabetes research and study the effects of childhood obesity, antioxidant treatment in pregnant diabetic women and their offspring, oral health in diabetics, and retinopathy.

NCRR awarded eight research facilities improvement grants for diabetes-related research.

The NCRR-supported mutant mouse resource for type 1 diabetes at The Jackson Laboratory now has 27 strains of mice ready for distribution and an active Web site for information dissemination to interested diabetes researchers. The Web site also allows the Steering Committee to review submitted type I diabetic mouse strains.

Researchers at the University of Washington National Primate Research Center are investigating pancreatic islet cell allograft survival in macaques and baboons and have found that transplanting islets without immuno-suppression followed by a second graft with immuno-suppression facilitates allo-tolerance of the second graft.

At the University of California-Davis National Primate Research Center, xenografts of islet cells from pigs to diabetic macaques were successful in 50 percent of the animals and showed functionality for at least 3 months.

Porcine models are being used to investigate the significance of coronary artery disease in type 2 diabetics.

Future Activities

Planned activities include:

- Define the incidence of b-cell autoimmunity by age, race/ethnicity, HLA-genotype, and family history of type I diabetes and formally evaluate candidate autoimmunity/diabetes risk factors available for all participants(e.g., early childhood diet, reported infections, and vaccination). Expected outcomes of the approach are filter paper blood sample testing to predict and assess relative risks associated with candidate environmental and genetic factors.

- Expand resources to maintain and supply genetically engineered mouse models for diabetes mellitus research including hyperglycemia, hyperinsulinemia, and insulin resistance. Expand and improve cryopreservation of murine embryo and gametes. Improve techniques associated with *in vitro* fertilization and intracytoplasmatic sperm injection methodologies.

- Continue efforts to develop the non-human primate model for diabetes, using molecular tools to search for naturally occurring diabetes in non-human primates and to detect genetic predisposition.

NCRR will continue to work with minority-serving institutions to provide access to Internet2 and advanced bioinformatics tools to facilitate participation in NIH-sponsored clinical trials, including those related to diabetes.

National Center on Minority Health and Health Disparities (NCMHD)

The mission of the National Center on Minority Health and Health Disparities is to promote minority health and to lead, coordinate, support, and assess the NIH effort to reduce and ultimately eliminate health disparities. In this effort NCMHD will conduct and support basic, clinical, social, and behavioral research; promote research infrastructure and training; foster emerging programs, disseminate information; and reach out to minority and other health disparity communities.

Building on the work of the former Office of Research on Minority Health (ORMH) through its partnerships with the NIH institutes and centers (ICs), the NCMHD has made remarkable achievements since its establishment just over 1 year ago. NCMHD is particularly committed to continuing its partnerships with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and other NIH ICs supporting diabetes research and training. While diabetes affects all groups in the U.S. population, Native Americans, Mexican Americans, Puerto Ricans, and African Americans suffer disproportionately compared to the general population. Findings in a recent National Eye Institute/NCMHD-funded study indicated that increased efforts are needed to improve diabetes detection in Mexican Americans.

Current Activities

The Center is addressing disparities in health status in racial and ethnic minorities with respect to diabetes through the support of research in three broad areas: preventing or delaying the early onset of diabetes through diabetes education and lifestyle changes, improving the management of and therapies for diabetes, and the identification of biological and genomic risk factors for diabetes.

Highlights of FY 2001–2002 diabetes-related specific accomplishments and activities include the Look AHEAD program and Project EXPORT Awards.

Look AHEAD (Action for Health in Diabetes) is a multicenter randomized clinical trial to examine the effects of a lifestyle intervention designed to achieve and maintain weight loss over the long term through decreased caloric intake and exercise. Look AHEAD will focus on the disease most affected by overweight and obesity, type 2 diabetes, and on the outcome that causes the greatest morbidity and mortality, cardiovascular disease.

Recently, NCMHD awarded grants under the Centers of Excellence in Partnerships for Community Outreach, Research on Health Disparities and Training (Project EXPORT). Three grant awards that are diabetes-related are: "Partnerships for Diabetes-Related Disparities in Hawaii," "South Hampton Roads EXPORT Center," and "The Drew/UCLA Project EXPORT Center." The Project EXPORT grants aim to build research capacity at designated institutions enrolling a significant number of students from health disparity populations and to promote participation and training in biomedical and behavioral research among health disparity populations.

National Eye Institute (NEI)

The National Eye Institute's mission is to conduct and support research, training, health information dissemination, and other programs concerned with blinding eye diseases, visual disorders, mechanisms of visual function, preservation of sight, and the special health problems and requirements of the blind. Diabetes is responsible for diabetic retinopathy, an eye disease that is the leading cause of blindness in people between the ages of 24 and 70 years. This disease is characterized by a progressive breakdown of the normal retinal vascular system.

Current Activities

NEI re-issued the program announcement (PA-02-020), "Strategies To Identify the Genetic Basis of Diabetic Retinopathy" in order to alert the scientific community of the continuing interest of NEI in encouraging research on the genetic basis of this disease. This PA seeks grant applications on gene discovery; genetic epidemiology; methodological studies of phenotypic assessment of retinopathy, including possible surrogate markers; and the development and application of novel statistical methods relevant to analyzing genetic data on diabeticretinopathy. This PA is co-sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). NEI is collaborating with other NIH institutes and the American Diabetes Association (ADA) on PA-02-153, "Translational Research for the Prevention and Control of Diabetes." This PA seeks to translate recent advances in the prevention and treatment of type 1 and type 2 diabetes into clinical practice for individuals and communities at risk. The NEI continues to participate with other NIH institutes in a PA entitled "The Role of Antioxidants in the Prevention of Diabetic Complications." The intent of this PA is to solicit applications on the role of antioxidants in preventing, delaying, or ameliorating the micro- or macrovascular complications of diabetes as well as the mechanism(s) by which antioxidants might prevent diabetic vascular disease.

NEI is collaborating with other NIH institutes in the re-issuance of the Request for Application (RFA) entitled, "Bench to Bedside Research on Type 1 Diabetes and Its Complications," (RFA-DK-03-001), which seeks applications involving partnerships between clinical and basic biomedical researchers with the goal of translating advances of the molecular basis of type 1 diabetes into new therapies.

NEI continues to participate with NIDDK, the National Institute of Dental and Craniofacial Research (NIDCR), the National Institute of Neurological Disorders and Stroke (NINDS), and the National Heart, Lung and Blood Institute (NHLBI) in a program announcement (PA–99–159) on "The Role of Growth Factors in the Development of Diabetic Complications." This PA encourages grant applications on the role of growth factors in the etiology and pathogenesis of the micro- and macrovascular complications of diabetes.

NEI continues to co-sponsor ACCORD (Action to Control Cardiovascular Disease Risk in Diabetes), a large multicenter trial supported by NHLBI and NIDDK to assess treatments to reduce risk of cardiovascular disease in type 2 diabetes. For this trans-NIH effort, NEI is sponsoring an eye examination component in order to collect epidemiological data.

Under the National Eye Health Education Program, the NEI is expanding its efforts to raise awareness about eye health among Hispanics. "Ojo con su Visión", under the National Eye Health Education Program (NEHEP), is developing a new national campaign targeting Hispanic adults. Through this effort, NEI hopes to increase awareness about the importance of dilated eye exams and to tailor vision loss prevention messages focusing on diabetic eye disease and glaucoma. NEHEP is developing messages and materials and identifying dissemination strategies through news media and community organizations. Implementation will take place in 2003.

The NEI has begun the development of a diabetic eye disease program for American Indians and Alaska Natives. A working group representing this target audience has been established to provide guidance to the NEI on this new program. The NEI is conducting focus groups and key informant interviews with the community. This research is being conducted in collaboration with the tribal networks nationwide.

NEI is supporting an initiative on evaluation of new treatments for diabetic macular edema, a major cause of visual loss in patients with diabetes. An RFA (EY–01–001) entitled "Diabetic Macular Edema Clinical Research Network" was issued in June 2001 calling for cooperative agreement applications to support core centers to plan, implement, and conduct clinical trials on the treatment of diabetic macular edema. The overall goal of this RFA is to develop an infrastructure to accelerate the development and conduct of clinical trials of the treatment of diabetic macular edema. These include both medical and surgical approaches. Grant awards have been made for a coordinating center in Tampa, Florida, a reading center in Madison, Wisconsin, and a chairman's grant in Boston, Massachusetts. Clinical centers will be added to the network during the first year of operation. A pilot study is being developed at the NEI clinical center and is intended to set the stage for a major multicenter randomized clinical trial for the treatment of diabetic macular edema.

Another initiative seeks to identify genetic associations in patients with microvascular complications of diabetes. NEI continues to supplement the FIND (Family Investigation of Nephropathy and Diabetes) study funded by NIDDK to investigate the genetics of individuals and special populations of patients with renal disease. NEI is supporting detailed eye examinations for these patients and will search for genetic associations with microvascular disease.

Future Activities

NEI will continue to incorporate the scientific priorities outlined in the *Report of the Congressionally Established Diabetes Research Working Group* in making funding decisions. NEHEP will continue to develop and implement outreach activities for people with diabetes. NEI will continue to encourage experienced investigators from outside vision research to apply their expertise to develop novel strategies for increasing knowledge about the pathophysiology and treatment of diabetic retinopathy.

National Heart, Lung and Blood Institute (NHLBI)

The primary cause of death in patients with diabetes is cardiovascular disease (CVD). NHLBI has continued to expand its comprehensive programs of basic and clinical research to understand the pathogenesis, improve treatment, and develop effective prevention strategies to reduce or postpone the cardiovascular complications of diabetes. Despite reductions in cardiovascular disease mortality in the general population, patients with diabetes continue to have 2–4 times the CVD rates of non-diabetics of the same age, gender, and ethnic group. In addition, recent studies indicate that current treatments to prevent these complications may be somewhat less effective among those with diabetes than in the non-diabetic population.

Current Activities

During the past year, NHLBI has continued work on three major clinical trials that will evaluate several therapeutic approaches designed to reduce cardiovascular complications of diabetes. The Action to Control Cardiovascular Disease Risk in Diabetes (ACCORD) trial successfully completed a 1,000 patient Vanguard phase. Recruitment for the main phase of ACCORD (9,000 additional patients) will begin shortly. The cohort will be followed over the next 5 years to evaluate the benefits of intensified control of hyperglycemia compared to conventional glucose control and also will test the benefits of aggressive blood pressure control and intensified control of the dyslipidemia associated with diabetes upon CVD rates.

The Bypass Angioplasty Revascularization Investigations II Diabetes (BARI 2D) trial is recruiting 2,800 patients to evaluate whether elective coronary artery revascularization plus optimal medical management of cardiovascular risk factors and symptoms is superior to optimal medical management alone. It will also evaluate the important issue of whether reducing insulin resistance provides protection against cardiovascular complications by testing whether insulin-sensitizing drugs are superior to injected insulin or to oral drug regimens that stimulate insulin secretion at levels of glycemic control that are attainable with current conventional treatments. The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is providing partial support for the ACCORD and BARI2D trials.

NHLBI is also helping to fund the NIDDK-sponsored Action for Health in Diabetes (Look AHEAD) trial, which is evaluating the effect of obesity treatment on cardiovascular complications in type 2 diabetic patients.

Taken together, these three trials should lead to new clinical approaches that reduce cardiovascular complications of both type 1 and type 2 diabetes.

A better understanding of how diabetes causes an increase in CVD may lead to innovative preventive treatments. NHLBI supports basic research to identify other ways in which the major vascular complications of diabetes can be retarded or prevented. In view of the complexity of the available treatments and the burden they place on patients with diabetes, it is particularly important to develop new therapies that can reduce the adverse effects of diabetes on the heart and large vessels without requiring intensive efforts at glucose control. NHLBI has expanded basic research related to macrovascular complications of diabetes including continuation of several large project grants originally cosponsored with the Juvenile Diabetes Foundation.

NHLBI has also participated, in collaboration with NIDDK, in the program of small, innovative grants aimed at improved understanding of diabetic macrovascular complications. These have involved studies of the effects of diabetes on vascular smooth muscle cells, its effect on circulating growth factors, and the effect of salt restriction on insulin sensitivity. Grants have been awarded to understand the etiology of diabetes-associated cardiomyopathy, an abnormality that contributes to the high rates of congestive heart failure in diabetic patients.

Other investigations include examining the proatherogenic effect of consumption of a high glycemic load diet on the endothelium, platelets, and monocytes. Studies will provide much needed information about the cardiovascular consequences of some of the commonly used diets in order to properly advise individuals and the public at-large about the long-term consequences of dieting. In addition, studies examining the role of enzymes such as the nuclear enzyme, poly (ADP-ribose) polymerase (PARP), in the development of diabetic endothelial dysfunction are being conducted. Preliminary data found that PARP regulates a key pathway that seems to mediate multiple organ vascular dysfunctions prevalent in the diabetic population.

NHLBI has also participated, in collaboration with NIDDK, in the program of small, innovative grants aimed at utilizing state-of-the-art gene therapy approaches for treatment of diabetes and its complications. The information that will be gained with the completion of these experiments will be significant in the continued development of angiogenic factor gene therapies, offering new technology that will render the therapies safer for treating cardiovascular ischemic disorders of diabetes.

Finally, it is important to recognize that many of the other research efforts supported by NHLBI may help to reduce or improve treatment for cardiovascular diseases occurring in patients with either type 1 or type 2 diabetes. This is because the effect of diabetes on macrovascular disease is, at least in part, to accelerate progression of the underlying atherosclerosis that is also common in non-diabetic individuals in middle and older ages. Thus, studies on treatment of congestive heart failure, treatment of arrhythmias, including public access to defibrillation, implantation of vascular stents that contain drugs that reduce restenosis rates, regeneration of cardiac muscle, and other treatments may have major benefits for patients with diabetes.

NHLBI support for studies of diabetes-related macrovascular disease has continued to increase. Funding for this work expanded further as the major clinical trials have moved into their main recruitment phases. Taken together, these clinical and basic studies should provide better guidance for physicians to reduce cardiovascular complications of diabetes in the near future and provide easier to use, more effective therapies to achieve this goal in later years.

National Human Genome Research Institute (NHGRI)

The National Human Genome Research Institute leads the National Institutes of Health's (NIH) contribution to the International Human Genome Project, which has as its primary goal the sequencing of the human genome. As this project nears successful completion, the NHGRI's mission has expanded to encompass a broad range of studies aimed at understanding the structure and function of the human genome and its role in health and disease.

To that end, NHGRI continues to support two major diabetes projects conducted by investigators in the Division of Intramural Research and their collaborators. Both studies aim to identify genetic variations that lead to increased susceptibility to type 2 diabetes mellitus.

Current Activities

Africa America Diabetes Mellitus (AADM) Study. There is a paucity of standardized, population-based data on genetic and epidemiological factors contributing to the disproportionate increase in complex diseases, such as diabetes and cancer, in African Americans and other minority populations. The NHGRI aims to collect family and population-based information in a way that maximizes the participation of minority physicians, research scientists, and the community. The identification of genes underlying susceptibility to common diseases and an understanding of the function of these genes and their interaction with environmental factors will lead to improved management and treatment of the diseases.

During the past several years, the National Center for Minority Health and Health Disparities and NHGRI have supported innovative research collaboration between investigators from Howard University and scientists in the intramural research program of the NHGRI. The collaboration involves support for projects involving African Americans affected with diabetes. To achieve this and other research goals, the NHGRI assisted Howard University in establishing a Center for collaborative research on genomic analyses of diseases that disproportionately affect African Americans. The National Human Genome Center at Howard University was formally dedicated on May 1, 2001. Initial efforts to define the scientific focus and objectives of the Center's diabetes research efforts were addressed through peer-reviewed contracts with Howard University as the Coordinating Center for the Africa America Diabetes Mellitus (AADM) Study.

Because of the high frequency of environmental risk factors for type 2 diabetes in the African-American population, it is more productive to study genetic risk factors in West Africans, since they are thought by many anthropologists to be the founding population of modern African Americans and have fewer dietary and nutritional confounding variables. To establish recruitment sites for the study, five sites were selected through a peer review process from a total of 24 applications, three of them in Nigeria and two of them in Ghana. Because of logistical challenges involved in doing a study of this type in West Africa, the study was planned in stages to allow assessment of the sites' ability to recruit appropriate patients and collect blood, urine, and other clinical data and successfully send the samples and data to the Coordinating Center at Howard University. The 2 year pilot project fully met its goal of recruiting 15 affected sibling pairs/site. Based on this experience, a full-scale study was implemented in September 1998 with an anticipated total of 400 affected sibling pairs and 200 spouse controls from West Africa by the end of the study period.

Genetic analysis of the blood samples was performed at the Center for Inherited Disease Research (CIDR), a centralized facility established in 1996 by eight Institutes at NIH to provide genetic services for investigators seeking to identify genes that contribute to human disease. Scientists at the National Human Genome Center at Howard University and the NHGRI are currently analyzing the results of the genome-wide scan performed at CIDR.

Finnish-U.S. Investigation of NIDDM Genetics.
Type 2 diabetes is one of the major causes of morbidity and mortality in the developed world. While environmental factors such as diet play a significant role, familial clustering indicates that there must be significant genetic susceptibility factors at work. The NHGRI assisted in the development of a consortium of groups who have agreed to pool their linkage data on type 2 diabetes in order to study the genetic factors involved in this disease. The consortium currently has support from the National Institute of Diabetes and Digestive and Kidney Diseases and includes all of the major groups in the United States with large family collections as well as a few European groups.

For 9 years, the Institute's intramural research program has been engaged in a major project, known as the Finland-United States Investigation of Non-Insulin Dependent Diabetes Mellitus (abbreviated FUSION), which aims to identify susceptibility genes for type 2 diabetes and for the related intermediate quantitative traits in a Finnish population. The data from the FUSION project represents a major component of the type 2 diabetes consortium's effort. Over 5,000 individuals with diabetes and suitable controls from Finland are being studied, using careful phenotyping of diabetes and diabetes-associated traits and genome-wide genetic linkage and association. This project has made significant progress, shifting almost entirely from microsatellite analysis to fine mapping using the mass spectrometer for high throughput single nucleotide polymorphism (SNP) genotyping. Further evidence has shown a diabetes locus on chromosome 22q, narrowing it down to a few hundred kilobases and confirming the association in a West African sample set. For chromosomes 11q and 20q, where evidence has shown the strongest linkage signals in a genome-wide scan, NHGRI has generated high density SNP maps and discovered narrow areas that demonstrate association at the 0.001 to 0.0001 level. The project is now focusing on genes in these intervals as possible diabetes susceptibility candidates.

Cultural and Ethical Issues Associated with Genetic Family Studies. The Institute's Ethical, Legal and Social Implications (ELSI) Program is designed to provide a novel approach to scientific research by identifying, analyzing, and addressing the ethical, legal, and social implications of human genetics research at the same time that the basic scientific issues are being studied. The ELSI Program is funding a project that aims to examine cultural and ethical issues associated with participation in genetic family studies by patients with a family history of type 2 diabetes mellitus in order to enhance the ascertainment process and establish strategies for genetic counseling of patients and relatives with a family history of type 2 diabetes and diabetic neuropathy.

Future Activities

Technology Development for Natural Genetic Variation. NHGRI started a program to establish new academic Centers for advanced genome research. These Centers of Excellence in Genomic Science (CEGS) will support multi-investigator, interdisciplinary teams to develop innovative genomic approaches to address biological problems. One of the CEGS aims to develop tools for studying natural genetic variation and to apply those tools to develop an improved understanding of the molecular basis of genetic susceptibilities to type 1 diabetes, progressive supranuclear palsy, and neutropenia. More broadly, the Center expects, through its development of new technology and close interactions between theory and experiment, to contribute indirectly to many research projects directed at understanding the genetic contributions to human health and disease.

National Institute of Allergy and Infectious Diseases (NIAID)

The National Institute of Allergy and Infectious Diseases supports a broad range of research on the immunopathogenesis of autoimmune diseases, including type 1 diabetes. Basic research focuses on understanding the genetics of autoimmunity, elucidating the mechanisms of self-tolerance, developing approaches to induce self-tolerance, and characterizing pathways of immune-mediated tissue destruction. These studies provide the knowledge to develop new treatments and diagnostic tests for autoimmune diseases, including type 1 diabetes, and novel treatments for ongoing disease.

The NIAID chairs the NIH Autoimmune Diseases Coordinating Committee (ADCC), established in FY 1998 at the request of Congress to increase collaboration and facilitate coordination of research among NIH Institutes and Centers, other Federal agencies, and private organizations. In FY 2002, the ADCC completed a comprehensive strategic and collaborative research plan for autoimmune diseases, which was mandated in the Children's Health Act of 2000 (P.L. 106-310). It is anticipated that this research plan will be presented to Congress in late 2002. The first ADCC report, published in December 2000, summarized basic and clinical research programs supported by NIH and non-Federal organizations, highlighting coordination and collaborative activities in the 10 thematic areas; described ADCC activities; and outlined emerging opportunities for research on autoimmune diseases.

Current Activities

The NIAID is committed to furthering understanding of the immunopathogenesis of autoimmune diseases, including type 1 diabetes, and to promoting the translation of basic research to clinical applications. During the past year, the NIAID has continued to expand its research program in type 1 diabetes. In FY 1999, NIAID established the Immune Tolerance Network (ITN), an international consortium dedicated to the clinical evaluation of novel tolerance induction approaches for autoimmune diseases, asthma and allergic diseases, and prevention of graft rejection. The goal of these therapies is to "re-educate" the immune system to eliminate injurious immune responses and graft rejection while preserving protective immunity to infectious agents. An important aim of the ITN is to explore the immune mechanisms underlying efficacy (or lack of efficacy) of candidate approaches. The ITN is conducting clinical trials involving multiple tolerance induction approaches for multiple autoimmune diseases, including type 1 diabetes. Examples of the ITN-supported clinical trials for type 1 diabetes include:

- Type 1 diabetes funds have been utilized by the ITN to develop cell replacement therapy for the treatment of disease. One of the initial clinical trials conducted by the ITN is the "Edmonton Protocol," an experimental islet transplantation protocol for brittle type 1 diabetics. To date, the initial study, conducted by the University of Alberta, resulted in insulin independence in the majority of patients. The ITN trial will further assess the safety and efficacy of this regimen; expand the capacity for islet preparation and clinical transplantation at nine sites in the U.S., Canada, and Europe; establish the baseline success rate for islet transplantation; and facilitate the evaluation of new tolerogenic approaches for islet transplantation.

- The ITN is developing therapeutic approaches for the prevention and reversal of type 1 diabetes. The ITN plans to initiate enrollment in two clinical studies to evaluate different approaches in the treatment of diabetes. One study will evaluate a humanized monoclonal anti-CD3 antibody recombinantly engineered to lack activating effects on target T cells. Another will evaluate the safety of giving insulin B chain with adjuvant in new onset diabetics. If this approach proves safe without the induction of immunity to the insulin B chain, further studies to test the ability of this combination to interrupt the autoimmune process in new onset or at-risk individuals will follow.

- ITN clinical trials will have integrated studies aimed at identifying the underlying mechanisms involved in disease progression and therapeutic actions of the treatment regimens. The ITN has received two proposals to sequence the regions of the NOD (non-obese diabetes) mouse genome involved in the development of type 1 diabetes. The proposals were reviewed in FY 2002, award took place in the third quarter of FY 2002, and it is expected that by the end of 2003 that sequencing will be completed.

The ITN includes more than 80 basic and clinical scientists and physicians from over 40 institutions in the U.S., Canada, Europe, and Australia and is co-sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the Juvenile Diabetes Research Foundation International (JDRF). More information on the ITN is available on their website at http://www.immunetolerance.org.

The NIAID, in collaboration with multiple NIH Institutes and Offices, has established several large multidisciplinary research programs for autoimmune diseases, including type 1 diabetes:

- Autoimmunity Centers of Excellence (ACEs) support collaborative basic and clinical research on autoimmune diseases and perform clinical trials of novel immunotherapies in multiple autoimmune diseases, including type 1 diabetes. These Centers conduct basic research into the pathogenesis of autoimmunity, immune modulation, and self-tolerance. Protocol development for clinical trials in type 1 diabetes are under development. The ACEs are co-sponsored by NIDDK, National Institute of Arthritis and Musculoskeletal and Skin Diseases, and the Office of Research on Women's Health.

- NIAID and NIDDK co-sponsored the Request for Application "Innovative Partnerships in Type 1 Diabetes Research" to provide access to specialized expertise or technologies and facilitate the formation of interdisciplinary research partnerships to investigate significant biological and medical problems associated with type 1 diabetes. This initiative provides for collaborative research partnerships between independent principal investigators with expertise in different aspects of type 1 diabetes.

- NIAID and NIDDK co-sponsored the RFA "Bench to Bedside Research on Type 1 Diabetes and Its Complications" to support partnerships between clinical and basic researchers to translate advances in the understanding of the molecular basis of type 1 diabetes into new therapies for the prevention, treatment, and cure of this disease. There were a total of 25 applications. NIAID funded three out of the eight supported applications.

- NIAID and NIDDK co-sponsored the RFA "Gene Transfer Approaches to Enhance Beta-Cell Transplantation" to support feasibility and pilot projects for methods to engineer beta cells or alter islets to enhance their viability. Successful projects could lead to an improved supply of islets for transplantation to treat type 1 diabetes.

- NIAID, with the NIH Office of Rare Diseases, NIH Office of Research on Women's Health, the American Autoimmune Related Diseases Association, and the Sjogrens Syndrome Foundation, co-sponsored a workshop titled "Autoantibodies as Predictors of Autoimmune Diseases." Using the T1D autoantibodies as a model, meeting participants explored the use of autoantibodies as potential clinical predictors of autoimmune diseases.

Other NIAID-supported research programs include:

- "Gene Therapy Approaches for Diabetes and Its Complications" to conduct research on the development of novel vectors and targets in the treatment of type 1 diabetes;.

- NIDDK "Diabetes Prevention Trial-Type 1," a multisite cooperative clinical trial for the prevention of type 1 diabetes in first-degree relatives of patients with the disease.

- NIDDK's "Type 1 Diabetes TrialNet," a consortia of clinical centers and core support facilities to enable rapid and efficient testing of additional promising new strategies, including vaccines, to prevent disease or delay its progression.

Future Activities

NIAID will support new and ongoing clinical trials of promising immune therapies for multiple autoimmune diseases through renewal of the Autoimmunity Centers of Excellence (ACEs) and through the ITN. The ACEs support collaborative basic and clinical research on autoimmune diseases, including single-site and multisite pilot clinical trials of immunomodulatory therapies. These Centers bring together many different subspecialists (e.g., neurologists, gastroenterologists, and rheumatologists) and basic research scientists, increasing clinical and research collaborations on autoimmunity.

National Institute of Biomedical Imaging and Bioengineering (NIBIB)

The mission of the National Institute of Biomedical Imaging and Bioengineering (NIBIB or EB) is to improve health by promoting fundamental discoveries, design and development, and translation and assessment of technological capabilities in biomedical imaging and bioengineering, enabled by relevant areas of physics, chemistry, mathematics, materials science, information science, and the computer sciences.

Current Activities

The Institute plans, conducts, fosters, and supports an integrated and coordinated program of technology development to improve health.

During the past year, the NIBIB, in collaboration with National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Dental and Craniofacial Research, National Institute of Deafness and Other Communication Disorders, and National Human Genome Research Institute, released an initiative entitled "Sensor Development and Validation." As a result of this initiative, seven applications specifically related to glucose sensors were supported. In addition, other grants designed to address basic technology development applicable to the treatment of diabetes were supported.

The Institute coordinates with the biomedical imaging and bioengineering programs of other agencies and NIH Institutes to support imaging and engineering research with potential medical applications and facilitates the transfer of such technologies to the clinical arena.

Within this mission, NIBIB supports hypothesis-, design-, technology- or problem-driven research relating to the discovery, design, development, translation, and physical assessment of new knowledge in biomedical imaging and bioengineering. The knowledge gained and the technologies developed in this endeavor will be transferred to other Institutes for the refinement and optimization that is uniquely organ- or disease-specific.

Future Activities

Diabetes research supported by NIBIB will encompass investigation of future methods to image and cope with this disease. The potential applicability of these research results will enable diabetes researchers to improve the well-being of individuals with diabetes.

Several NIBIB initiatives will be released and supported in FY 2003 to address basic technology development. Of particular interest to the diabetes community is one that addresses the need to prevent biofouling of sensors. The success of this initiative will prevent the rapid loss of sensor responsiveness seen with the present glucose sensors.

National Institute of Child Health and Human Development (NICHD)

The mission of the National Institute of Child Health and Human Development is to promote the development of healthy children. Understanding genetic and environmental factors that contribute to the development of diabetes is consistent with this mission, given the prevalence of both type 1 and type 2 diabetes in children and the serious complications of diabetes later in life. The NICHD focuses its efforts on the earliest pathogenesis of type 1 diabetes and on optimizing insulin therapy in children with type 1 diabetes. In addition, NICHD supports research on the origins of type 2 diabetes in adolescents and on improving the outcome of pregnancy in women with gestational diabetes mellitus.

Current Activities

In efforts to prevent type 1 diabetes, the NICHD pioneered methods in stratifying levels of risk for type 1 diabetes mellitus according to genetic and immunologic markers. This work forms the basis of the Diabetes Prevention Trial for Type 1 Diabetes, a major collaborative, trans-NIH study aimed at preventing or delaying the onset of type 1 diabetes. The NICHD also continues its collaboration with the Juvenile Diabetes Research Foundation (JDRF) to co-fund two large prospective studies of infants who have relatives with type 1 diabetes in order to ascertain the earliest immunologic changes in the pathogenesis of type 1 diabetes.

The incidence of type 1 diabetes has increased steadily over the past 30 years. It is presumed that environmental factors account for this striking increase in incidence. Epidemiologic studies and animal models implicate cow milk antigens in infant formula as an environmental agent that may trigger the autoimmune attack. In order to test this hypothesis, the NICHD is supporting a randomized controlled clinical trial. Screening began in FY 2002 to enroll 2,800 infants at high genetic risk of type 1 diabetes, based on family history and HLA genotype. The infants will be randomized to standard infant formula or to Nutramigen®, a casein hydrolysate. The investigators will follow the development of autoantibodies in these children through 2005. Meade- Johnson will provide the standard formula and the Nutramigen®. The study will be funded by the NICHD, JDRF, the Canadian Institutes of Health Research, the European Foundation for the Study of Diabetes, and the Netherlands Diabetes Foundation. Specially appropriated type 1 diabetes funds are being used to help support the first 3 years of the project. These funds are administered by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

Although genetic factors predispose children to type 1 diabetes, environmental agents are necessary to trigger the onset of the disorder. In order to elucidate this process, the NICHD recently joined NIDDK to support a Consortium for Identification of Environmental Triggers of Type 1 Diabetes. The consortium will be supported entirely by special type 1 diabetes funds in FY 2002 and FY 2003. In FY 2004-06 the NICHD will support one of the six centers of the consortium.

NICHD also emphasizes research on the earliest pathogenesis of insulin resistance and type 2 diabetes. In FY 2002 the Institute continued to support eight grant applications submitted in response to Request for Applications in the areas of fetal origins of adult disease and prevention of type 2 diabetes in adolescents. Both of these initiatives focus on early pathogenesis of insulin resistance and glucose intolerance prior to the onset of clinical diabetes. The investigators of one of these projects reported recently that oral glucose tolerance testing revealed states of impaired glucose tolerance in 25% of obese children.

NICHD is currently supporting a 15-site, prospective, international study of hyperglycemia and adverse pregnancy outcomes. This study of gestational diabetes mellitus will enroll 25,000 women early in their pregnancy and will follow them through their gestation, delivery, and postpartum period. Their infants will be studied as well. NIDDK is co-funding this large study.

Congressional Report 106-293 encourages NICHD to work with the National Institute of Allergy and Infectious Diseases (NIAID) and NIDDK on efforts to develop a vaccine to prevent juvenile, or type 1, diabetes. In response to this Report, NICHD joined NIDDK in co-funding TrialNet, a Network of 14 centers designed to perform clinical trials of new immunomodulatory agents to treat, delay, or prevent the onset of type 1 diabetes. The NICHD also joined NIDDK and NIAID in co-funding the Cooperative

Study Group for Autoimmune Disease Prevention, a network of investigators who are developing new methods to induce immune tolerance to self-antigens of the beta cells of the pancreas. Ultimately, this collaborative research promises to mitigate or reverse the autoimmune process that leads to type 1 diabetes.

NICHD also supports a Cooperative Multicenter Research Network to test the accuracy and efficacy of glucose sensors in children with type 1 diabetes. This effort is designed to reduce the incidence of hypoglycemic attacks in diabetic children on intensive insulin therapy. This multicenter trial of glucose sensors in children will utilize funds appropriated by Congress for research in type 1 diabetes for the first 3 years and will then be co-funded by NICHD NIDDK.

The Intramural Research Program of NICHD is following children in a 15-year study designed to understand the earliest pathogensis of insulin resistance and glucose intolerance in obese children and in non-obese children of obese parents. In two randomized clinical trials, these investigators are also studying the effects of metformin and orlistat in obese insulin-resistant children.

Future Activities

The Intramural program plans to initiate a case-control study of new-onset type 1 diabetes to elucidate the genetic and environmental factors that interact to initiate the autoimmune attack on the beta cells of the pancreas. The Pediatric Pharmacology Research Unit Network plans to augment its Phase 1 and Phase 2 studies of new molecular entities designed to ameliorate glucose intolerance in children and adolescents.

National Institute of Dental and Craniofacial Research (NIDCR)

The mission of NIDCR is to support research on the causes, prevention, diagnosis, and treatment of oral and craniofacial diseases and conditions. The oral complications of diabetes include greater prevalence and severity of periodontal diseases, increased susceptibility to oral mucosal infections, impaired wound healing, salivary gland dysfunction, and neuropathies resulting in loss or alteration of taste, smell, and mucosal sensory perception. NIDCR supports research on the oral complications of diabetes and the effects of oral diseases and conditions on the metabolic control of blood glucose.

Current Activities

Results of an April 2001 meeting evaluating linkages between oral health and diabetes were published in FY 2002 (*Annals of Periodontology* Vol 6(1), December, 2001). As reviewed in the publication, a well-documented relationship exists between diabetes and increased severity and incidence of periodontitis. Potential underlying mechanisms, including damage of oral tissues by glycosylated proteins in the diabetic patient, are discussed. New findings are also presented that suggest that periodontitis adversely affects blood glucose levels in diabetic patients.

FY 2002 findings from NIDCR-supported basic research include the following:

- IA-2, a major autoantigen in type 1 diabetes, was discovered several years ago in NIDCR laboratories. Autoantibodies to IA–2 have been shown to appear years before the development of clinical disease and are now being used as a predictive marker. Recent studies by NIDCR intramural investigators suggest that IA-2 plays a role in insulin secretion.

- Oral inoculation of normal and diabetic NOD mice with a periodontal diseases-causing bacterium resulted in exaggerated bone loss in diabetic mice. More inflammatory genes were upregulated and a prolonged inflammatory response occurred in diabetic mice compared to normal mice.

- Monocytes from patients with diabetes appear to produce more tissue-reactive oxygen products and to have enhanced enzyme activity associated with the inflammation.

In addition, studies were initiated on the role of defects of innate immunity found in diabetic NOD mice and on abnormal pro-inflammatory cytokine production in ob/ob diabetic mice and individuals with type 2 diabetes.

Translational and clinical research/clinical trials NIDCR supported in FY 2002 include:

- Studies on salivary gland dysfunction in animals and humans with diabetes.

- A randomized clinical trial to evaluate the effects of treating periodontal infection in reducing inflammation and immune cell activation associated with tissue destruction in patients with type 2 diabetes.

- Studies on host/pathogen interactions in endodontic patients with type 1 diabetes.

- Studies on host modulation and the effects of periodontal therapy on diabetic complications.

- A pilot case-control study on the role of periodontal disease in preterm deliveries among pregnant diabetic Asian and Pacific Islander women.

- A study of racially diverse children and adolescents with type 1 and type 2 diabetes to assess oral disease burden, determine the natural history of periodontal complications, and test a health care provider education program.

An ongoing training and career development program is developing researchers with the skills needed to study relationships between oral and systemic diseases, including diabetes.

Future Activities

NIDCR continues to participate in two active multi-Institute program announcements (PAs), "The Role of Growth Factors in the Development of Diabetes Complications" and "Enhancing Adherence to Diabetes Self-Management Behaviors." No additional initiatives are planned.

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is the lead agency of the Federal Government for research efforts to combat diabetes and its complications. The Division of Diabetes, Endocrinology and Metabolic Diseases has responsibility for extramural programs related to diabetes research and research training. The Division of Intramural Research; the Division of Digestive Diseases and Nutrition; and the Division of Kidney, Urologic and Hematologic Diseases support additional diabetes-related activities.

Section 330B of the Public Health Service Act provides the Secretary, HHS, special funding for research on the prevention and cure of type 1 diabetes in the amount of $1.14 billion for FY 1998 through FY 2008. The Secretary has designated to the NIDDK the lead authority for planning, implementing, and evaluating this program. The special diabetes programs were mandated for the period of FY 1998 through FY 2003 by the Balanced Budget Act of 1997 (P.L. 105-33) and the 2001 Consolidated Appropriations Act (P.L. 106-554). On December 17, 2002, the President signed the Public Health Service Act Amendment for Diabetes (P.L. 107-360), which extends the programs at the level of $150 million per year for FY 2004 through FY 2008.

Under the leadership of the NIDDK, the Special Statutory Funding Program for Type 1 Diabetes Research has engaged in a broadly consultative process that includes the participation of multiple NIH institutes and centers, the CDC, and other HHS components in all aspects of the planning, implementation, and evaluation of the special program. In addition, the active involvement of external scientific and lay experts with respect to type 1 diabetes and the major diabetes voluntary organizations--the Juvenile Diabetes Research Foundation International and the American Diabetes Association--has been vital to the program's success in establishing a vigorous and productive research enterprise.

The laws that established the special diabetes funding programs also mandate interim and final evaluation reports to the Congress. The interim report on the special funding program for type 1 diabetes research was transmitted to the Congress in June 2000. The enactment of P.L. 107-360 changed the due date of the final program evaluation report from January 1, 2003, to January 1, 2007.

The NIDDK is in the final stages of preparing the evaluation report that was originally intended to meet the January 2003 statutory reporting requirement. Now, with the enactment of P.L. 107-360, the NIDDK is proceeding to issue the current report because it provides an important interim assessment of the program by external scientific experts, grant recipients, and NIH and CDC staff who have analyzed the associated scientific literature and other relevant data on the program. Moreover, the report contains a highly useful summary of research opportunities identified by external experts in the field. These opportunities can thus serve as a scientific guidepost in developing this trans-HHS program in the years ahead.

The NIDDK also led the NIH-wide participation in preparation of a detailed progress report, "Conquering Diabetes: Highlights of Program Efforts, Research Advances, and Opportunities," describing research achievements and initiatives since 1999, when the Diabetes Research Working Group (DRWG), published its five-year Strategic Plan. The progress report reflects the advice of many scientists at the forefront of diabetes research and identifies new research opportunities that have emerged since the DRWG made it recommendations. It also outlines recent advances, both clinical and basic, in type 1 and type 2 diabetes and the pre-diabetic conditions, usually asymptomatic, that precede disease onset.

Current Activities

NIDDK supports a vigorous program of both basic and clinical research to further understanding of the development, treatment, prevention, and cure of diabetes and its complications. To maximize research on diabetes, the Institute has fostered collaborations among the many Institutes and Centers of the National Institutes of Health (NIH), as well as with the Centers for Disease Control and Prevention (CDC), the Juvenile Diabetes Research Foundation International (JDRF), and the American Diabetes Association (ADA).

Capitalizing on and responding to recent advances amd emerging opportunities, the NIDDK continues to foster cutting-edge research in diabetes—from the recognition and support for innovative ideas in investigator-initiated research, to the Institute-led establishment of consortia focused on important fundamental and clinical research issues. Examples of ongoing activities and new initiatives for FY 2002 follow.

Genetics of Type 1 Diabetes: Type 1 diabetes usually strikes in childhood or young adulthood but can affect an individual at any age. It is an "autoimmune disease," in which the body attacks is own tissue. Type 1 diabetes is characterized by the immune system's destruction of insulin-producing beta cells, contained in islets within the pancreas. Without insulin, the body cannot properly regulate glucose, lipid, and protein metabolism—resulting in physiologic alterations that can rapidly cause death. Researchers have yet to determine the precise factors that cause the immune system to initiate this misguided attack. However, many studies have suggested that an environmental exposure may trigger this autoimmune disease process in individuals who have an underlying genetic susceptibility to develop type 1 diabetes. Multiple genes are believed to be involved in this susceptibility and to interact with each other and with the environment to initiate the cascade that leads to the development of type 1 diabetes. Several comprehensive new initiatives are under way to identify genes conferring risk for type 1 diabetes.

International Type 1 Genetics Consortium: Established by the NIDDK, in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID), the National Human Genome Research Institute (NHGRI), and the JDRF, this consortium builds upon recommendations from a pivotal meeting of international experts held in November 2000. This consortium is striving to identify type 1 diabetes susceptibility genes by "scanning" human genome sequences in families from the U.S., Europe, and Australia. Thus far, the data from over one thousand diabetic sibling pairs have been combined and analyzed. These analyses have revealed several chromosomal regions that may be harboring diabetes susceptibility genes. Because large sample sizes are required to identify susceptibility genes, especially for complex diseases such as diabetes, the consortium proposes to continue this effort by collecting data on an additional 2,000 families for genetic analysis.

Genetics of Type 2 Diabetes and Obesity: As with type 1 diabetes, susceptibility to type 2 diabetes and obesity is determined by both genetic and environmental factors. We know that the environmental factors such as diet and activity are risk factors but we know much less about the genes involved in disease susceptibility. There are many different pathways that lead to the development of diabetes. The spectrum of clinical presentations of type 2 diabetes–and the close association of the disease with other conditions such as obesity, high blood pressure, and lipid abnormalities--add to the complexity of defining the causative genes. While these considerations make it particularly challenging to identify the genetic variations that predispose to type 2 diabetes, it is nonetheless critically important to meet this challenge, given the large and increasing health burden type 2 diabetes imposes on the American people and its disproportionately heavy burden on minority populations.

International Type 2 Diabetes Genetic Linkage Analysis Consortium: The NIDDK has bolstered the research efforts of this consortium, formed in 1998 to accelerate the search for genes. The pooling of genetic data from the many groups in the consortium increases the probability of identifying genes that influence this genetically complex disease. This combined effort also means that more samples are available for analysis of individual ethnic groups than is possible within a single study. With support from the NIDDK, the groups in the consortium are currently undertaking more precise mapping of a region of a potential diabetes susceptibility gene suspected to be on chromosome 1q as well as investigating potential susceptibility genes on other chromosomes. Because African Americans are disproportionately affected by type 2 diabetes and are underrepresented among the data in the consortium, the NIDDK has supported the collection of additional DNA samples from this population. These samples have been genotyped by the NIH-funded Center for Inherited Disease Research (CIDR) and will be combined with the other African American samples in the consortium for analysis of genetic variation that may be specific to this population. Biannual meetings of consortia participants are convened to monitor progress attained to date and to identify new research avenues and strategies.

Genetics of the Complications of Diabetes: Genes are a critical factor not only in the onset of type 1 and type 2 diabetes but also in the onset and progression of the complications that result from both forms of the disease. Familial clustering of complications of diabetes suggests an important genetic component to their development. Finding susceptibility genes for complications has important implications for identifying and intervening in individuals at increased risk as well as for developing new therapeutic approaches. Several new initiatives are under way to identify genes that predispose individuals with diabetes to the development of complications. Some of these will use samples obtained from populations that have been well characterized through participation in epidemiological studies or clinical trials.

Epidemiology of Diabetes Interventions and Complications (EDIC): An important genetics component has been added to the EDIC follow-up study of type 1 diabetes patients who participated in the landmark Diabetes Control and Complications Trial (DCCT). The DCCT demonstrated that patients who maintain their blood glucose levels as close to normal as possible throughout the day can prevent or delay eye, kidney, and nerve complications of the disease. In total, these patients with diabetes have been followed clinically for up to 15 years. Recently, the EDIC was expanded to include a genetic study that will acquire samples from 1,388 patients studied in the DCCT and their parents. Data will be used initially to study candidate genes that may predispose to diabetic complications.

Family Investigation of Nephropathy and Diabetes (FIND): Two studies have recently shown that diabetic kidney disease is a highly heritable trait. In response to this new information, the NIDDK established the FIND study to uncover candidate genes associated with development of kidney complications in patients with type 1 or type 2 diabetes. FIND has also incorporated a retinopathy study as part of its subject evaluation. A specific objective is to search for susceptibility genes in subpopulations of Caucasians, African Americans, Hispanic Americans, and Native Americans across the U.S.

Mouse Models of Diabetic Complications Consortium: This cross-disciplinary consortium will develop mouse models of diabetes complications to facilitate the study of disease prevention and treatment and the testing of candidate genes that emerge from human genetic studies. Mice developed through the consortium will be distributed to the research community. Co-sponsors of this initiative are the National Eye Institute; the National Heart, Lung and Blood Institute; the National Institute of Dental and Craniofacial Research, and the JDRF.

Beta Cell Biology and Cell Signaling: Further understanding of cell signaling in the beta cell has been a top priority because altered function of this cell is central to the pathogenesis of both type 1 and type 2 diabetes. Research momentum was spurred through a series of workshops, entitled "Pancreatic Development, Proliferation, and Stem Cells" and "Beta Cell Biology in the 21st Century," held in late 2001, to define the current state-of-the-art in signaling in the beta cell. These workshops were an important means of assembling key investigators, recruiting new researchers to the field, identifying new technologies and approaches to be applied, and defining goals for future work. Initiatives have been designed to promote the development of multi-disciplinary consortia among laboratories to bring resources to bear more effectively on cell signaling and cell regulation in the beta cell. The Beta Cell Biology Consortium will work to apply the tools of functional genomics to the endocrine pancreas, to identify the genes expressed in mouse and human pancreas at all stages of development, and to generate DNA arrays and other tools to facilitate the identification of important signaling components. This consortium will also attempt to delineate pathways of islet and beta cell signaling in development, and potentially, in beta cell renewal. A second initiative, Comprehensive Programs in Beta Cell Biology, will bolster investigator-initiated collaborative research focused on signaling networks within the adult beta cell and the integration of signaling networks within the pancreatic islet. It will seek to characterize each step in the molecular pathway by which glucose stimulates insulin secretion, mechanisms by which other signals modify beta cell function, and the factors that regulate beta cell growth.

Genome Anatomy Projects: To build upon the achievements of the Human Genome Project, the NIDDK has established a range of Genome Anatomy Projects (GAPs) to map the complex network of cellular interactions in normal and diseased tissues. The beta cell consortia described previously comprise one such GAP. Other related large-scale projects will foster multi-disciplinary team approaches applying genomic and proteomic technology to understanding, at the molecular level, the signaling events in tissues involved in the pathogenesis of diabetes and its complications. Efforts will focus on developing a comprehensive understanding of tissues that are major sites of insulin action—such as liver, muscle and fat—and how signaling and cell regulation are altered in diabetes.

The Diabetes Genome Anatomy Project (DGAP) will enable researchers to take a systematic approach to the complex problem of diabetes by cataloging all genes expressed in tissues relevant to the disease. The initial step in this multi-faceted program was an initiative on the Functional Genomics of the Developing Pancreas. This program has already identified 500 novel genes expressed primarily in the pancreas. These genes are being evaluated using microarray technology to understand their function in the pancreas and how their expression is altered in diabetes. Based on the success of this approach, the NIDDK now plans to expand this effort to other tissues affected by diabetes. To make these technologies widely available to researchers, the NIDDK also established Biotechnology Centers to provide gene profiling resources to investigators working on diabetes and other diseases.

Clinical Trials and Clinical Research: The NIDDK has significantly expanded clinical trials and clinical research directed at advancing the prevention and care of diabetes. In particular, considerable work has been done to establish the clinical infrastructure needed to efficiently conduct large, long-term trials by creating national, multi-center research networks or consortia. Many of these consortia provide opportunities for partnerships between the NIH, academia, and industry for collaboration and co-funding of clinical trials and for support of clinical research training in diabetes. They also provide for collection of biologic specimens for use in ancillary clinical research studies to address key questions of disease pathogenesis and mechanisms of response to therapies as well as opportunities for development and validation of surrogate markers that can be used to gauge the health of the patient before development of diabetes or its complications. This section of the report describes major new results achieved and new clinical research undertaken to address the prevention and treatment of diabetes and its many complications.

Prevention of Type 2 Diabetes in People at High Risk: The Diabetes Prevention Program (DPP) demonstrated that individuals at substantial risk of developing type 2 diabetes could prevent or delay disease onset and improve their blood sugar levels through modest improvements in diet and exercise. Minority groups who suffer disproportionately from type 2 diabetes—African Americans, Hispanic Americans, Asian Americans and Pacific Islanders, and Native Americans—made up 45% of the over 3,200 individuals enrolled in the trial. The DPP, conducted at 27 centers nationwide, is the first major clinical trial to show that diet and exercise can effectively reduce diabetes in a diverse American population of overweight people with pre-diabetes. The lifestyle intervention, which targeted a 7% (or an approximate 15 pound) weight loss, and 150 minutes of walking or other moderate-intensity exercise per week, reduced the risk of getting type 2 diabetes by 58% compared to the control group, which received standard medical advice. The same study found that treatment with metformin also reduces diabetes risk, though by a less dramatic 31%, in people at high risk for type 2 diabetes.

Long-term follow up studies are under way to assess the durability of the DPP interventions in preventing or delaying diabetes and to determine whether the interventions reduce cardiovascular disease and atherosclerosis, major causes of death in people with type 2 diabetes. This study will also provide important information on the clinical course of new-onset type 2 diabetes in this diverse study population.

Continued Benefits of Improved Blood Sugar Control: The Diabetes Control and Complications Trial (DCCT)—a large, randomized, and controlled clinical trial completed in 1993—definitively tested the hypothesis that improved blood sugar control prevents or delays complications in type 1 diabetes patients. In a report on a follow-up study to the DCCT, scientists demonstrated that the benefits of strict blood sugar control first observed in the DCCT persist for at least 7 years. When the DCCT trial ended, both groups were encouraged to use intensive therapy and were closely monitored. Overall blood sugar levels soon became similar in the two groups--with better control in the former conventional group and looser control in the former intensive group. Despite their similar levels of control during the subsequent 7 years, follow-up showed that those who had initially been in the intensive therapy group were still less likely to develop eye or kidney disease than those whose blood sugar was initially controlled using conventional therapy.

This follow-up study, the Epidemiology of Diabetes Interventions and Complications (EDIC) study, is still ongoing. Using the DCCT closeout examination results as a baseline for comparison, the scientists found that patients initially in the intensive treatment group were less likely to develop retinopathy and impaired kidney function than those in the conventional group. Individuals initially in the intensive treatment group were also less likely to develop high blood pressure.

The DCCT results demonstrated that by strictly monitoring and controlling their blood sugar, patients can significantly reduce their risks of developing complications. The new results from EDIC show that the benefits of a finite period of stricter blood sugar control persist for at least 7 years after levels of control were equalized. Because of this proven, persistent benefit, it is important to begin intensive treatment to control blood sugar as early as possible.

Diabetes Prevention Trial for Type 1 Diabetes (DPT-1): In this major clinical trial, NIDDK-supported researchers tested the hypothesis that low dose insulin injections can prevent type 1 diabetes in those most at risk–relatives of type 1 diabetes patients. Although the study did not demonstrate a benefit for this therapy in pre-diabetic patients, it did show that it was possible to accurately identify individuals at very high risk for progression to type 1 diabetes and it set the stage for future studies through a new clinical trial network, the Type 1 Diabetes TrialNet. The ability to recognize the onset of autoimmunity before damage is sufficient to cause diabetes and to identify individuals likely to progress to diabetes will be essential for the design of future clinical trials to prevent type 1 diabetes.

A parallel trial, testing the efficacy of orally administered insulin for preventing the onset of type 1 diabetes in persons at increased risk (25-to-50 percent risk of developing disease in 5 years), has finished recruiting and analyses of its outcome is expected in the Spring of 2003.

Type 1 Diabetes TrialNet: A consortium of investigators, clinical recruitment centers, and core support facilities has been established to perform intervention studies to preserve pancreatic beta cell function in patients with new-onset type 1 diabetes and to prevent type 1 diabetes in high risk individuals. TrialNet centers are completing the Diabetes Prevention Trial for Type 1 Diabetes (described previously). Furthermore, TrialNet will design and execute pilot and expanded studies of new agents to prevent or ameliorate type 1 diabetes as well as natural history and genetics studies in populations screened for or enrolled in these studies. Fourteen clinical centers and approximately 350 satellites and sites affiliated with these centers throughout the U.S. and Canada are participating in this consortium. The TrialNet will conduct studies in collaboration with the Immune Tolerance Network, a consortium of leading immunologists that is focused on assessing methods to reprogram the immune system to reverse autoimmunity in a number of autoimmune disorders, including type 1 diabetes.

Network for Type 2 Diabetes in Children and Adolescents: To combat the rising epidemic of type 2 diabetes in children, the NIDDK created a network of investigators to develop trials for treatment of type 2 diabetes in children and to develop and test interventions to reduce their risk of developing type 2 diabetes. The majority of children with type 2 diabetes are in the pre-adolescent or adolescent age range, a period that presents special challenges to health care providers and families when attempting to promote behavior and lifestyle changes. Prevention and treatment programs must also consider cultural differences among racial and ethnic groups that may influence acceptance of medical regimens. This is especially important for type 2 diabetes in children, which disproportionately affects minority populations.

In addition to those with frank diabetes, significant numbers of children may be at high risk of developing diabetes based on the presence of insulin resistance and blood glucose levels above normal but not as high as in diabetes. The Network for Type 2 Diabetes in Children and Adolescents is developing a prevention trial protocol that will focus on cost-effective, school-based interventions to decrease risk factors for type 2 diabetes and thus lower the incidence of this disease in children and adolescents. It is anticipated that the prevention strategies developed and tested will have the potential for broad, population-wide application.

To address its other major research goal, the Network will design trials to identify appropriate and effective treatment regimens for type 2 diabetes in children. The drugs currently available for the treatment of this disease in adults have not been used widely in children. Treatment options, including lifestyle changes and pharmacologic therapy, need to be studied in this population to determine the most efficacious, safe, and cost-effective strategies to achieve and maintain near normal blood glucose levels in the pediatric age group. Such treatment strategies are essential for reducing the long-term progression to diabetic complications for those who were diagnosed with diabetes during childhood and are at particularly high risk due to early development, and therefore longer duration, of their disease.

Obesity–Critical in Diabetes and a Major Problem of its Own: The number of overweight and obese Americans has risen dramatically in the past two decades and is now at epidemic levels. Obesity is a major risk factor for numerous serious diseases, including type 2 diabetes, heart disease, and cancer. Approximately 80 percent of the type 2 diabetes in the U.S. occurs in overweight or obese individuals. Overweight and obesity disproportionately affect minority populations, particularly African American, Hispanic, and Native American women and children. NIDDK-supported investigators are working to elucidate the molecular factors that control appetite, metabolism, and energy storage, and are identifying potential targets for the development of new pharmacological agents to promote safe, long-term weight loss. As demonstrated recently by the landmark Diabetes Prevention Program (DPP), a five to seven percent sustained reduction in weight–achieved through modest changes in diet and exercise--can delay or prevent the onset of diabetes in a high risk population. Investigators are continuing behavioral research like that employed in the DPP, to help people achieve lifestyle modifications that include increased physical activity and improved diet.

The NIDDK maintains a strong program of research on and related to obesity, both as a serious risk factor for type 2 diabetes and its complications and as an independent health problem. The National Task Force on the Prevention and Treatment of Obesity was established by the NIDDK and includes both NIH scientists and experts from the extramural community. This Task Force provides science-based guidance to aid research strategies. The Task Force also generates public health messages about obesity. The Director of NIDDK recently created the Office of Obesity Research within the Institute to coordinate obesity research across the many Institutes and Centers of the NIH. The NIDDK also supports Obesity/Nutrition Research Centers and Clinical Nutrition Research Units, which conduct both basic and clinical research studies.

Look AHEAD: Action for Health in Diabetes: With support from other NIH Institutes and Centers, the NIDDK has launched Look AHEAD—a multi-center clinical trial that will examine the health effects of intentional weight loss in 5,000 obese diabetic patients, with particular emphasis on cardiovascular health. Enrollment, begun in June 2001, is now at the halfway point at 16 Look AHEAD Clinical Centers and a Data Coordinating Center. Trial participants, who will be followed for up to 11.5 years, are randomly assigned to one of two protocols, the Lifestyle Intervention, which is designed to help participants achieve and maintain weight loss over the long term, or Diabetes Support and Education.

Translating the Results of Clinical Research into Clinical Practice: The past few years have seen encouraging progress in development of effective new treatments for diabetes. Now, a key challenge is to ensure the American people benefit from what researchers have discovered. One approach to this challenge is education—dissemination, to those at risk and their care providers, of information about measures proven effective for treating type 1 and type 2 diabetes and for preventing type 2 diabetes in individuals at high risk for this disease. However, providing information alone is not sufficient to translate what we know into practice. We need to develop methods to take interventions that have been demonstrated to be beneficial in careful clinical investigations, and extend or adapt them to larger populations or other settings. There is also increasing recognition that behavioral factors play a major role in the increased prevalence of obesity and type 2 diabetes and in the management of diabetes and its complications.

National Diabetes Education Program (NDEP): The NDEP is a collaborative initiative of the NIDDK and the CDC that uses over 200 public and private partnerships to promote, through education, routine clinical application of the therapies and other activities that have demonstrated value in the prevention of type 2 diabetes and diabetic complications. A key feature of this program is the participation of individuals who represent communities such as African Americans, Hispanics/Latinos, Native Americans/ Alaska Natives, and Asian and Pacific Islanders who are disproportionately affected by type 2 diabetes. Among its many educational efforts, the NDEP is the primary mechanism for translating the striking results of the DPP into real health improvements for the public.

A new national diabetes prevention campaign, launched on November 20, 2002, by HHS Secretary Tommy Thompson, will be coordinated by the NDEP. The program, entitled "Small Steps, Big Rewards," represents the first major NDEP effort to translate the DPP results on a national level, and its message is targeted at the 16 million Americans most at risk—those with pre-diabetes. The program emphasizes the practical application of the DPP findings and includes lifestyle-change tools for those at risk, patient education materials for healthcare providers and consumers, and TV, radio and print public service announcements.

While working to increase awareness about diabetes and effective means for prevention, the NDEP is continuing a core campaign, "Be Smart About Your Heart: Control the ABC's of Diabetes." This campaign is designed to make people with diabetes aware of their high risk for heart disease and stroke—the leading cause of death in these patients—and the steps they can take to dramatically lower that risk. The campaign emphasizes not only managing blood glucose, but also blood pressure and cholesterol.

The National Kidney Disease Education Program: This new program will raise awareness of the seriousness of kidney disease and the importance of early diagnosis, and increasing implementation of the appropriate management and prevention strategies for the disease and its complications. The number of people with end-stage renal disease has doubled each decade for the last two decades. These increases appear to parallel the rising prevalence of diabetes, the leading cause of kidney disease. Clinical trials have shown that optimal management of diabetes and blood pressure can reduce onset and progression of kidney disease.

Behavioral Research—Key to Prevention and Treatment of Diabetes: Recent clinical trials have provided definitive evidence that type 2 diabetes can be prevented with lifestyle change and that rigorous control of blood glucose, blood pressure and lipid levels can delay or prevent diabetes complications. Yet, this control can be arduous—requiring adherence to a complex regimen of medications, diet and physical activity–and it is optimal in very few Americans with this disease.

In response to the needs in this research area, the NIDDK has acted to stimulate application of behavioral science to diabetes through multiple initiatives. One solicitation called for research related to sociocultural, environmental, and behavioral mechanisms that contribute to successful self-management of diabetes. A subsequent solicitation specifically addressed diabetes self-management in the minority populations who are disproportionately affected by diabetes and its complications. A broader NIH-wide solicitation addressed the clarification of disease-relevant social and cultural factors and the linking of behavioral research to practices for improved prevention and treatment. More targeted research has focused on the role of psychological disorders--such as depression and eating disorders--on the risk of developing diabetes and its complications. People with diabetes have twice the rates of depression seen in the general population; moreover, people with depression have increased prevalence of diabetes. An NIH conference focused on research issues in depression in diabetes and other selected chronic diseases; this was followed by a solicitation to increase research on the relationships among depression, eating disorders, diabetes and obesity, and to explore how treatment of psychological disorders may improve outcomes in diabetes.

Translational Research for the Prevention and Control of Diabetes: Sadly, advances from "gold standard" clinical trials on therapy of diabetes and prevention of its complications have not been successfully incorporated into general health care practice. Under-utilization of current knowledge was highlighted in a recent study of individuals with diabetes that demonstrated a low frequency of self-monitoring of blood glucose, good glycemic control, regular foot care, and ophthalmic examinations, all of which markedly reduce the development and progression of diabetic complications. With the demonstration that modest lifestyle changes can dramatically reduce the risk of developing type 2 diabetes in high risk individuals comes the imperative to develop both population-based and clinic-based strategies to establish cost-effective programs to identify individuals at high risk who could benefit from prevention programs and/or successfully promote lifestyle change. Additional research is also needed on improved methods of health care delivery to patients with diabetes and to compare the effectiveness and use of different clinical practices, interventions, and technologies in particular population subgroups. These opportunities are being explored through new Diabetes Prevention and Control projects.

Diabetes-Based Science Education in Tribal Schools (DETS): American Indian and Alaska Native communities have the highest rates of diabetes in the world. Using the network of Tribal Colleges and Universities, the DETS program is developing supplemental curricula for Tribal elementary, middle and high schools to instruct students about lifestyle changes that can dramatically reduce the risk of diabetes and to encourage them to prepare for biomedical careers.

Strengthening Research Talent in Diabetes: Solving the puzzle of diabetes will require a cadre of exceptionally talented and dedicated researchers. To that end, a number of specific new initiatives were developed to recruit, train, and support new diabetes research talent.

Attracting New Talent to Diabetes Research: An innovative partnership program is promoting collaboration among diabetes researchers and those in areas other than diabetes who have expertise or technology that could advance diabetes research projects. This program was initiated with the special type 1 diabetes funding, using the diabetes centers as a catalyst to bring researchers together from disparate components of institutions for collaborative, multi-disciplinary research relevant to problems associated with type 1 diabetes. Subsequently, the program was expanded to investigators at all institutions. The goal is to encourage diabetes researchers to act as "talent scouts" to identify other researchers who could contribute to research breakthroughs in diabetes.

Bringing Together Basic and Clinical Researchers: An innovative program supports collaboration between basic research scientists, whose findings have potential direct applicability to development of new treatments or diagnostic tests, and clinical scientists, who can help to translate these basic discoveries into pre-clinical or clinical trials. The special type 1 diabetes funding allowed this program to be initiated with a focus on type 1 diabetes and diabetes complications. If successful, this bench-to-bedside research program will be expanded to all forms of diabetes.

Developing Clinical Researchers for Childhood Diabetes: In collaboration with the ADA and the JDRF, the NIH is intensifying efforts to expand the cadre of pediatric endocrinologists pursuing research careers. A new program addresses a critical shortage of clinical researchers in the important field of childhood diabetes. This effort will support a combination of complementary programs at institutions with particular strength in pediatric diabetes research. These combined programs will support development of new researchers by providing research training during pediatric endocrinology fellowships followed by a special career development award framed to provide research support for individuals who have completed their research training and have dedicated themselves to becoming independent clinical researchers.

National Institute of Environmental Health Sciences (NIEHS)

Many environmental agents have been investigated as contributing to the risk of type 1 diabetes. Environmental components have been suggested because concordance rates between identical twins, where one twin has type 1 diabetes, remain at 30-50%. NIEHS is pursuing research in several areas relevant to the etiology of type 1 diabetes, as summarized below.

Current Activities

Recent studies have raised the possibility that certain chemicals in the environment, such as nitrates in well water, increase the risks of juvenile diabetes. Studies in the United Kingdom, Finland, and Colorado indicate that the incidence of childhood diabetes is higher in areas with elevated levels of nitrate in the drinking water. This finding is significant for agricultural communities because well water can have elevated nitrate levels in areas where there is extensive use of fertilizers. Current and future activities in this area by NIEHS intramural scientists include.

- Further investigation of the possible association between nitrates and juvenile diabetes in a rigorous prospective study, such as the Agricultural Health Study.

- Evaluation of diabetes along with other health outcomes in the Agricultural Health Study.

In other studies, intramural investigators at NIEHS have reported an association between the body burden of a persistent organic pollutant (polychlorinated biphenyls) and type 1 diabetes. Current and future studies in this area include. Further studies to examine the relation between diabetes and body burden of persistent organic pollutants are either underway or being planned. For example, DNA is being collected from a cohort of men so that polymorphisms in the Ah-receptor (binds with dioxin-like polychlorinated biphenyls) can be examined in relation to body burden of persistent pollutants and risk of diabetes.

In extramural studies supported by the NIEHS, investigators are studying the possibility that arsenic in drinking water causes an increase in diabetes risk. Elevated levels of arsenicals in drinking water are common throughout the world, and oxidative forms of arsenic are known to have cytotoxic effects. These studies will:

- Investigate the effects of trivalent arsenicals and related compounds on glucose-stimulated insulin secretion in pancreatic islets and cell culture systems.

- Examine the effects of these compounds on insulin sensitivity in insulin-sensitive peripheral tissues and in intact animals.

Other extramural research efforts are examining the contributions of stress-activated protein kinases to insulin resistance and type 2 diabetes and the mechanisms of action of xenobiotic beta-cell toxins in animal models.

As noted above, the intermediate concordance rates for type 1 diabetes have stimulated the search for contributing environmental factors. Current and future activities in this area by intramural investigators include:

- In collaboration with investigators in the United Kingdom, NIEHS is investigating the hypothesis that persistant materno-fetal michrochimerism influences the development of type 1 diabetes in a set of monozygotic twins discordant for type 1 diabetes.

- NIEHS is investigating the possibility of establishing a discordant monozygotic twin registry in the United States for twins with type 1 diabetes, so that prospective studies of at-risk twins can be carried out.

Recent findings by intramural investigators using knockout mice have identified the guanine nucleotide regulatory or G protein G0 as an important regulator of glucose tolerance and glucose-stimulated insulin secretion in mice. Future studies will involve:

- Investigations into the molecular nature of the enhanced glucose tolerance seen in the intact mice.

- Studies of the molecular mechanisms of the enhanced glucose-stimulated insulin secretion seen in isolated islets from the G0 knockout mice.

NIEHS investigators are also investigating the role of menstrual and reproductive risk factors in diabetes and are looking at mechanisms of how environmental agents can affect pancreatic cancer cells.

National Institute of General Medical Sciences (NIGMS)

The National Institute of General Medical Sciences supports research and research training in the basic biomedical sciences that provide the foundation for a better understanding of fundamental life processes. Some of this work has relevance to understanding and treating diabetes.

Current Activities

NIGMS supports the Human Genetic Cell Repository, a collection of over 7,900 cell lines from individuals with a wide variety of genetic disoders, including diabetes, and from normal individuals. Cell lines in the collection include those from individuals with both type 1 and type 2 diabetes mellitus and its complications. The repository includes an extensive collection of cell lines from members of an extended pedigree with maturity-onset diabetes of the young. This collection is of value in studies designed to map and characterize the gene(s) responsible for these disorders.

DNA is also available for many of the cell lines in the Human Genetic Cell Repository. In new initiatives, the Repository has obtained two large panels of cell lines collected from individuals in ethnically identified, minority populations within the United States. These new collections supplement the panels of cell lines from 500 unrelated individuals that were acquired earlier, in cooperation with the National Human Genome Research Institute, in order to facilitate analyses of the genetic diversity of the U.S. population. This resource has proven to be of great value to researchers for the discovery of DNA polymorphisms important in pharmacogenetic studies and in the identification of genes involved in complex genetic disorders such as diabetes. The NIGMS Human Genetic Cell Repository will continue to cooperate with the National Human Genome Research Institute in the collection of cell lines from around the world for the HapMap project.

NIGMS has an interest in understanding how genetic and environmental components interact to result in complex diseases such as diabetes. The Institute supports a portfolio of grants to develop better statistical methods for mapping and identifying genes underlying complex traits, develop mathematical models for studying gene-gene and gene-environment interactions, investigate DNA sequence variation and its evolution, examine gene activities and the consequences of abnormalities in these activities, and optimize sampling strategies. NIGMS also supports pre- and postdoctoral training that emphasizes statistical and computational skills and workshops to provide additional training in statistical methods to biologists.

NIGMS support for research on the mechanisms underlying individual variations in drug response, while not specifically targeting diabetes, has the potential to have an impact on the treatment of diabetes and its complications. Researchers are studying the structural features of a powerful peripheral vasodilator related to insulin identified as an important prospective drug for peripheral angiopathies associated with diabetes.

NIGMS, in conjunction with several other Institutes, is supporting a mouse mutagenesis and phenotyping center whose emphasis is the high-throughput generation and identification of mice with mutations in biochemical and developmental pathways that may prove useful as models for human diseases.

NIGMS is also participating in the Trans-NIH Zebrafish Initiative, whose goal is to improve the genomic resources for the zebrafish, another potentially valuable model for diabetes studies.

Future Activities

In the future, NIGMS will continue to support basic research that focuses on underlying mechanisms and principles that are expected to shed light on both normal and disease processes and to lead to the development of new modes of treatment and prevention.

National Institute of Mental Health (NIMH)

The National Institute of Mental Health supports research on the processes and mechanisms underlying co-morbid mental disorders and diabetes. It also supports research to develop and test preventive, treatment, and rehabilitative interventions for mental disorders in people with diabetes. The interventions may be pharmacologic, behavioral, or psychosocial.

Current Activities

In FY 2000–2001, NIMH and the National Institute of Diabetes and Digestive and Kidney Diseases co-sponsored a major research conference, "Depression and Mental Disorders in Patients With Diabetes, Renal Disease, and Obesity/Eating Disorders," on January 29–30, 2001 at the Natcher Conference Center, National Institutes of Health. The papers resulting from the conference have been published in a 2002 special issue of the *Journal of Psychosomatic Research* (October 2002; 53(4)). The two Institutes jointly released a Request for Applications with a set aside of $1.5 million to fund new research projects in 2002. The NIMH supported two applications with its available funds.

In addition, NIMH re-issued in 2002 its program announcement calling for research applications on co-morbid mental and physical disorders, including diabetes.

National Institute of Neurological Disorders and Stroke (NINDS)

The National Institute of Neurological Disorders and Stroke supports a portfolio of research to study neurological complications of diabetes. Over 60% of people with diabetes are affected by neuropathy, and in many patients symptoms such as pain, numbness, weakness, or even paralysis are serious enough to interfere with daily activities. Symptoms of diabetic autonomic neuropathy can include heart rate abnormalities, hypertension, dizziness, digestive disturbances, and impotence. Autonomic neuropathy is an important cause of sudden cardiac death in people with diabetes. Prevention and treatment of neurological complications is a central therapeutic problem in diabetes mellitus, and research is conducted in such diverse areas as metabolism, sensory disorders, impaired wound healing, hypoglycemia, and pain.

Current Activities

NINDS has participated in nine initiatives related to the special type 1 diabetes appropriations, three as the lead institute. As the result of three Request for Applications published each year between FY 1998 and FY 2000, NINDS has greatly expanded its research into neurological complications of diabetes. New areas of study include early detection of diabetic neuropathy, gene transfer for prevention of neuropathy, autonomic neuropathy, behavioral effects of hyperglycemia, and mechanisms of neuropathic pain.

Several new NINDS applications were funded from two new FY 2002 RFAs. Applications in response to the RFA “Surrogate Endpoints for Diabetic Microvascular Complications” are looking for ways to detect early signs of diabetic neuropathy. Applicants whose grants were in response to the RFA “Effects of Hypoglycemia on Neuronal and Glial Cell Function” are studying mechanisms that may explain hypoglycemia’s effect on cells in the central nervous system.

NINDS continues to support a large epidemiological study of neurological complications of diabetes in the Rochester, Minnesota, area in the Caucasian and Mdewakanton Dakota Native American populations.

Future Activities

In addition to the Caucasian and Mdewakanton Dakota Native American populations, the Rochester epidemiological study will be expanded to include Hispanic subjects. Diabetes is characterized by large disparities in prevalence among ethnic groups, but little is known about the extent of neurological complications in these populations. This study will be the first to document the extent and progression of neurological complications in a longitudinal multiethnic cohort. Additional studies of this type have been solicited in a new jointly issued Program Announcement, "Race/Ethnic Disparities in the Incidence of Diabetes Complications" (PA-02-165).

National Institute of Nursing Research (NINR)

The mission of the National Institute of Nursing Research is to support clinical and basic research to establish a scientific basis for the care of individuals across the lifespan—from management of patients during illness and recovery to the reduction of risks for disease and disability, the promotion of healthy lifestyles, the improvement of quality of life in those with chronic illness, and care for individuals at the end of life. One purpose of this research, specific to diabetes, is to understand how to promote health-sustaining behavior and to improve quality of life by relieving the effects of disease processes and their progression. Nursing research focuses on how physical and psychological responses to diabetes symptoms and treatment of the disease affect health throughout the lifespan. NINR research programs pay particular attention to the effect of diabetes in minority and underserved populations.

Current Activities

NINR joined one new and one reissued program announcement (PA) in FY 2002: "Race/Ethnic Disparities in the Incidence of Diabetes Complications" and "Translational Research for the Prevention and Control of Diabetes," respectively. Additionally, NINR continued to encourage research in this area with three ongoing program announcements: "Enhancing Adherence to Diabetes Self-Management Behaviors", "Diabetes Self-Management in Minority Populations", and "Self-Management Strategies Across Chronic Diseases." These PAs are consistent with Diabetes Research Working Group (DRWG) recommendations (NINR was a participant in this working group).

In response to increased congressional support for type 1 diabetes research, NINR joined three requests for applications issued in FY 2002: "Innovative Partnerships in Type 1 Diabetes Research", "New Approaches To Prevent Hypoglycemia in Patients with Diabetes", and "Understanding Hypoglycemia Unawareness in Patients with Diabetes."

Funded grants relating to diabetes research included career development, postdoctoral training, and investigator-initiated research. Diabetes-specific topics included ethnic variations in type 2 diabetes prevention knowledge, adolescents with type 1 and 2 diabetes, autonomy and self-care in adolescents with type 1 diabetes, Spanish language self-management programs, biobehavioral intervention studies in several ethnic groups, a description of the integration of diabetes self-care in Mexican-Americans with type 2 diabetes in the southwest, an intervention for parents of young children with newly diagnosed diabetes, biophysical determinants of diabetes foot ulcer healing, weight loss in diabetes, and children's response when a sibling has type 1 diabetes.

Future Activities

NINR plans to continue to support research that focuses on problems experienced by persons with diabetes. Research efforts will be guided by the following goals:

- FY 2003: NINR will work collaboratively with other Institutes and organizations to increase and facilitate diabetes research activities.

- FY 2004: NINR plans to focus support on promising ongoing and new diabetes research areas, while building on recent nursing science advances.

In summary, NINR activities are designed to support research related to interventions for persons with diabetes, self-management, quality of life, special and diverse population needs, problems of defined age groups and across the lifespan, basic research, genetics, and other initiatives relevant to clinical practice and client outcomes. Translation of advances of science to the practice setting will be encouraged.

National Institute on Aging (NIA)

The mission of NIA as it relates to diabetes is to support biomedical and behavioral research leading to improved therapies to prevent diabetes and its complications, as well as improved quality of life for older diabetic patients.

Current Activities

NIA continues to support studies of potential metabolic mechanism(s)/factors that contribute to and/or underlie deleterious changes in body composition that can lead to metabolic disorders in old age. Ongoing studies in animal models have demonstrated a cause-and-effect relationship between visceral fat and major components of the metabolic syndrome. Surgical removal of visceral fat in aging (20-month-old) F344/Brown Norway (FBN) and in Zucker Diabetic Fatty (ZDF) (accounting for approximately 18% of their total body fat) rats was sufficient to restore peripheral and hepatic insulin action to the levels of young rats. While removal of visceral fat in ZDF rats prevented the progressive decrease in insulin action and delayed the onset of diabetes, it did not alter plasma-free fatty acid levels. This data suggest that insulin resistance and the development of diabetes can be significantly reduced in aging rats by preventing the age-dependent accumulation of visceral fat.

An NIA-supported project examined aging rats that underwent calorie restriction throughout their lives, maintaining their youthful body fat pattern and metabolic profile in order to examine whether leptin's failure in aging is due to aging per se or to changes in body fat mass or distribution. As assessed by a number of parameters of leptin action, it appears that the age-related decline in leptin action is independent of the body fat pattern. Leptin's failure in this model suggests a possible causative role in the metabolic decline seen with aging.

Numerous studies in laboratory animals have shown that chronic caloric restriction (CR), i.e., limiting caloric intake below ad libitum levels, extends maximum and average lifespan by as much as 40% and delays age-related pathologies correspondingly. CR increases life span whether initiated in early adult life or middle age, but its effects diminish with increasing age of onset of CR. The amount of lifespan extension increases with the degree of caloric restriction (up to approximately 40% restriction); substantial effects have occurred with 20% restriction. Among the aging, changes slowed by these regimens are declines in glucose tolerance and insulin sensitivity and increases in body weight.

Chronic CR in nonhuman primates has been found to produce parallel physiologic changes to those seen in rodents; studies of its effects on nonhuman primate lifespan have not been completed. To evaluate the effects of CR interventions in humans, NIA recently initiated the group of U01 projects known as CALERIE (Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy). CALERIE consists of exploratory controlled human intervention studies on the effects of CR interventions on physiology, body composition, and risk factors for age-related pathologies in non-obese persons. The CALERIE clinical sites and respective Principal Investigators include: Washington University, St. Louis, John Holloszy, M.D (PI); Pennington Biomedical Research Center, Eric Ravussin, Ph.D. (PI); and Tufts University, Susan Roberts, Ph.D.(PI). The CALERIE Coordinating Center is located at Duke Clinical Research Institute, James Rochon, Ph.D. (PI).

NIA was a cosponsor of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) study, Diabetes Prevention Program (DPP).

NIA was a cosponsor of the NIDDK Request for Application (RFA DK-03-002) "The Life Cycle of the Adipocyte." Application receipt date is March 13, 2003. Awards will be issued at the end of FY 2003.

NIA was a cosponsor of the National Heart, Lung and Blood Institute (RFA HL-03-008) " Role of Sleep and Sleep-Disordered Breathing (SDB) in Metabolic Syndrome." This RFA seeks to develop a better understanding of relationships between sleep deprivation, SDB, and the metabolic syndrome with the goal of reducing the risk of cardiovascular complications and age-associated pathologies. Application receipt date was February 11, 2003.

National Institute on Alcohol Abuse and Alcoholism (NIAAA)

The National Institute on Alcohol Abuse and Alcoholism encourages research to understand the role of alcohol consumption as a risk factor in the development of diabetes mellitus. NIAAA also supports research to determine the effects of moderate alcohol consumption on diabetes. Several studies suggest that alcohol consumption may directly or indirectly contribute to the development of type 1 diabetes. This line of reasoning is based on the following observations: a) alcohol impairs pancreatic insulin secretion; b) chronic alcohol intake increases plasma TNF (tumor necrosis factor) levels, which have been shown to cause pancreatic beta cell apoptosis leading to decreased beta cell number and insulin secretion; and c) chronic alcohol consumption may impair beta cell function by eliciting immunotoxicity.

Chronic alcohol consumption also has been implicated in the development of type 2 diabetes based on the following findings: a) chronic alcohol feeding in rats reduces the number of insulin-binding sites on isolated hepatocytes; b) alcohol impairs insulin-mediated tyrosine phosphorylation of insulin receptors in a tumor cell line; c) chronic alcohol exposure blunts tyrosine phosphorylation of insulin receptor substrate-1 in rat hepatocytes and a tumor cell line; and d) chronic alcohol exposure inhibits the activity of rat hepatocyte phosphotidylinositol-3kinase, which stimulates glucose transport. These effects of alcohol may lead to insulin resistance and impaired glucose transport.

Current Activities

Currently, NIAAA supports three projects that investigate the relationship between alcohol intake and diabetes. The following research areas are under investigation:

- Impact of moderate alcohol consumption on the risk of diabetes mellitus.
- Effects of fetal alcohol exposure on the biochemical and physiological changes in the insulin response and glucose homeostasis.
- Molecular mechanisms of disruption of insulin-mediated glucose transport by ethanol.

Future Activities

NIA has on going initiatives to build up our portfolio on the interaction between alcohol consumption and diabetes mellitus and tissue injury.

NIA is planning to hold a workshop on Alcohol and Diabetes in FY 2003.

National Institute on Deafness and Other Communication Disorders (NIDCD)

Disorders of hearing, balance, smell, taste, voice, speech, and language exact a significant economic, social, and personal cost for many individuals. The mission of the National Institute on Deafness and Other Communication Disorders is to support and conduct research and research training in the normal processes and the disorders of human communication that affect many millions of Americans. NIDCD supports basic and clinical research on diabetes mellitus in the area of taste. Taste preferences for sweet-tasting substances play a crucial role in the development of insulin and non-insulin dependent diabetes.

Current Activities

NIDCD is supporting research on taste and endocrine factors in women with gestational diabetes. Gestational Diabetes Mellitus (GDM) is a common complication of pregnancy with serious consequences for maternal and child health. Diet is an integral part of the management of GDM, but current diet strategies for pregnant women with GDM are poorly defined and often fail. NIDCD-supported scientists have observed that GDM increases the preference for sweet taste and dietary intake of sweet foods, which could have important implications for the management of this disease. At the time of diagnosis (approximately 30 weeks gestational age), pregnant women with GDM showed a higher preference for sweetened dairy drinks compared to pregnant women without GDM. In addition, increased plasma glucose in women with GDM was related to higher preference for the sweet taste of glucose and higher dietary intake of simple sugars as fruit and fruit juices. Because these studies were limited to a single observation point during gestation and excluded women with severe diabetes or those treated with insulin, further studies are needed.

The specific aims of this project are: 1) to determine the relationship between hyperglycemia and increased taste preference and dietary intake of sweet foods in GDM, 2) to compare the temporal pattern of taste and dietary changes in women with GDM to those of women without GDM across pregnancy stages, and 3) to relate these taste changes to alterations in gestational hormone and metabolic profiles. A single prospective study will be conducted to measure sweet taste preferences, food cravings, dietary intake of sweet foods, and plasma indices of selected hormones and metabolites (including insulin, cortisol, and leptin) during early, middle, and late gestation and at 6-week and 20-week post-delivery. The long-term goal of this project is to obtain a better understanding of taste changes in women with GDM to develop better preventative and therapeutic dietary intervention strategies for this disease.

National Institute on Drug Abuse (NIDA)

A study on glucose metabolism disorders in HIV-infected drug abusers will be considered for funding in FY 2003. Further, the proceedings of a workshop on "Interventions for Metabolic and Endocrine Complications of HIV/AIDS and Drug Abuse," guest-edited by Jag Khalsa, Sander Genser, and Henry Francis of the Center on AIDS and other Medical Consequences of Drug Abuse, NIDA, has been accepted as a special supplement volume in the *Clinical Infectious Diseases* journal.

National Library of *M*edicine (NLM)

NLM explores the use of new information technologies to enable diabetes patients to manage their disease and avoid or delay the onset of costly and debilitating complications, especially patients from minority and medically underserved populations.

In particular, we seek to learn how the use of NLM's MEDLINEplus Web site, and other computer-based health information resources, can be helpful to patients, their families, and members of the public to learn about and understand the latest research news on diabetes, nutritional requirements, tests, devices, secondary prevention techniques, and for obtaining answers to patient-specific questions. In the clinical setting, the principal hypothesis is that MEDLINEplus can reinforce and supplement the information provided by physicians, nurses, and health educators. A related hypothesis is that a combination of individualized training and access to publicly available computer resources at hospital libraries and elsewhere in the community can help bridge the "digital divide" experienced by minority populations that have less ready access to computers in the home, school, and workplace than the majority population.

Current Activities

NLM's diabetes-related objectives are to develop, design, implement, and evaluate a comprehensive program of diabetes-focused outreach initiatives in collaboration with academic health science centers and libraries, clinical centers, community-based organizations, and voluntary health organizations.

Project A. In collaboration with the Naomi Berrie Diabetes Center at Columbia/Presbyterian Hospital in New York City, study the benefits of MEDLINEplus and the Center's own Web site with Hispanic and African-American teenage type 1 diabetes patients who are on the insulin pump. These new resources are intended to reinforce and supplement the information provided by the Center's physicians,

nutritionists, and educators. The Center is also working with the medical informatics department at Columbia to build a type 1 diabetes module for a promising telemedicine system now under development for patients and hospital staff.

Project B. In collaboration with the Childrens Hospital of Los Angeles and the University of Utah School of Medicine, study how a diverse patient population, including Hispanic and African-American teens and the families of newly diagnosed type 1 patients can benefit from using MEDLINEplus to learn about and understand the latest research news, nutritional requirements, and uses of new medical devices for promoting better diabetes management and control.

Project C. In collaboration with two churches serving the African-American community in Montgomery County, Maryland, experiment with the concept of "peer tutors" as a means to recruit teenagers at risk for type 2 diabetes; enhance their diabetes knowledge with the use of MEDLINEplus; and observe changes in risk behaviors by them and by their peers.

Project D: Enhance the usability of MEDLINEplus for Spanish-speaking users by developing a Spanish language version of the more than 500 health topics, patient tutorials, medical encyclopedia, and drug information database and evaluate its acceptance among diabetes patients.

Project E. In collaboration with the University of Texas Health Science Center at San Antonio, and its regional health center and clinics in the Lower Rio Grande Valley, study how a computer workstation installed in the clinic waiting room can provide Hispanic patients with diabetes-related information. Health care providers will encourage use of MEDLINEplus with special information referral prescription pads.

.*Project F*. Explore with the Juvenile Diabetes Research Foundation (JDRF) a variety of mutually supportive uses of new information technologies. These include enhancement of NLM's MEDLINEplus diabetes content for children and teens; user evaluations of MEDLINEplus; inclusion of JDRF-sponsored trials in NLM's ClinicalTrials.gov database; creation of Spanish language resources based on JDRF's *Countdown* research magazine; experimentation with informatics tools to lessen the probability of misdiagnosis of type 1 diabetes, particularly in emergency departments serving minority and other medically underserved populations; and experiment with informatics and distance education tools for science teachers and nurses in low-income high schools.

Veterans Health Administration (VHA), Department of Veterans Affairs

The mission of the Veteran's Healthcare System is to serve the needs of America's veterans by providing primary care, specialized care, and related medical and social support services. To accomplish this mission, VHA needs to be a comprehensive, integrated healthcare system that provides excellence in healthcare value, excellence in service as defined by its customers, and excellence in education and research, and it needs to be an organization characterized by exceptional accountability and by being an employer of choice.

The mission of the VHA diabetes program is to improve the health of veterans with diabetes by decreasing the incidence of adverse health outcomes, especially macrovascular and microvascular disease. This will be accomplished through systems-level integration of guidelines, performance measurements, and data feedback to promote the increased use of evidence-based preventive and treatment processes. VHA research service supports this mission through clinical, basic science, and health services research. VHA reports the following progress in FY 2002.

Current Activities

Performance Measurement (Office of Quality and Performance, OQP). In FY 2002,VHA, through its External Peer Review Program, collected data from a random sample of 23,561 charts of veterans with diabetes. A patient, to be established in the "plan," (not just enrolled as a veteran) must have accessed VHA for any type of care some time at least once 2 years ago and at least once during the previous 12 months. OQP data analysis showed that the percentage of patients having chart documentation of the following Diabetes Quality Improvement Project (DQIP) measures using DQIP abstraction criteria within 12 months (or as noted) of chart review is as follows:

- HbA1c test (94%); 78% of HbA1c values less than 9%; 65% less than 8.0%; 41% less than 7%, and 17% greater than 9.5% (for less than 9.5% the results are 87%).
- Lipid profile within 2 years 94%; 70% less than 130 mg/dl, 64% of LDL-C values less than 120 mg/dl, 43% less than 100 mg/dl.
- Blood pressure control, 58% less than 140/90.
- Dilated retinal examination (72%).
- Nephropathy screening within 2 years (78%).
- Visual examination of feet 92%; palpation of pedal pulses 86%; sensory examination of feet 82%; referral of patients with "high risk feet" to a foot care specialist 84%.

Since VHA uses DQIP measures, comparison to the private sector is possible. In FY 2001, VHA national adherence to most measures was at the 90th percentile of the individual private sector plans, included in the National Committee on Quality Assurance (NCQA) Quality Compass Report.

VHA Diabetes Registry (Office of Policy and Planning). The VHA has developed a nationwide diabetes registry derived from administrative data. Veterans are identified as having diabetes using one inpatient or two outpatient codes with a diabetes-specific code or receipt of an oral agent or insulin. The denominator is defined as veterans who had at least one clinical visit during the year. For FY 2001 there were 764, 603 veterans with diabetes out of 3,843,832 unique veteran users, for a prevalence of 20%; this compares to 639, 323 (19% prevalence) for FY 2000; 503, 321 (16% prevalence) for FY 1999, and 420, 486 patients (14% prevalence) in FY 1998. This cross-sectional calculation technique probably yields an underestimate compared to the prevalence calculated from a longitudinal analysis.

Based on registry data analysis for patients with A1c performed in VHA laboratories, the mean HbA1c for FY 2001 was 7.37 compared with 7.61 in FY 2000; and the mean LDL was 104 mg/dl compared with 108 mg/dl in FY 2001.

Lower Extremity Amputation Programs (Offices of Policy and Planning and Patient Care Services). In collaboration with the Centers for Disease Control and Prevention, Division of Diabetes Translation, a 12-year Lower Extremity Amputation (LEA) Registry has been created by the Office of Policy and Planning. From FY 1997-FY 2000, the age-adjusted rate (standardized to the VHA 1998 User Population) of LEA in the entire veteran population has decreased from 2.18 (0.78 major amputations [e.g., below knee or above knee]) to 1.42 (0.65 major amputations) per 1,000 VHA users in FY 2000. The VHA is in the process of updating its data through 2002.

In FY 2001 the Under Secretary for Health reissued the VA Preservation, Amputation Care and Treatment Directive (PACT), which mandates multidisciplinary foot care programs, including screening, surveillance, and salvage components, at all VHA facilities.

VHA recently participated as a full partner with the American Diabetes Association, the Centers for Medicare & Medicaid Services (CMS), the American Podiatric Medical Association, and the Centers for Disease Control and Prevention in an initiative to improve foot care for Medicare beneficiaries with diabetes. CMS's comprehensive decision memorandum cites five VHA research papers as providing scientific evidence to support the requested coverage benefit.

Guideline Development (Offices of Quality and Performance and Patient Care Services). VHA, in partnership with the Department of Defense, has revised its February 2000 version of the Diabetes Clinical Practice Guidelines. The guidelines, covering outpatient management of glycemia, blood pressure, hyperlipidemia, diabetic retinopathy, foot care, and renal disease, emphasize transparency of the evidence underlying clinical recommendations as well as principles of absolute risk reduction and patient-clinician target (HbA1c) value negotiations.

Research Service. There are three VA Diabetes Centers of Excellence focused on diabetes research co-funded by Medical Research Service and the Juvenile Diabetes Foundation International. Investigators at these sites are investigating the effects of diabetes upon the vascular system; mechanisms of insulin resistance; cellular and molecular processes by which intensive therapy reduces insulin resistance; the role of exercise in modulating the effectiveness of therapy; and mechanisms responsible for defective low blood sugar regulation.

VHA has funded a 5-year cooperative study (VA Diabetes Trial (VADT), CSP #465) to evaluate the effect of near-normal glycemic control upon cardiovascular outcomes in type 2 diabetes. The VADT will enroll 1,700 men and women from 20 VHA sites randomized to intensive versus conventional control. The outcome will be assessed by evaluating composite cardiovascular events. Recruitment is ongoing.

The VHA Quality Enhancement Research Initiative (QUERI) has been cited as a model by the Institute of Medicine. The goals of QUERI initiatives are to translate research into improvements in patient care and outcomes. The primary focus of the Diabetes Mellitus QUERI–DM program is upon more–aggressive treatment of modifiable risk factors and the prevention of progressive complications among veterans with diabetes. These activities range from the implementation of interventions to assist "front-line" clinicians with targeting high-risk patients to the design and evaluation of alternate methods for constructing diabetes care quality indicators. QUERI–DM continues to work with partners outside VA, including the Centers for Disease Control (Translating Research Into Action for Diabetes). This project will produce a structural and organizational analysis of VHA diabetes care and allow direct comparisons with diabetes care in the private sector.

Joslin Vision Eye Network (Office of Patient Care Services). The VHA is a participant in the Telemedicine Project for Non-Mydriatic Retinal Examination in partnership with the Joslin Vision Network. The Joslin Vision Network is a congressionally mandated project, which currently includes the VHA, the Department of Defense (DoD), and the Indian Health Service. The project involves imaging the retina with a non-mydriatic camera and transmitting the images to a reading center. A recent VHA teleopthamology (digital imaging) consensus conference made recommendations on the technical aspects of data acquisition. DoD, and the VHA is in the process of evaluating the operational issues associated with the implementation of teleopthamology at the facility level.

Standardization of Glycated Hemoglobin Testing. Consistent with a directive from the Under Secretary for Health, all VHA facilities use methodology traceable to the Diabetes Control and Complications Trial (DCCT) standard as recommended by the National Glycosylated Hemoglobin Standardization Program (NGSP). This has been acknowledged by the NGSP in its publications and on its Web page.

Education. Over 30 VHA facilities have obtained American Diabetes Association Recognition of their patient education programs—more than any other national system of health care. VHA hosted the 4rd annual National Diabetes Symposium for over 250 endocrinologists and primary care clinicians, as well as the annual VA Diabetes Educators Conference for nearly 300 VHA clinician educators. These conferences represent an institutional commitment to translating agency priorities and research findings into results at the field level.

Future Activities

VHA remains committed to improving outcomes for veterans with diabetes. A nationwide approach to more aggressive blood pressure control, instituted last year, remains a priority. Research Service funded proposals for research to improve eye care and blood pressure control. The Under Secretary for Health, in the reissued PACT directive, has directed that senior management review network amputation rates. A national Web-based learning center is being pilot tested. VHA has a national Computerized Patient Record System (CPRS), with clinical reminders, and improvements to CPRS to support all clinical care, including diabetes, are ongoing. The VHA leadership role in the use of medical informatics has been noted by the Institute of Medicine.

THE NATIONAL DIABETES EDUCATION PROGRAM

THE NATIONAL DIABETES EDUCATION PROGRAM

Fiscal Year 2002 Accomplishments

INTRODUCING THE NATIONAL DIABETES EDUCATION PROGRAM

The National Diabetes Education Program (NDEP) is jointly sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the Centers for Disease Control and Prevention (CDC) and is a subcommittee of the Federal Government's Diabetes Mellitus Interagency Coordinating Committee (DMICC). The program speaks to a national audience of people with diabetes and their families, health care providers, payers and purchasers of health care, health care system policymakers, and the general public, including people with undiagnosed diabetes and those at risk for the disease.

The NDEP's efforts are aided by a Steering Committee comprised of representatives from diabetes-related, health care, racial/ethnic, and voluntary service organizations. Federal liaisons to the NDEP Steering Committee include several representatives from the DMICC. Members of the Steering Committee also serve on NDEP Work Groups that provide direction and help implement NDEP initiatives.

The NDEP also has developed a Partnership Network of about 200 organizations to help disseminate program messages through the mass media, community groups, and health systems serving people with diabetes. A new web site, called "Team Diabetes," has been launched to provide an interactive, online site for NDEP partners to exchange resources and information.

In June 2001, the NDEP published *Changing the Way Diabetes Is Treated, A Progress Report from the National Diabetes Education Program* that reviewed the NDEP's accomplishments since its inception in 1997 through Fiscal Year 2000. This booklet details the origins, development, activities, and future priorities of NDEP and has been distributed widely in the diabetes community. To obtain copies of this publication, please contact Joanne Gallivan, Program Director, NDEP, NIH at *Joanne_Gallivan@nih.gov.*

During FY 2002, NDEP supported a variety of activities to promote awareness about the importance of comprehensive diabetes care and to add an important new message about diabetes prevention. Highlights of NDEP's activities during the past year are summarized below.

NDEP Steering Committee

The Steering Committee met twice—in October 2001 and June 2002 in Washington, D.C. The purpose of the meetings was to coordinate and advise on program policies, initiatives, and goals and to help coordinate efforts. The October meeting was planned to outline the Program's three-year strategic plan and in June, the meeting included a discussion of plans to develop a diabetes prevention campaign, as well as program evaluation efforts.

Mass Media Campaigns

From June 1998, when NDEP launched its first Public Service Announcement (PSA) campaign, through FY 2002, NDEP's campaigns have obtained well over $13 million in free advertising time or print media space. The NDEP continues to promote its comprehensive care campaign and provided support for tailoring this campaign targeted to several minority audiences. The program also began planning the launch of its diabetes prevention campaign and initiatives. NDEP carried out extensive market research prior to initiating these campaigns and developed the materials in conjunction with appropriate NDEP Work Groups. The program also provided ongoing support for continuing campaigns targeted to African Americans, Hispanic/Latino Americans, American Indians, and Asian Americans and Pacific Islanders.

"Be Smart About Your Heart: Control the ABCS of Diabetes" creates awareness about the link between diabetes and heart disease and promotes comprehensive diabetes care to control blood glucose (hemaglobin A1c), blood pressure, and cholesterol—the ABCs of diabetes. In November 2001, the "Be Smart About Your Heart" brochure was completed and printed. A major promotion of the brochure was conducted in the media as part of National Diabetes Month. In February 2002, in coordination with the American Diabetes Association (ADA), U.S. Department of Health and Human Services Secretary Tommy G. Thompson announced the results of an ADA-commissioned survey showing the lack of awareness in people with diabetes about the link between diabetes and cardiovascular disease. In June 2002, NDEP and ADA announced results of an ADA commissioned survey of health care providers understanding and promotion of the comprehensive care messages. "Be Smart" messages and materials continue to be promoted by NDEP partners.

"Si Tiene Diabetes, Cuide su Corazón" is NDEP's campaign aimed at helping Hispanic Americans better understand the need to control all aspects of their diabetes to help prevent heart disease. Hispanic and Latino Americans with diabetes are at higher risk of heart disease, but they can reduce that risk, according to a new bilingual brochure, "Usted es el corazón de la familia...cuide su corazón" or "You are the heart of your family...take care of it." In July 2002, the campaign was announced at the National Council of La Raza's annual meeting.

"Move It!" is the call to action of the American Indian Youth Campaign, which addresses the rising prevalence of type 2 diabetes in American Indian young people. The campaign includes a series of three posters, a print ad, a fact sheet, and suggestions for ways to increase physical activity at school. A "Move It!" kit has been sent to the Bureau of Indian Affair's American Indian schools.

In May 2002, during Asian/Pacific Islander Heritage month, the NDEP promoted a specially tailored tracking card for comprehensive diabetes care for this population.

Media Outreach

In conjunction with these PSA campaigns, NDEP continued to conduct media outreach to obtain coverage about diabetes in the print and broadcast media. Program messages were featured in a number of national media outlets. In November 2001, a Video News Release was distributed to over 150 stations in top media markets that promoted the ABCs message and availability of the ABCs brochure. BET.com featured messages about the ABCs of diabetes and famous African Americans with diabetes during Black History month and *Heart and Soul* magazine featured an article on this topic. As part of the partnership with ADA, the "Be Smart" campaign has been covered in *Newsweek*, *Time* and *U.S. News & World Report*.

NDEP Conference Participation

Program spokespersons gave presentations and represented NDEP at several meetings in FY 2002. Conferences included the American Dietetic Association's annual meeting in October 2001; the American Public Health Association meeting in November 2001; the ADA Postgraduate Course in January 2002; the American Association of Diabetes Educators annual meeting in August; the CDC's Diabetes Translation Conference in May; the annual meeting of the ADA in June; and the annual meeting of the National Council of La Raza in July.

Diabetes at the Worksite

NDEP's Business and Managed Care Work Group has designed a web-based resource that employers and human resource and health professionals can use to assess the scope of the diabetes problem in their workforces and to conduct diabetes education at the worksite. Hosted by the Washington Business Group on Health, this resource was launched in April 2002 and is available at www.diabetesatwork.org.

Diabetes in Children and Adolescents

This Work Group has completed a set of resource materials for health care professionals, parents, and others concerned about diabetes in children and adolescents. Materials include fact sheets, an annotated bibliography, and a resource directory. The Work Group is developing a series of tip sheets for children with type 2 diabetes and their families. In addition, a manual for school personnel on managing children with diabetes at school is being finalized.

Health Care Professional Work Group Activities

NDEP's Health Care Provider Work Group provided guidance for the Comprehensive Care Campaign and continued to promote the "ABCs of Diabetes" message. The group is developing a Web site that will promote various system changes and approaches to improve the quality of diabetes care, including clinical practice tools.

The Pharmacy, Podiatry, Optometry, and Dentistry (PPOD) Work Group is developing a diabetes primer to expand PPOD professionals' understanding of their role in care for people with diabetes beyond their own specialty and to include education about the need for glycemic, blood pressure, and cholesterol control for people with diabetes. The group also helped revise the publication "7 Principles for Controlling Your Diabetes," adding messages about the ABCs of diabetes and caring for the feet, eyes, and teeth and proper medication use for people with diabetes.

The Older Adults Work Group is developing materials to promote the newest benefits for people with diabetes who are Medicare recipients, including Medical Nutrition Therapy and diabetes self-management.

Future Activities

During Fiscal Year 2003, NDEP will not only continue to promote comprehensive diabetes care but it also will take the lead in translating and promoting the findings of the recently completed Diabetes Prevention Program (DPP) clinical trial. The DPP demonstrated that the onset of diabetes could be prevented or delayed among people at risk for the disease through modest lifestyle changes such as 150 minutes of moderate activity per week and losing 5 to 7 percent of one's body weight. This important prevention message will add a new dimension to the NDEP and its goal of "changing the way diabetes is treated."

For more information about the National Diabetes Education Program, please visit our web sites at http://ndep.nih.gov and www.cdc.gov/team-ndep on the Internet.

MEETING SUMMARIES

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THE DIABETES PREVENTION PROGRAM (DPP) AND TRANSLATION

March 11, 2002
National Institutes of Health
Bethesda, Maryland

WELCOME
–Allen Spiegel

Dr. Spiegel opened the March 11, 2002, meeting of the DMICC for the purpose of discussing the critical issue of translating the results of the Diabetes Prevention Program (DPP). He stated that data from the Centers for Disease Control and Prevention (CDC) shows that the incidence of type 2 diabetes is growing at an epidemic rate in the United States and worldwide. Dr. Spiegel indicated that findings of the DPP have received extensive coverage and interest since Dr. David Nathan, DPP Study Group Chair, first presented them to the DMICC on August 8, 2001. Immediately after the August 8th DMICC meeting, Secretary Tommy G. Thompson of the U.S. Department of Health and Human Services (DHHS) held a press conference to publicly announce the results and declare his commitment to disseminating them. The DPP primary results were published in the February 7, 2002, issue of the *New England Journal of Medicine*.

Dr. Spiegel reminded the group of the statement of Dr. Claude Lenfant, Director of the National Heart, Lung and Blood Institute, who said, "It's great to have a paper in the *New England Journal* [but] if it sits on the shelf, we will have accomplished nothing." Dr. Spiegel asked that the group address the translation problem cohesively and that they apply their scientific, critical thinking to recommend pragmatic, effective ways to move forward and translate the reality of these prevention findings.

To prepare for developing a framework for action, the group first heard from representatives of the public sector. Dr. Nathan presented an overview of the DPP trial and its results. The potential role of the National Diabetes Education Program (NDEP) was given by Drs. Charles Clark and David Marrero. Dr. Richard Kahn then discussed the American Diabetes Association's concerns about the challenges of translating the results into effective action. Ms. Kathy Berkowitz spoke of the interest of the American Association of Diabetes Educators in DPP. Mr. Ned Calogne discussed translation issues at the State level, and Dr. Joseph Selby described the managed care perspective. The presentations are summarized here. Copies of their slides can be found at http://www.niddk.nih.gov/federal/dmicc/meetings.htm.

PRESENTATIONS

DPP Primary Results – David Nathan

An overview of the DPP primary results presented by Dr. David Nathan demonstrated that type 2 diabetes could be prevented or delayed in a group of participants at high risk for developing type 2 diabetes by reason of their having impaired glucose tolerance and that there are approximately 10 million individuals in the United States at comparable high risk. The DPP demonstrated that modest lifestyle changes or the use of metformin can help stem the growing diabetes epidemic of more than 800,000 new cases of type 2 diabetes a year. Dr. Nathan emphasized that, although the U.S. population is projected to increase only slightly, the risk of developing diabetes is projected to increase 100 percent over the next 50 years. Thus, diabetes and its complications will create an enormous health care and financial burden for our Nation.

The DPP, along with Finnish and Chinese studies, has shown that managing impaired glucose tolerance (IGT) can slow or prevent progression to diabetes in those at high risk and even reverse the IGT. Since most diabetics are not diagnosed until 4 to 7 years after developing the disease, at which time early complications such as cardiovascular disease have already started, screening for IGT and intervening early can produce significant human and financial cost savings. Results are still being analyzed, but early indications are that managing IGT also has prevention benefits for cardiovascular events and atherosclerosis.

The DPP selected participants from the upper half of a group considered to be at risk for developing type 2 diabetes. Since people are not normally identified as having IGT, the DPP screened for patients who were overweight and had a family history of diabetes. Eligible study candidates had both a 2-hour oral glucose tolerance test (OGTT) glucose level of 140 to 199 mg/dL and a fasting glucose level of 95 to 125 mg/dL. Forty-five percent were from minority groups and 20 percent were age 60 or older, both groups who are disproportionately affected by diabetes. Eligible participants at the 27 clinical centers were randomized to either intensive lifestyle; metformin, 850 mg BID; or to placebo.

Dr. Nathan made the distinction that the lifestyle intervention was a supportive, comprehensive, and intensive program with moderate exercise and weight loss goals. The goal of the lifestyle intervention group was loss of 7 percent of body weight (10 to 15 pounds), restriction of daily dietary fat to 25 percent and caloric intake to 1200-1800 calories, and 150 minutes per week of physical activity, such as brisk walking. Participation and retention were both excellent. At the end of the study, 93 percent of participants completed the study and 93 percent completed all study outcome visits. Dr. Nathan said that these retention and participation figures reflect the motivation and dedication of the study volunteers and the skill of the centers and the DPP staff members.

Because of the strong positive results achieved by May 2001 and the recommendations of the Study Data Monitoring Board, the NIDDK ended the study one year early. The study findings demonstrated that lifestyle intervention reduced the risk of developing diabetes by 58 percent and metformin reduced the conversion to diabetes risk by 31 percent for an average of 2.8 years of exposure.

Dr. Nathan said that to have a public health impact the target at-risk audience must be identified and their cooperation must be obtained in order for translation of the study results to the at-risk population. Whether public health results similar to those of the DPP can be obtained will depend a great deal on the public health message developed and channels used for communication.

Dr. Nathan pointed out that important questions need to be resolved about the cost-effectiveness of the DPP interventions, how the results will translate to the larger population group at high risk, and how to accomplish the translation. The DPP Research Group is conducting analyses and preparing for a 5-year followup study with the cohort of DPP participants to determine the clinical consequences and benefits of DPP interventions over time.

The National Diabetes Education Program Role in DPP Translation – Charles Clark, David Marrero

Dr. Charles Clark and Dr. David Marrero reported on a proposed multi-faceted, three-phase NDEP campaign with specific target audiences, objectives, messages, and plans of action. A tentative slogan for the diabetes prevention campaign is "Small Steps. Big Rewards." The program targets three separate audiences—health care providers and allied professionals, people at risk for type 2 diabetes and other stakeholders, and health care purchasers, payers, and the media. With the help of CDC, NDEP will conduct focus groups with each audience to test and refine the effectiveness of the campaign strategies and messages.

Following an initial 3-month provider phase, the campaign will target the at-risk population similar to the volunteers in the DPP. Diabetes tends to run in families and disproportionately affects racial/ethnic minority groups. The campaign will therefore target the at-risk group's family and friends, those who have diabetes and their supporters, and the community at large. Dr. Marrero emphasized that communicating the DPP results requires less a medical model as much as a community health model. Changing the behavior of the ten million high-risk people similar to those in the DPP is a community effort. The message will be that modest changes make a big difference. Individuals will be encouraged to see their doctors and be tested. Options will include lifestyle modification—eat better and get moving—and/or medication. Channels of communication will include local and culture-based media outlets, food editors and shows, celebrities, and community and faith-based groups. Messages will stress that diabetes prevention is not only for adults at risk; it applies to children and young people who are developing patterns that lead to increased risk.

Drs. Clark and Marrero pointed out that NDEP began with the goal of changing the treatment of diabetes today and ultimately trying to prevent diabetes. The "ultimately" came quicker than expected. Now the goal is not only to change the way diabetes itself is treated, but also the way pre-diabetes is treated as a health risk.

American Diabetes Association (ADA) Perspective – Richard Kahn

Dr. Richard Kahn, Chief Scientific and Medical Officer, ADA, stated that ADA took the lead many years ago to screen people for diabetes. Now, he said, perhaps we are going to screen people for pre-diabetes. Dr. Kahn presented the following issues that his organization considers crucial to creating a framework for action to translate the DPP results:

- Achieving results similar to the DPP will be difficult. There is no provision in today's health care systems to pay for the type and extent of the intervention done in the clinical trial. If we identify people and tell them they are at risk, then we must offer them specific, focused, doable interventions. This must be more than "lose weight and exercise." This public awareness message has been around for a decade and has not been very successful. We need a lifestyle intervention similar to DPP that is less expensive than DPP's. Or are there other, more cost-effective strategies that would produce the same results? Can the results be maintained?

- The means for identifying the target audience must be decided. Will the OGTT or fasting glucose test (FGT) be used? They are not interchangeable. What happens when the scientific community changes the values defining pre-diabetes and diabetes? Or is there another algorithm that can be used for which a scientific basis does not yet exist.

- The term for the condition that defines the at-risk population must be carefully selected. Is IGT or IFG, whichever is chosen, a pre-disease condition or a disease? Is it early stage diabetes or pre-diabetes? There are very few diseases we treat, and receive reimbursement for treating, in the pre-disease stage. What do we tell people they have? Deciding what to call the state is important for the message, the testing, the reimbursement, and the intervention.

It was also announced that ADA and NIDDK will publish a position statement on diabetes prevention in the April 2002 edition of Diabetes Care. (Diabetes Care, Vol. 25: 742, 2002).

American Association of Diabetes Educators (AADE) – Kathy Berkowitz

Ms. Kathy Berkowitz, President, AADE, assured DMICC that her group of some 10,000 nurses, dieticians, pharmacists, and other health care disciplines are experienced, qualified, and committed to a team approach to translate the DPP results. Most of AADE's members have been involved with diabetes for 10 or more years. Currently the country's 12,000 Certified Diabetes Educators must serve some 16 million persons with diabetes. To assist in the translation effort, many more educators will be needed to reach the 10 to 20 million persons at risk.

AADE expects the DPP to widen the scope of the diabetes educator's role, increase the demand for services, and enhance the value of the diabetes educator. AADE is in the process of developing a position statement on diabetes prevention and the impact of DPP on the diabetes educator's role. AADE has planned a multi-organizational Lay Health Worker Summit for April to reach community health workers. This effort is designed to identify those who are already delivering some diabetes education and reach consensus on a role for them in reaching more people with diabetes and those at risk for diabetes. DPP will be a prominent subject at their August 2002 annual meeting. The association will include some form of prevention education and the interventions in their practice standards, such as distributing the "Am I at Risk" pamphlet. They are planning to develop web-based, continuing education programs and articles in their publications.

Ms. Berkowitz noted that AADE will be developing both patient education materials and professional's toolkits to help their members understand, apply, and disseminate the DPP information. They also will be working with CDC's training program for community health workers.

Translation at the State Level – Ned Calogne

Dr. Ned Calogne, prior to becoming Chief Medical Officer and State Epidemiologist for the Colorado Department of Public Health and Environment, was Chief of Preventive Medicine for Kaiser Permanente and worked closely with the DPP principal investigator at the Denver center. Dr. Calogne pointed out that States do not receive much State funding for public health efforts. Funding for much of what they do comes from other sources, such as Federal grants from CDC, prevention block grants, tobacco settlements, local and national foundation grants, and non-public health community partners. State funds only allow for limited training, production of materials, and information dissemination. Another challenge to any role for States in translating DPP research is that most public health takes place at the local level. Matching State needs with Federal goals can be difficult, but trying to match local needs and State goals is often more difficult. Translating programs down into local health departments—which have their own issues, their own strategies for funding, their own county commissioners, their own local politics—is a huge issue.

Dr. Calogne identified three areas for translation of the DPP findings: (1) screening and definition of the glycemia problem; (2) behavior change; and (3) chemoprophylaxis.

There are no public health funds currently available for screening for impaired glucose tolerance. The State would need to influence supportive policies for screening through its community partners, including health systems, insurers, community health services, Medicare, and Medicaid. To translate DPP, Dr. Calogne said States would need assistance and cooperative efforts from DMICC member agencies. Funding through grants and cooperative agreements is a familiar and comfortable mechanism for States. Integration with existing programs, such as the cardiovascular, diabetes, and weight management programs, would ease the oversight and administrative burden.

Dr. Calogne described several things that have worked in public health. One was the use of tobacco money to fund a quit-line and the collaboration with Kaiser Permanente to provide smoking cessation pharmaceutical aids to quit-line participants. Although the effectiveness of the intervention is still unknown, it is an example of a collaborative effort to create awareness and facilitate an intervention. Use of the Internet as active deliverer of an intervention might be a low-cost possibility that could be applied on a broad basis.

Dr. Calogne asked rhetorically what the role of the public health service should be? Should it be primarily to raise awareness? Or to provide direct care?

Managed Care Perspective – Joseph Selby

Dr. Joseph Selby, Director of the Division of Research, Kaiser Permanente, is overseeing the TRIAD study in diabetes management in a managed care setting. Although he was speaking about Kaiser's reactions to DPP, he pointed out that other organizations were also very interested in DPP. One is the American Association of Health Plans (AAHP), the national organization representing the vast majority of health plans in D.C. AAHP coordinates a CDC-funded research program and sponsors a number of chronic illness initiatives relevant to translating the DPP. Working with NIH, it is actively engaged in promoting clinical trial participation for HMO-enrolled members in its health plans. Another organization is the HMO Research Network, a 6-year-old research center association of 14 large health plans covering 20 to 30 million people. Currently, the HMO Research Network is receiving more than $30 million in NIH, CDC, and Agency for Healthcare Research and Quality (AHRQ) research funds. This is an active, population-based research effort and group that will very likely participate in translation of the DPP.

Kaiser Permanente's Care Management Institute (CMI) responded very quickly to announcement of the DPP results. CMI was already working in the areas of overweight and diabetes. The Institute supports the development of evidenced-based population disease management across the nine separately incorporated regions of the Kaiser Permanente program. Nationally, Kaiser has 8.2 million members, 90,000 employees, and 11,000 physicians. CMI identifies affected populations; identifies and disseminates best practices; supports clinicians and specialized staff; provides feedback; and measures, reports, demonstrates, and, hopefully, improves outcomes.

Dr. Selby stated that diabetes is the paradigmatic chronic illness, the classic disease management disease, the care for which must be solved and resolved if we are ever to manage health care costs. Kaiser has been aware of the tremendous impact of diabetes on its membership for years. In 1994, Kaiser was spending $3,300 additional dollars per member per year on care for its diabetic members in the Northern California region alone. About half of this was spent on acute and chronic complications. In monitoring the incidence of chronic illnesses, using the same criteria from 1996 to 2000, Kaiser has found no change in the prevalence of congestive heart failure, no change in the prevalence of coronary artery disease, but a 33 percent increase in the prevalence of diabetes over just the past 5 years.

Shortly after the August press release on DPP, CMI convened a meeting in Portland of clinicians, other providers, and health educators interested in obesity and diabetes. They developed short- and long-term themes on strategies for preventing obesity including (1) development of partnerships with schools, employers, government agencies, and academic researchers; (2) establishing collaborations with other health plans on coverage and incentive issues, such as employer-based incentive programs around weight management; and (3) establishing a national advisory group on overweight and obesity.

The Kaiser Permanente Clinical Network managed and supported by CMI will risk-stratify the overweight population, including the subgroups with decreased HDL, hypertension, IGT, and gestational diabetes, to direct intensive efforts toward those at high risk. Dr. Selby said it is doubtful that Kaiser Permanente will push now to identify the IGT population per se.

Kaiser's strategies for ongoing improvement include the clinical network to rapidly disseminate new findings as they are published or as Kaiser becomes aware of them. CMI intends to see research conducted on translation within its membership and its research centers funded by internal Requests for Applications (RFAs). Kaiser also hopes to partner with Federal and State-level demonstration projects.

Presentation of Risk Assessment Concept

Discussions during the morning presentations centered on which risk assessment measurement should be used (IGT or IFG), which test should be used (OGTT or FGT), or whether there is another profile or test that could be used for risk assessment. It was suggested that a possible risk assessment model based on BMI and other factors might provide enough of a profile to justify lifestyle intervention for a subset of the population and further screening for another subset thought to be at higher risk. Before the group recessed for lunch, Dr. Allen Spiegel offered the following risk assessment concept that could be used for the afternoon discussions. He suggested that this tool could be Internet-based.

A potential at-risk group would be identified based on a weight and family history profile. The total group would then be stratified into low, middle, and high subgroups according to each person's risk assessment profile. Parameters would need to be defined for this stratification, and guidelines would be needed for each subgroup. For those placed in the low-risk subgroup, the guideline might be that there is no problem. For the middle subgroup, although it is arguable, some form of lifestyle counseling might be needed, such as the doctor simply advising them to lose weight and exercise. These persons would not be tested or receive medication.

In Dr. Spiegel's concept, persons in the high-risk subgroup would be screened for glucose tolerance. If the test indicated the person was in the normal range, then a retest would be done at some interval (e.g., 3 years). If the test showed the person was diabetic, then treatment would be necessary. If the test indicated the person was pre-diabetic according to the criteria established, then intervention would be required, either lifestyle or medication.

The ADA/NIDDK position statement on the result of recent prevention studies including the DPP recommends lifestyle intervention be tried first. What the lifestyle intervention would be and how it would be provided would have to be determined. There is a continuum in glucose intolerance to a point where diabetes is present. There may also be a continuum where exercise and diet are no longer effective enough to prevent diabetes without the assistance of medication.

DMICC Agency Actions and Perspectives

The plans and viewpoints of several of the DMICC agencies were presented by their representatives: Dr. Judith Fradkin, NIDDK; Dr. Daniel Stryer, Agency for Healthcare Research and Quality (AHRQ); Dr. Steve Phurrough, Centers for Medicare & Medicaid Services (CMS, formerly HCFA); Dr. David Stevens, Health Resources and Services Administration (HRSA); Dr. Kelly Acton, Indian Health Service (IHS); Dr. Leonard Pogach, U.S. Department of Veterans Affairs (VA); Dr. Frank Vinicor, CDC; and Dr. Jean Flagg-Newton, National Center for Minority Health and Health Disparities (NCMHD). The panel's presentations are summarized here.

NIDDK

Dr. Judith Fradkin, Director, Division of Diabetes, Endocrinology ,and Metabolism, NIDDK, stated that NIDDK is working with the ADA, CDC, and NDEP to translate the DPP results. There also are opportunities for collaboration among the DMICC members. One major NIDDK focus of translational research is R18s for demonstration-and evaluation-projects. These programs test clinical trial results with specific populations in the community setting.

The current R18 program announcement is focused on developing cost-effective strategies for improving treatment of patients with diabetes. NIDDK plans to reissue that R18 with several other components of the NIH and CDC and ADA. The re-issued version will continue the focus on improving care for people with diabetes, but it will now stress many of the research goals identified in the ADA/NIDDK position paper appearing in the April issue of *Diabetes Care*. The program announcement will incorporate many of the issues discussed at this meeting. Applications will be accepted three times a year following the standard R01 receipt date schedule. A special study section will be convened by the NIDDK review branch and meet three times annually.

Another NIDDK new initiative focuses on prevention of type 2 diabetes in children. NIDDK has been working with CDC to define the extent of impaired glucose tolerance and of type 2 diabetes in children. Given the anecdotal evidence and now the DPP science-based evidence for adults, the Institute felt it important to investigate methods for prevention of type 2 in children. Rather than the medical model used in DPP, this will be a public health-focused initiative. It will target school-based interventions that stress increased physical activity and dietary education. The outcome to be measured will be some form of metabolic outcome, such as reaching a glycemic threshold, rather than actual development of diabetes. Sites have been selected, and the first steering committee meeting has been held.

A third effort is benchmarking what we are achieving in translation through CDC's NHANES, the mechanism by which we know what is happening in the Nation and how well we are succeeding or failing in terms of reducing risk or treating persons with diabetes. NIDDK has long provided data collection support of NHANES. Following NHANES III, NIDDK stopped supporting glucose tolerance tests and supported fasting blood glucose measures, based on ADA's changed recommendations for diagnosis. Now NIDDK would like to hear from the community if that decision should be reviewed and oral glucose tolerance tests now be used for NHANES to monitor the prevalence of impaired glucose functioning.

AHRQ

Dr. Daniel Stryer, Medical Officer and Internist, Center for Outcomes and Effectiveness Research, Agency for Healthcare Research and Quality, explained that AHRQ is the Federal Government's organizational home for research on the delivery of health care. Quoting Andrew Balas, a researcher at the University of Missouri, Dr. Stryer said, "It takes 17 years to turn 14 percent of original research to the benefit of patient care." Dr. Stryer listed the following DPP-related activities as part of AHRQ's discretionary programs:

- The U.S. Preventive Services Task Force, an independent panel of experts that reviews the evidence of effectiveness and develops recommendations for preventive practices, reviewed the DPP and recommended diet and exercise changes, but not screening.

- AHRQ's Put Prevention Into Practice (PPIP) develops tools and resources for clinicians, office staff, and patients. They will be creating diet and exercise materials to incorporate the DPP message.

- The Office of Health Care Information will add DPP to its present prevention activities portfolio.

Dr. Stryer also mentioned his agency would welcome any submissions to a new RFA being issued in partnership with the VA for AHRQ's Translating Research Into Practice (TRIP) portfolio. Another TRIP RFA in partnership with HRSA will be coming out shortly to assess the Disparities Collaboratives, of which diabetes has been one, to find ways to improve their effectiveness and efficiency. There are also plans for a collaborative focused on diabetes prevention.

Information gained from the work of AHRQ's Excellence Centers to Eliminate Ethnic/Racial Disparities (EXCEED) should help implement the DPP message. Nine centers across the country are focused on understanding why disparities exist and identifying strategies to reduce or eliminate them. The University of Colorado center is looking at Native American health. Other programs are focused on risk communication and cultural competence. Other AHRQ community-based participatory research activities should also help in DPP translation by building on the strengths of these groups.

In closing, Dr. Stryer told the group of the sad loss the previous day of AHRQ's Director, Dr. John Eisenberg, with whom many of those present had worked over the years.

HRSA

Dr. David Stevens, Director of the Clinical Management and Professional Development Branch, Health Resources and Services Administration, presented a brochure and video, "Changing Practice, Changing Lives," to each DMICC member. Dr. Stevens stressed that HRSA realized that to get better results in diabetes, major system changes were needed. HRSA provides approximately 26 percent of the funding for community-controlled health centers offering comprehensive primary care to underserved, high-risk populations. Eighty percent are low income, more than 66 percent are below the Federal poverty level, and 40 percent are uninsured. A major goal is to reduce health disparities.

HRSA has identified four main areas in changing clinical care practices that Dr. Stevens stressed were very important. First is leadership; second is a documented model of care and a model for improvement and learning. Third is infrastructure, and fourth is strategic partnerships.

After the report of the DPP results, HRSA and CDC thought this provided a great opportunity for their health centers. They plan to set up an expert panel to develop concepts and evaluation measures for translating DPP recommendations into preventive care for the underserved, based on their diabetes primary care model. The centers' program will include weight reduction, exercise, and/or metformin. HRSA hopes to have a pilot established by the third quarter of 2002. The 9- to 12-month pilot will target their enrolled patients and other persons in their communities.

With their current resources plus other resources from CDC and a partnership with AHRQ, HRSA plans to integrate the DPP initiatives into a prevention collaborative currently being designed. If additional resources become available, they will develop a free-standing DPP prevention group, taking into account the complexities inherent in this effort. Either model—stand-alone or integrated—will be started by the latter part of 2002.

CMS

Dr. Steve Phurrough, Director of the Division of Medical and Surgical Services, Coverage and Analysis Group, Centers for Medicare and Medicaid Services, explained that one of his group's responsibilities is to recommend items for CMS coverage to the Secretary of DHHS. Diabetes issues have been prominent in their discussions the past couple of years and several new benefits have been added. When it comes to DPP translation, Dr. Phurrough had to say that there was not much CMS planned to do on this front. CMS buys health care for its 39 million beneficiaries, 34 million of whom are over age 65, based on what Congress tells CMS to purchase. Congress's specific requirements and specific limitations are basically limited to what is reasonable and necessary for the diagnosis and treatment of disease. Unless Congress directs CMS to provide a benefit over and above diagnosis and treatment of disease, it is not covered. Prevention, including screening, is a large category that generally is not paid for.

Currently DPP screening and interventions do not fit into a CMS benefit category. There does exist the potential for defining the risk state as a disease. Also, DPP may not be primary prevention, but rather secondary prevention for obesity, which is not currently a CMS disease. Secretary Thompson and former Surgeon General Dr. David Satcher rather took issue with that this past year, and there is discussion now at CMS on whether obesity is a disease. If obesity becomes defined as a disease, then there will be a whole host of new coverage decisions to define treatment and diagnoses associated with obesity. If this should happen, then treatment may fall in line with what DPP is recommending. The problem, obviously, in defining obesity as a disease is that the treatment of obesity in the Medicare population would cut physicians' income by 20 to 25 percent across the board to cover all the treatments that fall into the realm of treating obesity. Therefore, it is unlikely this will happen in the near future.

IHS

Dr. Kelly Acton, Director of the Indian Health Service National Diabetes Program, stated that IHS has a unique government-to-government relationship with American Indian and Alaska Native (AI/AN) Tribes. This puts constraints on the way IHS may do business with people. They may not dictate what will be done. The Tribes have considerable input about and control over their own health care.

As a federally funded primary health care agency, IHS takes both a public health and a clinical approach to diabetes. The program's basic components are conducting surveillance, describing the problem, providing standards of care and clinical guidelines generated from the bottom up, developing publications, and reviewing the science. A yearly diabetes care and outcomes audit looks at both process and outcomes measures around diabetes. A new activity has been the addition of 318 new diabetes grant programs under a special $100 million diabetes program funded through 2003 for American Indians. Since IHS is not a grant-issuing agency, monitoring 318 new grants has been a real adventure. The program priorities are set by local tribal communities. The director decided this was not going to be a top-down activity. Most communities are doing combinations of different preventions and two-thirds of the programs are doing primary prevention activities. Their efforts may have something significant to tell us about translating DPP activities at the local level.

Dr. Acton provided evidence that incidence and mortality from diabetes significantly disproportionately affect American Indians. Also rates in cardiovascular disease (CVD), for which diabetes is a risk factor, are decreasing in the overall U.S. population, but increasing in the AI/AN population. Fifty-six percent of cardiac events in American Indian men are in people with diabetes, and their relative risk of CVD mortality is 2.9. Seventy-eight percent of cardiac events in AI women occur in those with diabetes, and their relative risk of mortality is 3.8.

Other data provided by an epidemiologist from CDC shows that from 1990-98, there was a 6 percent increase in prevalence rates for diabetes in children under 15-years-old, a 68 percent increase in the 15-19 year-old group, a 47 percent increase in 20-24 year-olds, and a 50 percent increase in 25-34 year olds. IHS is deeply concerned about this trend in AI/AN youth. The National Diabetes Education Program, American Indian Subgroup, is working with focus groups to ask the youth how to get a message across to them, and they have provided some very insightful comments.

Dr. Acton researched the cost of care for diabetics and found that a few years ago managed care estimated the cost of treating diabetes was about $5,000 to $9,000 per person, per year. It has probably gone up. IHS currently cares for about 90,000 people with diagnosed diabetes, so a conservative estimate is that it should cost the Federal Government about $450 million a year. Unfortunately, the agency receives only $1,578 per person, per year, so there are significant economic disparities in terms of the ability to provide adequate diabetes care.

Since IHS and its providers already have difficulty handling the current volume of patients with diagnosed diabetes, they are concerned about how they can translate the DPP results. As an underfunded agency working with a unique, primarily rural, population, IHS must be creative to translate the DPP results into something meaningful. The agency would like to enhance the current lifestyle programs in prevention. Could the non-clinical part of DPP be done by trained community mentors or lay persons? They are also talking about how to adjust their pharmacy budgets to buy metformin when the budgets cannot afford other drug therapies at this time.

Dr. Acton said the agency's short-term plans for DPP translation included a press release sent to the Indian press and published around the country in all the Indian newspapers. DPP will be featured at the National Tribal Leaders Diabetes Conference in Denver in December 2002. Focus groups have been held at four sites and interviews been done with American Indian participants of the DPP. A special edition of *Health for Native Life* focuses on DPP and features DPP celebrities within American Indian communities. These celebrities tell how they accomplished the interventions to inspire people and give a positive message about what DPP could mean to the individual in American Indian communities.

IHS long-term plans include participating in discussions like those at the DMICC meeting to define screening criteria and resolve other issues. The agency wants to use experience being gained from the grant programs and other programs to develop lifestyle activities specific to AI/AN communities, based on best practices or promising practices. They will also be working to expand the funding base to be able to purchase pharmacy supplies and equipment, fitness equipment, and so forth.

Dr. Acton said that, personally, she feels DPP means HOPE to AI/AN communities. There is so much fatalism in the communities about diabetes. "You are just going to get it. There's nothing you can do." Hopefully, DPP can change this mindset by projecting a positive message. It can say, "This is not the same old story because now we have proof that diet and exercise work."

In the discussions on translating the research, Dr. Acton emphasized that since diabetes tends to occur within families, a method that has worked in the AI/AN communities to change behavior has been to relate it to preventing diabetes and its complications in the children.

VA

Dr. Leonard Pogach, National Program Director for Diabetes, U.S. Department of Veterans Affairs, presented the perspective of the Nation's largest integrated health care system. Its Chief Medical Officer is the Undersecretary for Health, who reports to the DHHS Secretary. The VA treated 3.3 million veterans in Fiscal Year 2000. The number is closer to 4 million now, approximately 15 percent of the Nation's veterans. The median age of a U.S. veteran is about 59. Thirty-eight percent were over 65 in 2000, which is a larger percentage than in the general U.S. population. Women and African-Americans tend to be younger than the white, male population, probably reflecting changes in the military over the past several decades. The health care agency uses an enrollment system with a global budget and the effect of a capitation system. In a sense, it is a giant staff model HMO for patients who are largely, but not completely, economically challenged. Their indigent population, many of whom are minorities, is larger than that of most other health care systems.

As a corollary to DPP, Dr. Pogach cited the 4S Study reported by Hafner and Herman in 1999. In a subgroup of persons with impaired fasting glucose, simvastatin significantly reduced the number of major coronary events, revascularizations, and total and coronary mortality. The significance is the relationship of IFG and cardiovascular disease, which is the major cause of morbidity and mortality in diabetes. Dr. Pogach added that the efficacy of aggressive blood pressure and cholesterol control in preventing morbidity and mortality in an IFG population also needs further study.

According to Dr. Pogach, there are several unresolved issues for the VA in translating the DPP results to its patients. The VA is dealing with an older population, with persons who have a number of disabilities that might interfere with lifestyle interventions, and with persons who are sick to begin with. The agency provides health care for about 750,000 people with diabetes. Some 1.2 or 1.5 million people with diabetes receive care in the combined. U.S. Department of Defense/VA care systems. Dr. Pogach estimated that there are roughly 1.8 million veterans who are not being treated for diabetes.

The agency is considering opportunistic screening for impaired fasting glucose in veterans with other DPP risk factors, but is not prepared to use the OGTT yet. VA expects to find that a lot of their patients will have the DPP risk factors. Fortunately, VA already provides access to dietary and lifestyle education. They also distribute and share NDEP materials. A prime issue is how to apply the DPP intervention, which was rather intensive, to the VA patient population. Use of metformin will be a fairly convenient option. However, for those over 60 and with lower BMIs, this was not shown to be a very effective intervention. Dr. Pogach felt that it was very important to vigorously identify and treat hyperlipidemia and hypertension in this same population.

To assist with DPP translation, VA has an active health services research and development program. Dr. Pogach indicated that for an issue of this magnitude, it probably would be possible to get service-directed research to study it. Investigators can obviously put in for individual grants at any time. Another asset the VA can offer is in terms of its established performance measurement system and computerized electronic medical records. They have a metric to identify individuals who should be targeted for screening and how they should be targeted. Based on their experience, they can quickly and cost-effectively develop and validate a performance measurement and collect data on how well a care mechanism is performing. Their electronic medical records system has computerized reminders that can embed health factors, such as medical risk factors or conditions that do not have codes, and then extract that data from the system. This capability is something that the VA could provide in collaboration with its Federal partners.

CDC

Dr. Frank Vinicor, Director of Diabetes Translation, Centers for Disease Control and Prevention, spoke of primary prevention from a public health standpoint. Specific CDC prevention activities for 2002 include:

- Developing population-based methods for identifying persons at very high risk.
- Conducting formative research through focus groups on views of primary prevention in collaboration with NDEP.
- Supporting demonstration projects with the CDC-funded Diabetes Control Programs and Community Health Centers.
- Serving as purchaser/insurer of a possible TRIAD pilot project exploring managed care and primary prevention.
- Establishing an international work group with the Finnish group on primary prevention in diabetes.
- Collaborating with NIH programs such as the DPP extension and "Environmental Approaches to Obesity."
- Expanding economic studies of primary prevention, such as the cost implications of possibly screening for unrecognized diabetes and IFG and IGT.

Dr. Vinicor was emphatic in expressing his CDC division's role as a leader in the public health community in diabetes. He insisted that the group must stick with the DPP science and what works. The impact that the power of science from DCCT and UKPDS had on policymakers should not be underestimated. An important issue is what investment in diabetes prevention are people, who do not see themselves as direct stakeholders, going to be willing to make. Also, what investment are providers willing to make?

There is a very large population at risk and there is not a huge amount of money in any group to translate the DPP findings. Increasing the caseload from 16 million persons with diabetes to 10 or 20 million at risk will be a challenge. If one case manager in the DPP took care of 20 or 25 people, and if the lifestyle intervention could be modified so that one case manager could take care of 100 people, 50,000 case managers would be needed to handle the minimum 10 million people with impaired glucose tolerance. The country does not have 50,000 additional case managers. There certainly are not the resources to take on 200 million people in this country. Like the bank robber Willie Sutton and the researcher Doctor Baruch Blumberg, going to where the money is, where the action is, and where the most likely effect can take place is the thing to do.

Another reason for targeting a DPP-type population is that there is not science to support that these interventions are "good for everyone," that they will prevent a whole array of diseases. Dr. Vinicor cited a study done in England in which ethicists looked at the quality of the evidence needed to make a difference for persons on a spectrum from terminal to healthy. A quality value of only 20 was satisfactory to the terminally ill but a value of 80 was needed for those at risk to pay attention and 90 was required by the healthy person. This again demonstrates the importance of the DPP science and the importance of applying it accurately.

Dr. Vinicor stressed it is essential to focus on what is known and what works and build on that beginning. What works best in public health efforts is using multi-faceted approaches. He said being an active partner with others in cardiovascular disease and obesity is okay, but that is not the primary role of those whose assigned area of public health responsibility is diabetes. Their role is to focus on and lead the DPP translation effort to prevent diabetes. Finally, Dr. Vinicor said, "We need to go slowly and move fast."

NCMHD

Dr. Jean Flagg-Newton, Deputy Director of the National Center on Minority Health and Health Disparities, said that NCMHD's vision is that there will be an America in which all populations will have an equal opportunity for long, healthy, and productive lives. In its first year, the Center has spent considerable time focusing on congressionally mandated programs, completing the development of the trans-NIH strategic plan on research to address and eliminate health disparities, and working to establish its Centers of Excellence networks across the country.

The law that established the Center was very specific in terms of the activities that NCMHD would carry out. There is a two-fold focus. First, the group is to continue the collaborations that the previous Office of Research on Minority Health had established. Those collaborations are primarily with the other NIH institutes and centers (ICs). There are also partnerships with AHRQ for their EXCEED Program and the CDC Reach 2010 Programs. Secondly, NCMHD has a mandate to develop independent programs focused on research, particularly in the areas of biomedical research, biobehavioral research, and the social sciences.

NCMHD was a partner with NIDDK in support of the DPP Program, as well as other programs related to diabetes in terms of research and capability building. It is now the Center's policy that the trans-NIH Strategic Plan on Health Disparities will guide its collaborations with the other NIH ICs. NIDDK's portion includes the DPP followup and another major initiative with a focus on racial and ethnic disparities in the incidence of diabetes and its complications. Dr. Flagg-Newton confirmed that NCHMD will certainly be working with NIDDK in these areas. NCHMD is also looking at what research needs to be initiated that is not now being done. Dr. Flagg-Newton promised that they will be looking at those areas in terms of future translation efforts. One of the areas that NCHMD might support would be research in why sustainability is a problem.

In summary, Dr. Flagg-Newton encouraged everyone to evaluate the proposed strategies for translation and guard against thinking that a one-size-fits-all translation program will yield equally successful results across all racial and ethnic groups.

Discussion Summary

Questions and lively discussions on the issues and challenges of translating the DPP findings took place after each of the presentations. The comments and recommendations centered on the following questions:

- What should the risk be named?
- Who is the target audience?
- How should the at-risk group be identified?
- How should the at-risk person be treated?
- What translation strategies are most effective?
- What are the challenges?

What Should the Risk Be Named?

Selecting the correct name for the risk that was responsive to the DPP interventions was thought to be crucial for implementing the DPP science, for reimbursement, and for the impact of the message on providers, persons at risk, payers, and policymakers. Of the many terms suggested (pre-diabetes, impaired glucose tolerance, hyperglycemia, homeostatis dysregulation), pre-diabetes seemed to provide the most promise. "Treating pre-diabetes" was deemed more apt to be taken seriously than "preventing diabetes."

Who Is the Target Audience?

Focusing on a high-risk population similar to that of the DPP trial was thought to have the greatest potential for success in translating the DPP results. Although "eat right and exercise" is good common sense and a message Americans have been hearing from many quarters in the past decade, it was felt that to make the DPP translation a general population appeal would dilute its impact and effectiveness. First, the current messages about behavior modification have been disappointingly ineffective. Second, the DPP results occurred with a selected high-risk group of persons who were overweight, had impaired glucose metabolism, and a family history of diabetes. Targeting a similar group from the 10 to 20 million at-risk persons will be more effective than targeting the entire U.S. population or even only those who are overweight. Other target groups should be health care providers, friends and families of this high-risk group, especially racial and ethnic minorities, and persons with diabetes and their supporters. Primary targets to assist in delivering the message would be the media, community-and faith-based groups, local and State governments, and employers.

How Should the At-Risk Group Be Identified?

The discussion centered on the risk assessment concepts presented before the lunch break by Dr. Spiegel and described above. For those persons considered at high risk, there is the issue as to whether they should be screened for glucose tolerance levels, and, if so, which test should be used. The OGTT tends to be the more reliable for identifying those with diabetes. On the other hand, an overnight fasting glucose test, currently being used under ADA guidelines for identifying diabetes, is less expensive. Other questions included: What parameters should be set for each of the tests? What will happen if the values identifying pre-diabetes change as they have done for both diabetes and hypertension? Is there a different test that could be used? Another issue was that it is unlikely that either test would be reimbursable for an at-risk rather than disease condition.

Some concern was expressed about categorizing the at-risk population. One problem in presenting people with categories is the tendency to think, "Well, I'm in the lower end, so that's okay for now" or "I'm a little bit in the upper part, but I'm on the lower end of the upper part." In other words, people tend to think "I'm sick or I'm healthy."

How Should the At-Risk Person Be Treated?

If the person is in the IGT- or IFG-positive group, by whatever test, then he or she already has increased cardiovascular disease risk and increased risk of developing frank diabetes, but it is not inevitable. The group felt that the cholesterol paradigm was very relevant. The significance at this point is that type 2 diabetes is very difficult to treat and may, at some stage, be irreversible because of beta cell failure.

In DPP, the lifestyle modification was generally the better intervention in all groups, but it was emphasized that medication as an intervention should not be dismissed. Both the DPP younger group and those who were more obese responded equally well to metformin and lifestyle intervention. It is also important to consider people's biases regarding medication or behavior changes.

There was concern that prescribing the comprehensive lifestyle intervention as practiced in the DPP trial would be unrealistic, too expensive, and probably not reimbursable under our health care system. Possibilities outside the private and public health care system were suggested such as community-based programs in schools and senior centers, advocacy group sponsorship, faith-based sponsorship, employer-sponsored programs, and Federal and State-supported prevention centers. Advocacy groups, private foundations, and the fitness, exercise, and food industries might also be sources of some financial support. An example given was the smoking cessation partnerships between physicians and the heart and lung associations.

What Translation Strategies Are Most Effective?

The group agreed that translating research results is always a daunting task. The greatest asset in the current case is DPP's science and impressive results. The science and its relationship to the risk can hopefully cut through the crowd of health care messages being issued today. A multi-faceted approach was deemed necessary. The messages should highlight that a very modest weight loss of only 10 to 15 pounds and walking 5 days a week can reduce one's risk by more than 50 percent. While emphasizing the benefits to be gained from modest behavior changes, the messages to health care providers should not neglect the importance of the metformin intervention.

The following are some of the group's recommendations:

- Keep the message simple and focused.
- "Brand" the lifestyle intervention; make it desirable from a health, not looks, point of view; make it feel achievable.
- Be clear that "eat well and exercise" might be a good message for everyone, but for the targeted group it is of extreme importance to prevent a serious disease.
- Partner with other agencies and other organizations, especially local groups.
- Rely on the willingness of adults to change their habits to benefit and protect their children and other family members even when they are reluctant to work to benefit themselves. This has been especially true in racial/ethnic groups.
- Use media avenues specific to professional and cultural groups.
- Test messages and programs with focus groups and ask for their suggestions.
- Leverage support from celebrity spokespersons and the fitness, sports equipment, and food industries.
- Imitate the health care marketing tactics of the pharmaceutical industry but with a smaller budget.
- Develop tools for at-risk persons to help them achieve and maintain their goals. Suggestions included a simple chart to show them they need to lose less weight than they probably think they do; recipes for lower-fat, lower-calorie foods that taste great; and a pedometer to track their 2,000 steps a day.
- Develop guidelines, tools, and toolkits for providers and other health professionals to help them assess and counsel their overweight patients.
- Develop toolkits to help local groups set up and sponsor their "DPP Lite" program.
- Use the Internet. Ensure important websites are easily found through search engines.
- Work with other Federal and State agencies to provide financial assistance, such as a tax break or part of the spa fee, to help the at-risk person carry out the lifestyle intervention.
- Work with other agencies through their programs, such as the food stamp program and the school food program, to provide access to lower-calorie, lower-fat, more nutritional food.
- Work with other agencies to increase physical activity at school and the workplace.
- Work with insurers and payers, decisionmakers and policymakers to determine the benefits of prevention over the difficulties and high cost of treating diabetes and to find ways to apply these interventions to stem the diabetes epidemic.

What Are the Challenges?

Marketing behavior change is a difficult task. The needed lifestyle changes will be up against society's current super-size everything and sedentary habits at work and at home. The message cannot come across as the same old/same old. It must clearly get across the seriousness of the targeted individual's ignoring the risk and not taking advantage of the interventions. Focusing the message and relying on the science are crucial to move over or around these obstacles. Implementing and funding the interventions will require support outside the health care system. People live in families, cultural groups, and communities; therefore, these groups can inhibit or facilitate behavior change. It will be necessary to raise awareness, motivate them, and rely on their resources and influence.

People are not afraid of cholesterol per se. They are afraid of heart disease. The association between the risk factors—being overweight, inactive, having impaired glucose function, family history, cultural background, and age—will have to be clearly associated with the consequences of having diabetes and heart disease.

Common perceptions are that one must lose a lot of weight to do any good, that any weight loss is very difficult to achieve, and it cannot be maintained. Inexpensive ways to highlight that a minor weight loss is effective and to provide motivation, support and encouragement will be needed. People are already spending millions of dollars on diet books and weight loss drinks and alternative drugs, and so on, but sustaining weight loss is what is proving to be the big failure and the big challenge.

Translational research messages take time to filter down. Patience, persistence, and creativity will be needed.

Framework for Action and the Road Ahead

The attendees agreed that the Diabetes Prevention Program has provided the group with an excellent opportunity to help stem the epidemic in type 2 diabetes. Consensus was achieved on the following elements in the development of a framework for action for the road ahead:

- Choose the appropriate term, pre-diabetes, to create recognition of the risk factor.
- Focus on a high-risk population similar to that of the DPP volunteers.
- Provide risk assessment testing and interventions as inexpensively as possible.
- Develop a multi-faceted translation approach.
- Establish partnerships and collaborations, especially at the community level.

The DMICC members are taking steps to translate the DPP science-based findings. Dr. Fradkin encouraged the DMICC members and others present to build on their current collaborations and partnerships to translate the DPP research. She spoke enthusiastically about NIDDK's newly designed initiatives and planned efforts in partnership with ADA and CDC. Dr. Fradkin also pointed out that it was important to remember that impaired glucose tolerance is a significant risk factor for cardiovascular disease, not the two- to four-fold risk that diabetes is, but a 50 percent elevation, which is substantial.

Dr. Spiegel summed up the success of the day's work by noting that many entities came together to discuss the road ahead in a challenging and productive way. He stressed that the fact that diabetes is very difficult and costly to treat is a compelling reason for primary prevention. In referring to Dr. Phurrough's presentation, he pointed out that both financial and human resources are needed to respond to the opportunity and challenge of translating the DPP results to clinical practice. On the other hand, some $18 billion a year is being spent on health care for end-stage renal disease (ESRD), 45 percent of which is largely due to type 2 diabetes. As the numbers of persons with diabetes continue to grow, it can be projected that this ESRD burden will also grow.

Dr. Spiegel said that costs saved by preventing or delaying diabetes and its complications cannot be saved immediately, and it is still unknown just how effective the DPP interventions will be in the long run, but it is daunting to consider what the numbers and costs will be if we do not at least try. He agreed that further followup and analysis are needed.

Dr. Garfield adjourned the meeting at 3:20 p.m.

Participants

Beena Akolkar
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
Two Democracy Plaza, Room 681
6707 Democracy Boulevard
Bethesda, MD 20892
Tel: (301) 594-8812
Fax: (301) 480-3503
ba92i@nih.gov

Richard Anderson, MD, PhD
Program Director, Division of Genetics
and Developmental Biology
National Institutes of Health
45 Center Drive, MSC 6200, Room 2AS-25
Bethesda, MD 20892-6200
Tel: (301) 594-0943
Fax: (301) 480-2228
andersor@nigms.nih.gov

Nell Armstrong, PhD, RN
Program Director
National Institutes of Health
Building 45, Room 3AN-12
45 Center Drive, MSC 6300
Bethesda, MD 20892-6300
Tel: (301) 594-5973
Fax: (301) 480-8260
nell_Armstrong@nih.gov

Kate Berg, MD, MPH
Deputy Scientific Director
National Institutes of Health
31 Center Drive, MSC 2152
Bethesda, MD 20892-2152
Tel: (301) 594-2481
Fax: (301) 402-2040
kab@helix.nih.gov

Perry Blackshear, MD, Dphil
Director, Office of Clinical Programs
National Institutes of Health
PO Box 12233
NIEHS, MD A2-05
RTP, NC 27709
Tel: (919) 541-4899
Fax: (919) 541-4571
black009@niehs.nih.gov

Susan J. Blumenthal, MD, MPA,
U.S. Assistant Surgeon General
200 Independence Avenue, SW
Room 719H
Washington, DC 20201
Tel: (202) 260-2255
SBlumenthal@osophs.dhhs.gov

Patricia S. Bryant
Director, Behavior, Health Promotion
and Environment Program
National Institutes of Health
Building 45, Room 4AN-24, MSC 6402
Bethesda, MD 20892-6402
Tel: (301) 594-2095
Fax: (301) 480-8318
bryantp@de45.nidr.nih.gov

Joan Chamberlain
Science Writer
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
31 Center Drive
Building 31, Room 9A04
Bethesda, MD 20892
Fax: (301) 496-7422
Tel: (301) 435-8112
chamberlainj@extra.niddk.nih.gov

Emily Chew, MD
National Eye Institute
National Institutes of Health
Building 31, Room 6A52
31 Center Drive
Bethesda, MD 20892
Tel: (301) 496-6583
Fax: (301) 496-2297
eyc@nei.nih.gov

Michelle A. Cissell, PhD
AAAS/NIH Science Policy Fellow
Office of Scientific Program
and Policy Analysis
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
9000 Rockville Pike
Building 31, Room 9A05
Bethesda, MD 20892-2560
Tel: (301) 496-6623
Fax: (301) 480-6741
CissellM@extra.niddk.nih.gov

Elaine Collier, MD
Centers Program Director
Division of Allergy, Immunology,
and Transplantation
National Institutes of Health
Soar Building, Room 4a20
9000 Rockville Pike
Bethesda, MD 20892-7640
Tel: (301) 496-7104
Fax: (301) 402-2571
ecollier@niaid.nih.gov

Peter Dudley, PhD
Director, Retinal Diseases Program
National Institutes of Health
6120 Executive Boulevard, Suite 350
Rockville, MD 20892
Tel: (301) 496-0484
Fax: (301) 402-0528
pad@nei.nih.gov

Chhanda Dutta, PhD
Chief, Musculoskeletal Section and Nutrition,
Metabolism, Gastroenterology Section
Geriatrics Program
National Institutes on Health
7201 Wisconsin Avenue, Suite 3E327
Bethesda, MD 20893
Tel: (301) 435-3048
Fax: (301) 402-1784
cd23z@nih.gov

Mark Eberhardt, PhD, Epidemiologist
National Center for Health Statistics
6525 Belcrest Road, Room 730
Hyattsville, MD 20782
Phone (301) 436-5979, x142
Fax (301) 436-8459
mse1@cdc.gov

Marguerite Evans
Health Science Administrator
6707 Democracy Boulevard, Room 106
Bethesda, MD 20892-5475
Tel: (301) 402-5860
Fax: (301) 480-3621
evansm@od.nih.gov

Jean L. Flagg-Newton, MD
Deputy Director
National Institutes of Health
2 Democracy Plaza
6707 Democracy Boulevard, Suite 800
Bethesda, MD 20892
Tel: (301) 402-1366
Fax: (301) 402-7040
flaggnej@od.nih.gov

Julia Freeman, PhD
Chief, Autoimmunity Section
National Institutes of Health
Building 45, Room 5AS-19F
45 Center Drive, MSC 6500
Bethesda, MD 20892-6500
Tel: (301) 594-5052
Fax: (301) 480-4543
freemanj@ep.niams.nih.gov

Joanne Gallivan
Director
National Diabetes Education Program
National Institutes of Health
Building 31, Room 9A04
31 Center Drive
Bethesda, MD 20892
Tel: (301) 496-6110
Fax: (301) 496-7422
joanne_gallivan@nih.gov

Rachel Greenberg
Hager Sharp
RGreenbe@hagersharp.com

Sanford Garfield, PhD, Senior Advisor,
Biometrics and Behavioral Science
National Institute of Diabetes and
Digestive and Kidney Diseases
National Institutes of Health
Two Democracy Plaza, Room 685
6707 Democracy Boulevard
Bethesda, MD 20817
Tel: (301) 594-8803
Fax: (301) 480-3503
garfields@extra.niddk.nih.gov

Gilman D. Grave, MD
Chief, Endocrinology, Nutrition
and Growth Branch
National Institutes of Health
9000 Rockville Pike
Bethesda, MD 20890
Tel: (301) 496-5593
Fax: (301) 480-9791
gg37v@nih.gov

Robert D. Hammond, PhD
Director, Division of Extramural Activities
National Institute of Diabetes
and Digestive and Kidney Diseases, NIH
Two Democracy Plaza, Room 715
6707 Democracy Boulevard
Bethesda, MD 20892-5456
Tel: (301) 594-8834
Fax: (301) 480-4125
hammondr@extra.niddk.nih.gov

Joan Harmon, PhD
Senior Advisor for Program & Acting Director,
Division of Bioengineering
National Institutes of Health
Building 31, Room 1B37, MSC 2077
Bethesda, MD 20892-2077
Tel: (301) 451-6772
Fax: (301) 480-4515
harmonj@nibib.nih.gov

Elke Jordan, PhD
Deputy Director
National Human Genome ResearchInstitute
National Institutes of Health
31 Center Drive, MSC 2152
Bethesda, MD 20892-2152
Tel: (301) 496-0844
Fax: (301) 402-0837
elkej@mail.nih.gov

Mary Beth Kester
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
31 Center Drive
Building 31, Room 9A05
Bethesda, MD 20892
Tel: (301) 496-6623
Fax: (301) 480-6741
kesterm@extra.niddk.nih.gov

Jag H. Khalsa, PhD
Pharmacologist Health Administrator
Center on AIDS and other Medical
Consequence of Drug Abuse (CAMCODA)
National Institute on Drug Abuse
6001 Executive Boulevard
Room 5098, MSC 9593
Bethesda, MD 20892-5953
Tel: (301) 443-1801
Fax: (301) 443-4100
jk98p@nih.gov

Richard Knazek, MD
Medical Officer
Center for Research Resources
National Institutes of Health
6705 Rockledge Drive
Rockledge 1, Room 6128
Bethesda, MD 20892
Tel: (301) 435-0790
Fax: (301) 480-3661
richardk@ncrr.nih.gov

Natalie Kurinij, PhD
Program Director
Collaborative Clinical Research,
Division of Extramural Research
National Eye Institute
National Institutes of Health
Executive Plaza South, Room 350
6120 Executive Boulevard
Rockville, MD 20852
Tel: (301) 496-5983
Fax: (301) 402-0528
kurinij@nei.nih.gov

John P. Lanigan
Health Insurance Specialist
Office of Professional Relations
Centers for Medicare & Medicaid Services
Hubert Humphrey Building
Room 435H
Washington, DC 20201
Tel: (202) 690-7418
Fax: (202) 401-7438
jlanigan@hcfa.gov

Saul Malozowski, MD, PhD, MBA
Division of Diabetes, Endocrinology
and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
Two Democracy Plaza, Room 679
6707 Democracy Boulevard
Bethesda, MD 20892
Tel: (301) 451-4683
Fax: (301) 480-3503
sm87j@nih.gov

Nancy E. Miller, PhD
Senior Science Policy Analyst
Office of the Director
National Institutes of Health
Building 1, Room 218
Bethesda, MD 20892
Tel: (301) 594-7742
Fax: (301) 402-0280
nm68k@nih.gov

Peter Muehrer, PhD
Chief, Health and Behavioral Science
Research Branch
Division of Mental Disorders,
Behavioral Research and AIDS
National Institute of Mental Health
National Institutes of Health
6001 Executive Boulevard, Room 6189
MSC 9615
Bethesda, MD 20892-9615
Tel: (301) 443-4708
Fax: (301) 480-4415
pmuehrer@mail.nih.gov

Paul L. Nichols, PhD
Program Director, Systems
and Cognitive Neuroscience Program
National Institute of Neurological
Disorders and Stroke
National Institutes of Health
6001 Executive Boulevard, Room 2118
Rockville, MD 20892
Tel: (301) 496-9964
Fax: (301) 402-2060
pn13w@nih.gov

Vishnudutt Purohit, PhD
National Institute on Alcohol Abuse and Alcoholism
National Institutes of Health
6000 Executive Boulevard, Suite 402
Bethesda, MD 20892
Tel: (301) 443-2689
Fax: (301) 594-0673
vpurohit@willco.niaaa.nih.gov

Peter J. Savage, MD
Acting Director, Division of Epidemiology
and Clinical Applications
National Heart, Lung and Blood Institute
National Institutes of Health
Rockledge 2, Room 8104
Bethesda, MD 20817
Tel: (301) 435-0421
Fax: (301) 480-1864
savagep@nhlbi.nih.gov

Shaio-Wei Shen, MD
Medical Officer
Division of Metabolism
and Endocrine Drug Products
Food and Drug Administration
Parklawn Building, Room 14B-04
5600 Fishers Lane, HFD-510
Rockville, MD 20857
Tel: (301) 827-6378
Fax: (301) 443-9282
shen@cder.fda.gov

Elliot R. Siegel, PhD
Associate Director of Health Information
Program Development
National Library of Medicine
National Institutes of Health
8600 Rockville Pike
Bethesda, MD 20817
Tel: (301) 496-8834
Fax: (301) 496-4450
siegel@nlm.nih.gov

Philip Smith, PhD
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Two Democracy Plaza, Room 693
6707 Democracy Boulevard
Bethesda, MD 20892
Tel: (301) 594-8816
Fax: (301) 480-3503
smithp@extra.niddk.nih.gov

Mehrdad Tondravi, PhD
Program Director
National Institute of Diabetes and Digestive and Kidney Diseases
National Institutes of Health
Two Democracy Plaza, Room 603
6707 Democracy Boulevard
Bethesda, MD 20892
Tel: (301) 451-9871
Fax: (301) 480-3503
TondraviM@extra.niddk.nih.gov

Elizabeth Warren-Boulton
Hager Sharp
Elizab@aol.com

Violet Ryo-Hwa Woo, MS, MPH
Program Analyst
Office of Minority Health
U.S. Department of Health and Human Services
5515 Security Lane, Suite 1000
Rockville, MD 20852
Tel: (301) 443-9923
Fax: (301) 443-8280
vwoo@osophs.dhhs.gov

Speakers

Kelly Acton, MD, MPH
Director, National Diabetes Program
Indian Health Service
5300 Homestead Road, North East
Albuquerque, NM 87110-1293
Tel: (505) 248-4182
Fax: (505) 248-4188
Kelly.Acton@mail.ihs.gov

Kathy J. Berkowitz, RN, CS, FNP, CDE
President
Grady Health System, Diabetes Unit
American Association of Diabetes Educators
69 Butler Street South East
Atlanta, GA 30303
Tel: (404) 616-3722
Fax: (404) 616-3717
kberkow@emory.edu

Charles Clark, MD
Professor of Medicine
Indiana University School of Medicine
6055 Sunset Lane
Indianapolis, IN 46228
Tel: (317) 554-0139
Fax: (317) 554-0092
chclark@iupui.edu

Ned Calonge, MD, MPH
Chief Medical Officer
Colorado Department
of Public Health and the Environment
4300 Cherry Creek Drive South
Denver, CO 80246
Tel: (303) 692-2622
Fax: (303) 691-7702
ned.calonge@state.co.us

Jean L. Flagg-Newton, MD
Deputy Director
National Center on Minority Health
and Health Disparities
National Institutes of Health
2 Democracy Plaza
6707 Democracy Boulevard, Suite 800
Betheda, MD 20892
Tel: (301) 402-1366
Fax: (301) 402-7040
flaggnej@od.nih.gov

Judith Fradkin, PhD
Director, Division of Diabetes,
Endocrinology, and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases, NIH
Two Democracy Plaza, Room 689
6707 Democracy Boulevard
Bethesda, MD 20892
Tel: (301) 594-8814
Fax: (301) 480-3503
fradkinj@ep.niddk.nih.gov

Richard Kahn, PhD
Scientific Chief Medical Officer
American Diabetes Association
1701 North Beauregard Street
Alexandria, VA 22311
Tel: (703) 549-1500 ext 2065
Fax: (703) 836-7439
rkahn@diabetes.org

David Marrero, PhD
Indiana University Diabetes Training
and Research Center
250 University Boulevard, Room 122
Indianapolis, IN 46202
Tel: (317) 278-0905
Fax: (317) 278-0911
dgmarrer@iupui.edu

David M. Nathan, MD
Study Chairman and Principal Investigator
Diabetes Prevention Program
55 Fruit Street
Boston, MA 02114
Tel: (617) 726-2875 or (617) 726-2066
Fax: (617) 726-6781
dnathan@partners.org

Steve E. Phurrough, MD, MPA
Director, Division of Medical
and Surgical Services
Coverage and Analysis Group
7500 Security Boulevard
Baltimore, MD 21244
Tel: (410) 786-2281
Fax: (410) 786-9286
Sphurrough@cms.hhs.gov

Leonard M. Pogach, MD, MBA
National Program Director Diabetes
Chief, Endocrinology VA
New Jersey Health Care System
Medical Service (111)
Diabetes Veterans Health Administration
VA Medical Center
385 Tremont Avenue
East Orange, NJ 07018
Tel: (973) 676-1000 ext.1693
Fax: (973) 395-7092
leonard.pogach@med.va.gov

Joseph V. Selby, MD
Kaiser Permanente
3505 Broadway
Oakland, CA 94611-5714
Tel: (510) 450-2106
Fax: (510) 450-2073
jvs@dor.kaiser.org

Allen M. Spiegel, MD
Director
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
31 Center Drive
Building 31, Room 9A52
Bethesda, MD 20892
Tel: (301) 496-5877
Fax: (301) 402-2125
spiegela@extra.niddk.nih.gov

David M. Stevens, MD, FAAFP
Director, Clinical Branch
Division of Community and Migrant Health
Health Resources and Services Administration
4350 East West Highway, 7th Floor
Bethesda, MD 20814
Tel: (301) 594-4323
Fax: (301) 594-4997
dstevens@hrsa.gov

Daniel B. Stryer, MD
Medical Officer
Center for Outcomes and Effectiveness Research
Agency for Healthcare Research and Quality
6010 Executive Boulevard, Suite 300
Rockville, MD 20852
Tel: (301) 594-4038
Fax: (301) 594-3211
dstryer@ahrq.gov

Frank Vinicor, MD, MPH
Director
Division of Diabetes Translation (K-10)
Centers for Disease Control and Prevention
4770 Buford Highway
Atlanta, GA 30341-3717
Tel: (770) 488-5000
Fax: (770) 488-5966
fxv1@CDC.GOV

DMICC: MACROVASCULAR DISEASE & DIABETES: TRANSLATION ISSUES

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NIH Campus, Building 31c, 6th Floor, Room 6
Bethesda, Maryland

Introduction

Dr. Sanford Garfield, Executive Secretary, DMICC, opened the meeting and introduced Dr. Allen Spiegel, Director of the NIDDK and Chairman of the Diabetes Mellitus Interagency Coordinating Committee (DMICC). Citing data that indicates an increased relative risk of cardiovascular disease (CVD) for those individuals who have been diagnosed with diabetes or pre-diabetes, Dr. Spiegel defined the purpose of the meeting: To determine the means and methods for translating the current scientific data from clinical trials and epidemiological studies to diabetic patients and the general public. Dr. Spiegel also took the opportunity to introduce Dr. Claude Lenfant, Director of the National Heart, Lung and Blood Institute (NHLBI), who further emphasized the need for translation efforts involving CVD and diabetes.

Diabetes and Macrovascular Disease: Scope of the Problem

Dr. Hertzel Gerstein, Professor of Clinical Epidemiology and Biostatistics and Medicine at McMaster University, Hamilton, Ontario, Canada, examined the increased relative risk of a macrovascular event in subjects with diabetes. CVD must be considered as a risk factor for people with diabetes, since 70 percent of diabetic subjects die of cardiovascular causes, and CVD represents more than two-thirds of the greater than $100 billion per year diabetes costs in the U.S. alone.

Data from clinical studies show that diabetes in men increases the relative risk of a CVD event two- to three-fold; in women the risk is increased from two- to five-fold. The OASIS database indicates that having diabetes at the time of admission for unstable angina predicts a higher risk of mortality. Even having experienced a previous myocardial infarction (MI) presents less risk than does having diabetes alone.

The absolute risk of a cardiovascular (CV) event in people with diabetes is difficult to accurately predict. Although less than ideal, the best data is obtained from clinical trial databases. Dr. Hertzel summarized data from the HOPE, RENAAL, IDNT, IRMA, and HPS studies, concluding that a person with diabetes and no previous CV event may have a risk equivalent to a non-diabetic subject who has experienced a CV event.

Blood glucose levels of >133 mg/dl and elevated hemoglobin A1c are consistently predictive of CV risk, independent of diabetes. Since these risk factors extend well below the diabetes threshold, Dr. Gerstein asserted that the prevalence of metabolic problems in the general public foretells a much larger epidemic of CVD.

Recent Clinical Trials: Projected Benefits

Dr. Steven M. Haffner, Professor of Internal Medicine at the University of Texas Health Science Center in San Antonio, Texas, reviewed recent clinical trials in the area of CVD and diabetes translation research. Dr. Haffner recommended that the focus of NIH strategy be on the primary prevention of diabetes for two reasons: 1) diabetic subjects have a high mortality rate within 1 year of their first MI, and 2) diabetics develop CVD at twice the rate of those individuals who are never diagnosed with diabetes.

Current clinical trials such as the ACCORD, Look AHEAD, and BARI studies are examining hemoglobin A1c, blood pressure, LDL, HDL, and smoking as risk factors. Clearly, data from these trials show that these conventional risk factors predict CV risk within diabetic subjects. Data further suggests that ACEs, ARBs, statins, and antihypertensive agents are particularly promising pharmacologic interventions.

The heterogeneity of the risk in diabetics for CVD is evidenced by data indicating that subjects with metabolic syndrome have an intermediate risk of CVD. Eighty-five percent of diabetic subjects have metabolic syndrome and a subsequent two-fold greater risk for CVD than do diabetics without metabolic syndrome.

Dr. Haffner emphasized that a multifactorial approach in clinical trials will be necessary to halt the CVD epidemic, one which addresses the prevention of type 2 diabetes, as well as the improvement and treatment of the disease, including examination of improved glycemic control, risk factor management, and special interventions.

Economics of the Problem

Dr. Vinkat Narayan, Chief of the Epidemiology Section at the Centers for Disease Control and Prevention (CDC), addressed the economics of diabetes and CVD translational research and application. The interaction of diabetes and CVD has a huge impact on the cost of health service in the U.S. Direct costs of diabetes are estimated at $44 billion per year, and CVD at $8 billion; of that, 56 percent of deaths and 55 percent of lost productivity are attributed to CVD. At all ages, the impact of CVD is substantial. Although the direct cost of diabetes in terms of medical expenses is but a small component, the indirect costs (i.e., mortality costs) are substantial. Among people with diabetes, macrovascular complications account for a large percentage of total costs.

Total lifetime costs of diabetes are probably underestimated at $82,000. This figure decreases with age, since younger individuals have longer lifetime exposure to risk of complications, and argues for better screening for diabetes at younger age levels.

QALY, which incorporates mortality, morbidity, and quality of life, is an important measurement tool. Data from the UKPDS study among others show that, per $1.00 of investment, blood pressure control is a clearly superior investment, although glycemic control may be more beneficial in younger age groups. Dr. Narayan suggested that other interventions, such as ACE inhibitors and aspirin use, should be more closely evaluated.

Diabetes Translation:
The Challenge for Primary Care

Dr. Evan Benjamin of the Bayside Medical Center, Springfield, Massachusetts, identified safety in health care as one of the challenges of providing comprehensive health care to patients. Misuse, underuse, and overuse of treatment are components that ought to be addressed in the health care system.

Although ultimately we ought to seek to prevent diabetes, our immediate goal must be to get treatment to patients with diabetes. Aggressive goals for blood pressure, LDL, hemoglobin A1c, aspirin, and anti-platelet therapies are laudable, but are not widely or consistently attained among diabetic patients, let alone the general population. In a Massachusetts General Hospital study, 92 percent of patients diagnosed with diabetes had A1c determined and 99 percent had blood pressure readings taken. However, only 76 percent had their cholesterol tested and just 61 percent had a fasting lipid profile for LDL. Of those tested, the majority were above the target levels, reflecting an underuse of testing for risk factors in diabetic subjects.

The message regarding aggressive treatment regarding blood pressure and lowered lipid levels has been well received by both physicians and patients. However, problems in translation persist in the areas of knowledge and attitude among physicians, systems issues, and patient adherence to treatment plans. Without clear guidelines for health care providers, physicians must rely on computerized systems or diabetes registries for standards. Alternatively, patients must be directly instructed by the health care system as to how to recognize the standards and demand the necessary treatment for high quality diabetes care.

Dr. Benjamin cited the diabetes clinic approach used by the Indian Health Service and Kaiser Permanente, which focuses on diabetes, glycemic control, blood pressure, lipid levels, standards of care, and secondary prevention related to diabetes as well as CVD, as being an effective tool that all health care systems ought to consider.

The Drug Industry and Its Role in Translation

Dr. Fred Fiedorek, Vice President of the Metabolics, Clinical Development, and Life Cycle Management Division, Pharmaceutical Research Institute at Bristol-Myers Squibb, related the current focus of the drug industry as the determination of surrogates that will lead to event reduction in clinical trials and clinical practice.

The drug industry is focusing on the metabolic syndrome because of concern that these are the events that most impact not only patients with diabetes, but those in the 10- to 15-year period prior to diagnosis. Those in the drug industry recognize that a balance of benefit and costs associated with risk is an important consideration where patients taking multiple medications are concerned.

To that end, Dr. Fiedorek suggests that two approaches be followed: 1) to do innovative science to understand core mechanisms underlying diabetes and how it is linked to CVD, and 2) to investigate "killer applications" (research of the use of multiple medications as effective treatment).

The drug industry grants the importance of prevention as well as drug therapy such as metformin, pravastatin, and aspirin-drug combinations; the investigation of metabolic syndrome; and the need for translation. However, the past emphasis on glycemic ranges may need to be downplayed, since diabetes does not involve simply a problem with sugar, but more precisely relates to an increased risk of CVD, together with its inherent health hazards.

The Managed Care Perspective

Dr. Joseph V. Selby, physician, health services researcher, and Director of the Division of Research at Kaiser Permanente in Northern California, presented the managed care perspective on diabetes, macrovascular disease, and translation. The prevalence of diabetes within the Kaiser Permanente population has risen 33 percent in the past 5 years, while coronary heart disease and congestive heart failure rates have remained stable.

Although hospitalization costs for diabetic patients have decreased slightly over the past 5 years, the current focus on lowering blood pressure and lipid levels has contributed to a significant rise in laboratory testing and pharmaceuticals, keeping overall costs relatively neutral. Still, health care costs for diabetic patients are significantly greater than for non-diabetics. Dr. Selby emphasized the importance of good disease management in reducing health care costs and recommended a systems approach to identify populations; to provide decision support, monitoring, and feedback on performance and outcomes; and to ensure that the highest risk patients receive the most intensive efforts.

The high co-occurrence rates of hypertension and dyslipidemia among diabetic patients suggests the benefit in risk-stratifying populations of diabetic patients lies in being able to identify subgroups having an increased risk of metabolic syndrome and accompanying complications. Using a multivariate model, Kaiser Permanente has identified three predictors that a patient with no previous event would suffer a major micro/macrovascular, infectious, or metabolic event within 12 months: 1) elevated serum creatinine levels, 2) use of two blood pressure medications, and 3) use of insulin.

Kaiser Permanente is currently expanding the training and responsibilities of diabetes nurse care managers to include CVD risk factor management and plans to re-design risk stratification algorithms to incorporate findings from the risk predictor study. Future and ongoing research will evaluate trends in coronary artery disease (CAD) and stroke incidence over time, with a particular focus on possible increases in end-stage renal disease (ESRD) as macrovascular disease rates decline.

Agency Overviews on Macrovascular Disease and Diabetes and Translation Issues

National Diabetes Education Program (NDEP)

Dr. Judith Fradkin, Director of Diabetes, Endocrinology and Metabolic Diseases, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), presented an update on the National Diabetes Education Program with regard to cardiovascular issues.

The NDEP is committed to expanding the glucocentric message to include more comprehensive care for patients with diabetes, with a particular focus on cardiovascular disease. The NDEP's ABC (A1c, blood pressure, and cholesterol) Campaign targets patients and is, therefore, complementary to the American Diabetes Association's (ADA) Make The Link Program, which is primarily aimed at health care providers.

A joint press conference with ADA emphasizing that two-thirds of patients with diabetes are unaware that CVD is the major source of mortality for diabetics generated a fair amount of publicity. Information is being disseminated through a variety of media, including the NDEP Web site, community publications, and television and radio news broadcasts.

Most recently, NDEP has turned its efforts toward sub-populations, such as African Americans, Asian Americans, and women.

National High Blood Pressure Education Program (NHBPEP)

Dr. Jeffrey Cutler discussed the translation efforts of the National High Blood Pressure Education Program. The NHBPEP, overseen by a coordinating committee comprised of approximately 45 members representing professional and volunteer organizations, as well as Government agencies, has recommended aggressive treatment of high blood pressure among patients with diabetes. While lifestyle changes, weight control, and increased physical activities are interventions that have been promoted for many years, new emphasis has been applied to the prevention of hypertension and diabetes.

Previously, treatment goals for hypertensive diabetic patients were determined strictly on risk considerations and lacked a basis in trial data. However, more recent trials have provided evidence of the improved effectiveness of beta blockers over earlier drug interventions and have identified diabetic patients as the high-risk level, resulting in the recommendation of immediate drug treatment initiation for those patients.

Most information regarding hypertension guidelines is shared internationally, and a broad awareness of the principles are apparent, even if their implementation is less clear.

Since the benefits from the treatment and control of high blood pressure seem to be leveling off, the NHBPEP is concentrating efforts in a new direction, including work with the National Committee on Quality Assurance, to adopt a HEDIS or control standard aimed at the CVD high risk populations. NHBPEP is also involved in contracts with the community-based consortia, or dissemination-utilization center, whose goal is to provide for CVD high-risk populations.

National Cholesterol Education Program (NCEP)

Dr. James Cleeman, Coordinator of the NCEP, discussed the translational efforts of the program with respect to diabetes. Dr. Cleeman explained that science must first be translated into guidelines for professionals before those guidelines can be extended into useful tools for health care professionals, patients, and the public.

The Adult Treatment Panel III (ATP III) Study regards diabetes as a coronary heart disease (CHD) risk equivalent. Within the study's statin trials, over 20 percent of those subjects in the placebo group suffered an MI plus coronary death within a 10-year period. In comparison, 15 to 25 percent of diabetic patients are at risk of developing CHD.

Data from the Heart Protection Study, which examined the effects of therapeutic lifestyle changes and the LDL level at which drug therapy ought to be considered, is currently being evaluated.

ATP III derived therapeutic objectives for metabolic syndrome, including the reduction of underlying causes (i.e., obesity and a sedentary lifestyle). The study produced an executive summary published by JAMA and a Quick Desk Reference (the ATP III At-A-Glance, which provides treatment instructions). These reference materials have been augmented by a NHLBI Web site, patient brochures, kits sent to 65,000 physicians, a palm device program, and implementation of National Cholesterol Education Month, all of which emphasize diabetes as a coronary disease equivalent.

Centers for Medicare & Medicaid Services (CMS)

Dr. Steve Phurrough, Director, Division of Medical and Surgical Services of the Coverage and Analysis Group, addressed the translation efforts of CMS. Medicare was authorized by Congress to pay for the diagnosis and treatment of injury and disease, covering 34 million Americans at an annual cost of $300 million. While coverage originally excluded screening or prevention, over the past decade, Congress has approved some limited screening procedures.

For diabetic patients, coverage has generally been available for secondary prevention in macrovascular care, since secondary prevention is considered the treatment of a primary disease. Coverage has recently been expanded to include nutritional counseling, selected foot exams, and a 10-hour diabetes education program. Medical benefits may also be covered in the future. However, translation at CMS remains an issue of coverage.

Currently, CMS publishes several pamphlets and manuals made available to both health care providers and patients. The agency is investigating the level and causes of disparities in diabetes treatment between gender, racial, and ethnic groups.

Indian Health Service (IHS)

Dr. Kelly Acton, Director of the National Diabetes Program at the IHS, spoke about the agency's approach to macrovascular disease and translation activities in terms of risk factors. CVD and cerebrovascular disease mortality rates in American Indians and Alaska Natives, although variable between tribes, exceed all other races in the U.S. combined. The Strong Heart Study, an NHLBI-funded, longitudinal study of CVD in 13 American Indian tribes, produced data showing diabetes is second only to age as the strongest determinant of CVD.

IHS updates its standards for care every 2 years and has recently instituted the CVD Risk Factor Report, a subreport from the agency's annual diabetes care and outcome audit, which calculates CV risk status for individual facilities, as well as for regions. Data from this report shows a substantial increase in the number of people within the population who are tobacco-free. Aspirin use has increased over the past 2 years as a result of changes in IHS standards of care. Levels of glycemic control, blood pressure, LDL and HDL, triglycerides, and albuminuria, while increasingly favorable, still present an area for improvement. The population continues to show a significant problem with obesity.

IHS targets the highest risk individuals, utilizing a systems approach with diabetes clinics in nearly every facility, electronic registries, and standards of care. Currently, IHS is gathering age-specific diabetes prevalence data.

Veterans Administration (VA)

Dr. Leonard Pogach, National Program Director for Diabetes for the Veterans Health Administration and Chief of Endocrinology for the VA Health Care System, offered information regarding cardiovascular prevalence, risk factors, and outcomes in the VA health care system. The VA health care system is a nationwide system that includes clinical reminders and an emphasis on prevention, care coordination, and chronic disease management. It provides health care services for a relatively challenged population, 40 percent of whom have known CVD.

To improve quality of care for its patients, the VA instituted the Quality Enhancement Research Initiative (QUERI) program in 1999, using health services research in its system for translation, feedback, and evaluation. Primarily, effort has been focused on ongoing organizational improvements and integration with existing tools, especially using the VA's electronic databases, with the goal of inducing behavioral changes within the population.

Aspirin use and maximal hypertension therapy (defined as three or more medications) interventions have shown promising results in lowering the incidence of hypertension among VA patients. Health care providers using the VA computer system are presented with reminders for blood pressure and lipid levels. Pilot data indicates clinicians are responding by entering data and making an appropriate intervention.

Centers for Disease Control and Prevention (CDC)

Dr. Frank Vinicor, Director of Diabetes Translation at CDC, suggested that the diabetes epidemic may cause a neutralization of the benefits of lowering blood pressure and lipid levels, together with a corresponding increase in CVD associated with diabetes.

Dr. Vinicor stressed the importance of science in underpinning public health translation approaches, since absent the essential scientific basis, controversies regarding treatment and programs will arise.

Dr. Vinicor raised the issue that discussion of CVD ought to focus on the large percentage of time patients spend away from their doctors or health care professionals, and that rather than making the best treatment available to a small number of diabetic patients, it would be better to make a good treatment available to many, at least insofar as CVD is concerned.

At CDC, the focus is currently on 1) collection of data from national sources such as the Diabetes Quality Improvement Program, 2) examination of the issue of proper CVD care for diabetics through systems of care and the development of health care workers as an essential part of the health care team, and 3) comprehensive diabetes control programs concerned with health systems changes, community interventions, and health communications. Future CDC endeavors include establishing a better definition of diabetes and examination of the metabolic syndrome.

Other Translation Efforts

Following the presentations by invited speakers, Dr. Garfield invited representatives from various agencies and associations to share current translational efforts.

Dr. Daniel Stryer, Center for Outcomes and Effectiveness Research, Agency for Healthcare Research and Quality (AHRQ), informed the group that AHRQ is conducting studies examining the impact of diabetes policies, disparities in diabetes, and systems level changes, including disease management programs and the use of diabetic clinics and automated telephone assessment and reminder systems. Implementation research includes TRIP studies (Translating Research Into Practice), such as the impact of opinion leaders, academic detailing, and patient empowerment tools. AHRQ's National Guidelines Clearinghouse puts guidelines into the public domain, making the information easily accessible. Data networks and surveys are also available.

Dr. Robert Misbin, Medical Officer of the Division of Endocrine and Metabolic Products, Center for Drug Evaluation and Research at the Food and Drug Administration, highlighted studies being conducted by the pharmaceutical industry regarding the benefit of treating insulin resistance with respect to hard endpoints.

Dr. Nathaniel Clark, National Vice President of Clinical Affairs at the American Diabetes Association, stressed the need for consistent, evidence-based, and achievable guidelines. Current projects involve issues of optimal lipid levels in children and the construction of guidelines for children with type 1 diabetes.

Dr. Robert Eckel, of the American Heart Association (AHA), expressed his association's goal that by 2010 morbidity and mortality from heart disease and stroke be reduced by 25 percent, and risk factors for heart disease and stroke also be reduced by 25 percent. To accomplish their goal, the AHA has placed a very high priority on understanding the connection between obesity and diabetes. Information from research and the agency's progress has culminated in several prevention conferences.

Panel Discussion

During the Panel Discussion, the following questions were raised:

- What, if any, are the public health responsibilities of agencies that are not public health agencies?
- How will the health care of patients with more than one chronic disease be effectively coordinated?
- How can agencies coordinate efforts on translation research in order to perform larger, more efficient studies?
- How can patients be risk-stratified so that translation efforts can be made more immediately usable?
- Would a trial research network be feasible?
- Given the accessibility to care and medications, why are patients not achieving goals?
- If interventions are effective, are they additive or subadditive?

SUMMARY

Participants reached a general consensus in recognizing that primary prevention research in the areas of diabetes and CVD will provide the greatest benefit for translation efforts. Future research in the following areas is therefore warranted:

I. Interventions

- Examination of pharmacologics, particularly ACEs, ARBs, statins, and antihypertensive agents.
- Determination of the benefits of glycemic control versus CV risk reduction.
- Investigation of multiple drug therapy and its metabolic effects.
- Identification of the underuse and misuse of pharmacologic therapies.
- Assessment of the effects of underuse of specific patient exams, such as A1cs, eye exams, and foot exams.

II. Health Care Costs/Economics

- Institution of incentives for health care providers.
- Promotion of earlier screening for younger subjects, in an effort to reduce lifetime costs.
- Examination of costs over a finite time period versus lifetime costs.
- Prospective data collection of costs in clinical trials.

It was strongly emphasized that extensive research efforts are demanded in the area of metabolic syndrome and its connection to diabetes and cardiovascular disease. Additionally, disparity issues between gender, race, and ethnicity must be addressed.

The traditional emphasis on metabolic control, while certainly effective to some degree, must be expanded to include CV risk reduction, such as boold pressure control and lowering of cholesterol levels. In order to go beyond the current levels of prevention and increase the effectiveness of treatment, the message must be expanded to include CV risk reduction.

It was noted that not all failure of individuals to achieve target levels is due to faults in the health care system or providers. There are important gaps in knowledge of the epidemiology of diabetes as a CV risk factor. Research efforts directed at promoting a system approach may correct the current paucity of databases available, as well as facilitate large outcome trials. Clinical reminders (i.e., those promoting aspirin use) are relatively easy to implement and have shown a good measure of success with respect to health care provider and patient use. As the message to be portrayed is more clearly defined, tools such as Quick References and Web sites ought to be put into place. Doing so will not only impart diagnostic and treatment data to health care professionals, but perhaps more importantly will place information in the hands of patients and the general public.

Participants

Kristin Abraham, PhD
Director, Cell Signaling Programs
Division of Diabetes, Endocrinology
and Metabolic Disease
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
2 Democracy Plaza, Room 607
Bethesda, MD 20892
Tel: (301) 451-8048
Fax: (301) 480-3503
abrahamk@extra.niddk.nih.gov

Beena Akolkar, PhD
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard
2 Democracy Plaza, Room 681
Bethesda, MD 20892
Tel: (301) 594-8812
Fax: (301) 480-3503
ba92i@nih.gov

Barbara Alving, MD
Deputy Director
National Heart, Lung and Blood Institute
National Institutes of Health
31 Center Drive
Building 31, Room 5A47, MSC 2490
Bethesda, MD 20892
Tel: (301) 594-5171
Fax: (301) 402-0818
alvingb@nhlbi.nih.gov

Diane M. Canova, Esq.
Vice President of Advocacy
Office of Public Advocacy
American Heart Assocation
1150 Connecticut Avenue NW, #300
Washington, DC 20036
diane.canova@heart.org

Michelle Cissell, PhD
AAAS/NIH Science Policy Fellow
Office of Scientific Program and Policy Analysis
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
31 Center Drive
Building 31, Room 9A05
Bethesda, MD 20892
Tel: (301) 496-6623
Fax: (301) 480-6741
cissellm@extra.niddk.nih.gov

Nathaniel Clark, MS, RD, MD
National Vice President, Clinical Affairs
American Diabetes Association
1701 North Beauregard Street
Alexandria, VA 22311
Tel: (703) 299-5533
Fax: (703)549-1715
nclark@diabetes.org

Catherine Cowie, PhD
Director, Type 1 Diabetes Clinical Trials Program
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
2 Democracy Plaza, Room 691
Bethesda, MD 28092-5460
Tel: (301) 594-8804
Fax: (301) 480-3503
cowiec@extra.niddk.nih.gov

Joel Finkelstein
Science Writer
Center for the Advancement of Health
2000 Florida Avenue, Suite 210
Washington, DC 20009
Tel: (202) 387-2829
Fax: (202) 387-2857
jfinkelstein@cfah.org

Joanne Gallivan
Director, National Diabetes Education Program
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
31 Center Drive
Building 31, Room 9A04
Bethesda, MD 20892
Tel: (301) 496-6110
Fax: (301) 496-7422
joanne_gallivan@nih.gov

Robert D. Hammond, PhD
Director, Division of Extramural Activities
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
2 Democracy Plaza, Room 715
Bethesda, MD 20892-5456
Tel: (301) 594-8834
Fax: (301) 480-4125
hammondr@extra.niddk.nih.gov

Barbara Harrison
Director, Obesity Special Projects Program
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard
Room 661, MSC 5450
Bethesda, MD 20892-5450
Tel: (301) 594-8858
Fax: (301) 480-8300
harrisonb@extra.niddk.nih.gov

Joyce Hunter, PhD
Deputy Director, Division of Extramural Activities
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard
Bethesda, MD 20892
Tel: (301) 594-0056
hunterj@extra.niddk.nih.gov

Mary Beth Kester
Program Analyst
Office of Scientific Program and Policy Analysis
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
31 Center Drive, Room 9A05
Bethesda, MD 20892
Tel: (301) 496-6623
Fax: (301) 480-6741
kesterm@extra.niddk.nih.gov

Maren R. Laughlin, PhD
Director, Metabolism Program,
Division of Diabetes, Endocrinology
and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
2 Democracy Plaza, Room 6101
Bethesda, MD 20892-5460
Tel: (301) 594-8802
Fax: (301) 480-3503
maren.laughlin@nih.gov

Barbara Linder, MD, PhD
Division of Diabetes, Endocrinology
and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard
2 Democracy Plaza, Room 699
Bethesda, MD 20892
Tel: (301) 594-0021
Fax: (301) 480-3503
linderb@extra.niddk.nih.gov

Saul Malozowski, MD, PhD, MBA
Senior Advisor for Clinical Trials
and Diabetes Translation
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard, Room 679
Bethesda, MD 20892
Tel: (301) 451-4683
Fax: (301) 480-3503
malozowskis@extra.niddk.nih.gov

Robert Misbin, MD
Medical Officer
Division of Endocrine and Metabolic Products
Center for Drug Evaluation and Research
Food and Drug Administration
Tel: (301) 443-9282
misbinr@cder.fda.gov

Salvatore Sechi, PhD
Director, Proteomic Program
Division of Diabetes, Endocrinology
and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard
2 Democracy Plaza, Room 611
Bethesda, MD 20892-5460
Tel: (301) 594-8814
Fax: (301) 480-2688
Salvatore_Sechi@nih.gov

Denise Simons-Morton, MD, PhD
Acting Director, Clinical Applications
and Prevention Programs
Division of Epidemiology and Clinical Applications
National Heart, Lung and Blood Institute
National Institutes of Health
6701 Rockledge Drive, MSC 7936, Room 8138
Bethesda, MD 20892-7936
Tel: (301) 435-0384
Fax: (301) 480-1669
simonsd@nhlbi.nih.gov

Elizabeth Singer
Director, Office of Communicatoins
and Public Liaison
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
31 Center Drive, Room 9A04
Bethesda, MD 20892
Tel: (301) 496-3583
elizabeth_singer@nih.gov

Susan Yanovski, MD
Director, Obesity and Eating Disorders Program
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard, Room 665
Bethesda, MD 20892
Tel: (301) 594-8882
Fax: (301) 480-8300
yanovskis@extra.niddk.nih.gov

Speakers

Evan Benjamin, MD
Baystate Medical Center
759 Chestnut Street
Springfield, MA 01199
Tel: (413) 794-2527
evan.benjamin@bhs.org

James Cleeman, MD
Coordinator, National Cholesterol
Education Program
National Heart, Lung and Blood Institute
National Institutes of Health
Building 31, Room 4A16
Bethesda, MD 20892
Tel: (301) 496-1051
Fax: (301) 402-1051
cleemanj@nhlbi.nih.gov

Fred Fiedorek, MD
Vice President, Metabolics, Clinical Development
and Life Cycle Management, Pharmaceutical
Research Institute
Bristol-Myers Squibb
3551 Lawrenceville Road
Princeton, NJ 08540-4700
Tel: (609) 252-4897
Fax: (609) 252-6791
fred.fiedorek@bms.com

Hertzel Gerstein, MD
Professor (Associate)
Clinical Epidemiology and
Biostatistics and Medicine
Faculty of Health Sciences
McMaster University
Health Sciences Centre, Room 3V38
1200 Main Street West
Hamilton, Ontario
CANADA
Tel: (905) 525-9140 x73371
Fax: (905) 521-4971
gerstein@mcmaster.ca

Steven M. Haffner, MD
Professor, Department of Medicine
Department of Medicine
Division of Clinical Epidemiology
The University of Texas Health Science Center
San Antonio, TX 78229-3900
Tel: (210) 567-4737
Fax: (210) 567-6955
haffner@uthscsa.edu

Claude Lenfant, MD
Director, National Heart, Lung
and Blood Institute
National Institutes of Health
31 Center Drive
Building 31, Room 5A-52
Bethesda, MD 20892
Tel: (301) 496-5166
Fax: (301) 402-0818
lenfantc@nhlbi.nih.gov

Vinkat Narayan, MD
Chief, Diabetes Epidemiology Section
Division of Diabetes Translation
Centers for Disease Control and Prevention
2858 Woodcock Boulevard, MS K10
Atlanta, GA 30341
Tel: (770) 488-1051
kav4@cdc.gov

Steve Phurrough, MD, MPA
Director, Division of Medical
and Surgical Services
Coverage and Analysis Group
7500 Security Boulevard
Baltimore, MD 21244
Tel: (410) 786-2281
Fax: (410) 786-9286
sphyrrough@cms.hhs.gov

Joseph V. Selby, MD
Kaiser Permanente
3505 Broadway
Oakland, CA 94611-5714
Tel: (510) 450-2106
Fax: (510)450-2073
jvs@dor.kaiser.org

Theresa Watkins-Bryant, MD
Chief, Perinatal and Child Health Branch, BPHC
Health Resources and Services Administration
U.S. Department of Health and Human Services
9-10A4 EWT
Bethesda, MD 20814
Tel: (301) 594-4423
TWatkins-Bryant@HRSA.gov

DMICC: THE SCIENCE OF TRANSLATION RESEARCH: OUTCOMES AND OPPORTUNITIES

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National Institutes of Health
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Introduction

Dr. Sanford Garfield, Executive Secretary of DMICC, opened the meeting and announced that Dr. Saul Malozowski, Senior Advisor for Clinical Trials and Diabetes Translation, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), would become the new Executive Secretary at the next DMICC meeting. Dr. Allen Spiegel, NIDDK Director, welcomed the attendees and stated "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."

Dr. Spiegel pointed out that understanding translation can sometimes be confusing because it is made up of two blocks. The first block is “from bench to bedside,” from laboratory research to impacting on the patient’s care. The focus of this meeting was the second translational block, the science of translation research that goes from scientific understanding to adoption and community practice. He emphasized that there is no sharp demarcation in the NIH mission; rather it is a continuum, a critical aspect of which is the partnership with academic partners and agencies of the U.S. Department of Health and Human Services (DHHS), many of whose members were represented in the audience. Dr. Spiegel said that the role of DMICC is to ensure that the entire continuum is realized from the most basic NIH-supported research out to the distal levels of clinical care, quality of care, and application. This meeting celebrates the 25th anniversary of the Diabetes Research and Training Centers (DRTCs) program and the initiation of the translation activities mandated to be a part of these DRTCs.

Dr. Spiegel also announced that Dr. Judith Fradkin, Director of NIDDK’s Division of Diabetes, Epidemiology, and Metabolism, is the recipient of the 2003 American Medical Association’s Nathan Davis Award for Career, Executive Branch, Public Service, a Government-wide award that recognizes her role as co-chairperson of the National Diabetes Education Program (NDEP) and in the framing of a trans-NIH strategic plan for diabetes research, and for her efforts, along with that of other NIDDK program staff, with the 1999 congressionally mandated Diabetes Research Working Group (DRWG) for research planning in type 1 and type 2 diabetes. DMICC participants received copies of a draft Executive Summary of the updated DRWG report and a summary of the May 16, 2002, meeting of external advisors on the special statutory funding program for type 1 diabetes research.

Morning Presentations and Discussions

National Diabetes Mellitus Research and Education Act, Diabetes Research and Training Centers, and Diabetes Translation—The First 25 Years

Dr. Roland "Red" Hiss, Director of Prevention and Control Division of the Michigan DRTC, University of Michigan Medical School, Ann Arbor, presented an historical overview of the DRTCs and their role in translation research, beginning with the National Diabetes Mellitus Research and Education Act of 1974 (Public Law 93-354, July 23, 1974). This far-reaching and informed act enacted by the 93rd Congress resulted from a 1970's national groundswell that was beginning to recognize diabetes as a serious disease, as had happened previously with hypertension. The Act established the regional DRTCs and recommended establishment of a National Commission on Diabetes to develop a long-range plan to combat diabetes. The Act also established the DMICC. In December 1975, the Commission, chaired by Dr. Oscar Crofford, submitted a four-part report consisting of nine volumes. The first volume was the mandated long-range plan, updated in 1976. The plan was intended to expand and coordinate national research on diabetes; advance the education of patients, health professionals, and the general public; and disseminate updated information.

The NIH agencies impacted by the report included the National Institute of Arthritis, Metabolism, and Digestive Disorders (NIAMDD, now NIDDK); the National Eye Institute (NEI); the National Institute of Neurological and Communicative Disorders and Stroke; the National Institute of Dental Research; the National Institute of Child Health and Human Development; the National Heart and Lung Institute (now the National Heart, Lung, and Blood Institute (NHLBI)); and the National Institute of Mental Health (NIMH). Inclusion of NIMH suggested that research be conducted on the behavioral aspects of diabetes. Also included was the Center for Disease Control (now CDC, the Centers for Disease Control and Prevention); the Veterans Administration; and the Bureaus of Indian Affairs, Quality Assurance, and Community Health Services. The report recommended the creation of a National Diabetes Data Group, the National Diabetes Information and Education Clearinghouse, and the CDC Diabetes Control Programs in each of the States' departments of health.The first Request for Applications (RFA) for a DRTC was issued in June 1976 by NIAMDD. The RFA stated two principal functions—research and translation. It stated that a key function "will be to translate, rapidly and effectively, appropriate results of research into health care so that particular activities can become standard practice, not only in the community in which it is demonstrated, but in other communities as well." Dr. Hiss said that the statement sounds clear, but it was not. For some 10 years, "what is translation" was argued about at site visits and annual meetings. He pointed out that we have come a long way from that early concept.

Dr. Hiss mentioned a number of barriers to adoption of new science and to the development of consensus regarding the science's message in its adaptation to clinical care and practice. Among these barriers are the asymptomatic nature of diabetes; attitudes, beliefs, and misconceptions on the part of clinicians and patients; the health care system's emphasis on acute, not chronic illness, and health care economics; the influence of obesity; and the difficulties of instituting and maintaining behavior change in adults. He stressed the importance of consensus in delivering a clear message and the resistance created by mixed messages from different groups. Following barrier identification, the big challenge is barrier removal or circumvention. Incorporation of feedback from clinicians and patients is also necessary.

Asked to provide an example of a good piece of science that has become bogged down in barriers, Dr. Hiss selected NEI's 1981 diabetes retinopathy study that showed that photocoagulation of periferative and pre-periferative retinopathy saved sight. Unfortunately, the report was initially publicized primarily in ophthalmologic literature and meetings. Subsequently as strong effort other health care professionals did not learn about it for about 3 years. Now a strong effort has been made to have an annual or biannual examination of a dilated pupil included in standard diabetes care. However, in Michigan, which Dr. Hiss believes is typical of the rest of the United States, 40 percent of patients with diabetes have never had this examination—21 years after the science was reported.

An example of what the DRTCs' translation components have accomplished collaboratively is the 1993 publication "Metabolic Control Matters," a nationwide translation analysis and recommendations based on the Diabetes Control and Complications Trial (DCCT). The report included recommendations for diabetes care from the DCCT, strategies and models for translation, and implications of the DCCT findings on the structure of the health care system. It also covered professional practice and training, implications of the DCCT for patient education and for social systems, and financing issues of intensified management of diabetes. In 1995, the six DRTCs provided an updated report on the recommendations.

Based on the DRTCs' 25 years of experience, Dr. Hiss offered a definition of translation. He echoed Dr. Spiegel's comments that translation is not a one-time event; it is a sequence of many events divided into two distinct phases. Phase I is the development (from the bench) and application (to the bedside) of new biomedical science to patient care. This is the clinical research or bench-to-bedside phase, the "R" in DRTC. Phase II is the application of new clinical science through clinical trials, the product of phase I, to community care. This second phase—the "T" role of the DRTC—involves the identification and overcoming of barriers to widespread adoption of the improved practices. Dr. Hiss stressed that these phases are different, essential, and sequential and performed differently by different people, who must remain in touch with each other to resolve their problems if we are to realize the social value of new biomedical science. Phase I benefits several hundreds of patients. Phase II benefits millions of patients.

Discussion. In the discussion following his presentation, Dr. Hiss described how attitudes towrad obesity serve as a barrier to better diabetes care because of the perception that the patient's weight is his/her own fault. Obese persons are seen as failures by their families and society in general, and thus obese patients with diabetes may receive less attention in the health care system and also may avoid the health care system because of their fear of being blamed or stigmatized.

It was suggested that translation and translation research are not identical. In addition to the phase I research, research can be done in phase II by studying how to foster the application of phase I research. Dr. Hiss agreed that there is an enormous amount of translation research that needs to be done in phase II.

Experimental Design Elements of Translation

Dr. Lawrence Green, Director of the Office of Extramural Prevention Research, CDC, gave two statements from a recent National Cancer Institute (NCI) conference on dissemination research to frame his presentation. The first quotation was "An ounce of prevention takes a ton of office system change" (Thomas Kottke). This relates to the need to bring research methods to bear that allow for working with complex systems. The second was about the culture of the research community itself. One of the cultural aspects of researchers is their conditioned concern about having their best ideas stolen. The second quotation was "Don't worry about people stealing your ideas. If you have a really good idea, you will have to cram it down their throats."

Because of the increased potential to address diabetes at the primary level, as well the secondary and tertiary levels, Dr. Green said he planned to go beyond the bedside in his presentation to examine the community population-based considerations that influence reaching the millions, both patients and those not yet patients, who deserve the health care system's attention. First, he presented five ideal elements of experimental design as aspired to by researchers in randomized clinical/controlled trials (RCTs). He considered only one element—one or more posttests to measure effects after the experimental intervention—as essential. The others are ways to control threats to internal and external validity. He feels that preoccupation with maximizing internal validity—threats to the validity of the conclusions about the causal effect of the intervention—has neglected external validation. Thus a lot of research is less than convincing to practitioners because it does not relate to their situation.

Dr. Green said he did not come "to bury experimental design, but to praise it." There are problems in applying "best practices" from RCTs because of the inability to achieve their controls in translation to the community. Better use needs to be made of other evidence beyond the clinical setting where there is such strict control. Other problems include generalizing from one population, place, or circumstances to another. Although there is a high degree of generalizability across the human species, because of its relative homogeneity, physiologically and pathologically, in social groups, there is heterogeneity. This makes generalization from one study setting or population to others increasingly difficult as one moves up the biopsychosocial spectrum.

Practitioners face three problems (identified by Brick Lancaster) in translation that cause them to question the high standards suggested by "best practices" based on research conducted elsewhere:

- Accessibility gap: Do I have the same resources as the experimenters had?

- Credibility gap: How different is their practice situation (i.e., university or large hospital setting with grant money) from mine?

- Expectations gap: Do I need to strive for such lofty goals in my practice?

Dr. Green noted that CDC has named 10 areas of great public health achievements in the 20th century. In the last third of the century, the smoking problem accumulated in the first two-thirds of the century was reduced by 50 percent. Similar public health success was achieved in stroke and cardiovascular disease deaths and in automobile crash-related deaths, especially alcohol-related crashes. Dr. Green described the various economic, social, regulatory, and historical events affecting the changes related to cigarette consumption. Strong influences on the decline in smoking included the Surgeon General's Reports on the hazards of smoking, the nonsmokers' rights movements, the ban on broadcast advertising and Federal tax increases, the development of over-the-counter cessation aids, and the master tobacco settlement.

Lessons learned from the smoking cessation achievement include:

- Surveillance data systems are needed to track population trends, to establish baseline and trend lines, put an issue on the public policy agenda, show change, and compare progress. The Behavioral Risk Factor Survey System maps showing the growth in the prevalence of obesity from 1985 to 1999 are an excellent example. They clearly indicate the growing epidemic in obesity over time and across jurisdictions. Dr. Green said we are more fortunate than smaller countries to have a 50-State laboratory with variations in policies and programs to compare treatment across jurisdictions and populations.

- Comprehensive programs using a combination of methods are more effective than individual methods; the more components, the greater the effectiveness and the better the coverage. In tobacco control programs, only tax increases could stand alone as an essential component. Successful components included community, statewide, chronic disease, cessation, and school programs; enforcement; surveillance and evaluation; countermarketing; and administration and management. Dr. Green suggested that these same components apply to diabetes.

- The ecological imperative means that a problem must be addressed at all levels—individual, organizational, institutional, community, State and regional, national and international—and these levels must be mutually supportive and complementary.

- There is a level of threshold spending below which there is little effect. A critical mass of personal exposure is needed to influence individuals and a critical mass of population exposure is needed to effect community response. To reach the less motivated, a critical distribution of exposure is needed. Dr. Green said the RE-AIM model demonstrates this well. Reach is a critical component of the effect of a program. In smoking, anything below $2 per capita achieved little effect. Local ordinances are another critical component.

- The environmental imperative addresses the opportunities, cues, and choices provided by the environment, the social reinforcement of positive behaviors and punishment of negative ones, and legal penalties and financial incentives. These create new social norms. Dr. Green reminded the group of how in the past the current room would have been heavy with smoke.

- The educational imperative includes public awareness of the risks and benefits, interest in lifestyle options, understanding of behavioral steps, attitudes toward options and steps, outrage at conditions putting them at risk, and personal and political actions. An informed electorate is necessary to get changes in public policy and legislation.

- The evidence-based imperative is the need to bridge best practices from research to application in practice. This means reaching the underserved, special populations, the less affluent, the less educated, and the community-centered practitioners. Most research occurs amongst highly motivated persons and off-the-shelf protocols do not translate well to other populations. Practitioners and health care systems need the tools of research to do their own immediate evaluation.

According to Dr. Green, viable alternatives to the strict RCT-based interpretations, the gold standard that has driven most "best practices" manuals, are beginning to gain increased credibility with practitioners. While the RCTs provide a valuable foundation, there is no single best practice that is appropriate for all patients and practitioners, or even for some of them all the time, as they go beyond the bedside. Behavior is influenced by a combination of forces—predisposition, enabling, and reinforcement. Paying attention to all three is necessary for sustained change, even with highly motivated persons, who, without support and reinforcement, can become frustrated and rationalize away the credibility of the source of the motivation. Different sources of evidence need to build on the initial structure and provide a menu of appropriate possibilities for different patients and populations.

Dr. Green recommended that the intervention-based research and planning habit be broken. This habit has grown out of the pharmaceutical model of testing specific drugs as interventions by assessing the response, increasing the dose to get a response, and evaluating the response. This tends to increase resource costs without necessarily ensuring they are the appropriate resources for the population being studied. The alternative is a population-based diagnostic planning approach in which the needs and capacities of the population are assessed and a program is designed and implemented based on these and a set of priorities and objectives. The program is then evaluated through a short-loop feedback process to reassess the assumptions, and the program is redesigned. The short-loop cycle becomes a management tool to improve performance in particular settings with specific populations. This approach uses evidence from the community or population; from behavioral, economic, and social research in addition to epidemiological and medical research to help assess causes of behavior and social change; from experimental studies and research and development; and from evaluations in other settings similar to the intended study.

Discussion. Dr. Hiss strongly supported Dr. Green's statement that translational efforts must be very specific to the target audience, the setting, and the situation. As an example, he pointed out that a translational effort with a 35-year-old primary care physician 4 years out of school working in a large hospital that has an active internal medicine residency with a large number of subspecialists in a large community is very different than that effort with a 58-year-old general internist who has been out of school for 25 years working basically alone in a small community hospital with few subspecialists and no in-house educational program.

Asked how the approach would be different, Dr. Green responded that in the hospital setting with an in-house educational program, one works with the house officer and builds into the training the changes in care with this captive audience and this works back through the attendees.

In response to a question as to what approach should be used in what situation to direct the translation, Dr. Leonard Pogach, Veterans Administration (VA), commented that it is the system of care that drives the approach. In the VA system there are a variety of types of hospitals, rural and academic, that are guided by a system of care with integrated electronic medical records, nationally promulgated evidence-based guidelines, quality improvement efforts, and performance measures that drive the system.

Dr. Spiegel pointed out that the obesity issue cannot be viewed solely from the provider perspective, because there are important environmental influences. Although there is arguably a difference between smoking and eating as addictive or nonaddictive behaviors, one does have to eat to live. He recommended *Food Politics*, recently published by Dr. Marion Nestle, head of the nutrition department at New York University. He noted the parallels in food and tobacco advertising to children and to underprivileged minority groups. This action has relevance in advertising to children and to underprivileged minority groups. However, rather than smoking cessation as an example for translation research for diabetes, Dr. Spiegel prefers the example of the decline in cardiovascular mortality. He asked if this decline indicated a public health success in reducing cardiovascular disease or are individuals developing congestive heart failure in larger numbers or other outcomes that are more lingering. Dr. Spiegel posed two related questions. Does the decline reflect control of blood pressure, control of cholesterol, and changes in diet and exercise? If so, then why do we have this increased obesity epidemic over the past two decades?

Dr. Green responded that tobacco cessation was the effort he knew best and it had contributed to the cardiovascular success, but obviously had run in the opposite direction from the obesity problem. The cardiovascular effort was much more complicated.

Dr. Denise Simons-Morton, NHLBI, answered that it was true that along with decline in mortality, there have been dramatic increases in heart failure. Over the years, improvements in quality of care has resulted in improvements in all the risk factors, except obesity, in spite of improvements in diet, in smoking, and some in activity and treatment improvements in blood pressure and cholesterol. There has been a positive impact on cardiovascular disease (CVD) mortality, but there is still a problem in CVD with obesity and the burgeoning diabetes epidemic, an important risk factor for CVD. There remains the relevant issue of competing risks: if people live longer, then what will they develop.

Dr. Garfield mentioned that the initial presentations and discussions had described barriers to translation. The later discussions would address how to revise translation research to combat those barriers.

Translation Research at the University of Chicago DRTC

Dr. Marshall Chin, Associate Professor of Medicine, University of Chicago, discussed the importance of collaborative community-academic-government partnerships in diabetes translational research, especially to improve care in vulnerable or hard-to-reach populations. He offered the Public Health Service's Community Health Centers (CHCs) and the MidWest Clinicians' Network (MWCN) of CHCs as examples and as a basis for later discussion on what types of translation research might be funded by NIH and the other DMICC agencies, many of whom are key partners in the current efforts. He stated that community-based participatory research has come to the forefront in the efforts to find innovative ways to reduce racial and social-economic disparities in health care and outcomes.

CHCs were created by Public Health Service Acts 329, 330, and 340 to provide a broad community health perspective, serve the medically underserved, and focus on community participation. In 1995, MWCN chose diabetes as their number one priority for improvement and established a 55-member research network with pilot funding from the Agency for Healthcare Research and Quality (AHRQ) and the Bureau of Primary Health Care (BPHC). The mission was to conduct credible, meaningful research on health care access and delivery issues in special populations served by CHCs. In 1997, MWCN sought an academic partner through NIDDK, and the University of Chicago became that partner in the research group along with BPHC.

Reviewing CHC performance against the American Diabetes Association's (ADA's) quality of care guidelines, the committee determined in its first study that improving quality care meant achieving the difficult goals of critical self-examination, courage to adopt new ideas, and rigorous evaluation of interventions. The second study was a needs assessment at the CHCs to determine barriers and produced three major findings: Physicians wanted help in facilitating behavior change in patients, wanted improved efficiency in the CHC, and wanted macro health policy issues (insurance, access) addressed. At about this time, BPHC, CDC, NIDDK, and others developed a three-prong diabetes breakthrough series (BTS) that included continuous quality improvement cycles, a chronic care model, and learning sessions to work collaboratively and share lessons learned.

A study of 19 midwest CHC's that applied the diabetes BTS showed improvement in key ADA recommendations of care such as eye and foot exams and urine microalbumin testing, improvement in A1c levels, and enthusiastic support for the intervention. In interviews, physicians noted several issues that impacted their ability to improve standards of care in the community and that are relevant to translation: They needed more time and resources to provide the intervention, paper registries needed to be converted to electronic recording, and lack of senior leadership and support and staff turnover were problems. Another major concern was how to sustain gains after the first year. In response to these studies, Dr. Chin listed current intervention efforts of the group including an RCT-based study of the BTS intervention, provider training in behavioral change, patient empowerment, and hypertension and lipid projects. One evaluation technique was audio tapes of patient-doctor encounters to assess if patients asked questions based on the ADA standards.

As an example of some of the diabetes translation questions and issues at the CHCs, Dr. Chin next described evaluation of a BPHC-sponsored 6-year initiative to improve chronic care in CHCs, with an emphasis on diabetes. The evaluation was based on a conceptual model of a health disparities collaborative that was assessed at two sites, Chicago DRTC being one them. Incentives and assistance flowing between BPHC, the CHC leadership, and the CHC collaborative team, providers, and staff are key components of the model. Organizational and environmental characteristics are recognized as affecting the next level of the model, the improved organizational structures and processes, which then impact the clinical processes of care and patient outcomes, the sustainability and distribution of the interventions, and the costs.

The evaluation of the health disparities collaborative model had three aims: (1) to determine if the model improved health care quality and outcomes; (2) to determine if it enhanced effectiveness, sustainability, and spread by providing understanding and improving incentives and assistance for leaders and staff; and (3) to evaluate costs and cost-effectiveness. Dr. Chin said the second aim might be the most important in providing answers to the translation challenge of how to get something to work in the real world over time.

Dr. Chin characterized diabetes translation research issues as being diverse and complicated, involving quality of care, outcomes, access, and costs across the multiple intervention levels of patients, including children and older persons, providers, centers, and health care systems. They require multiple methods from multidisciplines. Methodological resources include biostatistics, economic analysis, and database management, along with a large variety of research areas. From the funding agency perspective, a major challenge is how to evaluate proposals and encourage innovative, creative research that takes advantage of multidisplinary approaches.

In summary, Dr. Chin named the following three issues faced by community-based participatory research:

- Developing and funding relationships of trust and equality that recognize the partners' different goals, needs, and skills and accepting that building such relationships takes time.

- Dealing with the time constraints and need for flexibility required by the real world and recognizing which partners are ready to change.

- Promoting a common vision across the partners' agendas and obtaining senior leadership's buy-in.

Discussion. Since not all standards are equally evidence-based and those that are can vary by populations, especially by age, the question was asked whether there was a need to prioritize delivery of services within constrained systems and related costs, and if so, how should they be prioritized. Dr. Chin responded that there is a lot that needs to be done in several areas at this time. A primary determining issue currently is what is practical. In CVD and diabetes management, Dr. Chin sees hypertension control as being easier to work on than glucose control. As progress is made, there may be more of a role for prioritization. CMS, for example, is considering whether outpatient quality indicators for the Medicare population should vary by age. In diabetes risk factors, should some areas require more attention than others. Dr. Chin said, possibly, but on the other hand, there is so much room to grow that group autonomy needs to be respected. Groups may have different priorities for very good reasons, so it may not make sense to apply the same standards in the VA and the health centers and the Medicare population. Some may overlap and some may be different.

Dr. Russell Glasgow, Kaiser Permanente AMC Cancer Research Center in Colorado, raised the point that there is considerable variability in success across the centers in applying the BTS approach. Dr. Chin agreed and attributed this to issues of leadership and culture, although on the whole all are enthusiastic and idealistic groups. He emphasized that the CEO or the medical director is crucial to supporting the changes needed in the organization and in making the sustainability of the approach a strategic |priority and to ensure incentives are developed to combat burnout over time.

Dr. David Stevens, Health Resources and Services Administration (HRSA), commented that translation involves system change, not just removal of barriers. He noted that three main tools have been effective so far in promoting system change. One of these is moving from an acute care model to a multi-element chronic care model, that is population-based as well as patient-based. The assumption is that one cannot change or improve a system by maximizing only one element, as was illustrated by the tobacco interventions. Teams need to work on all the elements simultaneously to make changes. A second tool is an improvement model that relates to taking a general idea proven in research and applying it in various settings. The model provides measures acceptable to the research field to test the idea in the settings. The third tool is the learning model that allows for learning and changing over time, such as a year, rather than attending one or two CME courses.

Dr. Chin stated that placement of the focus depends to some extent on the individual organization. For example, for the individual practitioner or health care organization, the system is where one must get the most result from their investment. An agency such as NIDDK can take a broader viewpoint.

Translation Research: Insights from Cardiovascular Research

Dr. Harlan Krumholz, Professor of Medicine and Epidemiology, Yale University School of Medicine, said that those who are interested in diabetes are a special community of people who focus on a large population in the country, are concerned with the acute stages in diabetes care, and then follow up with efforts to manage the chronic nature of the disease. In carrying out their mission, they are used to working in multidisciplinary teams and thinking about a populations' health and about individual patient care decisions from initial diagnosis through the patient's lifetime. There is so much that researchers and providers need to know to inform the

way to bring about change. He stressed that as NIH's budget is increased and applied to support discovery, the application side needs equal enthusiasm. Dr. Krumholz gave two examples of how little is known about promoting behavior change. It is not clearly understood why there is a stigmatism of bad health behaviors amongst health professionals, but this change was not because of legislation, or adaptation of quality measures, or educational sessions. Likewise, dress fads sweep the country, especially amongst teenagers, but there is no understanding or documentation on how this happens.

Dr. Krumholz asked "What is the paradigm?" The conventional paradigm is that great discoveries happen, research is conducted to demonstrate that something should be done, and then the discovery is applied. This is rarely a linear process. It goes backwards and forwards. There are also terminology issues—translation research, translational research, differences between type 1 and type 2 translation research, outcomes research, and so forth. He defined outcomes research as "applied clinical research that generates knowledge to improve clinical decision-making and health care delivery to optimize patient outcomes." This research has a broad focus related to providing evidence applicable to enhancing and promoting quality patient care and population health. It strives to understand factors and consequences of patterns of care and to develop strategies to address current deficiencies and knowledge. Outcomes research is about questions, not methods, and takes advantage of observational, quasi-experimental, and clinical trial approaches to address the challenges and do timely, relevant research. He stressed the necessity of embracing a broad range of approaches in a variety of areas and in moving to develop models to gather information quickly, process and evaluate an intervention, and get it to the public, and then evaluate its effect on the next generation. This will require thought and a change in the paradigm of what constitutes good research. The traditional journals do not always appreciate such real world approaches because they do not fit easily into a current paradigm.

Applying public health discoveries will always present challenges. It is thus important to study and develop an infrastructure to do this translation. Dr. Krumholz stated one goal is to have evidence-based health policy, acknowledging that there will never be absolute evidence of the right thing to do. A second goal is appropriate adoption of innovation. Surveillance, knowledge of what is taking place, is important to this goal. Finally, rigorous evaluation of changing practices at the community and clinical level is a necessary aim to understand the implications of the process changes being made. He cited the example of the change in hospital stay for bypass patients from 10 days to 4 days, without any requirement for monitoring the effect of this earlier dismissal, unlike the stringent requirements on prescription drug usage. Domains to be considered include safety, effectiveness, efficiency, equity or access, patient-centeredness, and timeliness.

The good news/bad news, according to Dr. Krumholz, is that there is great progress in diabetes but not as great as it could have been, advances in knowledge along with substantial gaps in applied science, and a focus on discovery with a relative neglect of application research. He recommended that NIH take the lead in showing Congress and the public the value of not only research to find a cure for cancer, for example, but research to find a way to better apply the cure. This will draw the best people to the field, identify the best problems, and obtain the best answers.

The age-adjusted incidence of CVD has dropped dramatically for a variety of reasons, including health care changes and secular changes. However, prevalence of CVD cases is expected to explode because of the epidemics in diabetes and obesity and the aging of the population. The issue is not just mortality or years of life, but morbidity, quality of life.

Applying discoveries is not as simple as "just do it." Variations in population characteristics and settings affects the generalizability and validity of an intervention as well as changes that take place between the time of the initial discovery and study and the present day. Besides the cost of the intervention, there is usually a question of just what part or strategy of the intervention actually caused the positive result. Dr. Krumholz gave the use of beta-blockers after an acute myocardial infarction event as an example of these translation challenges. Following the NIHLBI-funded trials in 1981, guidelines were issued with a number of contra-indications, and basically it was left up to physicians what to do, with no surveillance of practices for a long time. Then in the 1990s, a few studies showed that less than half of those who were ideal candidates for the beta-blockers were receiving them. Further studies showed that in 1995, this was still true. Questions were also raised about effectiveness, so observational studies were done with the elderly and with diabetics. Finally, additional application issues have been raised. What are the key success factors to adopting this? How can we do studies to enhance this approach? Currently, about 75 percent of prime candidates are being treated.

Other trials have been conducted in management of heart failure, lipid management, and the role of diet in CVD. In general, each disease management intervention has shown approximately a 50 percent reduction in readmission rates. A major issue is who will pay for an intervention that may actually reduce the health care system's revenue stream. Therefore, a number of potentially valuable applications are not being used in practice or being evaluated for effectiveness. With regard to diet, there is not a clear definition of what the right diet is. Billions are spent on diets, but the knowledge of what works for whom is not being collected. If known, there would remain the question of how to get people to do it.

Effectiveness involves both efficacy and knowledge of what in the setting, the population, the intervention, or the administration of the intervention is working or not working, during the trial and beyond in the community practice. Dr. Krumholz cited reperfusion therapy as an example. There were many trials, but few studies on the right way to organize the hospital in order to administer the medication and successfully replicate the trial results. He suggested that such studies would result in more "bang for the buck" from funding these trials. Hypertension has similar issues. Treatment efficacy studies compare drugs that the pharmaceutical industry chooses to compare, which leaves providers confused about which are the most efficient strategies. Also, there are few studies on the most efficient way to screen. Should everyone have a blood pressure measure by age 45? Screening and identification strategies do not have the attention that treatment does. In addition, measurements in a trial are administered much differently than they are in a doctor's office. In other words, there is a whole range of questions and issues that are downstream from the original discovery or knowledge.

Dr. Krumholz listed several issues of particular significance to him. These included decision making based on the patient's characteristics and preferences and the complex world in which the person lives. Should we assume that everyone wants to minimize risk regardless of the level of their risk and their circumstances? He quoted Dr. Feinstein's statement that "clinical judgment depends not on a knowledge of causes, mechanisms, or names for disease, but on a knowledge of patients." He noted that the quality of the research spanned a large spectrum. He asked that NIH recognize that implications for the field include external perceptions, training needs, and enhanced funding opportunities.

In the hierarchy of research, RCTs, according to Dr. Krumholz, are not necessarily the best way to answer questions. It depends on whether the question is one of comparing direct medical treatment procedures or one regarding effective care in general, for example. The first calls for an RCT, the second for a real-world observational study. He urged that existing data, even if it is still debatable, be made available more rapidly, citing the 7-year delay since the Framingham study. Partnerships with agencies and quick grant mechanisms are needed to take advantage of the data sets already collected. He also recommended that although industry has contributed much to research, NIH should look at opportunities and challenges that industry is not interested in, ones that are important to patients even though not profit-making.

In summary, Dr. Krumholz presented a set of perspectives or needs. These included:

- Directing resources toward application and surveillance as a complement to the investment in discovery.
- Training future clinical investigators.
- Using multidisciplinary approaches.
- Forging public policy links.
- Making improved health a paramount goal.
- Gaining insight into enhancing translation of the best science.
- Continuously evaluating and refining the definition of best science as applied in the real world.
- Relying on parallel efforts, not perfect science, for appropriate evidence to implement practices in the community.

Discussion. It was observed that a large part of NIH efforts seems to be based on a model that there will be a breakthrough that will lead to a cure. Although there has been some modification of this, this is still the driving force. In CVD and stroke, the age-adjusted death rates have declined 70 percent without understanding all the genetics underlying the disease risk. There is likely to be a breakthrough in type 1 diabetes, but in type 2 diabetes, due to its being intricately intertwined with obesity and metabolism and environmental influences, the benefit may be incremental and dependent on studies about how to do things in the real world.

Dr. Spiegel added that an intriguing scenario in type 2 diabetes is when the University of Pennsylvania's Dr. Mitchell Lazar discovered that insulin resistance is possibly affected by a secreted hormone coming from fat from an endocrine organ. It was thought that perhaps a pill, not lifestyle, could uncouple being fat from insulin resistance. If so, then there might be obesity, but not type 2 diabetes. He noted that it is interesting to contemplate if that would be a good thing.

Regarding using case studies to promulgate information, Dr. Pogach said that the VA did a gap analysis and performance measures and learned that heart patients were not getting the proper education, or at least it was not documented. The VA implemented a performance measurement mandating the delivery of the information, developed health tip tools for patients and templates for providers, and sampled the 140 facilities over several months. Improvement varied between 20 and 100 percent. The agency has researched rigorous tools to reevaluate risk-adjusted readmission rates for heart failure nationwide using administrative data sets. Now the group is prepared to conduct observational studies. Dr. Pogach agreed that perhaps it is now time to get the information out more quickly, recognizing that there is a role for case studies as well as observational studies and well-conducted health services research.

Dr. Krumholz agreed that such publication is important, along with rigorous collection of data to accompany the intervention and rigorous, systematic evaluation of exact impacts. It is important to be able to trust the data.

Diabetes Translation Research: The Next 25 Years

Dr. Russell Glasgow, Senior Scientist at the Kaiser Permanente AMC Cancer Research Center in Colorado, opened his presentation by quoting Yogi Berra who said "In theory, there is no difference between theory and practice. In practice, there is." In looking at the next 25 years for diabetes translation research, he reviewed the key accomplishments and lessons learned from the initial 25 years, discussed needed changes based on the RE-AIM model and recommended responsive new approaches, and identified key areas and opportunities for future translation focus.

In looking back, Dr. Glasgow noted there has been almost a paradigm shift in diabetes management to a patient-centered focus that did not exist as late as 10 years ago. There have also been guidelines and systems change interventions that share such commonalities as having nurses do diabetes care management; using proactive, planned, population-based interventions; and recognition that the fault is not the patient's or the provider's, it is a systems issue. It has been shown that practical behavioral and office-based interventions do bring about effective change.

Dr. Glasgow cited successful robust, replicable interventions across populations and settings and programs to reduce health disparities that have provided valuable lessons in spreading and generalizing knowledge. For the latter, he referred particularly to the Diabetes Prevention Program (DPP), the CHC partnerships, the VA and the Indian Health Service, and the National Diabetes Education Program. He emphasized that diabetes and its management are extremely complex. Accompanying the many attributes of self-management are the impact of individual, social, and environmental variables. A person may do well in one self-management area and less well or poorly in others. The relationship of the variables and performance to outcomes is also complicated.

Using aspects of the chronic care model and the RE-AIM model, Dr. Glasgow listed changes that need to take place. These included:

- **(R)Reach:** expand the focus on creating and documenting broadly applicable interventions for diverse populations and persons with comorbid conditions (who are usually excluded from studies, even though most diabetes patients have multiple chronic problems). Dr. Glasgow noted that designing a perfect intervention does not mean people will choose to use it.

- **(E)Effectiveness:** broaden the outcomes so they are more sophisticated and comprehensive; include economic outcomes and quality adjusted life years (QALYs) from the patient's perspective.

- **(A)Adoption:** pay more attention to settings and agents, particularly to learn who can most effectively deliver the program.

- **(I)Implementation:** pay more attention to issues such as what level of intervention can non-professionals implement, the consistency of the intervention as a variable, and the error in concluding that the intervention was not successful when, in fact, it was never truly delivered. Accurate delivery of a research discovery is a challenge in the real world.

- **(M)Maintenance:** pay more attention to social/-environmental factors influencing maintenance, conduct long-term followup studies of participants and settings, and better understand the effects of policies and the interaction of policies and behavioral treatment.

Dr. Glasgow prefaced his recommendations for future translation research by quoting Einstein's statement that "The significant problems we face cannot be solved by the same level of thinking that created them." It is necessary to "think out of the box." Future interventions need to reach those who can most benefit, be adaptable to different settings, be implemented consistently by staff with moderate levels of training and expertise, and produce replicable, long-lasting effects with minimal negative impacts and at a reasonable cost. Dr. Glasgow said there needs to be a cultural change on the part of all relevant parties, not just researchers, but funding agencies, reviewers, and policymakers. He then listed specific recommendations for each of these groups.

Researchers need to reach large, representative populations, especially the underserved. They also need to report on implementation and outcomes across a range of interventions, agents, and settings. Funding agencies should support studies in multiple settings representative of real world practice and report both mediator and moderator effects. They should fund innovative ways to enhance reach, adoption, implementation, and maintenance and require and fund a maintenance/sustainability phase. There should be standardized reporting of exclusions, participation rates, and representativeness of participants and settings.

Reviewers need to undo bias and old learning, provide greater balance in looking at internal and external validity, relax criteria on long-term maintenance, and include the potential for translation as a standard, as has been done with innovativeness. In policymaking, it is time to "put our policies and money where our mouth is." Rather than talking about the importance of translation and patient-centeredness and other issues, we should include behavioral counseling indices in performance measures and provide incentives for individuals and systems.

Dr. Glasgow stated that there are incredible opportunities at this crossroads in translation research. Key areas for future diabetes translation research include:

- Comprehensive evaluations of interventions that address social context, noting that "things are not always what they appear."

- Genetic and behavioral issue interfaces, especially gene-environment interactions and the future of genetic counseling, shared decisionmaking, and risk perception science.

- Prevention issues learned from DPP, including cost-effectiveness and less-motivated populations.

- Integrated technology applications to facilitate and support patient/provider interactions and enhance reach, implementation, and maintenance.

- Health care systems change, including policy factors that impact systems.

Proponents of the chronic care model believe changes are needed in all components of the model in order to see lasting, significant change. The ultimate goal is to see productive interactions between a prepared, proactive practice team and an informed, activated patient. For the future, the impact of policy and the social environment also needs to be evaluated.

Dr. Glasgow offered an exercise looking at a future discovery of an amazing weight-loss intervention to deal with the obesity issue on a population basis. If an unprecedented 40 percent of the clinics adopted the intervention in their setting and 40 percent of the agents adopted it, the overall effect on the population would be only 16 percent. If a phenomenal 40 percent of the patients who tried the intervention were successful, the population effect would still drop to 6 percent. Including the factors of consistent delivery, behavior change, and sustainability, the cumulative effect would fall to less than half of 1 percent. The good news is that with greater attention to these factors, there can be a greater public health impact and perspective.

Dr. Glasgow said that if we are serious about seeing greater translation change, then we must require fundamental improvement and change in the culture at all levels of participation. The stepped care pyramid model illustrates this. To date, the largest amount of research has been at the top of the pyramid at the level of a very small segment of people, some at the primary care and health care systems levels, but relatively little at the community/neighborhood, media, and policy levels at the base of the pyramid. Whereas reach is highest at the lower levels, intensity and cost are highest at the upper level. Dr. Glasgow suggested that it might be more cost-effective and efficient to do more interventions at the lower levels for everyone.

In conclusion, Dr. Glasgow recommended, "the best way to predict the future is to create it" but to keep in mind that as H.L. Mencken said, "to every complex question, there is a simple answer—and it is wrong."

Discussion. Dr. Green identified that one thread running through the presentations and discussions was the degree to which those present really believe, as one moves out beyond the bedside, that there are interventions that can be packaged and made generalizable. The attendees fall along a continuum with respect to this thread. He said he took the position that no off-the-shelf, generalizable interventions exist. Interventions must vary with the person and the circumstances. However, RE-AIM seems to imply that there is something concrete, specifiable, exportable, and generalizable. He asked if Dr. Glasgow would be revising the RE-AIM model.

Dr. Glasgow replied that what we should learn from research, if it is cumulative, is some generalizable principles, not just theories or hypotheses, and this result can be enhanced by studying mediators and moderators. There are some common principles in self-management education that apply across settings, such as collaborative goal setting, followup, or integrating self-management into primary care. Dr. Glasgow did agree that one cannot take an intervention, even one as successful as DPP, off the shelf and apply it exactly the same. It must be tailored to the setting, working with partners to apply the principles of the intervention in the setting.

Dr. Stevens asked that in order to have a concept implemented or replicated, does it not have to be specific and not so generalizable that it is "messy" to apply. Dr. Glasgow said that the level of specificity is a good challenge. Most people cannot take the general principle, such as collaborative goal setting, and do it. Everyone thinks they do that, but actually few really do it in a way that is patient-centered. People need options, concrete examples, and tools in order to not have to reinvent the wheel. By being creative and willing to try things, centers have taken the principles of goal setting and having an action plan from the study setting and made them work in their settings. They have taken ideas and examples from academic researchers and adapted them to a lower literate, even almost illiterate level, to be used as tools for interventions.

Dr. Glasgow was asked if he would recommend the use of QALYs to set areas of priorities for interventions, and if so, what would be the implications for DMICC. Dr. Glasgow said one clear implication was that number one on the list would be redoubling efforts for smoking cessation for anyone with diabetes who smokes. That would be the single most cost-effective intervention, and there is a lot of information on how to produce system change in smoking. The questioner agreed and said that blood pressure would probably be second. Dr. Glasgow concurred and addded that one of the important lessons learned is that diabetes is about more than just Alc, although we must continue to improve our efforts to control that while broadening our focus.

Afternoon Presentations and Discussions

Dr. Saul Malozowski, who has been appointed as the new DMICC Executive Secretary, announced that the afternoon's format would vary from that of previous meetings. Rather than agency representatives providing a position statement and update of their current and proposed activities in relation to the meeting's subject, they would be discussing a set of questions posed by the speakers about emerging issues in diabetes translation research and implementation. The exception would be a presentation by Dr. Desmond Williams, Centers for Disease Control and Prevention (CDC).

Desmond Williams, MD, PhD, Division of Diabetes Translation, CDC

Dr. Williams began by stating that many people at CDC have been working to learn new techniques and strategies to address the complex issues of diabetes research translation. CDC views translational research as a way to identify and test strategies of change aimed at achieving optimal diabetes care, to assess the level and quality of care practices, to explore factors affecting variations in care, and to identify barriers and enablers of change.

Dr. Williams presented a CDC graphic depicting translation research in the context of other models of research, such as basic science/epidemiology, surveillance, and clinical trials, that are used together to better characterize and understand problems and track changes over time. CDC sponsors, conducts, and participates in clinical trials to understand solutions to problems. There is an ongoing translational process in which progress is made from one step to another and much is learned from mistakes made.

Current translational efforts embody a variety of approaches at different governmental levels. Translating Research Into Action for Diabetes (TRIAD) is a health system's approach, Diabetes Control Programs (DCPs) are administered by State health departments, Diabetes Collaboratives take place at the CHCs, Project DIRECT (Diabetes Interventions Reaching and Educating Communities Together) is another community-level effort, and the U.S.-Mexico Border Study is an international project.

The CDC/NIDDK multi-center TRIAD study, funded by a 5-year cooperative agreement, involves 11 plans and 63 provider groups and 194,000 persons with diabetes. The TRIAD centers are located in Hawaii, Texas, Indiana, California, Michigan, and New Jersey. The study uses baseline and longitudinal analyses to investigate structural factors, processes and quality of care, and health outcomes issues and interactions. This ongoing study is expected to produce information on the status of diabetes care in managed care organizations.

Levels of funding distinguish core and comprehensive nationwide DCPs, with cores receiving up to $240,000 and comprehensives, up to $800,000. Although CDC-funded, the groups operate as autonomous bodies, so all have different activities of concentration. CDC encourages the establishment and maintenance of statewide diabetes coalitions and each State has a Diabetes Advisory Committee. Examples of activities include diabetes surveillance and services, community-based programs to control complications, and public and provider education. The groups strive to identify barriers and enablers

to changes in diabetes care and develop outreach programs for minority populations.

Project DIRECT is the largest community-based diabetes project in the United States. It is an equal partnership among CDC; the community of southeast Raleigh, North Carolina; the Division of Public Health in the North Carolina Department of Health and Human Services; and North Carolina's Wake County Human Services. The community has developed a coalition, supported by the partners, that guides intervention activities. The coalition-written goals are to improve quality of care and self-management practices, detect undiagnosed patients and ensure persons with diabetes are in the health care system, and reduce risk factors by advocating and encouraging lifestyle changes.

The 5-year U.S.-Mexico collaborative study will be taking place in medically underserved communities on both sides of the border. The study communities have high poverty levels and many of the Hispanic members are uninsured or underinsured. The project's purpose is to determine the prevalence of diabetes along the border and to develop bi-national prevention and control programs. Besides CDC, international partners include the Pan American Health Organization, the U.S.-Mexico Border Health Association, the Secretaría de Salud de México, State Health Authorities and DCPs, Paso del Norte Health Foundation, El Paso Diabetes Association, the Border Health Foundation, and the California Endowment/ Project Concern International.

Other CDC research activities used to support translation efforts include surveillance and evaluation projects using both quantitative and qualitative methods. Along with efforts to learn more about barriers and enablers, CDC is trying to find ways to institutionalize activities in the community to make them more self-sustaining. CDC is committed to and actively engaged in translational research as a way to reduce the burden of diabetes and its complications. The agency sees translation research as a necessary bridge between basic and clinical research and diabetes care practices. It is an ongoing process of developing, testing, and implementing new strategies. Dr. Williams said CDC believes it is important to have opportunities like the DMICC meeting and other forums in which to share experiences with other agencies.

Discussion. Dr. Green spoke about the announcement of a new urban research center to be established in El Paso, funded by his office and the epidemiology program office. There are currently three such centers engaged in participatory research. Asked if the U.S.-Border Study was connected to this, Dr. Williams replied that it was a separate project. In response to the status of Project DIRECT, he said a contract for evaluation had recently been awarded and that CDC feels they have learned a great deal from this project, including lessons learned about collaboration. The evaluation will look at the study's achievements, analyze methods both qualitatively and quantitatively, look at differences in diagnosed and undiagnosed diabetes, and examine other issues set up by the primary study objectives. Important items to assess will be about how was the community accessed, what were the initial problems and how were they resolved, what was learned from this, and what lessons can be gained from the study to share with others. The study is ongoing with final results expected in approximately 3 years.

Emerging Issues in Diabetes Translation

Dr. Malozowski said that speakers had submitted about 20 questions earlier. These thoughts were used to form the following set of issues to be discussed by the DMICC representatives:

- What is the most important translation issue for your agency?

- What do you see as the unique role of your agency related to diabetes translation and how do you envision your agency responding to the outcome of today's meeting?

- What are the barriers to diabetes translation that your agency faces and what is the single most important thing that can be done to accelerate the translation of research to practice?

- At your agency level, what can be done to address the challenges of diabetes translation involving:

  – *patient and provider,*

  – *health care organizations, and the*

  – *health care system?*

- At your agency level, what can be done to ensure that there is the breadth of expertise needed to develop, nurture, and evaluate diabetes translation initiatives, such as:

  – *health services research,*

  – *behavioral research,*

  – *organizational theory,*

  – *epidemiology, and*

  – *economics, etc.?*

- How can your organization form collaborative partnerships with other funding agencies, academic institutions, and community partners to work on diabetes translation efforts?

Veterans Administration. Dr. Leonard Pogach referred the audience to www.oqp.med.va.gov where the VA's performance measures are posted on the Web. For diabetes care, the VA average nationwide is equal to or exceeds the 90th percentile of all NCQA reporting plans. The VA embraces change in translation at every level—systems, management, and research—which is why they are successful, according to Dr. Pogach, along with the Indian Health Service and the U.S. Department of Health and Human Services.

Dr. Pogach said that the VA's primary translation issue at this time concerns the nature of its patient population, which is economically disadvantaged, with 10 percent homeless and 30 to 40 percent with a mental health condition. Even with the mental health problems, their process measures and intermediate outcome measures for diabetes are comparable. With distal outcomes, mortality, amputations, and so forth, there are still disparities. Understanding that is a challenge for the agency. Another issue is that the VA cares for about 800,000 persons with diabetes, of whom 70 percent are Medicare eligible, with attendant policy-level considerations. The VA has a computerized system of medical records, computerized reminders, outcome information, and nationwide automated data sets. This enables him to have a research set of all diabetes patients with their Medicare data, which offers extraordinary opportunities to look at the delivery of health care within their system.

Competing resources for the patients' wide range of health problems, such as stroke and mental health conditions, can be a translation research barrier. Hepatitis C affects about 12 percent of the population. The VA is also the Nation's largest provider of AIDS care. There is tension between quality improvement and research. There is also a lack of consensus often as to what measures most need to be tightly controlled in seniors—hypertension, hyperlipidemia, or glycemia. Glycemia usually wins, which Dr. Pogach disagrees with, and he challenged DMICC to send out a unified message that for seniors, while not demeaning glycemic control, it is blood pressure and smoking that should be the priorities in using the health care systems' limited time and resources.

The VA has a Quality Enhancement Research Initiative (QUERI), which is funded for eight or nine disease entities, of which diabetes is one. The research coordinator is Dr. Rod Hayward at Michigan. Dr. Pogach is the clinical director. There was a Medicare supplement report on the initiative in June 2000. The goal throughout the VA is to systemize the quality of care. To accomplish this, the QUERI groups are integrated as much as possible with operations, with efforts made to overcome research/operations barriers as much as possible. Both researchers and policymakers serve on the executive committees for the QUERI groups. This system helps to bring the efforts of the whole VA health services community to bear on problems. In addition, a number of QUERI investigators serve on the VA/DoD national guideline council that integrates guidelines and performance measurements and implementation evaluations for both agencies.

In summary, Dr. Pogach said the VA has a unique system of care that, although sometimes somewhat bureaucratic and para-military and, like most of the other agencies, responsible to Congress, it does embrace change and innovation.

Discussion. Dr. Speigel asked if the VA was considering primary prevention of diabetes. Dr. Pogach answered that revisionary guidelines were coming out that would incorporate the ADA position statement on screening as a consensus-based statement. The VA population's average age is 67 and even among non-diabetics, there is 40 percent hypertension and hyperlipidemia is endemic, so the agency is looking for opportunistic screening in the population. Primary prevention has not been addressed directly, just implicitly. Because of the Institute of Medicine's finding that Agent Orange is possibly related to diabetes, it is now enshrined and benefited as a service-connected disease, so there might be some possibilities to target some appropriate populations.

National Heart, Lung, and Blood Institute. Dr. Denise Simons-Morton said the most important issue for NHLBI regarding diabetes is that diabetes is a CVD risk factor. In translation research, NHLBI has projects related to prevention such as diet, weight control, and physical activity programs. The most important challenge is balancing the portfolio with all the basic science that needs to be done along with the translational research. NHLBI also has a research continuum, with feedback loops, that goes from basic research to epidemiological studies to efficacy RCTs to effectiveness trials to translation and dissemination research that then results in translating and disseminating interventions. In this context, NHLBI is sponsoring the TAAG and ACCORD trials and the National High Blood Pressure Education Program and the National Cholesterol Education Program, which are not research programs but are translational.

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) is partly an efficacy and partly an effectiveness trial asking if intensive control of glycemia in adults (less than 6 percent HbA1c vs. the average 7.5 percent) would prevent CVD events. This study of 10,000 participants also will ask blood pressure and lipid questions. It will be implemented in 60 clinical sites across the United States and Canada, including HMOs, VA sites, Canadian health systems sites, and private doctors' offices. Thus, ACCORD will test the HbA1c reduction intervention in settings where patients are normally seen. Patient characteristics have been selected to be generalizable also.

The Trial of Activity in Adolescent Girls (TAAG) is another relevant study that is being implemented in 36 schools nationwide with a representative sample of minority students. TAAG's purpose is to study a school-community link to intervention to prevent the decline in activity seen in adolescence, particularly in girls. It is really a primordial prevention study of sedentariness. Phase I was a needs assessment. After the intervention, there will be a sustainability evaluation, which is important for programs to be implemented in the real world.

An example of translation research is the Activity Counseling Trial, an RCT to test patient education and counseling approaches for physical activity. The interventions were designed to be feasible and appropriate for delivery in primary care settings. The completed study was published in 2001 and showed an effect in women but not in men. CATCH-ON is an example of an observational study of the implementation and institutionalization of the previous CATCH (Child and Adolescent Trial for Cardiovascular Health) school-based intervention. These are examples of an RCT that tested real-life interventions in real-life settings and an observational study to identify the characteristics of schools that would make them adopt an intervention that was successful in improving diet and physical activity in children. The major characteristic identified was having a person in the school who was dedicated to behavioral change.

NHLBI just released and funded a Request for Applications (RFAs) for trials to assess innovative strategies to improve clinical practice through guidelines. The purpose is to test multi-faceted interventions delivered in clinical practice with the outcomes being the provider practices. The interventions are intended to help providers use guidelines that are evidence-based in heart, lung, and blood diseases. RCTs were not required, but quasi-experimental designs were requested in order to have comparison groups. Needs assessments were encouraged for phase I. Eight studies have been funded that are going to provide a lot of experience relevant to diabetes. Other investigator-initiated studies are testing similar events.

NHLBI recently had a retreat on translation to discuss both the bench to bedside and bedside to community steps. One of the results of that retreat is a new policy, which has been posted on the Web, that NHLBI will require dissemination plans in RFAs, Request for Proposals (RFPs), and large investigator-initiated studies for clinical or public health research.

NHLBI is making a strong effort to make data available for epidemiologic studies and clinical trials. There are a number of data sets that are available now from Framingham and the epidemiologic studies. Within the next year, additional clinical trial data will be available from NHLBI.

Dr. Simons-Morton noted that NHLBI also has training programs for clinical researchers, as do other NIH groups.

Discussion. Dr. Glasgow mentioned that each group has a research model going from basic research to translation and these models are useful. However, because of time, occasionally there is a problem going from one stage to another, particularly from efficacy (tested under experimental design conditions) to effectiveness (Does it work in the real world?).

Dr. Simons-Morton agreed that these were excellent points and ones NHLBI staff had discussed frequently in designing studies. In ACCORD, they conducted a vanguard phase in all 60 clinics because they wanted to know, although this was an efficacy study, that the intervention being tested could actually be implemented in the real world. It takes time and resources to reduce HbA1c to 6 percent and stay there, so the next question may be will it be implemented. In the history of CVD, researchers have asked in efficacy trials the causal question or proof of principle question: Is hypertension a risk factor for CVD and stroke? The way one proves evidence of causality is to have experimental evidence that lowering blood pressure prevents or reduces CVD and stroke events. Internal validity has been considered the most important thing, but now, there is a move toward valuing external validity and generalizability.

Dr. Simons-Morton stated that NHLBI is putting a lot of resources into ACCORD to do intensive glycemia treatment. If the study finds that there is a significantly positive effect, there will be a question of whether or not providers will or can do this. If the effect is not positive, then they will know that it is not worth their time.

In response to Dr. Green's query about the results of CATCH, and what CATCH-ON will do differently, Dr. Simons-Morton explained that CATCH was a randomized school-based trial of 96 schools randomized to intervention and control. The intervention being tested was a health promotion intervention to improve diet and physical activity in elementary school-age children. The primary outcome was identified as blood cholesterol. Improvements were achieved in diet and physical activity, but there was not a significant effect in blood cholesterol. Still the intervention was considered worthwhile because of the improvements in the health behaviors. It was then decided to do a followup observational study of three groups, the original CATCH intervention schools, the original CATCH control schools, and a naïve group of schools selected to be roughly comparable. For the original intervention schools, the questions were "was the intervention institutionalized, was it maintained, and what were the factors associated with that, if it was." The control schools were given all the materials and brief training and the question was whether or not the program was adopted. The third group was used for comparison for secular trends. As mentioned earlier, the most important factor for maintenance, institutionalization, or adoption was a change agent or a dedicated person who was committed to having the program happen in the school.

NIDDK. Dr. Garfield reiterated that studies such as DCCT clearly have no purpose unless they are translated. One approach NIDDK has taken is to implement a translation research program. A recent program announcement is asking for studies that involve translation of known effective interventions. The proposals are reviewed by the Institute's review branch. There is also an R21 small grant program to make it easier for persons to develop pilot data to feed into the translation research program. NIDDK is clearly emphasizing translation and setting up programs to promote that. The NDEP that NIDDK and CDC co-fund is also a translation program and is actively developing plans to disseminate and implement the DPP results.

Discussion. Dr. Williams asked how NIDDK sees the implementation of the DPP results in the general population. Dr. Garfield responded that HRSA is developing interventions to try to study that in their community centers and NIDDK's translation research program will assist with that. NIDDK is also working with the Indian Health Service, which is developing plans to implement DPP lifestyle intervention programs. NIDDK is also working with ADA to develop recommendations based on the DPP results. Dr. Malozowski added that NIDDK is working with the DPP nutritionists and those who implemented the intervention to put together a toolbox based on DPP to distribute to practitioners to help them implement the intervention.

Dr. Spiegel commented that Dr. Williams' question touches on the crux of the issue with DPP. In a clinical trial population, motivation is always a factor that limits generalizability. However, in DPP, by selecting 45 percent of the participants from minority groups, the rationale was that it should be generalizeable to the U.S. population, in contrast to the earlier Finnish study, with the caveat of having to motivate individuals. The two critical challenges to real-world effectiveness are first, identifying those at risk, which was done in DPP through the formal oral glucose tolerance testing, an issue we have been in dialogue about. The second issue is about implementing the highly structured, individualized, intensive lifestyle intervention that was shown to be effective; the calculations are that that cannot be done on a population basis simply in terms of available trained individuals and cost. Other interesting implications are that metformin, which is now generic, was shown to be equally effective to lifestyle in a subset of individuals with a body mass index (BMI) over 34 or 35 and age 25 to 44. So one issue will be pharmacological intervention and the cost effectiveness and implementation of that, which does not raise all the lifestyle issues. Returning to the first challenge, the identification of the target population, Dr. Spiegel said that it is not the message of DPP to suggest that there is no need to select individuals since the lifestyle changes would be good for everyone. The question is should persons be identified by

a checklist or a questionnaire, as has been done for cardiovascular risk, in which family history, obesity, membership in a minority population, sedentary behavior, and so forth are assessed. How would such a questionnaire track as a surrogate for formal glucose tolerance testing, which raises more complex questions about which test is appropriate.

Dr. Williams said that CDC is discussing these issues and as Dr. Spiegel clearly illustrated, there are no easy answers to the questions. Eventually, there probably would have to be some surrogate measures developed for administering the oral glucose tolerance test, possibly specific items in the patient's history that would indicate increased risk for impaired glucose tolerance. Those at risk might—only might—then be included in a testing program. Dr. Williams thought that developing such surrogate measures are a major stumbling block in translating DPP's results to a broader population.

Dr. Spiegel stated that the studies in the NIDDK translation research program that Dr. Garfield referred to are potentially important vehicles for testing hypotheses for identification and for modified lifestyle interventions.

Dr. Pogach said that one of his concerns about DPP implementation and generalizability issues was that the control groups did as well as they did, even though poorly, perhaps because they had access to one annual session with a diabetes educator, which is more than most people ever have, and they seemed to be a highly motivated, self-selected group who exercised more than most Americans do, although they had no significant weight loss. Also, for some persons in the VA population, vigorous exercise might be difficult because of knee problems and other health problems.

Dr. Spiegel and Dr. Garfield pointed out that 11 percent of the control group per year developed diabetes and that the intervention group attained an overall 4 to 5 percent weight loss and actually exercised more minutes per week than requested. In fact, exercise was the most adhered to component of the lifestyle intervention.

Dr. Simons-Morton commented that the issue of the control group comes up over and over in CVD trials. What is appropriate to deliver to the control group is one issue and another are the changes seen over time in the control group, but the internal validity of the study is still a comparison between the control and intervention group. In randomizing people who agree to go into one or the other group, there is often a highly selected group in terms of motivation whether or not they are representative in terms of gender, minority status, or other characteristic. Clinical trials in general have to deal with this issue.

Dr. Malozowski added that in drug trials, the patients tend to be more homogenous than they were in DPP. An interesting result in DPP was that patients in the control group did not gain weight as it had been expected they would, possibly due to the difference of participating in a study versus not participating in a study. He felt that it was very important information that elderly patients in particular benefited substantially from the exercise.

Dr. Peter Savage, NHLBI, stated that DPP was an extremely valuable study because no one would even be talking about preventing diabetes if the time and effort had not been taken to do a study of this sort. This is a good illustration of why there is a need for fairly complex clinical trials to change the mindset. The speculation is, however, that it was a complicated enough study in terms of effort and cost so if these data are turned over to relatively low-level efforts in routine clinical settings, there is a likelihood that there might not be a major reduction in development of type 2 diabetes. He asked if there

was a need for some other type of more formal research studies, maybe treatment for 6 months or a year with an insulin sensitizer—which drug companies are studying— plus some form of weight loss regimen and then stopping to see if persons can be kept non-diabetic for a period. Such a study could bridge the gap between an expensive, complicated intervention and something more affordable that could be done in a clinical setting.

Dr. Speigel responded that Dr. Thomas Buchanan had just published in *Diabetes* his study of the insulin sensitizing drug troglitazone, which has now been withdrawn, in gestational diabetes in Hispanic women. He had strikingly positive effects, which offers a theoretical framework of beta cell preservation. There was an arm of DPP that involved troglitazone that was discontinued after 9 months due to safety concerns and the group given modified lifestyle. The data from that group is not yet publicly available, but it will be at some point and it may be a test of what Dr. Savage just proposed because the group will have been treated with medication for a while and then lifestyle. A paper on data from this group is nearing completion, according to Dr. Garfield.

Dr. Pogach referred to a screening issue in the European UKPDS study about whether early detection for type 2 diabetes will actually improve outcomes. In general, it is thought that there is insufficient evidence to recommend screening for type 2 diabetes in the general population because it is unknown whether or not outcomes will be improved. Hypotheses could be posed that more rigorous treatment of the risk factors would improve outcomes. But these are questions for which there are not yet answers. The intensive nature of DPP has meant that there is a sense of caution about its adaptation. The question remains as to where the effort and resources should be put. That is different than saying who should lose weight and who should exercise.

Dr. Garfield said that the outcome study from the DPP is following all of the newly diagnosed patients and is the only cohort for which it is known, within a 6 month window, when a person became diabetic.

Dr. Glasgow suggested the group consider the situation if the DPP results had been reversed and the pharmacological intervention had been dramatically more effective than the behavioral intervention. The current discussions would probably not be taking place. There would not be much concern about the run-in period. There would not be any consideration about the fact that drugs are never implemented in the real world the way they are in an efficacy studies. There is a huge multi-billion dollar industry out there to support their implementation. This is a cultural mind-shift issue that is real and needs to be studied, but often different standards and issues arise because of how we have been trained in our culture.

Dr. Simons-Morton supported this point by commenting that there was an extensive effort in DPP to achieve the level of compliance for the metform in arm that they needed. Dr. Garfield added that just as there was a lifestyle corps to help people adhere, there was a drug corps for adherence..

Dr. Savage said that exercise may be more efficacious in preventing diabetes than in helping those who already have diabetes in terms of the levels at which people are likely to exercise, although some people may do spectacular things with diet and exercise. There are spun-off questions from the DPP that are not likely to be asked in the community and need to be followed up by NIH. Another question is the use of the fasting glucose test to screen for high-risk people. There are some large data sets from people who have been tested and followed for some time that are becoming available for public use from NIDDK and NHLBI. These will provide an opportunity to analyze that data and see if there is some combination of obesity and fasting glucose that would be a reliable predictor of diabetes risk and substitute for a formal oral glucose tolerance test. Dr. Garfield said they were also analyzing the effects of exercise versus weight loss.

Agency for Healthcare Research and Quality (AHRQ). Dr. Daniel Stryer said that AHRQ is a relatively small agency that is tasked with research on all problems within the "ICD-9 book" for all populations and in all settings, which becomes a bit overwhelming. Therefore, AHRQ cannot concentrate too many resources on diabetes, although it is obviously a major cause of morbidity and mortality. AHRQ is focused on the delivery of health care, so the agency is looking at clinical issues, but also at organizational and structural factors, which is important in translational research. In AHRQ studies, the agency is looking at these factors to understand the interplay between the organizational and structural levels and to understand some of the subtleties in interventions that make them work in one setting and not another.

AHRQ does go through the efficacy and effectiveness stages mentioned by the other speakers and other DMICC members. The agency refers to translation as implementation or TRIP, Translating Research Into Practice. The TRIP 1 initiative focused on efficacy. TRIP 2 was more of an effectiveness model. The agency is now in a third generation of implementation research and has issued a TRIP 3 Public Announcement in partnership with the VA. AHRQ is also a partner with NIDDK in its new RFA for translational research in prevention and control of diabetes. In this third generation, AHRQ is especially interested in the factors that account for variability in success or failure from one setting to another. This is considered important for generalizability and for adjusting or selecting one intervention or another in a particular setting.

Dr. Stryer said that the research base is important, but tools are also needed. There is no off-the-shelf intervention, most need to be adapted, but a lot of good work is taking place and it is unnecessary for everyone to reinvent the wheel. AHRQ is developing a tool box—or maybe a tool shed—that is going to come out in about a year to put these tools in the public domain.

Dr. Stryer stressed that partnerships are another important level in translation research. There is a chasm between what is known from research and what is being put into practice. A key in implementing findings is going to be developing partnerships with those on the front line of health care to understand their needs and address them, but also to get them involved early in the process in the research so they will come to the agencies with their needs and learn what is available. Dr. Styer said that establishing this level of partnership does not just happen; there is a science to it.

AHRQ's partnership with HRSA will assess the Health Disparities Collaboratives to enhance the research basis for quality improvement. It will look at real world situations; it is not an efficacy model. It is getting at the failure and success factors, generalizability, sustainability, and return on investment. All of which are important next steps for translation.

Discussion. In response to Dr. Green's inquiry about AHRQ's activities in community-based participatory research, Dr. Stryer said this sprung up from the disparities initiative but is also a part of implementation. This is really a subset of user-driven research. The communities are one of the types of users that AHRQ feels it needs to reach out to and ensure that their needs are being met. It is very important that these users are incorporated into all stages of the research process from identifying a topic, to development of the question, the development of the hypothesis, the actual choice of methods, the analysis, and the implementation. This is a key component of AHRQ's implementation research.

Health Resources and Services Administration (HRSA). Dr. David Stevens said that the most important issue in translation research for HRSA is the change in practice from the acute to the chronic care model. To do that involves four main elements. First, HRSA is using a learning model and Dr. Ed Wagner's improvement model that relies on productive interactions between a prepared, proactive, practice team and an informed, activated patient and interactions with community resources and policies and the health system. Second, the agency has a leadership program at the national and local levels. The third element is the agencies strategic partnerships. Fourth, and of major importance, is a heavy investment (nearly $20 million) and effort in building infrastructure at the State and national levels.

Dr. Stevens said there is a difference between research and quality improvement. HRSA does not do research to generate knowledge; they do evaluation, so their methods are different than those of researchers. One difference is that research uses blinded tests, and HRSA's are observable. Other differences are researchers are looking for no bias, whereas HRSA studies have a stable bias; researchers collect all possible data and HRSA wants just enough data to know if they are accomplishing what they want. Research works from fixed hypotheses; HRSA studies have changing hypotheses. In research, there is one large test and HRSA has many hundreds of sequential small tests. Research has stable cohorts; HRSA has a changing population.

In answer to the question about HRSA's unique role, Dr. Stevens explained that 86 percent of the patient population the agency works with are low income persons, 40 percent are uninsured, 28 percent are African American, 30 percent are Hispanic, and 8 percent are Asian. This is a very important population to be serving. HRSA has gone into many clinical areas with its model—diabetes, depression, CVD, asthma, and cancer. There is a potential synergism and HRSA has found a tremendous affinity with changes across the conditions, which is good news for a provider, because it means there is a finite number of things to do to produce multiple good results.

Dr. Stevens said he believed that DMICC can do a great deal in providing national leadership on the importance of translational research. This can help in removing barriers and making change in policy. It says that what agencies like HRSA is doing is important; it is not marginalized. It also provides HRSA with access to information. Dr. Stryer said that HRSA is actually a researcher's customer. There is no reason for HRSA to duplicate the expertise of the research agencies, and they are not equipped to do so. That is why HRSA wants to partner with the research groups. In return, HRSA can provide access to populations and provide information on spreading innovation to change and improve health care practices to complement what researchers are doing.

Dr. Stevens stressed that it is important to involve early on those to whom the research is going to be applied. This should be as early as at the hypothesis stage in the clinical research stage. HRSA is translating DPP now, but Dr. Stevens wishes they had been involved when the study was being designed. He said that the use of the DPP results is exciting, even though there are problems to be resolved. However, they wish that the study had considered a non-biological test to identify the target population or tested less than a 150-minute per week exercise intervention, even though this would have cost more money. It would be good to build in collaboration earlier. It could shorten the time. Currently, it has been found that 14 percent of original research takes 8 years to get into practice. It would help to have persons who can straddle the world of research and the world of application. If they do not exist, they should be trained.

Dr. Stevens said he sees translation research as developing inter-disciplinary discipline. If the translation units within NIH and CDC would form a collaborative themselves and had an overall strategy for moving the field forward, that would be tremendously helpful to HRSA. There would be less duplication and more synergism, and it would be easier for those who are in systems to get more feedback to the collaborative. This could be an ongoing activity, where the translation work results could be evaluated. Dr. Stevens said that every month he has outcomes and does not have time to look at the data. He suggested that this is true for the VA and NIDDK and it could be of interest and use to a larger group such as a collaborative.

HRSA does expect to have outcomes from its prototype of five CHCs on the DPP translation by July or August 2003. There will also be important outcomes from the work with AHRQ. Dr. Stevens said he would like to share those results in a group such as DMICC where it might influence research questions of colleagues in other agencies or in academia.

Discussion. Dr. Spiegel expressed his appreciation to the speakers and the attendees for their participation and acknowledgement of the 25th anniversary of the DRTCs and their important work. He said he felt a renewed sense of partnership and of the importance of collaboration. It needs to be made meaningful, and Dr. Speigel intends to work with the group in that capacity.

Dr. Pogach asked if there would be another meeting on translation that might bring together other NIH groups with DMICC. Dr. Spiegel responded that such a forum need not be limited to DMICC meetings. Dr. Williams said that CDC would strongly support such a meeting or conference, and it could include scientists from other organizations and from academia also.

The meeting was adjourned at 2:35 p.m.

Participants

Kristin Abraham, PhD
Director, Cell Signaling Programs
Division of Diabetes, Endocrinology
and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard
2 Democracy Plaza, Room 607
Bethesda, MD 20892-5460
Tel: (301) 451-8048
Fax: (301) 480-3503
abrahamk@extra.niddk.nih.gov

Richard Anderson, MD, PhD
Program Director, Division of Genetics
and Development Biology
National Institute of General Medical Sciences
National Institutes of Health
45 Center Drive, MSC 6200
Natcher Building, Room 2AS-25
Bethesda, MD 20892
Tel: (301) 594-0943
Fax: (301) 480-2228
andersor@nigms.nih.gov

Ricardo Brown, PhD
Program Director, Biomedical Research Branch
Division of Basic Research
National Institute on Alcohol Abuse and Alcoholism
National Institutes of Health
6000 Executive Boulevard, MSC 7003
Willco Building, Room 402
Bethesda, MD 20892-7003
Tel: (301) 443-2239
Fax: (301) 594-0673
ricbrown@mail.nih.gov

Francisco Calvo, PhD
Chief, Review Branch
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard, Room 752
Bethesda, MD 20892
Tel: (301) 594-8897
Fax: (301) 480-3505
calvof@extra.niddk.nih.gov

Michelle Cissell, PhD
AAAS/NIH Science Policy Fellow
Office of Scientific Program and Policy Analysis
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
31 Center Drive
Building 31, Room 9A05
Bethesda, MD 20892
Tel: (301) 496-6623
Fax: (301) 480-6741
cissellm@extra.niddk.nih.gov

Laura Cole, PhD
Senior Policy Analyst
Office of Scientific Program and Policy Analysis
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
31 Center Drive
Building 31, Room 9A16, MSC 2560
Bethesda, MD 20892-2560
Tel: (301) 496-6623
Fax: (301) 480-6741
colel@extra.niddk.nih.gov

Catherine Cowie, PhD
Director, Type 1 Diabetes Clinical Trials Program
Division of Diabetes, Endocrinology
and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard
2 Democracy Plaza, Room 691
Bethesda, MD 28092-5460
Tel: (301) 594-8804
Fax: (301) 480-3503
cowiec@extra.niddk.nih.gov

Jeffrey Cutler, MD
National Heart, Lung and Blood Institute
National Institutes of Health
Rockledge 2, Room 8130
Bethesda, MD 20892
Tel: (301) 435-0414
cutlerj@nhlbi.nih.gov

Maria Davila-Bloom, PhD
SRA/NIDDK Review Branch
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard,
Room 758, MSC 5452
Bethesda, MD 20892-5452
Tel: (301) 594-7637
Fax: (301) 480-3505
davila-bloomm@extra.niddk.nih.gov

Thomas Eggerman, MD, PhD
Director, Islet Transplantation Program
Division of Diabetes, Endocrinology
and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard
2 Democracy Plaza, Room 697
Bethesda, MD 20892-5460
Tel: (301) 594-8813
Fax: (301) 480-3503
eggermant@extra.niddk.nih.gov

Jody Evans
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
2 Democracy Plaza
6707 Democracy Boulevard, Room 713
Tel: (301) 594-8843
evansj@extra.niddk.nih.gov

Lawrence Fine, PhD
Medical Advisor
Office of Behavioral and Social Sciences Research
National Institutes of Health
1 Center Drive
Building 1, Room 256
Bethesda, MD 20892
Tel: (301) 435-6780
Fax: (301) 402-1150
finel@od.nih.gov

Carol Feld
Director, Office of Scientific Program
and Policy Analysis
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
31 Center Drive
Building 31, Room 9A07
Bethesda, MD 20892
Tel: (301) 496-6623
Fax: (301) 480-6741
feldc@extra.niddk.nih.gov

Sanford Garfield, PhD
Senior Advisor, Biometrics and Behavioral Science
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
2 Democracy Plaza
6707 Democracy Boulevard, Room 685
Bethesda, MD 20892-5460
Tel: (301) 594-8803
Fax: (301) 480-3503
garfields@extra.niddk.nih.gov

Alan Guttmacher, MD
Senior Clinical Advisor to the Director
National Human Genome Research Institute
National Institutes of Health
31 Center Drive, MSC 2152
Building 31, Room 4B09
Bethesda, MD 20892-0844
Tel: (301) 402-0955
Fax: (301) 402-0837
guttmach@mail.nih.gov

Stephen James, MD
Deputy Director
Division of Digestive Diseases and Nutrition
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard, Room 675, MSC 5450
Bethesda, MD 20892
Tel: (301) 594-7680
Fax: (301) 480-8300
jamess@extra.niddk.nih.gov

Mary Beth Kester
Program Analyst
Office of Scientific Program and Policy Analysis
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
31 Center Drive
Building 31, Room 9A05
Bethesda, MD 20892
Tel: (301) 496-6623
Fax: (301) 480-6741
kesterm@extra.niddk.nih.gov

Jon Kerner
National Cancer Institute
National Institutes of Health
6130 Executive Boulevard
Rockville, MD 20852
Tel: (301) 594-7294
Fax: (301) 594-6787
kernerj@mail.nih.gov

Richard Knazek, MD
Medical Officer
Clinical Research
National Center for Research Resources
National Institutes of Health
6705 Rockledge Drive, MSC 7965
One Rockledge Centre, Room 6030
Bethesda, MD 20892
Tel: (301) 435-0790
Fax: (301) 480-3661
richardk@ncrr.nih.gov

Maren R. Laughlin, PhD
Director, Metabolism Program
Division of Diabetes, Endocrinology
and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard
2 Democracy Plaza, Room 6101
Bethesda, MD 20892-5460
Tel: (301) 594-8802
Fax: (301) 480-3503
maren.laughlin@nih.gov

Barbara Linder, MD, PhD
Division of Diabetes, Endocrinology
and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard
2 Democracy Plaza, Room 699
Bethesda, MD 20892
Tel: (301) 594-0021
Fax:(301) 480-3503
linderb@extra.niddk.nih.gov

Robert Kuczmarski, Dr.P.H.
Director, Obesity Prevention and Treatment Program
Division of Digestive Diseases and Nutrition
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard, Room 673, MSC 5450
Bethesda, MD 20892-5450
Tel: (301) 451-8354
Fax: (301) 480-8300
rk191r@nih.gov

Saul Malozowski, MD, PhD, MBA
Senior Advisor for Clinical Trials
and Diabetes Translation
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
2 Democracy Plaza
6707 Democracy Boulevard, Room 679
Bethesda, MD 20892
Tel: (301) 451-4683
Fax: (301) 480-3503
malozowskis@extra.niddk.nih.gov

Carolyn Miles
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
2 Democracy Plaza
6707 Democracy Boulevard, Room 641
Bethesda, MD 20892-5452
Tel: (301) 594-7791
milesc@extra.niddk.nih.gov

Judith Podskalny, PhD
Program Director, Division of Digestive
Diseases and Nutrition
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
2 Democracy Plaza
6707 Democracy Boulevard, Room 667, MSC 5450
Bethesda, MD 20892-5450
Tel: (301) 594-8876
Fax: (301) 480-8300
podskalnyj@extra.niddk.nih.gov

Patricia Robuck, PhD, MPH
Director, Clinical Trials Program
Division of Digestive Diseases and Nutrition
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard, Room 659
Bethesda, MD 20892
Tel: (301) 594-8879
Fax: (301) 480-8300
pr132q@nih.gov

Peter Savage, MD
Acting Director, Division of Epidemiology
and Clinical Applications
National Heart, Lung and Blood Institute
National Institutes of Health
Rockledge 2, Room 8104
Bethesda, MD 20817
Tel: (301) 435-0421
Fax: (301) 480-1864
savagep@nhlbi.nih.gov

Marcia Scott
Prevention Research Branch
National Institute on Alcohol Abuse and Alcoholism
National Institutes of Health
6000 Executive Boulevard, Suite 505
Bethesda, MD 20892
Tel: (301) 402-6328
Fax: (301) 443-8774
mscott@mail.nih.gov

Salvatore Sechi, PhD
Director, Proteomic Program
Division of Diabetes, Endocrinology
and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard
2 Democracy Plaza, Room 611
Bethesda, MD 20892-5460
Tel: (301) 594-8814
Fax: (301) 480-2688
Salvatore_Sechi@nih.gov

Robert Selwitz, PhD
Senior Dental Epidemiologist
National Institute of Dental
and Craniofacial Research
National Institutes of Health
Natcher Building, 3AN-44D
Bethesda, MD 20892
Tel: (301) 594-3977
Fax: (301) 480-8254
selwitzr@de45.nidr.nih.gov

Elliott Siegel, PhD
Associate Director of Health
Information Program Development
National Library of Medicine
National Institutes of Health
8600 Rockville Pike
Bethesda, MD 20892
Tel: (301) 496-8834
Fax: (301) 496-4450
siegel@nlm.nih.gov

Elizabeth Singer
Director, Office of Communications
and Public Liaison
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
31 Center Drive
Building 31, Room 9A04
Bethesda, MD 20892
Tel: (301) 496-3583
Fax: (301) 496-7422
singerb@extra.niddk.nih.gov

Allen Spiegel, MD
Director
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
9000 Rockville Pike
Building 31, Room 9A52
Bethesda, MD 20892
Tel: (301) 496-5877
Fax: (301) 496-9943
spiegela@extra.niddk.nih.gov

Robert Star, MD
Chief, Renal Diagnostics and Therapeutics
National Institutes of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
Building 10, Room 3N108, MSC 1268
Bethesda, MD 20892-1268
Tel: (301) 402-6749
Fax: (301) 402-0014
starr@extra.niddk.nih.gov

Dorothy West
Program Analyst
Division of Diabetes, Endocrinology
and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard
2 Democracy Plaza, Room 687
Bethesda, MD 20892
Tel: (301) 594-8820
Fax: (301) 480-3503
westd@extra.niddk.nih.gov

Desmond Williams, MD, PhD
Centers for Disease Control and Prevention
4770 Buford Highway, N.W.
Atlanta, GA 30341
Tel: (770) 488-1158
Fax: (770) 488-5966
zhx0@cdc.gov

Violet Woo, MS, MPH
Program Analyst
Office of Minority Health
Department of Health and Human Services
5515 Security Lane, Suite 1000
Rockville, MD 20852
Tel: (301) 443-9923
Fax: (301) 443-8280
vwoo@osophs.dhhs.gov

Speakers

Kelly Acton, MD, MPH
Director, National Diabetes Program
Headquarters Office
Indian Health Service
5300 Homestead Road, NE
Albuquerque, NM 87110-1293
Tel: (505) 248-4182
Fax: (505) 248-4188
kelly.acton@mail.ihs.gov

Marshall Chin, MD, MPH
Associate Professor of Medicine
University of Chicago
5841 South Maryland Avenue
MC2007, Room B216
Chicago, IL 60637
Tel: (773) 702-4769
Fax: (773) 834-2238
mchin@medicine.bsd.uchicago.edu

Judith Fradkin, MD
Director, Division of Diabetes,
Endocrinology and Metabolic Diseases
National Institute of Diabetes
and Digestive and Kidney Diseases
National Institutes of Health
2 Democracy Plaza
6707 Democracy Boulevard, Room 689
Bethesda, MD 20892-5460
Tel: (301) 594-8814
Fax: (301) 480-3503
fradkinj@ep.niddk.nih.gov

Russ Glasgow, PhD
Senior Scientist
Kaiser Permanente Clinical Research Unit
Post Office Box 349
Canon City, CO 81215
Tel: (719) 275-6540
Fax: (719) 275-5704
russg@ris.net

Lawrence W. Green, Dr.P.H.
Director, Office of Extramural Prevention Research
Associate Director for Prevention Research
and Academic Partnerships
Centers for Disease Control and Prevention
4770 Buford Highway, N.W.
Mail Stop K-56
Atlanta, GA 30341-3724
Tel: (770) 488-2458
Fax: (770) 488-8200
lgreen@cdc.gov

Roland Hiss, MD
Professor of Medicine and Chair
Department of Medical Education
University of Michigan Medical School
G1103 Towsley Center
Ann Arbor, MI 48109
Tel: (734) 763-1426
Fax: (734) 936-1641
redhiss@umich.edu

Harlan Krumholz, MD
Professor of Medicine and Epidemiology
& Public Health
Yale School of Medicine
333 Cedar Street
PO Box 208025
New Haven, CT 06520-8025
Tel: (203) 737-1717
Fax: (203) 737-1718
harlan.krumholz@yale.edu

Leonard Pogach, MD, MBA
National Program Director Diabetes
Veterans Health Administration
East Orange Veterans Affairs Medical Center
385 Tremont Avenue
East Orange, NJ 07019-1095
Tel: (973) 676-1000 ext.1095
Fax: (973) 677-4408
leonard.pogach@med.va.gov

David Stevens, MD, FAAFP
Director, Clinical Branch
Division of Community and Migrant Health
Health Resources and Services Administration
4350 East West Highway, 7th Floor
Bethesda, MD 20814
Tel: (301) 594-4323
Fax: (301) 594-4997
dstevens@hrsa.gov

Daniel Stryer, MD
Center for Outcomes and Effectiveness Research
Agency for Healthcare Research and Quality
6010 Executive Boulevard, Suite 300
Rockville, MD 20852
Tel: (301) 594-4038
Fax: (301) 594-3211
dstryer@ahrq.gov

APPENDICES

APPENDIX A

NATIONAL DIABETES MELLITUS RESEARCH AND EDUCATION ACT, SECTION 429: Interagency Coordinating Committees

Sec.429. [285c—3]

(a) For the purpose of—

(1) better coordination of the research activities of all the national research institutes relating to diabetes mellitus, digestive diseases, and kidney, urologic, and hematologic diseases; and

(2) coordinating those aspects of all Federal health programs and activities relating to such diseases to assure the adequacy and technical soundness of such programs and activities and to provide for the full communication and exchange of information necessary to maintain adequate coordination of such programs and activities;

the secretary shall establish a Diabetes Mellitus Interagency Coordinating Committee, a Digestive Diseases Interagency Coordinating Committee, and a Kidney, Urologic, and Hematologic Diseases Coordinating Committee (hereafter in this section individually referred to as a "Committee").

(b) Each committee shall be composed of the Directors of each of the national research institutes and divisions involved in research with respect to the diseases for which the Committee is established, the Division Director of the Institute for the diseases for which the Committee is established, the Chief Medical Director of the Veterans' Administration,[1] and the Assistant Secretary of Defense for Health Affairs (or the designees of such officers) and shall include representation from all other Federal departments and agencies whose programs involve health functions or responsibilities relevant to such diseases, as determined by the Secretary. Each Committee shall be chaired by the Director of NIH (or the designee of the Director). Each committee shall meet at the call of the chairman, but not less often than four times a year.

(c) each Committee shall prepare an annual report for—

(1) the Secretary;

(2) the Director of NIH; and

(3) the Advisory Board established under section 430 for the diseases for which the Committee was established, detailing the work of the Committee in carrying out paragraphs (1) and (2) of subsection (a) in the fiscal year for which the report was prepared. Such report shall be submitted not later than 120 days after the end of each fiscal year.

[1] The reference is deemed to be a reference to the Under Secretary for Health of the Department of Veteran Affairs. See section 302 (e)(1) of Public Law 102-405(106) Stat. 1985 and section 10(4) of Public Law 100-527 (102 Stat.2641).

APPENDIX B

DIABETES MELLITUS INTERAGENCY COORDINATING COMMITTEE

ROSTER OF MEMBERS (2002)

CHAIRMAN

Allen Spiegel, MD

Director
National Institute of Diabetes and
Digestive and Kidney Diseases
National Institutes of Health
Building 31, Room 9A52
31 Center Drive, MSC 2560
Bethesda, MD 20892-2560
Tel: (301) 496-5877
Fax: (301) 402-2125
spiegela@extra.niddk.nih.gov

EXECUTIVE SECRETARY

Sanford Garfield, PhD

Senior Advisor, Biometrics and Behavioral Science
National Institute of Diabetes and
Digestive and Kidney Diseases
National Institutes of Health
6707 Democracy Boulevard, Room 685
Bethesda, MD 20817
Tel: (301) 594-8803
Fax: (301) 480-3503
E-mail:

MEMBERS

Agency for Healthcare Research and Quality

Daniel B. Stryer, MD
Medical Officer
Center for Outcomes and Effectiveness Research
6010 Executive Boulevard, Suite 300
Rockville, MD 20852
Tel: (301) 594-4038
Fax: (301) 594-3211
dstryer@ahrq.gov

Center for Scientific Review

N. Krish Krishnan, PhD
National Institutes of Health
Two Rockledge Centre
Room 6164
Bethesda, MD 20892
Tel: (301) 435-1041
Fax: (301) 480-2065
krishnak@mail.nih.gov

Centers for Disease Control and Prevention

Frank Vinicor, MD
Director, Division of Diabetes Translation
4770 Buford Highway, NW MSK-10
Atlanta, GA 30341
Tel: (770) 488-5000
Fax: (770) 488-5966
fxv1@cdc.gov

Mark Eberhardt, PhD
Epidemiologist
National Center for Health Statistics
6525 Belcrest Road, Room 730
Hyattsville, MD 20782
Tel: (301) 436-5979, x142
Fax: (301) 436-8453
mse1@cdc.gov

Centers for Medicare & Medicaid Services

John P. Lanigan
Health Insurance Specialist
Office of Professional Relations
Hubert Humphrey Building
Room 435H
Washington, DC 20201
Tel: (202) 690-7418
Fax: (202) 401-7438
jlanigan@hcfa.gov

Department of Health and Human Services

Susan J. Blumenthal, MD, MPA
US Assistant Surgeon General
200 Independence Avenue, SW
Room 719H
Washington, DC 20201
Tel: (202) 260-2255
Fax: (202) 690-4631
SBlumenthal@osophs.dhhs.gov

DHHS Office of Minority Health

Violet Woo, MS, MPH
Program Analyst
Department of Health & Human Services
5515 Security Lane, Suite 1000
Rockville, MD 20852
Tel: (301) 443-9923
Fax: (301) 443-8280
vwoo@osophs.dhhs.gov

Food and Drug Administration

Shaio-Wei Shen
Director, Division of Metabolism
and Endocrine Drug Products
Parklawn Building, Room 14B-45
5600 Fishers Lane
Rockville, MD 20857
Tel: (301) 827-6430
Fax: (301) 443-9282
orloffd@cder.fda.gov

Health Resources and Services Administration

David M. Stevens, MD, FAAFP
Director, Clinical Branch
Division of Community and Migrant Health
4350 East West Highway, 7th Floor
Bethesda, MD 20814
Tel: (301) 594-4323
Fax: (301) 594-4997
dstevens@hrsa.gov

Indian Health Service

Kelly Acton, MD, MPH
Director, National Diabetes Program
5300 Homestead Road, NE
Albuquerque, NM 87110-1293
Tel: (505) 248-4182
Fax: (505) 248-4188
Kelly.acton@mail.ihs.gov

National Center for Complementary and Alternative Medicine

Marguerite Klein
Health Science Administrator
6707 Democracy Boulevard
Room 401
Bethesda, MD 20892-5475
Tel: (301) 402-5860
Fax: (301) 480-3621
kleinm@mail.nih.gov

National Center for Research Resources

Richard Knazek, MD
Medical Officer
National Institutes of Health
6705 Rockledge Drive
Rockledge 1, Room 6128
Bethesda, MD 20892
Tel: (301) 435-0790
Fax: (301) 480-3661
richardk@ncrr.nih.gov

National Center on Minority Health and Health Disparities

Jean L. Flagg-Newton, MD
Deputy Director
National Institutes of Health
2 Democracy Plaza
6707 Democracy Boulevard, Suite 800
Betheda, MD 20892
Tel: (301) 402-1366
Fax: (301) 402-7040
flaggnej@od.nih.gov

National Eye Institute

Peter Dudley, PhD
Director, Retinal Diseases Program
National Institutes of Health
6120 Executive Boulevard
Suite 350
Rockville, MD 20892
Tel: (301) 451-2020
Fax: (301) 402-0528
pad@nei.nih.gov

National, Heart, Lung and Blood Institute

Peter J. Savage, MD
Acting Director, Division of Epidemiology
and Clinical Applications
National Institutes of Health
Rockledge 2, Room 8104
Bethesda, MD 20817
Tel: (301) 435-0421
Fax: (301) 480-1864
savagep@nhlbi.nih.gov

National Human Genome Research Institute

Alan E. Guttmacher, MD
Senior Clinical Advisor to the Director
National Institutes of Health
Building 31, Room 4B09
Bethesda, MD 20892-2152
Tel : (301) 496-0844
Fax : (301) 402-0837
guttmach@mail.nih.gov

National Institute of Allergy and Infectious Diseases

John Ridge, MD
Program Officer
Diabetes and Autoimmunity Section
of the Clinical Immunology Branch
National Institutes of Health
6700B Rockledge Drive
Bethesda, MD 20892
Tel: (301) 496-7104
Fax: (301) 402-2571
jr34g@nih.gov

National Institute of Arthritis and Musculoskeletal and Skin Diseases

Julia Freeman, PhD
Chief, Autoimmunity Section
National Institutes of Health
Building 45, Room 5AS-19F
45 Center Drive, MSC 6500
Bethesda, MD 20892-6500
Tel: (301) 594-5052
Fax: (301) 480-4543
freemanj@ep.niams.nih.gov

National Institute of Biomedical Imaging and Bioengineering

Joan T. Harmon, PhD
Senior Advisor for Program & Acting Director,
Division of Bioengineering
National Institutes of Health
6707 Democracy Boulevard
Room 241
Bethesda, MD 20892-2077
Tel: (301) 451-4776
Fax: (301) 480-4515
harmonj@nibib.nih.gov

National Institute of Child Health and Human Development

Gilman D. Grave, MD
Chief, Endocrinology, Nutrition
and Growth Branch
Center for Research for Mothers & Children
National Institutes of Health
6100 Executive Boulevard
Suite 4B-11
Bethesda, MD 20892-7510
Tel: (301) 496-5593
Fax: (301) 480-9791
gg37v@nih.gov

National Institute on Deafness and Other Communication Disorders

Barry J. Davis, PhD
Scientific Programs Branch
National Institutes of Health
6120 Executive Boulevard
Rockville, MD 20892-7180
Tel: (301) 402-3464
Fax: (301) 402-6251
barry_davis@nih.gov

National Institute of Dental and Craniofacial Research

Patricia S. Bryant, PhD
Director, Behavior, Health Promotion
& Environment Program
National Institutes of Health
Building 45, Room 4AS-43A, MSC 6402
Bethesda, MD 20892-6402
Tel: (301) 594-2095
Fax: (301) 480-8322
bryantp@de45.nidr.nih.gov

National Institute of Diabetes and Digestive and Kidney Diseases

Judith E. Fradkin, MD
Director
Division of Diabetes, Endocrinology,
and Metabolic Diseases
National Institutes of Health
Building 31, Room 9A27
31 Center Drive MSC 2560
Bethesda, MD 20892-2560
Tel: (301) 496-7348
FAX: (301) 480-6792
jf58s@nih.gov

National Institute of Environmental Health Sciences

Perry Blackshear, MD, DPhil
Director, Office of Clinical Programs
National Institutes of Health
PO Box 12233
NIEHS, MD A2-05
RTP, NC 27709
Tel: (919) 541-4899
Fax: (919) 541-4571
black009@niehs.nih.gov

National Institute of General Medical Sciences

Richard Anderson, MD, PhD
Program Director, Division of Genetics
and Developmental Biology
National Institutes of Health
Natcher Building, Room 2AS-25
45 Center Drive, MSC 6200
Bethesda, MD 20892-6200
Tel: (301) 594-0943
Fax: (301) 480-2228
andersor@nigms.nih.gov

National Institute of Mental Health

Peter Muehrer, PhD
Chief, Health and Behavioral Science
Research Branch
Division of Mental Disorders,
Behavioral Research and AIDS
National Institutes of Health
6001 Executive Boulevard
Room 6189, MSC 9615
Bethesda, MD 20892-9615
Tel: (301) 443-4708
Fax: (301) 480-4415
pmuehrer@mail.nih.gov

National Institute of Neurological Disorders and Stroke

Paul L. Nichols, PhD
Program Director, Systems and Cognitive
Neuroscience Program
National Institutes of Health
6001 Executive Boulevard
Room 2118
Rockville, MD 20892
Tel: (301) 496-9964
Fax: (301) 402-2060
pn13w@nih.gov

National Institute of Nursing Research

Nell Armstrong, PhD, RN
Program Director
National Institutes of Health
6701 Democracy Boulevard
Room 710
Bthesda, MD 20817
Tel: (301) 594-5973
Fax: (301) 480-8260
armstrongn@nih.gov

National Institute on Aging

Chhanda Dutta, PhD
Chief, Musculoskeletal Section & Nutrition,
Metabolism, Gastroenterology Section
Geriatrics Program
National Institutes on Health
Gateway Building, Suite 3C-307
7201 Wisconsin Avenue
Bethesda, MD 20893
Tel: (301) 435-3048
Fax: (301) 402-1784
cd23z@nih.gov

National Institute on Alcohol Abuse and Alcoholism

Ricardo A. Brown, PhD
Program Director, Biomedical Research Branch,
Division of Basic Research
National Institutes of Health
Willco Building, Room 402
6000 Executive Boulevard, MSC 7003
Bethesda, MD 20892-7003
Tel : (301) 443-2239
Fax : (301) 594-0673
ricbrown@mail.nih.gov

National Institute on Drug Abuse

Jag H. Khalsa, PhD
Pharmacologist Health Administrator
Center on AIDS and Other Medical
Consequences of Drug Abuse (CAMCODA)
6001 Executive Boulevard, Room 5098
MSC 9593
Bethesda, MD 20892-5953
Tel: (301) 443-1801
Fax: (301) 594-6566
jk98p@nih.gov

National Library of Medicine

Elliot R. Siegel, PhD
Associate Director for Health
Information Programs Development
National Institutes of Health
8600 Rockville Pike
Bethesda, MD 20817
Tel: (301) 496-8834
Fax: (301) 496-4450
siegel@nlm.nih.gov

Veterans Health Administration

Leonard M. Pogach, MD, MBA
East Orange Veterans Affairs Medical Center
385 Tremont Avenue
East Orange, NJ 07018
Tel: (973) 676-1000, ext. 1693
Fax: (973) 395-7092
Leonard.pogach@med.va.gov