Diabetes and Cardiovascular Disease in the Elderly
Diabetes Mellitus Interagency Coordinating Committee (DMICC) Meeting

November 4, 2013
Meeting Abstracts

Report from the Association of Specialty Professors (ASP) Workshop on Diabetes Mellitus and Cardiovascular Disease in Older Adults—Susan Zieman, M.D., Ph.D., National Institute on Aging

The Association of Specialty Professors Workshop on Diabetes Mellitus (DM) and Cardiovascular Disease (CVD) in Older Adults was held April 4 – 5, 2013. The goal of the workshop was to review the state of the science and identify existing research gaps. DMICC member agencies, including NIA, NIDDK, NHLBI, FDA, and CMS participated in planning. Slides from the 25 lectures may be found on the website. (Some—but not all—require Alliance for Academic Internal Medicine login.) A summary paper is currently in preparation. (That summary is now available here.) Workshop sessions included clinical epidemiology related to DM and CVD; the impact of age-associated metabolic changes on DM; heart and blood vessels vulnerability due to aging and DM; complications and disability due to DM and CVD; prevention and treatment of DM and CVD in older adults; and challenges to interventions in older adults. Future research directions were compiled after each presentation, including: How aging influences mechanisms that lead to DM and CVD; potential effects of gut microbes on metabolic and cardiovascular health and functional status; determining ways in which diagnostic tests should be changed or interpreted differently as people age; treatment of "competing" complications resulting from a common (*i.e.*, microvascular) pathway; improved research models and clinical trial approaches; assessing the relative importance and goals of DM treatment in older individuals with CVD in light of relevant functional, cognitive, and quality-of-life outcomes; determining what biological differences contribute to ethnic/racial DM and CVD health disparities, and to what extent these disparities are driven by access to care; and identifying protective adaptations of aging, both to promote them, and to prevent medical interference with their potentially beneficial effects.

Centers for Medicare & Medicaid Services (CMS) Diabetes and CVD Programs for Older Americans—Elizabeth Koller, M.D.

Taken together, ischemic heart disease, cerebrovascular disease, and other heart disease account for 65 percent of deaths among people with DM. Thus, one must consider the importance of controlling blood glucose relative to other risk factors, such as smoking, hypertension, and unhealthy cholesterol levels. When type 2 diabetes (T2D) is diagnosed in a younger individual, reduced survival relative to people of the same age without DM becomes apparent after 10 years, and the difference increases significantly through at least 20 years. In contrast, the difference of survival in people diagnosed at age 65 or later relative to age-matched individuals without DM is apparent almost immediately, and widens, modestly, though the first 10 years post-diagnosis. After that, and particularly after 15 years post diagnosis, the difference in life expectancy diminishes. These observations suggest that prevention of DM and treatment of glycemia may be of lower importance than treatment of comorbidities in people diagnosed with DM relatively late in life. The significant reduction in CVD from intensive blood glucose control in people with type 1 diabetes reported by the Diabetes Control and Complications Trial required a large cohort, and a 17-year follow up. Major T2D prevention and treatment trials have not identified significant differences in CVD morbidity or total mortality with various interventions, although several changes in surrogate markers were found. Despite the lack of clear CVD benefit, some interventions were linked with increased risk of hypoglycemia. Thus, it is worth considering whether glucose control is an appropriate focus of care in T2D, or whether it is just a marker of a metabolic disorder that has CVD at

its core. An observational analysis of disease clustering in Medicare beneficiaries found that one-third of beneficiaries—accounting for 15 percent of expenditures—mapped to 100 prevalent disease combinations; while less than one-third of beneficiaries—and 79 percent of expenditures—mapped to 2 million disease combinations. Thus, the likelihood of a varying array of comorbid diseases in older adults limits the utility of prevention measures and single disease management programs. Recognizing this, Medicare directs efforts toward screening for CVD risk factors and offers behavioral therapy and other services (*e.g.*, tobacco use counseling, intensive behavioral therapy for obesity, and obesity treatment with bariatric surgery) that help to reduce risk.

Reports on Federal Programs Specific to Older Americans with Diabetes and CVD

Agency for Healthcare Research and Quality—Barbara Bartman, M.D., M.P.H.

The Center for Outcomes and Evidence at the Agency for Healthcare Research and Quality (AHRQ), applies rigorous methodologies for studies that involve a synthesis or systematic review, such as evidence generation or observational studies. Many of the grants funded by the agency address care delivery for people with diabetes, with CVD, and for the elderly, although few studies intersect all three topics. A notable exception is Developing Evidence to Inform Decisions about Effectiveness Program (DEcIDE), a retrospective comparative effectiveness study that investigated the impact of intensification of DM treatment with insulin on CVD outcomes in individuals with and without this comorbidity. DEcIDE, led by Marie Griffin, M.D., M.P.H., at Vanderbilt University, utilized claims data from national Veterans Health Administration (VHA) and CMS databases to compare types and combinations of drugs used to treat diabetes in 33,084 individuals who initiated diabetes treatment with metformin between October 2001 and September 2008, and intensified treatment with either sulfonylurea or insulin. Primary outcomes included MI, stroke, and mortality, as well as the impact of treatment on development of CVD and chronic kidney disease. Event rates for sulfonylurea versus insulin were not significantly different, but mortality rates were higher for the insulin group. Furthermore, a subgroup analysis revealed an increased risk for mortality for insulin treatment in individuals with a history of CVD. These data indicate that elderly individuals with diabetes taking metformin might be at increased risk for death if insulin is added as a supplementary therapy. Dr. Bartman noted that the study results would be published soon, and a clinical trial will extend and validate those results.

Look AHEAD: Action for Health in Diabetes—Mary Evans, Ph.D., NIDDK, NIH

The Look AHEAD study compared the long-term health effects of an intensive lifestyle intervention (ILI) with a less intensive program of diabetes support and education (DSE) in overweight and obese persons with T2D. Look AHEAD was conducted at 16 geographically diverse areas across the United States. The primary hypothesis was that incidence of the first occurrence of a composite outcome (*e.g.*, CV mortality, non-fatal MI and stroke, and hospitalized angina) during a 13.5-year followup is reduced in the ILI as compared to DSE. Secondary outcomes included CVD risk, costs, diabetes control and complications, general health, and quality of life.

The inclusion criteria for Look AHEAD participants required patients with T2D on any treatment, BMI greater than 25, 45 to 75 years of age, and A1c below 11 percent. Patients also had to pass an exercise test and demonstrate ability to adhere to the interventions. Prior history of CVD was allowed if it was deemed safe. One-third of the cohort was racial and ethnic minorities, 15 percent of participants were insulin users, and 14 percent had experienced a prior CVD event. The DSE focused on health education topics of diet, exercise, and social support, while the ILI supported a 7 percent weight loss through caloric restriction and exercise.

Year four results indicated that the ILI group lost 8.6 percent of the baseline weight in the first year, with a slight regain to 5 percent during subsequent years. Improvements in CVD risk factors, fitness, reduced medication usage, sleep apnea improvements, mobility-related disability, and diabetes remission also were found for the ILI group. The intervention was terminated in September 2012, however, because a

futility analysis indicated that the probability of observing a significant positive result at the end of the trial was 1 percent. The ILI was associated with significantly greater weight loss than DSE, although the DSE group began losing weight starting at year 5. A1c levels were initially reduced sharply in the ILI group but increased over the years, remaining modestly but significantly below DSE. ILI participants also sustained improvements in systolic blood pressure, HDL, and reduced use of anti-hypertensive medications, lipid-lowering drugs, and insulin. The cumulative hazard ratio for the primary outcome, however, showed no difference over 10 years, and subgroup analysis did not demonstrate significant differences between genders or races/ethnicities. Although the study was sufficiently powered, the lack of significant differences between the ILI and DSE groups might indicate that larger sustained weight losses are required. Earlier intervention during the course of diabetes also might be needed. Interestingly, older participants lost more weight, possibly because of better self-monitoring, improved diet and increased exercise. Thus, the Look AHEAD study demonstrated that individuals with diabetes can successfully lose weight and maintain modest long-term weight loss; that the ILI improved fitness and CVD risk factors and was associated with lower medication use; and that participation in ILI did not reduce incidence for CVD events. Analysis of results for other outcomes is ongoing.

The following individuals made informal presentations on behalf of their agencies:
Dr. Sharon Saydah (CDC)
Drs. Susan Karol and Bruce Finke (IHS)
Dr. Denise Bonds (NHLBI)

Speakers
Dr. Zieman (NIA)
Dr. Koller (CMS)
Dr. Evans (NIDDK)

DMICC Members Attending
Dr. Fradkin, NIDDK, Chair
Dr. Roberts, NIDDK, Executive Secretary
Dr. Alekel, NCCAM
Dr. Atkinson, NIDCR
Dr. Bainbridge (for Dr. Wong), NIDCD
Dr. Bartman, AHRQ
Dr. Bonds (for Dr. Alvilés-Santa), NHLBI
Dr. Bourcier, NIAID
Dr. Branch (for Dr. Gracia), OMH
Dr. Dutta, NIA
Dr. Eberhardt, CDC
Dr. Grave, NICHD
Dr. Karol, IHS
Dr. Krosnick (for Dr. Conroy), NIBIB
Dr. Li, NHGRI
LCDR Plummer (for Dr. Kugler), DOD
Dr. Pogach, VHA
Dr. Roman, CMS
Dr. Saydah (for Dr. Albright), CDC

DMICC Members Not Attending
Dr. Bosetti, NINDS

Dr. Chavez, NIMH
Dr. Dankwa-Mullan, NIMHD
Dr. Frant, NLM
Dr. Gao, NIAAA
Dr. Graves, CSR
Dr. Heindel, NIEHS
Dr. Khalsa, NIDA
Dr. Krasnewich, NIGMS
Dr. Olson, HHS
Dr. Parks, FDA
Dr. Post, DOA
Dr. Rosenblum, NCATS
Dr. Shen, NEI