Diabetes Mellitus Interagency Coordinating Committee Meeting: Approaches Integrating Epidemiological Data on Diabetes

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Rockledge 2, Room 9100-91
Bethesda, MD

Summary Minutes

Opening Remarks

Dr. Saul Malozowski, Executive Secretary, Diabetes Mellitus Interagency Coordinating Committee (DMICC), welcomed the Committee members and guests and said that this would be the final meeting of the fiscal year 2004.

Dr. Allen Spiegel, Director, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), said that the meeting's theme would be "Approaches Integrating Epidemiological Data on Diabetes." Although the National Institutes of Health budget will be limited during the next two years, it is important to maintain momentum in addressing the diabetes epidemic. Therefore, diabetes research resources must be leveraged by studying existing cohorts, tapping into ongoing studies, and gleaning data from completed studies that were note designed to focus specifically on diabetes.

Assembling a Raw Data Meta-Analytic Database: The Joys and Sorrows

Sue Duval, PhD, CODA Study Group, University of Minnesota

Dr. Duval discussed the use of meta-analyses and the Collaborative Study of Obesity and Diabetes in Adults (CODA), which is led by investigators at the University of Minnesota. She began by explaining that meta-analyses can prolong the lives of individual studies and seek to enhance inferences of individual studies. With individual studies, observed findings are subject to random variation that could lead to incorrect inferences. By combining data from individual studies, statistical power can be increased and consistency across studies can be assessed.

The aim of the CODA project is to use meta-analysis of individual participant data (MIPD) methods to address the following diabetes epidemiology questions:

- What simple anthropometric indices most closely predict the risk of type 2 diabetes mellitus in adults?
- Do ethnicity and other factors modify that prediction?
- Is the association of these anthropometric indices with cardiovascular disease morbidity and mortality exacerbated by their association with type 2 diabetes mellitus?
- Is it possible to predict several diabetes-related risk states using noninvasive or minimally invasive methods?
- Should screening tools differ by ethnicity?

Dr. Duval further explained that many people think of a meta-analysis as a systematic review. However, the term meta-analysis actually refers to the quantitative component, in which summary data abstracted from the published literature are synthesized to produce a powerful summary estimate that incorporates many studies. Meta-analysis of the published literature (MAL or MPL) involves an exhaustive exploration, critical evaluation, and quantitative synthesis of all unbiased evidence from published reports. In contrast, MIPD involves pooled analysis of individual, original epidemiological data, not just combining data that are available in the literature. MIPD can be conducted retrospectively or prospectively. Prospective studies can be carefully designed to help ensure that data collection is consistent across studies.

Studies using the MIPD approach are beginning to appear in the literature (e.g., meta-analyses of cancer trials) and can be considered the "gold standard" of systematic reviews. The key to success in conducting a MIPD is good international collaboration and communication with researchers who have collected the data. This type of review also requires central collection, checking, and analysis of individual participant studies, and an attempt to include all relevant studies.

In contrast to MAL, MIPD involves many researchers who become very invested in the project, and international networks of collaborating investigators develop. Other advantages of MIPD include that: more data are available; data are standardized; and it is possible to do better time-to-

event analyses, to produce better adjusted/multivariate models, and to evaluate subgroup effects. In addition, heterogeneity and sampling bias in specific studies can be assessed. Disadvantages of MIPD include that: data may not be available from all published studies; there is potential for conflicts with collaborators regarding findings that are different from those published by the investigators; and substantial financial resources and infrastructure are required to get the investigators on board and to gather the data.

Dr. Duval then discussed the CODA project MIPD experience. She stated that having a large dataset allows the researchers to study broad questions with great precision. For example, questions can be asked about waist circumference versus body mass index (BMI) in fine-tuned demographic groups and in different ranges of adiposity. However, very detailed questions (e.g., about the utility of thigh circumference as a measure) may not be answerable through MIPD because only a few studies may have measured a variable of interest. Therefore, Dr. Duval emphasized the importance of prospectively identifying all variables that should be studied and developing a protocol to test important hypotheses.

One of the biggest advantages of the CODA project has been the establishment of personal relationships with the collaborators. These relationships were accomplished by phone, e-mail, and face-to-face meetings, with phone conversations and face-to-face meetings being the most productive forms of communication. In general, the collaborating researchers have been very responsive, particularly when well-known colleagues have been involved. Collaborators have also become more engaged as actual results, papers, and abstracts were developed.

Benefits of the collaborative effort have included more complete identification of studies, more balanced interpretation of the results, wider endorsement and dissemination of results, and collaboration on further research. Important factors in the CODA project's success have been assurances to the collaborating researchers that all data sent to the data management site are secure and held in confidence, and that all published results will be in the name of the CODA Study Group. The collaborators are asked to join writing groups and have the opportunity to review drafts before publication. Other important aspects of the project are ensuring that individual studies have first rights in publishing their data and that all studies' local review rules are followed.

Operation of the CODA MIPD has involved a commitment to obtain accurate, up-to-date data for all individuals in all relevant studies, and the greatest effort has involved establishing and maintaining collaboration, and processing the data. In addition, in merging the datasets, it has been important to determine whether the study protocols are similar and the source populations can be pooled. The least problematic task may be the data analysis.

Funding for the CODA Project began at the end of 2001, and the database now includes 37 studies, although some available databases are not yet included. Resource requirements for the project have included time, expertise (clinical, scientific, statistical, data management, computing, and administrative), money (researchers were offered up to $1,000 per study), and staff costs (which have totalled approximately 80% of the budget). The data are held at the University of Minnesota, the central project site, and a nominal steering group has been established.

Dr. Duval emphasized the importance of establishing study inclusion criteria. Inclusion criteria for the CODA project include baseline measures of age, sex, race/ethnicity, and one or more anthropometric indicators of obesity (e.g., waist circumference, BMI, or waist-to-hip ratio). Studies included in the CODA project were identified through WHO MONICA, DECODE, DECODA, and Medline searches; screening of abstracts of major international diabetes conferences; and personal communication with experts in the field. The project began by looking at follow-up studies for type 2 diabetes mellitus incidence and later expanded to include cross-sectional studies with newly diagnosed cases type 2 diabetes mellitus. Dr. Duval stressed the importance of identifying and including as many relevant studies (published and unpublished) as possible. If key studies are excluded, the results will be biased. Moreover, a large number of missing or unrepresentative trials could affect the meta-analysis results.

To establish collaboration, the CODA project team initially wrote a letter to all known investigators doing relevant research. The letter requested basic study information and protocols, but did not ask for data. It also discussed the CODA project aims and objectives, importance of the collaborative group, publication policy, collaborative group policy, and confidentiality of data. Many investigators were interested but time constraints were an issue. Ninety-nine studies received the initial letter, and 55 of the recipients gave a positive response. Of them, 52 studies

were eligible, of which 37 datasets have been received and included in the CODA database. Most of the data sources are in the United States and Europe; only one dataset is in South America and only two are in Africa.

Dr. Duval listed classes of variables that would be included in an ideal dataset. These variables include:

- Class 1: Variables that can be measured using questionnaire/self-report only
- Class 2: Clinical variables that do not require drawing blood
- Class 3: Clinical variables that require drawing blood, but do not require a provocative challenge oral glucose tolerance test (OGTT **)**
- Class 4: Clinical variables that require OGTT
- Dependent variables—IGM (excluding diabetes), previously undiagnosed diabetes, previously diagnosed diabetes, and diabetes incidence

The CODA Project team found that data collection and transfer issues included the need to accept a variety of data formats, to assist collaborators by providing forms and payment incentives, and to accept a variety of data transfer methods. They also needed to maintain regular contact with collaborators through correspondence and meetings.

The CODA Project team has analyzed the data by stratifying the analysis by study, taking each study's raw data and applying the same model across studies.

Discussion

The meeting participants briefly discussed the impact of the Health Insurance Portability and Accountability Act (HIPAA) on studies such as CODA. Dr. Duval commented that HIPAA has changed the face of research, but the project has not yet been impacted by the law because secondary data are being used. However, HIPAA may restrict the types of new research questions that could be asked in the future. Dr. David Jacobs of the CODA project team noted that initial study investigators may not have received patients' consent if hospitalization records were used for studies included in the database. This issue will have to be monitored carefully.

Body Mass Index vs. Waist Circumference as Predictors of Diabetes in an International Context: An Individual Participant Data Meta-Analysis (the CODA Study)

David Jacobs, PhD, and Sue Duval, PhD, CODA Study Group, University of Minnesota

Dr. Jacobs, presenting on behalf of Dr. Duval and the CODA Study Group, described the methodology and findings of the CODA project's meta-analysis of the association of BMI versus waist circumference (WC) as predictors of diabetes. He noted that there is overwhelming evidence that obesity is strongly associated with type 2 diabetes mellitus. The meta-analysis research questions were (slide 2):

- Which is the better predictor of type 2 diabetes, WC or BMI?
- What is the shape of the relation?
- Is the association the same in different populations?
- Is the association the same in different age groups, and for both sexes?

All projects included in the multinational collaborative CODA project (slides 3 and 4) gathered baseline glucose measurements (fasting glucose and/or oral glucose tolerance test) or incident diabetes, and baseline measurement of abdominal obesity. Analyses were restricted to studies with information on both WC and BMI, and the age range for the meta-analysis was restricted to ≥30 years at baseline; those under 30 will be included in future publications. Age- and sex-specific analyses used generalized linear mixed models, with random effects (slide 5). Age- and sex-adjusted risk ratios for diabetes were predicted from WC and BMI. Single-parameter models included a logistic regression model for baseline data, a proportional hazards regression model for follow-up data, and estimated absolute risk curves based on either logistic or Poisson regression. Multi-parameter models were also used. Diabetes outcomes, both prevalent and incident, included (slide 6):

- ADA definition 2003 (fasting plasma glucose ≥126 mg/dl),
- WHO definition 1999 (fasting plasma glucose ≥126 mg/dl or plasma glucose ≥200 mg/dl 2-h OGTT),

- Self-reported diabetes (medication, physician diagnosis, etc.), and
- Medication per pharmaceuticals registry.

Newly diagnosed diabetes was based on satisfying a blood glucose criterion in the absence of self-reported pre-existing diabetes.

Dr. Jacobs presented descriptive statistics for the 21 prospective studies and 13 cross-sectional studies included in the meta-analysis (slides 7-9). The prospective studies ranged in size from 658 to 52,468 subjects, with incident diabetes mellitus rates per 10,000 ranging from 16.2 to 401.7. The WC-BMI correlations ranged from 0.71 to 0.89, suggesting that the two variables are well correlated. The cross-sectional studies ranged in size from 466 to 25,902 subjects. The WC-BMI correlations ranged from 0.59 to 0.85.

The meta-analysis findings (slides 10-13) suggest that newly diagnosed diabetes, based on the latest ADA guidelines, can be predicted from BMI and WC using a logistic model, although BMI was slightly less predictive than WC. Incident diabetes was predicted from both BMI and WC using a proportional hazards model. WC appeared to be a slightly better predictor than BMI. The study also showed that when data were stratified by age group and gender, women had a slightly lower odds ratio for BMI, but not for WC, compared to men (slide 14). Dr. Jacobs noted that the cross-sectional studies produced the same kinds of results as the longitudinal studies, giving the investigators greater confidence in the poolability of the results for the cross-sectional and longitudinal data. In other words, Dr. Jacobs stated that the cross-sectional studies, with newly diagnosed diabetes as the outcome variable, and the longitudinal studies, with incident diabetes as the outcome variable, offered similar kinds of information about the association of adiposity and risk of diabetes. On the other hand, he stated that the associations of the two measures of obesity with prevalent (known) diabetes were much weaker than were those with newly identified (unknown) diabetes, perhaps because people who know they have diabetes have lost weight (data not shown). Therefore it is important to separate out the known diabetics in most studies of diabetes risk.

The above findings pertained to relative risk. To get some idea of the absolute magnitude of diabetes risk according to level of adiposity, the researchers also predicted the absolute risk of

either newly diagnosed or incident diabetes for a 50-year-old individual based on the pooled data and adjusted by study (slides 15-17), and found that "the gradient is tremendous," Dr. Jacobs reported. At the 90th or 95th percentile of obesity, the probability of newly diagnosed diabetes was much larger than at the lower percentiles of obesity. For incidence after 10 years follow-up the probabilities were also steeply graded, although they were lower than the corresponding values for newly diagnosed diabetes. Despite this high gradient of risk, however, these data suggest that even among the most obese people, 85% were not predicted to have previously unidentified diabetes or incident diabetes within the time frame examined. More cases would undoubtedly emerge with longer followup, but the data support the concept that, while obese people are at very high risk for developing diabetes, some obese people will not develop diabetes.

In addition, the investigators compared single vs. multiparameter models for both newly diagnosed and incident diabetes in relation to BMI and WC (slides 18-19). While single parameter models properly weight each study according to its precision, multiparameter models potentially introduce a peculiar kind of study bias. For example, one might use a multiparameter model to represent increasing categories of adiposity. In this case each category will be weighted optimally according to precision of the several studies contributing; however, different studies contribute differently across the range of adiposity, so the weighting of studies may vary between categories. Therefore comparison of a low adiposity category to the reference category may be greatly influenced by one set of studies, while comparison of a high adiposity category to the same reference category may be greatly influenced by another set of studies. When comparing the single-parameter vs. multi-parameter logistic and proportional hazards models, they found that the two models essentially agreed (so that no serious bias had been introduced) until the higher adiposity levels. The more flexible multiparameter models flattened compared to the less flexible single parameter models, probably reflecting difficulty in accurate measurement of weight and waist circumference in the most obese, rather than a true flattening of risk for diabetes. This finding suggests that the relationship between BMI and WC and diabetes is smooth and increasing; from the public health perspective, there appears to be no cut point for who is and who is not at risk. However, despite the graded risk, the researchers noted that the absolute increment in risk is very small for changes in BMI and WC within thin persons.

Several meta-regression analyses were presented (slide 20). These analyses use as dependent variable the study-specific slope estimating the ln(OR), in the cross-sectional studies, or ln(HRR), in the longitudinal studies, derived from each study's individual participant data. Other ecologic characteristics of the studies were predictor variables. As with the analyses based on individuals, these ecologic analyses suggested that WC and BMI are good predictors of diabetes. Whereas the individual participant data meta-analyses suggested that the association between adiposity and risk for diabetes increased slightly with age, the meta-regression analyses did not find an age gradient (likely representing an ecologic fallacy). However, the association between adiposity and risk for diabetes was slightly weaker in the studies with low overall diabetes risk than in the studies with high overall diabetes risk. The investigators had no obvious explanation for this phenomenon, although it appears to be some sort of ceiling effect on diabetes risk.

A slide was presented that considered differences in estimated slopes according to protocol used for waist measurement (slide 21); this analysis found no significant difference in predictability of diabetes according to the 4 different waist measurement protocols, although the slope was nominally least when the measurement was taken at the narrowest point.

Dr. Jacobs noted that copious evidence in the literature suggests that visceral fat is a stronger predictor of diabetes than is subcutaneous fat. The motivation for the meta-analysis was therefore that, for screening and prediction purposes, it would be desirable to use a measure of obesity that is more specific to visceral fat. Such a measure should be easy to use and generalizable so a practitioner could readily and more accurately assess a person's level of risk. WC is a reasonable candidate for such a measure, but perhaps it should be modified for frame size by height or hip circumference. BMI intuitively relates to fat generally, rather than specifically to visceral fat. However, the correlation between waist and BMI is about 0.8; with this high level of correlation, BMI and WC seem to offer similar information about adiposity. Therefore, it is important to ask whether WC offers an empirical improvement over BMI in prediction of diabetes, and whether other simple modifications such as incorporating hip circumference or height improve the prediction. A series of analyses (slides 22-23) was presented showing that there was little gain in predictivity of a variety of such models over use of BMI or WC alone. Some slight improvement, however, was afforded by combinations of BMI, WC, and hip circumference. Investigations of these more complex models continues.

In summary, the meta-analysis suggested that (slides 24-26):

- Waist circumference and BMI are both strongly and consistently related to diabetes risk.
- The association is largely similar whether using newly diagnosed diabetes (based on either the ADA or WHO diagnostic criteria) or incident diabetes. The association using total diabetes prevalence or known diabetes as the outcome variable is substantially weaker.
- Even modest overweight is associated with increased risk.
- There is a smooth gradient across the range of adiposity; the flexible multi-parameter models demonstrated this. They did not introduce much bias compared to the single-parameter models.
- Using several different analytic techniques, WC was consistently a *slightly* better predictor of risk diabetes than was BMI.
- There was further slight improvement in the prediction model when using height in the model.
- There is statistically significant heterogeneity among studies: nevertheless, all but one study showed the same qualitative increase in risk of diabetes as adiposity increased. Differences between studies suggest that adiposity is a stronger predictor in some studies than in others.
- The risk gradients were similar for men and women, but are slightly stronger at older than younger ages.
- Diabetes prevalence or incidence in the population is inversely related to the strength of the diabetes-obesity association, explaining part of the heterogeneity.

The researchers concluded that WC does not appear to offer substantial advantages over BMI and that the two are almost interchangeable in diabetes prediction. Whether there is an interaction between BMI and WC has not been investigated, although enough data are probably available through the meta-analysis to do so.

In conclusion, Dr. Jacobs said that "To prevent diabetes you have to know who will get it." The meta-analysis showed that adiposity is important but other information indicates that it is not the only factor in diabetes risk. This study provides a good example of what can be learned by synthesizing existing data from different studies.

Discussion

During the discussion that followed Dr. Jacobs' presentation, a participant asked whether the researchers will be able to look at duration of obesity over time (i.e., how long someone was overweight before diabetes is diagnosed). Dr. Jacobs responded that the meta-analysis would be suited to answering that type of detailed question, providing that the CODA dataset includes weight at a particular age or change in weight over time. However, only studies that asked about weight history or that developed a weight history by following participants over time could contribute information to this question. Another participant noted that subcutaneous abdominal fat could contribute to abdominal circumference, especially in some ethnic groups. Dr. Malozowski and Dr. Jacobs commented that the roles of subcutaneous versus visceral fat are of current interest. Dr. Grave suggested that it would be important to look at BMI and WC in the African-American population; a person's descent (African versus European) may play a role in risk. However ethnicity may play a different role in one culture (e.g. African-Americans or Mexicans in the United States) than in another (e.g. native Africans or Mexicans), so that such studies may need to be restricted geographically.

Access to Data from NHLBI Population Studies

Peter J. Savage, MD, Division of Epidemiology and Clinical Applications, National Heart, Lung, and Blood Institute

Dr. Savage discussed the availability of data from NHLBI-supported intervention and population studies. In particular, he provided an overview of participant privacy versus public access, how to protect privacy, the types of study data that are available for release by NHLBI, and the procedures for accessing the data. He noted that data from existing studies can be used for several purposes, including confirmation of results, analysis of secondary hypotheses, analysis of data for new study designs and samples, sample size estimation for future clinical trials, and teaching.

The advantages of making data available to outside investigators must not lead to violation of participants' rights. When using data from existing studies, all investigators (original or those

getting access later) have an obligation to respect the privacy rights of study participants. In recent years, there has been an evolution in understanding of informed consent and defining the boundaries of how data can be used in different kinds of studies. Investigators must consider whether informed consent forms for a given study allow specific new questions to be addressed.

NHLBI grants limited access to data from several of its large intervention and observational studies. Data requests and proposed analyses must be approved by the data recipient's IRB. When data are provided, obvious identifiers, inadvertent identifiers, and sensitive information are removed, although such data are not completely anonymous. Individuals requesting data must sign an agreement about how the data will be used. Violation of these agreements can have serious consequences both for the outside investigator and his/her institution including restrictions on approvals of future data requests.

An alternative to using limited access data is to collaborate with investigators already involved in ongoing studies. In many cases, this is the most fruitful and efficient approach. For example, interested investigators can identify primary study investigators to serve as ancillary study sponsors. The new study and paper proposals are developed with input as needed from the primary study sponsor. Proposals and manuscripts from such collaborations must be reviewed by the study Steering Committee of the study)or its designated representatives) and NHLBI.

Dr. Savage said that advantages to working with ongoing studies include: potential access to the complete main study dataset; access to biological samples, images, recordings, etc.; access to the expertise and experience of the study investigators and, possibly, access to the cohort for new data collection and assistance with administrative requirements. The only disadvantage he listed is the additional "red tape" and delays that result from the review process.

The success of NHLBI's promotion of data sharing is demonstrated by results to date in the Cardiovascular Health Study (CHS), a study originally established to investigate cardiovascular disease and its risk factors in the elderly. Several training grants have made use of CHS data. More than 130 approved ancillary studies have been conducted using CHS data, and collaborators have been the principal investigators for almost 70 percent of these studies. In

addition, during the past three years, collaborators from outside of the original study have been primary authors for more than 60 percent of the study manuscripts.

Epidemiology datasets that are currently available from NHLBI include the Framingham Original Cohort, Framingham Offspring, Honolulu Heart Program, Atherosclerosis Risk in Communities (ARIC), and Coronary Artery Risk Development in Young Adults (CARDIA), and the CHS studies. Clinical trials datasets are available for the Asymptomatic Cardiac Ischemia Pilot (ACIP), Intermittent Positive Pressure Breathing (IPPB), Post Coronary Artery Bypass Graft Study (Post CABG), Thrombolysis in Myocardial Infarction Study (TIMI II), Lung Health Study (LHS), Digitalis Investigation Group (DIG), Beta Agonist in Mild Asthma (BAGS), Antiarrhythmics Versus Implantable Defibrillators (AVID), and Colchicine in Moderate Asthma (CIMA) studies. The NHBLI seeks to make new datasets available to others in a timely fashion. This list continues to expand.

However, NHLBI has an obligation to give the primary study investigators the opportunity to publish their findings first. For epidemiological studies, public access datasets are available five years from the close of data for examination or follow-up, and for clinical trials, datasets are available three years after publication of the primary results report. Information about how to obtain data from NHLBI can be found at: http://www.nhlbi.nih.gov/resources/deca/default.htm. The Website provides data documentation, distribution agreement forms, information for recipients' IRBs, and policies for use of the data. Data are provided at no cost to the recipient. So far, NHLBI datasets have been requested less often than hoped, especially for studies that have not been widely publicized. From April 2000 to December 2001, the Framingham study was requested most often (35 requests), followed by the ARIC Study (13 requests) and CHS (11 requests).

Dr. Savage summarized his remarks by stating that data from a large number of NHLBI contract-funded studies are available through public access and that investigators are encouraged to access the data for new studies. Privacy is protected by reducing risk of identification, by requiring binding agreements, and by requiring IRB approval. Although not a mandate, investigators who access data are encouraged to communicate with the original study investigators to try to prevent misunderstanding about the data. Collaborations between outside

investigators and investigators already involved with a study are encouraged. Overall, these policies facilitate getting the most value from the information we collect while protecting the rights of all involved.

Brief Overview of Ongoing Activities

Michael Engelgau, MD, Centers for Disease Control and Prevention (CDC)

Dr. Engelgau commented that one part of the CODA study is examining population-based strategies to detect people with pre-diabetes, which is an important CDC focus. The DETECT-2 study, a complementary study based in Copenhagen, combines approximately 27 European surveys and 23 Asian surveys in a dataset that will be used to look at strategies for detection of people with pre-diabetes. The CODA and DETECT-2 investigators are working together in this effort.

A year ago, the CDC convened 15 investigators from around the world to discuss methods for identifying people with pre-diabetes. In general, two different strategies to detect people with pre-diabetes are being studied: first, direct measurement of glucose and explicit assessment of glycemic status, and second, prediction of future diabetes risk without actually measuring a glucose value. Both strategies hold promise in various settings, Dr. Engelgau said. The recent decrease in the impaired fasting glucose (IFG) cut point from 110 to 100 changes the pool of people with undiagnosed pre-diabetes from 20 million to 40 million. Most of these individuals have isolated IFG, not impaired glucose tolerance (IGT). Scientific evidence about the IFG population is not as well-documented as the evidence for the IGT population. This has an impact on policy issues related to pre-diabetes detection and primary prevention efforts.

Furthermore, isolated IFG was not part of any of the prevention trials, so it is unclear whether that measure will have the same benefit as IGT. The group that developed the IFG criteria in 1997 recently reconvened to review four longitudinal studies from around the world. When they lowered the cut point to 100 impaired glucose tolerance, it predicted future diabetes about the same as when using previous cut points. This was an attempt to align IGT criteria with the IFG criteria.

Myrlene A. Staten, MD, National Institute of Diabetes and Digestive and Kidney Diseases

Dr. Staten said there is a critical need for a better diagnostic test for diabetes, as well as pre-diabetes and IGT. The current method requires patients to be fasted and then have a 2 hour OGTT, which must be reconfirmed on a separate occasion.. To this end, NIDDK is creating a Translational Research Program Announcement to stimulate research into a better diagnosis method. The Institute currently is supporting an application to look at a one-hour non-fasting test to determine if it is comparable to the fasting, 2 hour OGTT and if it would be more acceptable and easier for patients and providers.

Another NIDDK program announcement (PA-04-076), issued March 18, 2004, is addressing proteomic and metabolomic approaches to diagnose diabetes and pre-diabetes. It solicits applications of proteomic and metabolomic technologies for the development of novel methodologies and/or identification of new biomarkers for the diagnosis of diabetes and type 2 diabetes. The first receipt date is July 20, 2004. Additionally as part of the previously mentioned grant to study a non-fasting, one hour test for diabetes diagnosis, the investigator is collecting samples from a 2,000 people that will be put into the NIDDK sample repository for use for proteomic/metabolomic approaches..

In addition, NIDDK is interested in epidemiologic approaches to identify those at risk for diabetes.

A participant commented that a significant percentage of people with impaired glucose tolerance will not become diabetic, at least for not for a number of years. However, the window of opportunity to intervene with people who are moving toward diabetes is narrow. Having two glucose tolerance tests showing IGT is a good predictor.

Discussion

The Committee discussed the merits of hemoglobin A1C as a diagnostic indicator for type 2 diabetes. Dr. Staten said that it has been shown to a poor indicator for diagnosis of type 2 diabetes. An OGTT and single fasting glucose test have some variability but are more robust

measures than is the A1C. The A1C is good way to monitor glycemia, but near the normal range, it is not a good indicator of diabetes. Nevertheless, the hemoglobin A1C was a positive advance. Other proteomic measures could also be as useful. Dr. Spiegel commented that other diagnostic research directions include epidemiology efforts and scientific technologies. In addition, work in the genetics arena includes the study of genetic polymorphisms that may be important because genetic tests could be used to assess a person's diabetes risk.

Dr. Spiegel then introduced a brief discussion about longitudinal trends in height and the relationship of BMI to height. Increases in height have leveled in the United States and other populations' height gain is greater, which could have implications for BMI. For example, the heights of discrete populations that move from one country to another have been shown to increase. The U.S. military has routinely gathered height data for personnel, and these data might be useful for studies in conjunction with the Department of Veterans Affairs. Data on the leveling of height in the United States may also have implications for nutrition. In addition, the Committee discussed the use of height squared versus height cubed in calculating BMI.

Closing Remarks

Dr. Malozowski stated that work to establish a Committee agenda for fiscal year 2005 will begin in July. In October, members will receive a letter requesting information for the Committee's annual report. Finally, the participation of the attendees was acknowledged and the meeting adjourned.