Translational Research and Grantee's Advisory Meeting
National Institute of Diabetes and Digestive and Kidney Diseases
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Double Tree Hotel and Executive Meeting Center
Rockville, MD

SUMMARY REPORT

Introduction and Charge to the Group and Overview of the Program

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Dr. Fradkin reviewed the evolution of NIDDK support of translational research She noted that NIDDK had supported "research to practice" translational research through the Diabetes Research and Training Centers (DRTCs) for over 25 years. However, substantial expertise in translation and dissemination research exists outside the limited number of institutions with DRTCs. Therefore, NIDDK took advantage of the doubling of the NIH budget to expand support for translational research beyond the DRTCs through the R18/R34 mechanism.
A major goal of the R18/R34 program has been the translation of information from major multi-center clinical trials on treatment and prevention of diabetes into clinical practice. Clinical trials have documented the value of intensive glycemic control and improved approaches to maintain tight glucose control have been developed. However, data from the National Health and Nutrition Examination Survey (NHANES) monitoring hemoglobin A1c (HbA1c) levels demonstrates that poor glucose control is still a problem, particularly among minorities, suggesting that research results are not being efficiently translated to clinical practice. A further incentive for enhanced translation comes from the Diabetes Prevention Program demonstrating that lifestyle or medication can prevent or delay onset of type 2 diabetes. The pragmatic purpose of the translational research program is to develop and validate approaches to enhance care and give the American people the benefits gleaned from the clinical trials research they have supported.

NIDDK's National Diabetes Education Program (NDEP) is another venue for moving information from clinical trials into the community. Materials developed by the NDEP may be useful components of dissemination research efforts undertaken through the diabetes prevention and control solicitation.

Goals of the Meeting

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The five goals of this meeting:

1. Foster a sense of community among translational researchers;

2. Share information among translational researchers;
3. Discuss design and analytical approaches applicable to translational research;
4. Stimulate new ideas for translational research; and
5. Provide guidance on potential future directions for NIDDK translational research efforts.

How the Scientific Question Leads to Specific Trial Design With Examples/ Considerations for the Biostatistical Section and Power Estimates

Carol Mangione, M.D.
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Selection of Designs

Carol Mangione

Study designs should build on theoretical, qualitative, and modeling work and should be linked closely to the purpose of the evaluation. The design should mitigate the independent influence of unmeasured structural, environmental, or behavioral factors on the outcomes of interest, minimize bias, and maximize generalizability to other settings. A major challenge of translational research in clinical settings is that it tends to involve complex, multifaceted interventions, with simultaneous measured and unmeasured changes occurring in different parts of the organization. In real world settings, the researcher has variable control over how the intervention under evaluation is implemented. Factors such as dose and timing of the intervention may not be easily controllable, and identifying true control groups is difficult.

Before commencing the definitive translational study, the researcher must develop a theoretical basis for the intervention; define the components of the intervention (both measurable and nonmeasurable); perform exploratory studies of observational data and qualitative research to further refine the intervention and planned evaluation; and develop plans for a definitive evaluation. Criteria for design selection include ethics/feasibility; strengths of casual evidence/internal validity; strength of external validity/generalizability; and true statistical cost-effectiveness. Ethics are of particular concern when working with minority or disadvantaged communities. In many settings a control group receiving usual care is not acceptable, because "usual care" often means "no care." To work effectively in partnership with disadvantaged communities and/or organizations, an activity or treatment that confers a valued health benefit in a domain that will not mask observed benefit from the active intervention of interest must be provided to the control group.

Concerning statistical cost-effectiveness, the two main types of designs, qualitative and quantitative, have trade-offs in terms of costs associated with data collection and needed sample size. Quantitative designs include experimental studies, which feature randomization at the individual level or group or cluster randomization (often the only options for the evaluation of organizational interventions), and non-experimental studies. Results from qualitative studies can provide critical information in the translation of interventions shown to be effective in clinical

trials to real world settings. These designs usually use focus groups or interviews with people similar to those who will receive the intervention.

An example of a qualitative research design is a study that sought to modify and implement an existing empowerment intervention to enhance self-management skills among older African Americans and Latinos with diabetes. The study also sought to determine whether the content areas of the intervention were relevant to the population of interest and to identify modifiable barriers to participation in the intervention. Investigators presented the intervention to 11 focus groups with providers and patients. They found that older African Americans and Latinos were more interested in the dietary information presented as part of the intervention than in the exercise information. They identified coping with disability as an important missing content area that affected participants' ability to care for their diabetes; many participants reported that the presence of disability made them less confident they would be able to carry out exercise plans. Barriers to participation included transportation, language, family influences, and competing family demands. Qualitative methods employed before commencing the main study were useful for identifying ways to enhance the acceptability of planned intervention. Qualitative research can also inform scale or survey development and can provide an assessment of the validity of specific measurement approaches in various study population. Qualitative methods can identify structural, cultural, and personal barriers to participation in an intervention and can provide critical information that will ultimately enhance recruitment and retention of participants.

Qualitative and quantitative work are often divorced, to each other's detriment. Statistical issues in qualitative research include cognitive testing, item development, and scale development, which are key to minimizing measurement error in self-reported data; measurement error, though often invisible, is of critical importance in quantitative work. Quantitative non-experimental designs include cross-sectional designs, longitudinal observational cohort studies (uncontrolled before and after), nonequivalent cohorts (controlled before and after), and time-series studies. In translational research, there can be political, practical, and ethical barriers to randomized designs; therefore, these other designs may be the best options. Despite offering little control over the implementation of the intervention, the strengths of quantitative non-experimental designs include very "real world" test conditions which provide robust external validity. If such a study shows that an intervention has an effect, this enhances the ability to translate the intervention into other real world settings. Weaknesses include the fact that it is difficult to know what really happened or which "outcomes" are likely to have changed. Data on implementation of an intervention also may help to understand why some groups benefit and others do not. Lack of randomized controls always is a threat to internal validity, but this trade-off must be considered in the context of the research question and goals of the study. To this end, the research community, particularly study sections, must become more comfortable with non-randomized designs.

Bias, Causation, and Analysis in Observational Designs
Marc N. Elliott

Selection Bias and Theories of Causal Inference
A key issue in observational designs is selection bias, including considerations of which people receive an intervention. In theory, biases can go in either direction, but empirically, it is more

common that observational studies, overestimate effect sizes. Approaches to reducing bias include eliminating potential sources of bias in the design, adjusting for sources of bias in the analysis, and acknowledge any remaining bias as "limitations." Two theories of causal inference are a "traditional" theory, such as that articulated by Cook and Campbell, and the more recent Rubin-Rosenbaum-Holland (RRH) theory.

Criteria considered in the Cook and Campbell theory include covariations (changes in the presumed cause must be related to changes in the presumed effect), temporal precedence (the presumed cause must occur before the presumed effect), and the absence of plausible alternative explanations. To have confidence in a causal inference, the presumed cause must be the only reasonable explanation for changes in the outcome. To illustrate the Cook and Campbell perspective, let us consider an intervention, such as insulin therapy, in which the treatment was associated with severity; in other words, treatment was provided only to the most severe cases. The design has covariation (insulin and outcome are associated) and temporal precedence (insulin comes before the measured outcome), but has alternative explanations (severity could be the cause of the outcome, rather than insulin). We will return to this example to illustrate much of what follows.

The RRH theory of causal inference has come to prominence because it provides a framework that accommodates many designs and corresponding analyses. The theory states that every subject in a two-arm study has two potential outcomes- the outcome that would have occurred if the subject had received the experimental treatment and the outcome that would have occurred if the subject had received the control treatment. The *causal effect* of an intervention for a subject is the difference between the outcomes for that subject. Generally, only one of these two potential outcomes is actually observed. Causal inference can therefore be thought of as a problem of "missing" data, in that one potential outcome is missing for each subject. This is a simple problem for randomized controlled trials (RCTs), because in a randomized experiment, the data are missing completely at random (MCAR), and inference is easy. Observational studies may have if selection bias, resulting in more complex situations in which potential observations are merely missing at random (MAR) or not missing at random.
Let us illustrate this approach with the insulin theory example. Here, each diabetic has a potential outcome if they had received insulin (experiment) and if they had not (control), but for each diabetic, only one outcome can be observed. If the unobserved value in each case could be accurately imputed, this would give an unbiased estimate. In a "perfect" RCT, this is possible because people in the experimental group are similar to those in the control group (no selection bias). In an observational study, data are "missing at random" (MAR) after accounting for covariates or "missing not at random (MNAR)."

<u>Systematic and Unsystematic Error (Bias and Variance)</u>
An important distinction in observational studies is that between systematic and unsystematic error. Systematic error (bias) has magnitude and an expected direction. Systematic error can be invisible or hard to measure, but is unaffected by sample size. It does not exist in RCTs with no nonresponse or measurement error. Unsystematic error (variance) has no expected direction, only a magnitude. This error is mainly a function of sample size. In some contexts, total error (Mean Squared Error) is a useful way of considering both types of error together. Mean Squared Error is calculated as the sume of Systematic and Unsystematic Error, or Variance + $Bias^2$. In

the example concerning insulin use, bias (systematic error) is the expected difference in outcomes between the diabetics who received insulin and those who did not *if they had both received the same treatment* (in an RCT, the expected difference would be zero). Variance (unsystematic error) is the random deviation of the estimates from their expected values. This "small sample noise" represents error in estimates based on "small" (finite) sample sizes that would not exists if the sample size were infinite.

Let us consider how analysis affects bias and variance in an RCT. Because an RCT with complete response and compliance has no selection bias, the RRH Causal Effect (Average Treatment Effect) is the difference in experimental and control means. While covariates that are associated with the outcome can reduce variance, as in linear regression, and can be used to examine subgroups, they are not *necessary* to unbiased estimates of causal effects.. Let us consider a hypothetical example of *random assignment* of insulin (unlike the observational version discussed before). Here even a t-test would be a valid test. The analysis of such data might also be a multiple regression that included age, gender, duration, and severity measures as covariates. This would improve power by reducing unexplained variance. Analysis might also include evaluation of subgroups (perhaps by gender).[1]

In nonexperimental (nonrandomized) designs, simple *t*-tests are not valid tests, because the difference between experimental and control means is a biased estimate of the Average Treatment Effect (ATE) in the presence of selection into treatment. Covariates related to outcomes (sometimes referred to as "confounders" in epidemiology) may be systematically different between experimental and control groups. There are two types of confounding covariates: those that affect the outcome and are measured, and those that affect outcome but are not measured. In our observational insulin example, the difference in outcomes means and the corresponding *t*-test for insulin versus non-insulin treatment would provide biased estimates of ATE (Copas & Li, 1997 JRSS). Here, the effects of insulin probably would be underestimated, because of inherently worse expected outcomes for those prescribed insulin compared to those who were not prescribed insulin.
In observational studies, covariates may be selected to explore subgroups or to reduce variance (as with RCTs), but may also be selected to reduce bias. To completely eliminate bias via regression on covariates, all variables that affect the outcome must be included, the correct functional form must be used for all predictors, and the true relationship between predictors and selection bias must be linear. The advantages to using regression in nonexperimental designs are: 1) linear models are easy to fit, and 2) covariates are generally not costly in terms of variances. Disadvantages include serious confounding that can inflate standard errors and the difficulty in meeting the conditions required for valid causal inference (e.g., including all relevant covariates). As a partial solution to the latter issue, sensitivity tests can calculate the minimum bias that would make findings nonsignificant (Rosenbaum, 2002, *Observational Studies)*. In some cases, the necessary bias is implausibly large, so that one can be reasonably confident that of a causal rejection of the null hypothesis.

<u>Modern techniques for the analysis of observational data</u>

[1] Evaluating subgroups would increase sample size needs, which must be addressed during the study design process. In general, evaluating X subgroups multiplies sample size needs by *at least* X, and formally comparing X subgroups in pairwise fashion multiplies sample size needs by *at least* 2X.

In the past 30 years, work in the fields of statistics and econometrics has led to improvements in the analysis of nonexperimental data, including techniques that attempt to directly address selection bias through selection models, rather than doing so indirectly. Analyses that target selection bias are typically costly in terms of variance, requiring large sample sizes are needed. This variance reflects the fact that observational studies contain less information per observation than RCTs. Two such techniques that will be discussed further are propensity score matching and instrumental variables.

In propensity score matching (Rosenbaum and Rubin, 1983), instead of modeling everything that determines an outcome, the investigator instead models the determinants of treatment assignment. In this approach, variables related to treatment assignment are used to model who receives an intervention. Predicted probabilities of receiving the intervention are created for all subjects (both those who did and those who did not actually receive the intervention). Matched blocks of those with similar probabilities are created, with subjects in the intervention and control groups represented in each block. Treatment effects are then estimated within blocks, and these within-block effects are averaged to calculate the ATE. To apply propensity score matching to the observational insulin treatment example, treatment decisions would be modeled, using as many predictors (such as medical history, patient characteristics, physician characteristics) as are available. Patients then would be grouped by the degree to which they resemble those who typically receive insulin. If done properly, this in essence generates a set of miniature "pseudo-RCTs" which can be averaged to generate the ATE. If well executed, propensity score matching in practice results in less bias than regression, although probably more than an RCT; bias can be equivalent to that of an RCT (zero) if all assumptions are met.

An actual example of the use of propensity score matching can be seen in a study in which new Medicaid beneficiaries in New Jersey were randomized to either receive or not receive a report in which other beneficiaries evaluated a set of health maintenance organizations (HMOs) along with their enrollment materials (Farley, Short, Elliott et al., 2002, HSR. All beneficiaries were then asked to select an HMO; the outcome of interest was the average consumer rating of the selected HMOs. An initial intention-to-treat analysis was essentially a *t*-test of an RCT. One difficulty with this study was that only approximately half of those receiving the evaluation report said they had noticed and read those materials when asked in a subsequent survey. Selection bias occurred within the experimental group because those who read the materials were better educated and sought more other sources of health information, making it difficult to determine if their better choices were due to the material received from the investigators, or whether that subgroup would have chosen more highly rated plans in the absence of any intervention. Propensity scores were used to find an equivalent subset of the control group-those would have read the materials if they had been mailed to them. This allowed the investigators to conclude that the evaluation materials did cause beneficiaries to choose the more highly rated HMOs among the subset of beneficiaries who read those materials.

Instrumental variables estimation can be used to understand the causal effect of a treatment on an outcome. A perfect instrument causes the experimental condition, but has no direct effect on the outcome. Such an instrument can be used to produce unbiased estimates of causal effects. Unfortunately, valid instruments of this sort are difficult to find, and this technique is especially costly in variance. In our hypothetical example, let us imagine that male physicians are more

likely to prescribe insulin but otherwise do not differ from female physicians in their effects on diabetic outcomes (otherwise similar care). Physician gender would then be an instrument for estimating the effects of insulin on diabetic outcomes. In this instance, physician gender could be thought of as an indirect source of randomization to treatment, because the physician gender affects the likelihood that patients will receive insulin, but other care is the same. Power is best, i.e., sample size needs are least, when male and female physicians differ strongly in prescribing-in other words, when the instrument is very predictive of treatment decisions.

In an actual example (McClellan, McNeil, and Newhouse, JAMA, 1994**)**, Medicare claims data from 1987 to 1991 were examined for patients with acute myocardial infarctions (AMI). The predictor of interest was catheterization and revascularization treatments, and the outcome was survival to four years after AMI. There were observable and unobservable health differences in those receiving the treatments. The authors were not confident that *t*-test or regression analysis would result in a good measure of difference. The instrument used was the distance from the nearest hospital of a given type. This was a strong independent predictor of treatment decisions, unrelated to observed health characteristics, and effectively randomized subjects to treatment. Results showed less than a five percent improvement in mortality, and all of this occurred on the first day of hospitalization, and so was not attributable to these procedures themselves. Instead, improvement was attributable to other aspects of first-day care that were associated with these procedures.

Examples of Nonexperimental Designs
Carol Mangione

Legal, ethical, or practical considerations can make it impossible to conduct a true experimental research in many settings and situations. Random assignment may not be possible and it may not be possible to incorporate control or comparison groups into the design. Often times, non-experimental designs take an experimental approach but do not have the level of control of a true experiment. Different types of non-experimental designs include non-equivalent control group design, in which discrete observations are made before and after an intervention; interrupted time-series (ITS) design, in which multiple observations are made before and after the intervention; and multiple time-series design, which is the same as interrupted time-series design but outcomes of interest are collected in two or more settings.

An example of non-experimental, observational study is the Translating Research Into Action for Diabetes (TRIAD) study. The research question asked in this TRIAD analysis was, “Do Latinos and Whites in managed care settings self monitor blood glucose at similar raters and are their HbA1c values similar?” The design used was an observational cohort study, with a sample of 4,685 persons with diabetes cared for in 8 health plans from various regions in the U.S. The study observed differences between the groups regarding self-monitoring of blood glucose and seemingly related differences in mean HbA1c levels, with groups reporting the highest levels of self-monitoring seeming to achieve the best control. In this study, however, the causal assumption that more self-monitoring lead to better control cannot be made. The uncontrolled before and after design is simple to conduct, but secular trends and other unmeasured variables make it difficult to attribute changes to the intervention. There are no easy analytic fixes to studies of this sort. In organizational interventions, this design is likely to lead to an over-

estimation of benefit, particularly if poorly performing units (i.e., the sickest people) are selected for participation.

The controlled before and after design, also called the nonequivalent control group design, has no randomization and is often called a "natural experiment." A control population with similar characteristics is identified, and baseline and post-intervention data are collected on both the control and intervention populations. This design provides some protection from bias due to secular trends. But even in well-matched groups, baseline characteristics can differ and these differences can be associated with the outcomes of interest. The strength of this design lies in how similar the controls are to the exposed persons; if very similar, this design controls for selection effects and regression to the mean. For analysis of controlled before and after designs, differences-of-differences is the simple (naïve) approach; looking at the significance of within-group change is less informative, and quality of matching is critical. Because matching is critical, propensity score techniques are applicable for this type of analysis.

ITS designs can be useful if data are being collected for a different purpose and if the outcome of interest is whether an intervention improves care more than the observed secular trend. In this situation the overall trend can serve as a control. This design requires the collection of data multiple times both before and after implementation of the intervention to understand the magnitude of the secular trend. The analysis also must account for the autocorrelation of data collected at multiple time points. ITS often is used in sociological or educational research. It provides the best way to control for history in a time-series design, when one group is exposed to the treatment of interest, the other is not, and there are multiple measures of the outcome in both groups in a pre-post design. The strength of the design depends on how similar the control group is to the exposed group. For example, a good research question for this sort of design could ask what the impact of removing vending machines from public schools is on childhood obesity. To use this design one would need demographically similar schools with similar amounts of physical education, standardized assessment of height and weight across multiple schools, and some schools with and without vending machines.

Quantitative experimental designs include individual patient-level RCTs and cluster RCTs. These are the strongest designs for establishing a causal relationship but often are not appropriate for health plan, community-level, or other system-level interventions. RCTs are the gold standard, but are time consuming, expensive, complex, and may require a large number of clusters. Additionally, tight inclusion criteria can limit generalizability. Highly controlled experimental designs also are unlikely to determine whether an intervention will improve routine practice. For trials of this sort, a pretest-posttest control group design is best, because it helps to ensure that groups are similar at baseline, and, whether the outcome varies more across individuals than across time. Controlling for baseline can greatly reduce the error variance and thus the sample size needed to detect clinically and/or statistically important differences. A posttest only group design, however, is often the design that is used in many settings. This type of design tends to be less expensive, but to properly use it, sufficient sample size is needed to increase the probability of equivalence, because preexisting differences cannot be controlled for between experimental and control subjects due to a lack of baseline data.

Analytic Issues of Group Randomization Trials (GRTs): Clustering versus Contamination
Marc N. Elliott

Cluster randomization may be a good design strategy for interventions at the provider, system, or community level, because randomization at the individual patient level may be logistically infeasible or likely to introduce "contamination" in which some of those assigned to the control group inadvertently receive at least part of the intervention through contact with experimental subjects. Randomization at a higher level reduces contamination, but exacts a high price in power to detect clinically meaningful differences in outcomes because of inflated variance through clustering.
A simple approach, analysis of the cluster level means, uses the cluster as the unit of both randomization and analysis. Unfortunately, treating each cluster as a single data point is often very inefficient. There are two broad classes of valid patient-level analyses of GRTs. The first adjusts for the clustering using the "sandwich estimator." This approach is very robust and requires only weak assumptions, but limits the degrees of freedom for predictors. The other approach, hierarchical modeling, allows the correlation between clusters to be explicitly modeled. The variance components generated by the latter approach are often of inherent interest.

One problem with group randomization is reduced power, because information can be lost if randomization is at the level of large, homogenous groups. The intraclass correlation coefficient (ICC) r measures the degree of similarity of participants within a randomized unit, whereas B is used to represent the number of completes per randomized unit. If $r = 0$, patients within the same units are no more similar than those in different units, an uncommon situation. If $r > 0$, patients within the same units are more similar than those in different units. Typical values of r are between 0.01 and 0.10. The design effect (DEFF) of a group randomized trial (GRT) is the relative increase in the variance of an estimate as a function of clustering, as compared to the variance for an individually randomized trial of the same total sample size.

The DEFF of a GRT can be calculated as $1+(B-1)r$. For example, if $r = 0.05$ and a cluster sample of 15 patients from each of 20 practices is chosen (total sample size is 300), $DEFF = 1+(15-1)(0.05) = 1.7$. The variance of a sample mean estimated from the cluster design is 1.7 times as large as it would be based on an individual RCT of 300 patients. Therefore, this study would have the same power as an individual RCT of 176 patients ($300/1.7 = 176.5$). If 25 patients are chosen from each of 12 practices (total sample size also is 300), then DEFF = 2.2, and the study would have the same power as an individual RCT of 136.4 patients. For a given total same size, there is a loss in power as the number of patients used per practice or the ICC increases. With a large ICC, increasing the number of patients per practice beyond a certain level (typically 1/r-3/r) produces very little benefit, and statistical power can be increased only by increasing the number of practices.

One motivation for performing GRTs is concern regarding contamination, which occurs when an intervention is adopted by some proportion of the control group. Randomization at the individual level might increase contamination through contact between patients, physicians, or others. For example, if patients with the same physician interact and inadvertently discuss an intervention, patients in the control group might spontaneously adopt some aspect of the

intervention (e.g., dietary changes). This is less of a problem if the intervention is implemented at the level of the practice. Intention-to-treat and other simple analyses will be (conservatively) biased if contamination occurs. Selection-based techniques (such as propensity score techniques) can correct this bias if contamination can be detected by retrospective survey. Contamination causes a loss of power to detect true effects; therefore, if contamination is suspected, the sample size must increase, although the costs are typically modest for plausible levels of contamination. For example, 5 percent contamination increases sample size needs by 11 percent and 10 percent contamination increases sample size needs by 23 percent. Variance inflation from group randomization is often much larger than this. In general, contamination must reach approximately 30 percent, which is rare, for it to outweigh the variance costs of group randomization (Torgerson, 2001, BMJ).

Discussion

Dr. Joe Selby asked about a situation in which the investigator would like to use individual randomization to an intervention after obtaining consent, but only 30 percent of those approached agreed to participate. He asked if propensity scores would be useful to determine which subjects in an intervention arm would participate, so that one could then the scores to match them to controls. He also asked what 30 percent participation meant for determining the generalizability of the intervention. Dr. Elliot answered that if a highly selected sample is randomized, valid inferences can be drawn about treatment within that group because of the random assignment. This does not, however, lead to automatic inference about the effect of treatment in the larger group from which the 30 percent who consented came. Evaluating whether the intervention will have an effect in the larger population is a classic problem of nonresponse. Here, a key question is whether the effectiveness of the treatment is associated with the basis on which people choose to enter the trial. The investigator could perform nonresponse modeling based on what is known about those who chose to participate versus those who do not choose to participate. Gathering as much information as possible about nonparticipants will help determine generalizability. Nonresponse fits nicely with these other issues of selection bias because it illustrates how bias can arise from a stuffy that starts out as an RCT.

Dr. Kim Gans asked about using group randomization at a work site. At intervention sites, random sampling of employees is performed, and a subset will attend several different interventions. She asked how the techniques described in Dr. Elliott's presentation could be used in the analysis of process evaluation when considering dose. Dr. Elliott answered that there likely will be differential adherence through attendance, and Dr. Gans could expect people to differ systematically with respect to attendance. Propensity scores could be used to estimate and predict who would attend an intervention. In answer to questions from participants, Dr. Elliott noted that propensity analysis techniques require a much larger sample size than RCTs and that, when these techniques are used to analyze one treatment with complex interventions, there are techniques to determine sample size needed to accommodate multiple arms and multiple interventions.

Dr. Edwin Fisher mentioned that group randomization techniques are useful for studies pertaining to community health practice. He cautioned against assuming a perfect RCT as a

standard for comparison, because RCTs are not perfect in translational research. When considering the pros and cons of RCTs and other designs, investigators should compare a "real world" RCT with a "real world" other design. As an example, 30 percent recruitment to an RCT may underestimate the effect of an intervention if those recruited are less likely to take advantage of interventions. There may be better ways to recruit subjects to improve generalizability. Dr. Elliott noted that a perfect RCT is often used as a reference point, because it is easy to understand all the issues and techniques discussed for observational studies, which can also be used to assess the failures of RCTs. Dr. Benjamin Littenberg added that RCTs are preferable because they represent the method least likely to be invalidated by selection bias. He proposed that community organizations tend to oppose randomization for ethical reasons, but the source of resistance lies more with the investigators and providers than the participants. Dr. Mangione clarified the idea of ethical considerations, explaining that the issue that usually arises is that of control groups receiving no or minimal care. She urged that investigators think creatively about design and offer valuable alternatives to controls without contaminating what is being studied. This pertains strongly to underserved minority communities, especially if investigators want to maintain good relationships with these communities.

Grantee Presentations

Improving Diabetes by Primary Care Translation (IMPACT)
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The IMPACT study examines how to successfully translate empirical knowledge regarding diabetes management and treatment into clinical practice. IMPACT is a GRT involving 24 primary care clinics. The diabetes-specific TRANSLATE interventions (Targeting, Reminder systems, Administrative review, Networked information system, Site coordinator, Local opinion leaders, Audit and feedback, Teamwork, and Education) were introduced to each site and evaluated over a 12 month period. The specific clinical outcomes assessed were changes in HbA1c and systolic blood pressure among all patients with type 2 diabetes, and quality of diabetes care as measured by the distribution and prevalence of HbA1c measurement, microalbumin, low density lipoprotein, and foot exams. Intervention cost from the perspective of the health care system also will be analyzed. The study seeks to improve clinical outcomes while reducing the time commitment required of the local team, having a neutral or positive impact on revenue, accounting for diversity, and involving administrative personnel and information services.

As part of the intervention, electronic reminder systems targeting patients and physicians were developed, which delivered electronically generated reminders to patients 3, 6, or 12 months overdue for visits, as well as to all patients with no visits in 6 months. Patient-specific profiles were generated for all visits, which detailed current disease status, provided a graphic history of previous test results, and recommended tests for the current visit. The system also helped to facilitate appropriate coding for procedures and visits, so correct reimbursement could be obtained; this increased clinic revenue because previously many visits were not properly coded or charged for. A networked information system also was established, which consisted of a distributed database with synchronization, with reporting and tracking systems and a laboratory

import facility. Regularly scheduled downloads permitted reference laboratories to provide patient files with relevant diabetes laboratory test results. The system also alerted clinics to new patients, patients with missing test data, and test results in need of updating.

An Administrative Oversight Board was created to monitor clinic performance. The Board received quarterly reviews of progress and also was able to designate and leverage resources to assist the clinics. The study made use of site coordinators, who facilitated interactions between the practice team and patients, contacted target patients, and generated monthly reports for the Diabetes Intervention Team (DIT). Site coordinators were overseen by local opinion leaders, who were clinic physicians recognized by their peers and well versed in diabetes care. These individuals worked as part of the DIT, which also included clinic managers, medical directors, local physician champions, and other personnel as designated by the clinics.

Preliminary outcomes have been measured in 16 clinics and include increases in frequency of microalbumin and HbA1c monitoring and eye and foot exams in the intervention group compared to the control group. Significant decreases in average blood pressure and average HbA1c levels among targeted subjects also were observed. The study successfully implemented protocols resulting in increased numbers of appropriate return visits and followup, development of a chart organization that was up-to-date and reliable, increased provider awareness, and increased staff communication and teamwork. Remaining barriers included an inability to change provider work styles, certain technical problems, issues of time constraints and continuity of care, and clarification of the roles of local champions.

The IMPACT team also has begun implementation of an electronic registry for translational research as part of the NIH Roadmap to promote translation of research to practice and harmonize these efforts across the country. This will be a single registry covering all diseases and focused on clinical support for translation. Standard features include integration of Internet-2 capability (Grid), and involvement of caBIG (NCI), Health Level 7 (HL7), the Clinical Data Interchange Standards Consortium (CDISC), and Abstract Syntax Tree Meta Modeling in Unified Modeling Language, creation of an enterprise vocabulary system, and development of standardized ontology and XML exchange. Additional functions will include remote training, patient safety and decision support information, improved meta-analysis, real time video conferencing, remote instrumentation, and opportunistic identification of subjects for large collaborative national studies.

Promoting Healthy Lifestyles Among Women
Edith Kieffer, Ph.D., M.P.H., University of Michigan School of Social Work

Exercise, dietary and weight-related beliefs and practices during pregnancy often result in excessive pregnancy weight gain. Stress, depression and the multiple demands of work, parenting and family life further contribute to behaviors that result in excessive pregnancy weight retention for many women. The effects of cumulative weight gain and weight retention during first and subsequent pregnancies may contribute to the development of chronic obesity, insulin resistance and increased risk for type 2 diabetes. **Promoting Healthy Lifestyles Among Women (a.k.a. Healthy Mothers on the Move/Madres Saludables en Movimiento) is** a randomized controlled study to determine whether a culturally and linguistically tailored healthy

lifestyle intervention can reduce risk factors for type 2 diabetes among pregnant and postpartum African American and Spanish-speaking Latino women in eastside and southwest Detroit, Michigan. This study demonstrates methods for apply findings from the DPP regarding prevention of type 2 diabetes to preventive efforts in a "real world" setting. Primary project aims are to increase the proportion of women who eat healthfully (increased fiber, fruits and vegetables, decreased fat and sugar), and exercise regularly at moderate levels. Secondary aims are to increase the proportion of women who have appropriate levels of pregnancy weight gain and postpartum weight reduction and have improved metabolic profiles (glucose, insulin, lipids). The project also assesses and documents challenges and contributors to implementation to understand the conditions necessary to translate this intervention to other settings.

This study is an RCT with two arms: the Healthy Lifestyle Intervention and the Healthy Pregnancy Education (control) Intervention. In these medically underserved communities, a control group receiving no care or intervention was unacceptable. The Healthy Pregnancy Education Intervention (prenatal and postpartum stress and depression, maternal, fetal and infant growth and development, labor, birth, and infant care) was designed in response to finding that women in the community (even those with children) had little to no education about pregnancy and infant care and were eager to learn about these subjects. The study was designed so that all women (both in the intervention group and the control group) receive this education.

Preliminary community-based participatory research identified community residents' beliefs, practices, and recommendations regarding weight, eating, and exercise during and after pregnancy. These findings resulted in an intervention structure, curriculum and activities designed to modify beliefs and attitudes and to increase perceived behavioral control by reducing physical, social, and environmental barriers to adopting healthy lifestyles. The intervention design reflects the importance of social support by providing one-on-one and twice-weekly group meetings with trained community resident Women's Health Advocates and peers. The Healthy Lifestyle Intervention group has 2 home visits, 9 group meetings, and 10 optional activity days during pregnancy, followed by 2 home visits and 1 group meeting during the postpartum period. The curriculum includes instruction on diabetes and its risk factors, stress and depression, discussion of beliefs, barriers and strategies for adopting and maintaining healthful eating, safe physical activity and stress reduction practices into daily life during and after pregnancy. Participants develop behavioral goals and discuss how to overcome potential family or social disapproval. During activity days, group members participate in food and cooking demonstrations, a variety of physical activities and group discussion.
Healthy Pregnancy Education (control) Intervention participants receive three group meetings during pregnancy and one group meeting postpartum led by staff from a community partner organization. Participants receive written information on healthy eating and exercise prepared by organizations such as the March of Dimes. Members of both groups participate in "Pamper Me Day", which includes massages, baby and mother gifts, social interaction and process evaluation as their last meeting. To aid with recruitment and retention, all meetings and data collection took place at trusted community organization host sites. Healthy food, transportation, childcare and small gift incentives are provided. A monetary incentive is provided following data collection sessions. Contact is maintained with participants through birth announcements and newsletters (in English and Spanish).

Data collection methods include questionnaires, anthropometry, and blood draws taken at baseline (15-20 weeks), pregnancy followup (33-36 weeks) and postpartum followup (6-8 weeks postpartum). Process evaluation data are derived from participant observer, facilitator, and participant, focus groups with participants and project staff, and interviews with host site representatives and members of the community-based steering committee. Data regarding rates of recruitment, randomization, withdrawal, reasons for declining to participate and withdrawal, meeting attendance, and types of other contacts and referrals are also collected and analyzed.

Many challenges can mostly be attributed to the "real world" in which this project is being undertaken, including fragile structures of Detroit health and community organizations supporting the trial. Budgets cuts that resulted in hospital, clinic and prenatal outreach program closings, undependable public transportation and overstretched private transportation have resulted in three moves of our staff offices, late entry of women into prenatal care and difficult project logistics that have affected recruitment and retention, particularly of African American women. Maintaining host site, transportation and childcare contracts, trouble shooting, initial staff recruitment (since stabilized) and ongoing intervention staff training, and assuring that our data collection subcontractor maintained a well trained staff needed for data quality have required extensive project resources and staff time. Extensive resources were also needed to develop the curriculum and materials since the DPP materials were not originally available and were not designed for pregnant women. Most healthy lifestyle interventions and materials were designed for older, more educated or higher income women, did not address cultural and literacy needs and were usually available only in English. The project has invested substantial resources in development of new materials and provision of staff training, continuing education and ongoing support for staff working with few resources, in often frustrating low resource environments with women who face tremendous social and economic challenges.

Accomplishments to date include development and implementation of well-received, culturally-tailored curriculum and retention materials and processes for pregnant and postpartum African American women and Spanish-speaking Latinas, completion of intervention activities for 7 cohorts of women and strengthening of community partnerships needed for sustainability. Community residents have been successfully trained to implement the program. They, and project steering committee members have a wealth of experience needed for ongoing problem-solving. Evaluation suggests that social support from the advocates and peers is key to success. Participants have self-reported increased adoption of healthy eating, physical activity and problem-solving behaviors. Outcome data is not yet analyzed.
Concerning sustainability, the materials and methods developed and lessons learned could be used to build the capacity of existing health providers and community based organizations (such as federally qualified health centers, Healthy Start and Extension Service home visitor programs) to provide aspects of the interventions as part of their ongoing activities. This has been requested by a key partner federally qualified health center, Community Health and Social Services, which serves pregnant and postpartum Latinas in southwest Detroit. Development of funding mechanisms also is key and could perhaps be achieved by educating health service and insurance providers on successful project components with the aim of encouraging reimbursement for services provided. Suggestions for some revisions of the curriculum and related materials have been made by project participants and staff. After resources are obtained

to make these revisions, these materials could be made available locally and nationally for other groups seeking to undertake similar interventions.

Behavioral Intervention for Type 2 Diabetes in Youth
Alan Delamater, Ph.D., Department of Pediatrics, University of Miami

Although the incidence of type 2 diabetes in youth has increased dramatically in recent years, little is known about psychosocial and behavioral issues affecting management of the disease in youth, particularly for lower income, minority youth. Additionally, little is known about the efficacy of programs to improve health behaviors and outcomes for these patients. The study aims to identify key psychosocial and behavioral issues related to diabetes management for lower income, minority youth. The study also will determine the efficacy of a behavioral intervention targeting weight control and diabetes self-care behaviors in a family context. Exploratory focus groups were conducted with lower income minority teens and their parents, and information from these groups was used to design behavioral interventions. Patients were approached at clinics; of 26 interested patients, only 12 participated in the focus groups.

Based on review of transcripts from the exploratory focus groups, investigators found that patients and their families had inaccurate information about type 2 diabetes and its treatment. They admitted to emotional upset and fear upon diagnosis and feelings of stigmatization; teens disclosed their diabetes diagnosis only to a few friends. Teens also indicated that they were less likely to follow diabetes care protocols outside of the home. Families were seen to be motivating and supportive but had difficulty defining specific treatment goals. Teens and their families felt comfortable with the focus on losing weight and increasing physical activity as part of diabetes management and showed enthusiasm for the idea of meeting in groups at the clinic with other teens with type 2 diabetes and of having a "diabetes buddy." They preferred mixed gender and ethnic groups and wanted a combination of structure and open format. The families reviewed the intervention approach and written materials, and were enthusiastic about both, indicating they would be interested in participating in such a program.

Intervention objectives include increased motivation and self efficacy for diabetes management, increased social support from peers and family, improved glycemic control and reduced health risk, weight loss through improved diets and increased physical activity, improved diabetes self-care behaviors, and improved quality of life. Initial individual sessions with teens and their parents included motivational interviewing and education about research participation. Small groups (four patients in the same age group) met initially and then three times at 2-week intervals, followed by monthly meetings over 12 months. Parents were involved in part of each of the sessions, which were led by a psychologist and dietician. The meetings addressed diabetes and nutrition education issues, changes in eating behavior and physical activity, and also addressed psychological adjustments to having diabetes to help motivate self-care and make teens more aware of the risks associated with diabetes.

Challenges faced by this study mainly concern recruitment and retention. After diagnosis and initial treatment, some patients do not return to the clinic and many patients do not keep regularly scheduled outpatient appointments. To increase recruitment, patients diagnosed with type 2 diabetes were contacted by letter and follow-up phone calls, rather than waiting for

patients to come to the clinic. Because of these difficulties, too few patients were recruited to realistically conduct a randomized study with 80 patients within the time constraints of R34 funding. The design was therefore changed to within group analysis, with all subjects receiving behavioral intervention; this will allow better estimation of effect sizes. Additionally, 10- and 11-year-olds were included to increase sample size. It was found that although interventions held at clinics for multifamily groups could be logistically difficult, groups may be more cost effective than individual interventions. Staffing for the intervention (psychologist and dietician) is feasible, with the ability to bill insurance for some services, and building the intervention into the clinic routine rather than conducting it separately (for example, weekday afternoon meetings rather than Saturday morning) will help sustain the intervention.

Expanding the Reach of Diabetes Prevention: Challenges of Community-Based DPP Translation

Ronald Ackermann, M.D., M.P.H., Indiana University School of Medicine

The DPP trial resulted in a 58 percent reduction in new cases of diabetes, but 4 years after the trial, no generalizable models for DPP implementation have been developed. Barriers to translation of DPP findings include difficulties in identifying people with impaired glucose tolerance (oral glucose tolerance testing is costly and difficult) and the challenges of implementing intensive lifestyle interventions (cost-recovery is delayed and most settings cannot provide the necessary resources). To overcome these barriers, we developed a model in which simplified methods are used to identify community residents likely to have impaired glucose tolerance, and these individuals are offered access to a diabetes prevention intervention that has been adapted for feasible delivery in a community setting. For this study, the YMCA was chosen as a partner, because it has more than 2,500 facilities across the United States, and has experience with lifestyle programming and with implementing scientific programs, and financial aid packages so all who wish to can join despite an inability to pay.

The primary aim of this study is to determine if a group-based adaptation of the DPP lifestyle intervention can be implemented at a YMCA facility. The cluster-randomized (YMCAs) pilot trial involves direct mailing of information describing risk factors for diabetes and an invitation to one of several screening events to households in the primary market areas of two matched YMCAs. This will result in recruitment and enrollment of 200 high-risk adults. Adults are allocated to intervention or control groups through enrollment at matched YMCA facilities that have been randomized as intervention or control sites; both groups receive marketing materials for YMCA risk screening events, assignment to low-moderate or high-risk groups, and brief advice about risk reduction. Those in the intervention group are offered free access to a group-based adaptation of the DPP intervention at the YMCA, whereas those in the control group are offered access to existing YMCA programs for a fee. Measures and outcomes include patient characteristics; self-report of physical activity and diet; and body mass, blood pressure, blood lipids, and HbA1c measurements. Costs and quality-of-life issues will be assessed, and internal direct program observation is being performed using a trained observer unknown to the group leader to determine if the intervention was delivered correctly. Predictors of enrollment, participation, attendance, and success in the program also will be evaluated.

Caveats to this method include the possibility that control group members also will lose weight and decrease risk for type 2 diabetes through use of YMCA facilities. Benefits of community-based participatory research with the YMCA include providing an expanded reach beyond healthcare systems to enhance the impact of preventive and chronic care interventions, investment of community members in the processes and products of DPP translation, enhancement of the generalizability and sustainability of the translation effort, and opportunities for future dissemination at YMCA sites throughout the United States. Barriers include the time required to build trust and support, limited community incentives or resources to conduct research, versus immediate action, lack of local or federal "bridge" funds to develop the partnership, and complicated study design issues.

Discussion

Several of the presenters responded to questions about costs and how to measure them. Dr. Ackermann said that his group has not completed the first round of followup. They will use DPP forms for costs not related to the intervention. Information is available concerning costs for YMCA delivery, training, and instruction, and they will soon have data for costs such as athletic shoes and exercise equipment. Dr. Littenberg asked about the costs of delivering interventions poststudy. Dr. Peterman answered that they are currently performing analyses to determine the costs of site coordination, physician champions, medications, and hospitalization. He said that his initial impression is that the intervention will be very cost-effective because it will decrease hospitalizations, emergency room visits, and complications; additionally, all 24 of the clinics he worked with plan to adopt the intervention. Dr. Ackermann mentioned that the YMCA has determined that the fee needed to recover their costs is approximately $25 per patient per month. Dr. Delamater said that recruitment costs will be handled through the clinics, and having one meeting per month will be very cost-effective. Psychologists will be able to bill for this through insurers. Dr. Kiefer said that she had not yet calculated costs, but more than half the funds are spent on data collection. The primary cost will be that of training the Health Advocates, which involves a 1-month training session as a community health advocate, training in pregnancy health and on the intervention, and mentoring sessions on research strategies, communication issues, and setting boundaries; these costs should be low.

Dr. Kiefer was asked about retention of participants between baseline and randomization, given that three baseline interviews are performed before participants are randomized. Dr. Kiefer answered that the three baseline interviews occur within 3 to 4 weeks. The largest loss of participants occurs between the point when the participant indicates she will participate and the introductory session; those who attend the introductory session tend to stay with the program. Loss of participants can largely be attributed to infrastructure problems such as transportation and data-collector absences.

Dr. Ira Ockene commented on difficulties identifying prediabetics and suggested using a system in which easily measured single blood test parameters, instead of the glucose tolerance test, in conjunction with high-density lipoprotein (HDL) levels, body mass index (BMI), family history, and ethnicity are used to predict diabetes. Dr. Ackermann answered that for his study they used capillary HDL and blood glucose. Fasting glucose was not used so that they would not miss postprandial glucose measurements.

The participants discussed Health Insurance Portability and Accountability Act (HIPAA) issues concerning access to diagnoses to locate diabetic patients. Dr. Delamater said that his group presented an amendment to the protocol to their Institutional Review Board (IRB) and received permission to contact existing patients by mail. Dr. Peterman described the business associate agreement he had with the clinics, which stipulated that the intervention would function under clinic rules. Clinic researchers did not have access to identifiable data and physicians were asked to resolve any conflicts of interest. Another participant mentioned that after his group failed to recruit an adequate sample under HIPAA rules, they contacted the IRB and were allowed to send potential subjects a postcard, which recipients were asked to send back if they were not interested in participating; those who did not send the card back were contacted by telephone. A participant commented that IRB research rules should be the same as HIPAA rules. Because community-based research cannot be performed without participation of the community, using passive, rather than active, consent is permissible; in this case, subjects must actively ask to be excluded. In general, communities are agreeable to this approach. Another participant added that her group sought to broaden the definition of informed consent to include the ability to share unidentifiable data with other researchers after the study has been completed. Dr. Gary Welch commented that perhaps a document should be generated detailing how others have coped with issues of consent, recruitment, and participation. Dr. Delameter described a program in which participants were randomized to receive or not receive education on research participation, which found that those who received the education tended to stay in the study.

Potential Future Directions for NIDDK-Sponsored Translational Research
David Marrero, Ph.D.
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Standards for grant evaluation are one set of factors influencing promotion of translational research. In particular, the methodologies used are a critical factor. RCTs are considered to be the "gold standard" by many grant reviewers, but RCTs often are the best option for translation research, and frequently are not feasible in a community setting. In addition, methods that support sustainability are often not emphasized. Reviewers tend to have variable experience with translational research and can be biased toward physicians and basic scientists. To address these issues, a database of potential reviewers should be developed; in particular, grant recipients could be required to review future applications. , NIH could also provide reviewers with examples of alternative design methodologies and their impact on study conclusions in the form of seminars, presentations or monographs. . Training monographs describing designs used and issues faced by translational researchers, along with examples of successful studies using alternative designs also would be useful.

Translation research often will require partnerships between community groups and research entities. This should be considered in future program announcements and Requests for Applications (RFAs). Greater emphasis should be placed on research investigating community outreach and coalition building; dissemination research versus efficacy; cooperative research agreements between partners and applying institutions; and sustainability of programs. Funding could be provided for research concerning how to sustain a program; these funds would not necessarily support sustaining the program itself.

Challenges to R34 and R18 grant recipients include recruitment and participation issues, technical problems, HIPAA regulations, and personnel turnover, especially when partnering with outside agencies. Community partners, academic institutions, and family agencies that participate in translational research need to be educated on how this research is performed. Many of these partners will not accept randomized designs and regulations concerning access to data can interfere with evaluation methods. Most community partners also do not appreciate the timeline inherent in proposals seeking federal funding; because of this lack of understanding, the length of funding cycles for R18 and R34 grants can discourage some partners. A monograph discussing funding agency expectations and restrictions, which would highlight the need for evaluation and describe design alternatives, could be developed and targeted to community partners. Community partners meetings modeled after or integrated with programs currently conducted by the National Diabetes Education Program could be hosted to integrate investigators and support agencies with community partners.

The NIH needs to consider these issues, particularly the considerable time lag in the grant review process, which could jeopardize relationships with partners and make it difficult to build longer term, integrated approaches to translational research. As possible solutions, "pilot" and "feasibility" applications that allow for limited pilot data could be developed. Applications could focus on feasibility and access, and require robust evaluation methods, although not necessarily RCT designs. A rapid funding pilot grant application, with a short turnaround time (6 months rather than 1 year), with flexible design requirements and a limited time frame, could be developed. NIH also could create Centers of Excellence in Translational Research, which would support integrated translation programs to allow development of pilot and feasibility studies, enable more comprehensive development of community partnerships, provide core support for other investigators, and assist in translation of large-scale clinical trials.

Discussion

On the topic of sustainability, a participant commented that it can be difficult to renew an R18 showing 2 years of an effective intervention because new material is not proposed. Dr. Welch commented that some studies include economic analyses, which could help structure translation of the intervention so it can be better sustained in the community once the study has been completed. Dr. Gans described an NCI mechanism in which investigators can apply for a dissemination grant in the last year of funding as long as data has been collected. These applications are not subject to traditional review; instead, they are reviewed by a special committee or possibly by administrative review.

Several participants commented that the 18-month cycle for grant evaluation needed to be shortened. Dr. Fradkin said that there is now a new Director for the Center for Scientific Review (CSR), who is trying to implement a system with a faster turnaround time. One problem is that R34 and R18 grants are reviewed by a single study section, and reviewers cannot be identified until the grants are received; reviewers have expressed displeasure with the limited time they are given to review the grants, but a longer timeframe for review would lead to an even longer application cycle. Dr. Ackermann suggested recruiting more reviewers and perhaps allowing submission of applications throughout the year, rather than just four times per year. Dr. Marrero

agreed that investigator-initiated submission with more frequent review cycles might be preferable for translational research grants. A participant suggested that perhaps the formality of review could be tailored to the type of grant, with a more formal review process required for larger grants.

Dr. Kate Lorig suggested that Centers of Excellence should be created across Institutes, rather than within Institutes, because the mechanisms of dissemination are not always disease- or age-specific. Dr. Peterman mentioned the Clinical and Translational Science Awards (CTSAs), which span institutes. The DRTCs may want to become involved in creation of new CTSAs. Dr. Marrero commented that there are interesting aggregations of people performing translational research across the United States, but they should be organized into a more cohesive unit with a better focus. The DRTCs have a role, but should not be the only outlet. A research agenda for dissemination and translational research is needed. Dr. Pat Coon described Action Grants, in which an academic center applies for the grant on behalf of partners unable to perform all aspects of translational research. These grants allow health institutions with limited resources access to research funding within a partnership with an academic institution with useful resources.

History of the DRTCs – How DRTCs Add Value to Translational Research: What Do They Do Well? With What Do They Struggle?
Kristin Abraham, Ph.D., Program Director, Division of Diabetes, Endocrinology, and Metabolic Diseases, NIDDK, NIH

The NIDDK's Diabetes Centers serve as integral components of the national research effort to improve prevention and treatment of diabetes and related endocrine and metabolic diseases. Goals of the Centers include raising awareness and interest in diabetes research; serving as catalysts for new ideas and approaches, particularly for interdisciplinary efforts; stimulating collaboration; enhancing education opportunities for patients, physicians, students, and scientists; providing core services to leverage funding and provide expertise to the wider research community; and attracting new investigators into diabetes research.

The Diabetes Center program consists of two types of centers: Diabetes Endocinology Research Centers (DERCs), and Diabetes Research Training Centers (DRTCs). Each center type provides core facilities, pilot and feasibility funds, and program enrichment activities. In addition, the DRTCs house cores designed to provide expertise and services to assist in translating research advances into new clinical and community practice. Providing overviews of these DRTC Prevention and Control cores are investigators representing each of the following DRTCs: Washington University-St. Louis University (Drs. Edwin Fisher and Debra Haire-Joshu); Albert Einstein College of Medicine (Dr, Elizabeth Walker); Vanderbilt University – Meharry Medical College (Drs. David Schlundt and Margaret Hargreaves), and the University of Michigan (Dr. William Herman).

Edwin Fisher, Ph.D.
Professor and Chair, Department of Health Behavior and Health Education
School of Public Health, University of North Carolina at Chapel Hill

In the 1970s, the National Diabetes Commission mandated a training and information transfer component to the DRTCs, with an emphasis on developing, evaluating, and disseminating materials and programs. An early problem was the lack of a community of researchers focusing on translational research in the areas of diabetes prevention and control. Strong communities of health behavior and health services research did not exist at this time. Development of prevention and control activities in the DRTCs can be divided into two phases: 1) cultivation phase, and 2) current phase. During the cultivation phase, innovative professional and patient education programs were developed. Currently, cores for prevention and control research have been established that facilitate research of established health services and health behavior communities and extend state-of-the-art health services and health behavior research methods to clinical research.

A general consideration regarding prevention and control research with the DRTCs and within a broader biomedical context is that of the complementarity of the role of behavior versus the roles of biology and medicine. Medical advances, instead of eliminating the role of psychology or behavior, increase behavioral challenges through development of more complicated treatment or prevention protocols. Reduction in the uncertainty of the results of treatment through increased precision of medicine (e.g., pharmacogenetics) also has led to advances in self-management, which is necessary to fully realize the benefits of improved medicine. Diabetes is a disease of disadvantage and aging; therefore, reaching key audiences will require sophistication in health education, social marketing, cultural influences on health behavior, and understanding of social stratification of health and health care, among other issues. Translation of the results of the DPP will require influencing at-risk populations to engage in moderate physical activity, healthy eating, and weight loss, which will require multidimensional campaigns.

Analysis of the current literature showed that a large proportion of diabetes research takes place at or is facilitated by the DRTCs. The DRTCs provide health behavior/health services research expertise to clinical and translational researchers, provide clinical expertise to health behavior/health services researchers, provide infrastructure to prevention and control research (such as sample identification, recruitment, data management, etc.), and bring established investigators into diabetes research and also facilitate the careers of new diabetes investigators.

Debra Haire-Joshu, Ph.D., Professor and Division Director of Behavioral Science, Department of Community Health, St. Louis University School of Public Health

The DRTC at Washington University–St. Louis University consists of 3 cores: a clinical research core (Washington University School of Medicine); a mental health services and behavior core (Washington University School of Social Work); and a community and vulnerable populations core (St. Louis University School of Public Health).

The DRTC facilitates the research of investigators by providing consultation on metabolic measures, recruitment strategies for physicians, instruction in participatory research methods and community-based health measures, and assistance with behavioral intervention development. The expertise and infrastructure provided by the DRTC attracts investigators across broad levels of background and experience to diabetes research. As an example, this DRTC has attracted established investigators from other fields to diabetes research, such as Dr. Ross Brownson the

director of the Prevention Research Center of the Centers for Disease Control and Prevention (CDC). Dr. Brownson is an epidemiologist renowned for his work in cancer, tobacco, and physical activity. In collaboration with the DRTC, Dr. Brownson was funded to conduct a study to increase physical activity in rural settings as a strategy for preventing diabetes. Most recently, Dr. Haire-Joshu has collaborated with Dr. Matthew Kreuter, Professor and Director of the Center Health Communication Research Lab, whose work has primarily focused on cultural communication, patient/physician communication, and risk perception for cancer. Dr. Kreuter is now involved in the conduct of a variety of studies with a focus on reducing diabetes risk behaviors and is an active member of the DRTC. Finally, the center has helped facilitate the careers of new investigators. For example, Dr. Sarah Barlow is a physician with expertise in pediatric obesity and author of the recommended pediatric assessment guidelines. Dr. Barlow received assistance from DRTC staff, which helped her to secure a career development award addressing pediatric obesity in the clinical setting. The support provided by the DRTC helps investigators of diverse backgrounds and experience pursue and conduct state of the art diabetes research.

The DRTC also helps in the development of the evidence base for community practice. The Diabetes Initiative, in conjunction with the Robert Woods Johnson Foundation, seeks to advance diabetes self-management and build community supports for diabetes care. The Diabetes Initiative National Program Office is located at Washington University and has 14 demonstration projects in primary care and community settings and provides a collaborative learning network, consultation, and training. The program reaches diverse populations in rural and urban settings. This initiative will help build the evidence base for community research and practice and help achieves the goal of sustainability and viability of translation efforts. The DRTCs inform practice-based evaluation methods, provide assistance in shaping findings and drafting papers and reports, and facilitate collaborations with community investigators to promote the "discovery to change" evidence base. This collaboration between the DRTC and the Diabetes Initiative provides a model for dissemination of diabetes research findings.

David Schlundt, Ph.D., Associate Professor of Psychology, Department of Psychology, Vanderbilt University

The Vanderbilt University DRTC was funded in 1977 as a DERC and in 1978 as a DRTC, with a focus on patient education using a model demonstration unit. It was the first DRTC to make the transition to the new prevention and control core model in 2001. This DRTC has two cores related to translation research, the Clinical Outcomes and Behavioral Sciences core, at Vanderbilt University, and the Behavioral Health Disparities Core, at Meharry Medical College.

Vanderbilt DRTC work on health disparities got started because of the need to include research on minority populations in the DRTC renewal. However, we soon came to see that addressing health disparities was "the right thing to do." Two community-based disparities projects were developed in 1992-1993, serving the Eastern Band of Cherokee Indians and Nashville's African American community. To facilitate these projects, a partnership was formed with Drs. Margaret Hargreaves and Mac Buchowski at Meharry Medical College in 1994. The early efforts of this collaboration involved developing and validating self-report measures specifically tailored for assessing eating behavior in African Americans. In 1998, the Nashville Health Disparities

Coalition (NHDC) was formed with Vanderbilt University and Meharry Medical College as charter members. In 1999, the NHDC received a 1-year CDC planning grant for Racial and Ethnic Approaches to Community Health (REACH) 2010; in 2000, the CDC funded the Nashville REACH 2010 implementation until 2007. The DRTC cores at Vanderbilt and Meharry are leading the evaluation of the project and providing support to the interventions.

Other recent accomplishments related to health disparities include Meharry's receipt of an EXPORT center grant, participation of Vanderbilt, Meharry, and the International Epidemiology Institute in the Southern Community Cohort Study, and receipt of a Healthy Communities Access Program grant to implement primary prevention and brief behavioral interventions in community health centers. Investigators associated with the core have received funding to study type 2 diabetes in children and their families (Dr. Russell Rothmann) and promotion of physical activity in rural African American women (Dr. Stephania Miller). Work is also underway on the BRIDGES to Care project, a safety network providers created to develop a Web-based home for patients without insurance. The core also has developed expertise in community-based participatory research through the REACH 2010 project and in measurement technology, such as validation of the Southern Community Cohort Study food frequency questionnaire and physical activity questionnaire, and the development of a web-based system for collecting process evaluation data. The core also has developed skill in using Geographic Information Systems (GIS) to analyze REACH 2010 evaluation data. By combining data on health and behavior with the GIS, the core is able to produces maps that show the geographic distribution of health disparities in a community. The Vanderbilt-Meharry team is currently: preparing an R18 application; continuing to support clinical and behavioral research not focused on disparities; expanding local health disparities coalitions; and developing expanded capabilities in dietary behavior assessment, physical activity assessment, public policy and behavior, and health economics. The team also has begun work to address disparities in local Latino populations.

Elizabeth A. Walker, DNSc, RN, CDE, Professor, Department of Medicine,
Diabetes Research and Training Center, Albert Einstein College of Medicine, Bronx, NY

The Prevention and Control Division (P&C) of the DRTC at the Albert Einstein College of Medicine has two cores, a Translation and Effectiveness core, and a Clinical Research Facilitation core. The Translation and Effectiveness core provides guidance in selecting or developing appropriate survey instruments, developing behavioral interventions, biostatistical and database support, and advice to pilot and feasibility grant applicants and funded investigators. The Clinical Research Facilitation core provides consultation to new investigators on study design, appropriate selection of metabolic variables and biologic markers, and clinical and behavioral research training. The core also maintains a registry of patients who have consented to be contacted for studies. Through these activities, the Einstein DRTC fosters research across the spectrum of basic research, clinical research, clinical practice and public health.

Examples of unique interdisciplinary collaborations fostered by the DRTC P&C include: work by Drs. DiLorenzo and Fleischer on beta cell antigens triggering autoimmunity in type 1 diabetes; work on mechanisms of insulin-sensitizing thiazolidinediones in type 2 diabetes by Drs. Kishore, Scherer, and Hawkins; and work on the glucosamine pathway and reactive oxygen

species in the pathogenesis of diabetic complications by Drs. Brownlee and Hawkins. The DRTC created an infrastructure that fosters the communication needed for this research to take place.

DRTCs will prove instrumental in overcoming barriers impeding translation of research findings to clinical practice or into the community. The DPP experience provides guidance for this process. The behavioral investigators from the four DRTCs awarded DPP center-funding facilitated coordination of efforts toward planning behavioral interventions and measures through formation of a behavioral subcommittee. This evolved into several subcommittees for lifestyle, medication adherence, recruitment, and retention. After the DPP, these centers were involved in translation of DPP findings, while continuing with the follow up outcomes study for the DPP. DRTCs can provide efficient infrastructure for facilitating communication between multi-disciplinary scientists and for promoting diabetes research across these disciplines.

William H. Herman, M.D., M.P.H.
Department of Internal Medicine, University of Michigan Health System

The Michigan DRTC Prevention and Control Division helps in the design, implementation, measurement, and evaluation of behavioral, clinical, and health system interventions in diabetes and related endocrine and metabolic disorders. The MDRTC receives more than 2,000 requests per year for measurement tools, approximately 200 requests for patient education materials, and approximately 100 requests for professional education materials. More than 16,600 laboratory analyses are performed, encompassing more than 30 assays, 39 projects and 33 investigators. The center manages 6 to 8 data entry projects each year, covering more than 10,000 pages.

The DRTC Pilot and Feasibility Grant Program is open to full-time faculty beginning their careers in diabetes research; to established investigators focusing their expertise on diabetes; and to established diabetes investigators moving their research into a new diabetes-related direction. These applications are reviewed by 3 external reviewers and a Grants Advisory Committee, and the average award is $50,000 with a total award of $250,000 per year. Prevention and Control Pilot Grants for 2002-2005 include studies to detect causes of preventable blindness in patients with diabetes, feasibility of a sustained diabetes self-management program for African Americans with type 2 diabetes; and examination of the role of elevated fatty acid availability on skeletal muscle fatty acid metabolism and the exercise-induced increase in insulin sensitivity, among others.

Questions for Speakers

Several participants asked how the DRTCs might be able to help young investigators applying for grants. Dr. Walker answered that the Einstein DRTC has several cores that support funded research and also can be used during the grant writing process. Investigators can ask to partner with the DRTC to use DRTC core services. She added that the DRTC could provide perhaps 15 percent of the help a new investigator would need to develop a successful grant application. Dr. Littenberg described a program at the University of Vermont in which money from the Health Resources and Services Administration is available for young investigator development and clinical investigators seeking their first grant. This money is used to provide training in

translational research; training is done by teleconference, mentoring, and online courses in subjects such as statistics and grant writing. Data from surveys performed at the University of Vermont also is available.

Participants asked if there was a central site at which investigators could find surveys, measurements, and tools to use in their own research. Dr. Schlundt explained that there was no central site for this information. Each center has its own site, and contacting the directors of the centers by e-mail is the best way to obtain this information. At the University of Michigan, investigators can register with the DRTC and download what they need. Dr. Walker added that Dr. Welch helped develop a clearinghouse on the American Diabetes Association Web site for many of the instruments used in diabetes research. Dr. Lorig mentioned that Stanford has approximately 40 instruments in both English and Spanish available at the Website, www.patienteducation.stanford.edu. Dr. Kiefer mentioned that her research would have been impossible without the support of the University of Michigan's DRTC but added that the materials she developed in the course of her project are not available through the DRTC's Website. Because the material was developed using taxpayer funds, she believed it should be made more broadly available, particularly to other researchers.

Dr. Milagros Rosal asked if the infrastructure of the DRTCs facilitated communication between basic and behavioral scientists. Dr. Herman answered that the center director tried to raise investigator awareness of mutual interests through newsletters, progress reports, and word of mouth. Dr. Walker commented that at the Einstein DRTC, both basic scientists and translational researchers are housed in the connected buildings and attend each other's seminars. Dr. Schlundt said that there was not much interaction between behavioral and basic biomolecular researchers at the Vanderbilt DRTC. In response to questions about changes in the structure of the DRTCs, directors agreed that overall the changes have had a positive effect on research, but because there is no longer direct funding for intramural research, more time must be spent raising funds for this. Nonetheless, this has resulted in better research and broader collaborations.

TUESDAY, NOVEMBER 15, 2005

Report from Breakout Group Leaders and Discussion

Translational research often involves the coordination of three domains, each with its own set of demands, constraints, and culture (i.e. norms, values, goals): the funding sector (both federal and foundation), community partners, and the academic organizations to which many of us belong.

Participants were divided into three breakout groups and used the Nominal Group Process (Delbecq, et al., 1971) to brainstorm and rank ideas addressing one of three discussion questions. Participants were then asked to choose 8 ideas they believed were most important and rank them from 1 (least important) to 8 (most important). Points assigned to the ideas were totaled to determine which ideas the group found most important.

Group 1: What do you see as the unique challenges/barriers in conducting translational research that meets the requirements of all three domains?
Carol Mangione

Group 1 identified 69 barriers to conducting translational research. Some of the barriers overlapped, pointing to different aspects of the same problem. The top 4 barriers identified received rankings of between 19 and 36 points. The highest-ranked barrier was determined to be insufficient attention to sustainable business models from all involved parties. After performing careful studies and developing interventions, investigators should demonstrate that the interventions make a difference; this chain of events often is not completed. There is no model to sustain an observed benefit and no place for storing methods and tools for others to use. The second highest barrier was described as tension between scientifically valid evaluations versus the "real world" realities of partnered research. This conflict can have implications at the levels of proposal writing through the review process and through implementation in the field; for example, an investigator may have an excellent proposal, but difficulties in implementing it as a result of conflicts with or different priorities than community partners. Another barrier identified by the group was a lack of shared resources across interventions and projects; there appear to be many investigators who are interested in studying similar topics, but communication between them is lacking. A fourth barrier was that of limited funding for pilot and feasibility studies across all organizations funding translational research.

The second five most important barriers received between 15 and 17 points. The barrier of competing missions across domains, particularly conflicts between the different missions of research versus providing service. Another problem is that each NIH Institute with a stake in chronic disease is developing translational research initiatives separately rather than collaboratively with a similar mission or vision. There should be more synergy and coordination between these efforts. Additionally, the level of support for translational research across all of NIH is small. A long time lag between problem identification (perhaps identified in conjunction with a community partner) and the actual research process outcome causes difficulties in maintaining community engagement. Finally, developing and sustaining academic-community partnerships beyond and across projects is a significant issue, particularly because resources for this are lacking.

Discussion

Participants agreed that the program announcements creating the R18 and R34 programs need to be extended. Suggestions and recommendations from this meeting will be used to develop the next set of program announcements and to create strategies to support translational research in general.

Several participants discussed other options for funding translational research, particularly seeking funds from others who may have an economic interest in funding this research, such as CMS, insurers, and others. These groups should not consider services delivered during the course of a protocol as unreimbursable; rather, they should be encouraged to view translational research experiments as ways for patients to receive cutting edge treatment and care, usually at reduced cost. In the past, Congress has mandated collaborations with CMS, and because diabetes is a top expense for CMS, perhaps collaborations pertaining to diabetes research will be of interest to CMS in the future. As a precedent, coverage for certain types of clinical trials, particularly cancer clinical trials, already is mandated.

Group 2: What suggestions/strategies would you offer to help conduct translational research that meets the requirements of all three domains?
David Marerro

Group 2 identified 57 strategies to help improve translational research. The highest ranked item scored in the 50-point range and called for development of a resource center containing materials, protocols, and instruments to support translational researchers, perhaps as a Web-based repository. The second highest ranked strategy was to support more theoretical and empirical research on dissemination. Improving the speed of grant review and commencement of funding also was highly ranked, because this would help facilitate relationships with community partners. Participants also wanted NIDDK and NIH foster innovative ways to expand funding, perhaps through partnerships with other agencies (Centers for Medicare & Medicaid Services [CMS], foundations, insurers) and coalition building to expand the amounts of money available for research.

Group 3: What are potential future directions for NIDDK's Translational Research Program?
Bob Anderson, Dr.Ed.
Diabetes Research and Training Center
University of Michigan

The highest ranked item arising from this group's discussion was to fund academic-community translation centers for practice-based research networks. The second most highly ranked item concerned funding community academic partnership through community based participatory research—RFAs, R01s, R18s. The first item involves a center mechanism for funding, the second, individual grants to address the same need. Sharing resources (measures, tools, etc.) also was highly ranked. Group members suggested development of career awards in translational and dissemination research for investigators at all levels. Dissemination research focusing on

training community-based health care professionals also was recommended. Developing program project grants for translational research was seen as important. The group also asked for funding for small, pilot studies; this funding should be for grants averaging $50,000, which should be reviewed and funded quickly. Further research also was deemed necessary in the area of organizational, provider, and patient barriers to translation.

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Summarization and Integration (With Q&A)
Joe Selby, M.D., M.P.H.
Director, Division of Research
Kaiser Permanente

The purpose of this meeting was to foster a sense of community among translational researchers, provide an opportunity for information-sharing and discussion of design and analytical approaches, stimulate new ideas for translational research, and provide guidance on potential future directions for the NIDDK's translational research effort. The meeting also presented an opportunity for participants to familiarize themselves with each other's projects and to learn about DRTC activities.

During early presentations, we agreed that RCTs are often optimal for minimizing bias, but translational research presents unique problems: ethical, logistic/political, and recruitment issues may make it difficult to use this design. Randomizing in groups or clusters addresses a number of these concerns, particularly the problems concerning a community's willingness to accept randomization and issues of crossover and contamination. Using group randomization to avoid contamination, however, has down-sides as well; specifically the potential loss of power may be worse than the effects of contamination or crossover. Rigorous non-randomized evaluation methods offer different and valuable perspectives; these methods are most often used to evaluate identifiable interventions that are already in place. Researchers seldom use these quasi-experimental approaches to evaluate interventions that they themselves have newly developed. Most likely as a result of the selectivity of study sections, almost all funded projects of this R-18

Translational Research Initiative to date have been randomized studies of interventions developed by the investigators rather than proposals to analyze interventions put into place by others (for example, state health departments).

Despite the potential biases of non-randomized studies, these observational methods are useful for performing modest or even well-powered pilot studies. These studies allow determination of standard deviations, covariances, intraclass correlation coefficients, and other parameters needed for planning a strong RCT. Additionally, if an intervention already is in place, there is value to observational methods in that entire populations can be studied, rather than having to recruit and randomize volunteers. This ability to estimate the effect of an intervention in an entire population rather than just those who chose to participate allows us to estimate true effectiveness. In this respect, such nonrandomized studies may prove more informative than RCTs. Newer methods for evaluating and controlling for selection bias in observational studies and adaptations of propensity score-like approaches for analyzing low participation rates and their effects on generalizability are available, but these methods are very power hungry.

This meeting allowed participants to familiarize themselves with other translational research projects. The projects presented at the meeting comprised a large group of very well-specified, theory-driven, mostly multifactorial interventions. Many of the projects targeted minority populations, an important issue particularly because HbA1c levels are higher in every nonwhite community in the United States compared to white communities. Most studies also are assessing health care costs, an outcome now appreciated to be very important. Challenges to nearly all investigators have included recruitment, developing partnerships, the importance of pilot data, and development of funding mechanisms for collection of pilot, pre-randomization data. A suggestion that many participants found important was better resource sharing, preferably through electronic means. There was a great deal of enthusiasm for Web-based ways of sharing and discussing issues such as recruitment and health policy. Another innovative idea involved developing a list of successful, IRB-approved interventions and strategies tried at different sites, so that this could be presented to investigators' IRBs to help the IRBs better understand the research strategy.

After the most recent re-competitions, the DRTCs have been urged to develop expertise that adds particular value for translation and dissemination. The DRTCs support large communities of translational researchers, often extending beyond their home institutions. They enhance translation at both ends of the spectrum, from bench to clinical research, and from clinical research to community practice. Expertise differs somewhat by DRTC and is made available in different ways by the different DRTCs, but all seem prepared to support translational researchers.

Although biological understanding and medical solutions to problems are increasing, the importance of behavior is not decreasing. Instead, behavioral changes are becoming more complex. As medicine becomes more precise, however, behavioral change may become easier for patients to achieve.

New Ideas for Translational Research—Discussion

A participant mentioned the CDC Prevention Research Center Program, which is composed of 33 Prevention Research Centers across the United States, focusing on chronic diseases. Approximately12 of these centers have an interest in diabetes. The centers have ongoing community relationships, which could provide another potential resource to diabetes investigators.

Several participants advocated the creation of "centers of excellence" as partnered efforts between academic medical centers and communities. Dr. Lorig cautioned against efforts of this sort that would result in clustering of resources in established academic centers. Instead, she suggested involving institutes in places such as Kansas and Nevada, which will never have DRTCs, to provide infrastructure and support to investigators in those areas. Dr. Anderson suggested funding "visiting professorships" that would allow investigators from DRTCs to visit overlooked universities to assist with development of research groups and grant writing.

Dr. Gans suggested an R18 for translational research for preventing obesity through the use of diets and physical activity. Many effective interventions exist that could be translated and disseminated, but mechanisms to do this are lacking. This sort of activity would apply to the prevention end of the diabetes research spectrum.

A participant suggested that better sustainable business models are needed to facilitate "connecting the dots" between R01, R18, and the Small Business Innovation Research (SBIR) program. There should be support to encourage people to modify the result of translational research for sustainability and to help bridge the gap between translational research and commercialization to provide consumers with what they need and want. The biomedical research community has addressed commercialization as a way to support local economies. A caveat is that it can be difficult to obtain an SBIR grant if one does not have or is not associated with a company. Dr. Kiefer cautioned that commercialization of translational research products could heighten disparities because poor communities could not afford the product. Dr. Lorig mentioned that products from her research have been licensed yet are provided for free to some communities. It is likely that even after commercialization, many products still will be available for free or at reduced cost for needy communities. Dr. Walker pointed out that although it may be relatively easy to translate and disseminate the results of a large clinical trial, this process can be more difficult for small trials. The DPP, for example, had the infrastructure to fund production of materials and make them freely available, but smaller R01 and R18 studies might not have this level of support. Dr. Delamater suggested a funding mechanism for sustainability in the form of supplements to grants.

Although most participants agreed that the nominal group process was a useful exercise for generating suggestions, the process did not result in any "cutting edge" ideas. One participant suggested that to facilitate breakthrough research, NIDDK could set aside funds to support proposals that reflect breakthrough thinking. Study sections that specifically fund novel ideas, rewarding innovation and risk taking, could be convened.

Dr. Mangione mentioned that although major universities such as Stanford and the University of North Carolina may not need extra support, the communities they partner with often are in need of support. She suggested a funding mechanism was needed that could help to stabilize the community organizations that work with the universities. The funding the centers receive from the NIH does not trickle down to community partners, which causes difficulties with research programs because stable relationships cannot be built with community organizations that are not financially stable and may not exist from one year to the next. Support to these organizations would help to build continuity into relationships with community partners.

Future Directions for NIDDK—Discussion

NIDDK should consider new mechanisms to support true pilot work. If effective R34 and R18s are desired, it may be in NIDDK's interest to fund pre-R34s, smaller grants that do not involve randomization and instead allow collection of genuine pilot data. Academic institutions also should support this work. NIDDK should give attention to supporting and funding partnered work pertaining to sustainability. Rapid cycle funding also is desirable, perhaps modeled after the DECIDE mechanism, which supports research aimed at the Medicare population to address questions of interest to CMS. This work is funded by task orders; investigators have 6 weeks to respond to an order and their application is reviewed in 2 months and funded within 3 months. This might particularly be useful for funding small pilot grants. Additionally, to facilitate review, investigators receiving translational research grants are encouraged to serve as reviewers.

Dr. Garfield raised the issue of methods to design studies in which sustainability is a component built into translational research and how it could be included in grant objectives. He asked whether sustainability would be considered at every level or only once the level of dissemination is achieved. Dr. Selby suggested that sustainability would apply to successful proposals and might need to be funded separately from the originally funded proposals. A participant mentioned Dr. Ackermann's YMCA project as an example of how to consider sustainability. Results are not yet available to determine if the intervention is effective in this setting, but if it is, there already is a clear-cut business case for how to disseminate the intervention. Sustainability and dissemination should be addressed in the proposal, even if these activities are not a funded part of the proposal. Additionally, once an intervention has been shown to be effective, the investigator could be eligible for an administrative supplement to assist with development of a dissemination plan. A participant suggested that R01 grant applications should include discussions of compatibility of the intervention with existing delivery systems and analysis of cost effectiveness. Dr. Fischer cautioned that clarification was needed to distinguish dissemination from sustainability from maintenance of behavioral change.

Dr. Ackermann suggested that community and practice partners could be asked for commitment letters indicating that they participated in the design of the intervention and the choice of outcomes to measure. The letter also should indicate that the community will make an effort to sustain the intervention if the outcome is meaningful. Dr. Anderson cautioned that organizations change, and although an organization may be willing to try to sustain a program, they ultimately may have other financial and logistic issues to consider that would prevent them from committing resources to sustaining interventions. A participant suggested that those developing the interventions should consider these problems; interventions dependent on the fiscal health of

certain community organizations might not be long-term solutions to public health. Because organizations that serve the poor and powerless often are poor and powerless themselves, interventions should be robust to financial problems or should help drive changes in policy that strengthen organizations that serve the poor. Additionally, interventions should be able to be easily transferred to a different organization through use of rapid training programs and other means of addressing changes in staff. Another participant suggested looking at multifactorial interventions to determine which part was most effective and sustaining that part of the intervention rather than the entire intervention. Dr. Walker cautioned that multicomponent interventions have value because "one size does not fit all." Multiple racial and ethnic groups struggle with obesity and diabetes, and multicomponent interventions create a toolbox with different interventions that may be more desirable and effective for specific groups. Dr. Mary Nies suggested that to promote sustainability, communities should be asked about what they need and want concerning interventions.

Summarization and Integration (continued)
Joe Selby

Challenges and barriers to translational research include insufficient attention to the economics of sustainability, such as the conflict between scientific rigor and the reality of "real world" partnerships; lack of shared resources across studies; limited funding for pilot and feasibility studies; long lag times between problem identification and research findings; and the level of support for translational research across all of NIH. Specific strategies to overcome some of these barriers include development of resource centers for sharing findings; more support for theoretical and empirical research on dissemination; improving the speed of grant review and funding; and expanding the pool of research funders to include agencies outside of the NIH.

Recommendations to NIDDK include funding academic/community translation centers for practice-based research networks and funding academic/community partnerships through community-based participatory research grants. Career awards to translational researchers were recommended and also support for research on training community-based professionals. Several participants recommended small pilot grants that could be rapidly reviewed and funded.

NIDDK has succeeded in funding a set of projects that is diverse and faithful to the Requests for Proposals that were issued. Translational research is a new discipline, but it seems that an appreciation of its methods and challenges is growing. One question to consider is if publications about the theory and methods of translational research are keeping pace with gains in knowledge. Increasing the numbers of these publications could help draw attention to translational research, and wider dissemination of this information could be of use to study sections and IRBs charged with evaluating translational research proposals. Key questions in translation are being addressed in multiple projects, underscoring need for synthesis. The RFA process could be improved to decrease duplications of effort and harmonize the translational research field.