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Independent but Coordinated Trials: Insights from the Practice Based Opportunities for Weight Reduction (POWER) Trials Collaborative Research Group

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Abstract

Background—The National Heart, Lung, and Blood Institute (NHLBI) funded three institutions to conduct effectiveness trials of weight loss interventions in primary care settings. Unlike traditional multi-center clinical trials, each study was established as an independent trial with a distinct protocol. Still, efforts were made to coordinate and standardize several aspects of the trials. The three trials formed a collaborative group, the “Practice Based Opportunities for Weight Reduction (POWER) Trials Collaborative Research Group.”

Purpose—We describe the common and distinct features of the three trials, the key characteristics of the collaborative group, and the lessons learned from this novel organizational approach.

Methods—The Collaborative Research Group consists of three individual studies: “*Be Fit, Be Well*” (Washington University in St. Louis/Harvard University), “*POWER Hopkins*” (Johns Hopkins), and “*POWER-UP*” (University of Pennsylvania). There are a total of 15 participating clinics with ~1,100 participants. The common primary outcome is change in weight at 24 months of follow-up, but each protocol has trial-specific elements including different interventions and different secondary outcomes. A Resource Coordinating Unit at Johns Hopkins provides administrative support.

Results—The Collaborative Research Group established common components to facilitate potential cross-site comparisons. The main advantage of this approach is to develop and evaluate several interventions, when there is insufficient evidence to test one or two approaches, as would be done in a traditional multi-center trial.

Limitations—The challenges of the organizational design include the complex decision making process, the extent of potential data pooling, time intensive efforts to standardize reports, and the additional responsibilities of the DSMB to monitor three distinct protocols.

Conclusions—The POWER Trials Collaborative Research Group is a case study of an alternative organizational model to conduct independent, yet coordinated trials. Such a model is increasingly being used in NHLBI supported trials, especially given the interest in comparative effectiveness research. Nevertheless, the ultimate utility of this model will not be fully understood until the trials are completed.

Keywords

POWER; clinical trial; weight loss; effectiveness; primary care; obesity

INTRODUCTION

Obesity has emerged as one of the most important and prevalent public health problems in the U.S. More than one-third of U.S. adults — over 72 million people -- are obese, defined as a body mass index (BMI) ≥ 30 kg/m² (1). Obesity is associated with several major, modifiable cardiovascular risk factors, including hypertension, dyslipidemia, and diabetes (2). Hence, obesity and its cardiovascular consequences are common, serious health problems that physicians routinely encounter in medical practice. Furthermore, obese persons use more health care and have higher health care costs than non-obese individuals (3).

Numerous trials have demonstrated the efficacy of behavioral interventions as a means to reduce weight and improve short-term health outcomes in overweight or obese adults (4–9). However, few of these trials have been conducted in the primary care setting (6–9). Furthermore, in most trials, primary care physicians have had a limited role in delivering the interventions or promoting weight loss (10). Nonetheless, the medical setting provides a potentially effective opportunity to advocate lifestyle changes, including weight loss, as a means to promote health. Indeed, the U.S. Preventive Services Task Force recommends that “clinicians screen all adult patients for obesity and offer intensive counseling and behavioral interventions to promote sustained weight loss for obese adults” (11). However, these activities occur infrequently in routine clinical practice.

To evaluate the effectiveness of interventions delivered in routine clinical practice, in December 2005 the National Heart, Lung, and Blood Institute (NHLBI) issued a Request For Applications (RFA) entitled, “Weight Loss in Obese Adults with Cardiovascular Risk Factors: Clinical Interventions”, for cooperative agreements (U01) to conduct randomized clinical trials in these settings. Unlike traditional multi-center trials that implement the same protocol across study sites, this RFA proposed that each center implement its own interventions and collaborate with the other RFA-funded trials to use several common measures. Because the optimal approach for weight loss in routine medical settings is uncertain, NHLBI believed it would be beneficial to develop and evaluate multiple interventions, rather than testing one or two interventions in a traditional multi-center trial. In September 2006, three institutions were funded under the RFA: Washington University (St. Louis, MO)/ Harvard University (Boston, MA), Johns Hopkins University (Baltimore, MD), and the University of Pennsylvania School of Medicine (Philadelphia, PA). Each study is conducted independently under the direction of a site principal investigator, and final data collection will occur in the spring of 2011. Although the trials share some common design features, each trial has distinct study aims and is implementing distinct interventions. To promote standardization where reasonable, the three trials formed a collaborative organization, the “Practice Based Opportunities for Weight Reduction (POWER) Trials Collaborative Research Group”. The aims of this paper are to: 1) describe the common and distinct features of the three trials; 2) describe key processes and

characteristics of this Collaborative Research Group; and 3) discuss the advantages and disadvantages of this novel organizational approach to organizing multi-center efforts.

METHODS

The POWER Trials Collaborative Research Group consists of three individual studies: “*Be Fit, Be Well*” (Washington University/Harvard University), “*POWER Hopkins*” (Johns Hopkins University), and “*POWER-UP*” (University of Pennsylvania). All three trials started a one-year recruitment period in early 2008. Figure 1 shows the timeline of the Collaborative Research Group, and Table 1 presents the key features of the three trials. In total approximately ~1,100 participants were recruited from 15 participating clinics. Common components were established to facilitate potential cross-site comparisons, but each protocol also incorporated distinct, trial-specific elements including different interventions and different secondary outcome measurements. The common components included some inclusion and exclusion criteria, a common primary outcome (change in weight from baseline to 24 months), standardized physical measurements, several questionnaires, and a common analysis plan for the primary analysis of principal outcomes. A single Resource Coordinating Unit (RCU) provides administrative support to the Collaborative Research Group. Each study was approved by a local Institutional Review Board. NHLBI established a common Protocol Review Committee (PRC), that was responsible for approving all the trials, and a single Data and Safety Monitoring Board (DSMB), to monitor the trials.

Description of the Three Trials

The “*Be Fit, Be Well*” study is being conducted by investigators from Washington University, Harvard University, and Kaiser Permanente. This study recruited participants from three Boston area community health centers: participants are predominantly low-income and from racial/ethnic minority groups. Participants were randomized to one of two arms: The Usual Care group received NHLBI’s “Aim for Healthy Weight” brochure and continued their medical care as usual. Participants in the Intervention group were assigned a health coach who provides support through 18 counseling phone calls and 12 bi-monthly group sessions. Participants set behavior change goals, self-monitor their progress, and receive skill training using either a website or a combination of telephone-based interactive voice response system and print materials. Additionally participants receive tailored “prescriptions” for weight-related behavior changes, as well as plans to increase the use of community resources.

The “*POWER Hopkins*” at Johns Hopkins University recruited participants from 6 primary care practices in the Baltimore area. Participants were randomized to one of the three arms. Those assigned to the control condition, Self-Directed (SD), received written materials as well as ongoing access to a static web page. Participants assigned to the Call-Center Directed (CCD) intervention are receiving a multi-channel, behavioral intervention with telephone, web, and email contacts, without in-person visits, implemented by trained coaches of Healthways, Inc, a disease management company. Those assigned to the In-Person Directed intervention (IPD) receive a multi-channel behavioral intervention with in-person, group and individual sessions, along with telephone, web, and email contacts. The IPD interventions are being delivered by coaches at the Hopkins clinical center. Both active interventions use established behavioral techniques to accomplish weight loss (i.e. frequent contact; self-monitoring of weight and physical activity; use of food records; accountability), and a web-based hub to facilitate communication among counselors, participants, and the primary care provider (PCP), as well as to promote behavior change in participants. At Hopkins, PCPs have a supportive, rather than a primary role in delivering the interventions. At routinely scheduled visits, the PCP reviews participants’ weight loss

reports and encourages participants in the CCD and IPD interventions to remain active in the weight loss program.

“*POWER-UP*” at the University of Pennsylvania (UP) recruited participants from 6 primary care practices within the Penn Medicine system. Individuals were randomized to one of three interventions: Usual Care, Brief Lifestyle Counseling, or Enhanced Brief Lifestyle Counseling. Participants in the Usual Care condition receive educational materials (i.e. NHLBI’s “Aim for a Healthy Weight”) that are distributed at quarterly visits with a primary care provider. Those in the Brief Lifestyle Counseling condition receive the same PCP visits, plus 26 brief counseling sessions with an auxiliary health care provider (e.g., a medical assistant). During the first year, participants receive 14 lifestyle counseling visits, scheduled at approximately monthly intervals. Visits that cannot be completed on-site may be conducted by phone. During the second year, participants are provided 12 lifestyle counseling sessions, at least six of which are scheduled in-person visits, with the option of conducting others by phone (in view of time or travel constraints). Participants in the Enhanced Brief Lifestyle Counseling condition receive the same treatment as those in the Brief Lifestyle Counseling group, plus the choice of adjunctive meal products or pharmacotherapy (i.e. orlistat or sibutramine). PCPs and auxiliary health care providers were trained and certified in implementing the protocol. Extensive attention was devoted to educating PCPs about the use of pharmacotherapy. At the start of the intervention, physicians reviewed with participants the potential benefits and risks of both meal replacements and weight loss medications and asked participants to choose the approach they preferred (i.e., meal replacements vs. medications). Participants did not begin their adjunctive treatment until the third visit with their lifestyle coach, to allow time to consider their choices.

Developing Common Protocols

During the early phase of the studies, the NHLBI Project Officer and the Principal Investigators of each trial established a *Steering Committee* to set policies for the Group, establish subcommittees and *ad hoc* working groups, and resolve cross-study issues. The following sections describe the key cross-trial components.

Eligibility—After extensive deliberations, the Collaborative Research Group decided that some eligibility criteria would be identical for the three studies (e.g. all participants must have a BMI ≥ 30 and ≤ 50 kg/m² and weight ≤ 400 lbs), while other criteria would be trial-specific (Table 1). For example, participants in the “*Be Fit, Be Well*” study were required to have treated hypertension; participants in “*POWER Hopkins*” could have any of the major weight-related cardiovascular (CVD) risk factors (hypertension, dyslipidemia, or diabetes, whether or not the condition was treated with medication); and participants in the “*POWER-UP*” trial were required to have at least two components of the metabolic syndrome.

Recruitment—As shown in Table 1, the three studies implemented different recruitment strategies, which largely reflected the study populations, arrangements with clinical practices, and other logistical considerations. The Collaborative Research Group provided a forum to share best practices and lessons learned about recruitment strategies.

Intervention Monitoring—Comprehensive reviews of behavioral weight loss studies were conducted independently by each trial site as part of the grant preparation. The three trials implemented different interventions, but shared information and discussed common issues related to staff training, delivery, and quality assurance and control, particularly related to intervention fidelity. The Collaborative Research Group also developed a common approach to report, compare, and monitor intervention

Outcomes—The three trials adopted a common primary outcome: change in weight from baseline to month 24. The Collaborative Research Group required the use of specific blood pressure devices and scales and implemented standardized protocols for physical measurements (including weight, height, and blood pressure) from other established studies (e.g. ACCORD (12) and OMNI-Heart Trials (13)). Measurement training and certification sessions were conducted annually and led by master trainers for staff involved in study data collection.

Common Questionnaires—During the developmental phase, the Collaborative Research Group reviewed relevant literature and had extensive discussions before selecting common questions and survey instruments to capture the following data: demographic characteristics, weight history, medical history, fruit and vegetable intake, fat intake, quality of life, physical activity, depression, sleep quality, and cost to participants. A survey was designed by the Research Group to describe current weight management practices by providers in their respective clinic settings.

Data Collection Mechanisms—The three trials chose to use different mechanisms to collect self-reported data. “*Be Fit, Be Well*” used a computer-assisted data entry system for participants to enter data on-site. In “*POWER Hopkins*”, a study website was developed for participants to complete questionnaires while at home, prior to clinic visits. In “*POWER-UP*”, standard paper- questionnaires were developed for participants to complete on-site. Although the three studies implemented their own quality control procedures, investigators and study staff exchanged local experiences through the Collaborative Research Group structure to further improve local operations.

Analysis Approaches—Each trial performed its own sample size calculations for its grant application, but after the grants were awarded the statisticians in the Collaborative Research Group re-computed sample size and power using a common, strategic approach. For example, studies used the same minimal detectable weight change difference, the same population standard deviation, and the same structure and values for longitudinal correlation of repeated weights. “*POWER Hopkins*” and “*POWER-UP*” trials also used a common approach to multiple comparisons for their three group designs. These commonalities produced an identical target sample size of 390 for these two trials. “*Be Fit, Be Well*” required smaller sample size (n=360), because no multiplicity adjustment was needed for the two-arm trial. In addition, the Collaborative Research Group developed a common approach for accommodating missing data and for outlier detection.

Cost Analysis—The Collaborative Research Group developed a data collection template to obtain intervention-related cost data and recommended common questionnaires (e.g. EuroQoL (14)) to capture medical events, quality of life, and cost to participants. “*Be Fit, Be Well*” and “*POWER-UP*” adapted a similar approach and are using monthly recall from physicians, interventionists, coordinators, and investigators to estimate time spent in different activities such as recruitment, intervention, or administration. “*POWER Hopkins*”, on the other hand, is directly sampling site intervention staff in representative weeks to document time spent in interventions. For the cost analyses, all sites plan to apply standard labor rates at the national level, in addition to local rates. The goal is to estimate total intervention costs, costs associated with interventions relative to the comparison group, costs per participant, and the marginal costs per incremental improvement in the primary outcome.

Safety Monitoring—Based on NIH policies and guidelines recommended by the common DSMB, the Collaborative Research Group developed and standardized reporting procedures

and formats to document adverse events and unanticipated problems. Annual safety training sessions are conducted to help ensure a standardized approach across the studies.

Dissemination—The Collaborative Research Group plans to disseminate the main results to target audiences through collaborative efforts. Targeted audiences include participants, health care providers, professional organizations, health care organizations, insurance companies, and policy makers. To translate and maximize the relevance of research findings to clinical settings, the Collaborative Research Group is developing plans according to the RE-AIM framework (15), which evaluates the representativeness of programs, and consistency of implementation across different settings, interventionists, and patient populations.

Resource Coordinating Unit

In the POWER Collaborative Research Group, a single coordinating unit at Johns Hopkins University was funded to support administrative functions and certain scientific activities for the three trials. This Resource Coordinating Unit (RCU) assisted in developing standardized protocols for the physical measurements and common questionnaires. It also developed standardized DSMB reports. Another function of the RCU is to design and maintain a Collaborative Research Group website to provide up-to-date information, document repository, and other resources. The RCU continues to arrange and coordinate conference calls and in-person meetings, and provide monthly reports on recruitment and retention to monitor progress at each study. The RCU is also developing a public access website to facilitate dissemination of study results.

DISCUSSION

Comparison with Traditional Trials

The POWER Trials Collaborative Research Group is a unique collaborative program of three independent trials with the goal of testing the effectiveness of multiple, distinct weight loss interventions for obese individuals in out-patient settings. Here we compare the ‘hybrid’ model of the POWER Collaborative Research Group to other types of trial organizations, namely, a single center clinical trial, a traditional multi-center trial with a common protocol, and a research network with one or multiple protocols implemented simultaneously or sequentially (Table 2).

Unlike other trial organizational structures, in the hybrid model, each trial is conducted independently under the direction of the site principal investigator. This model provides an opportunity to evaluate multiple interventions when there is insufficient evidence to mount a single, large scale multi-center trial that tests one or two interventions. Because there was no well-accepted approach to weight loss in the medical setting, such an approach was deemed appropriate for this research program. Nonetheless, to maximize what NHLBI can learn from this hybrid model, some degree of administrative and scientific coordination was needed across trials. In traditional multi-center trials or research networks, a Data Coordinating Center provides administrative and scientific coordination related to protocol development and standardization of data collection, as well as data management and analysis. On the other hand, the hybrid model utilizes a smaller scale unit, termed the RCU in POWER, which coordinates administrative and various scientific components, but is not taking primary responsibilities for data collection, management, or analysis.

For quality control, individual trials in the POWER Collaborative Research Group set local policies and procedures, while trials share information and learn from each other through regular conference calls, meetings, and informal site visits. A single DSMB monitors quality

and safety with side-by-side comparison from each trial. During the dissemination stage, the Collaborative Research Group will disseminate the principal findings collectively, as well as individually.

Trial sponsors have different levels of involvement in studies, depending on the type of funding mechanism. For investigator-initiated trials (e.g. R01), which are often single centers, the NHLBI project officer has minimal involvement in the trial design and its conduct as these are funded through grant mechanisms. In contrast, NHLBI staff is heavily engaged in the design and implementation of trials funded through contract mechanisms. Many multi-center trials are funded through contracts. The POWER Trials are funded through the cooperative agreement U grant mechanism. In this mechanism, NHLBI has a collaborative role on advising the design and implementation of trials.

In terms of costs, the hybrid model does not fund a large, expensive data coordinating center. However, in the hybrid model and in single center trials, each trial must instead develop its own data collection, management, and analysis infrastructure. It's not currently known as to whether this may or may not actually exceed the costs of a single data coordinating center.

Lessons Learned from the Collaborative Research Group Structure

The hybrid model implemented by the POWER Collaborative Research Group has several potential advantages. First, the Collaborative Research Group design can test several interventions simultaneously (five interventions in POWER). Second, the Collaborative Research Group enhances the expertise in areas that might not have been the case in a single trial. For example, the POWER Collaborative Research Group brings together three senior statisticians from different institutions to guide and develop the analysis plan with excellent interactions among biostatisticians. In contrast, most multi-center trials or research networks rely on one or two senior statisticians from the data coordinating center. In addition, specific expertise at one site (e.g. dissemination, cost-analysis, and safety) can be shared with other sites. Finally, the efforts to standardize collection and timing of measurements should enhance the potential for pooled analyses and comparisons across trials.

Nevertheless, there are several challenges associated with this mechanism. First, the decision making process can be complex. Since this is a relatively new way to conduct multi-center trials, it was often unclear which aspects of the trials should be identical. For example, early discussion revolved around philosophical considerations, i.e. what constitutes an effectiveness trial, particularly with respect to the different study populations. One trial enrolls participants whether or not they are interested in weight loss. Another trial enrolls individuals as long as they expressed interest in losing weight, while the third trial is somewhat more selective and conducted a brief behavioral assessment prior to enrollment. Other issues include medical eligibility criteria, data collection elements, outcome variables, measurement protocols, PCP role, and logistic issues (e.g. paper- vs. computer-based data entry).

Another challenge relates to maximizing the potential for pooling data. While the trials collected weight in a similar fashion, there were numerous other differences, particularly, the interventions and some enrollment criteria. Also, the RCU was not designed to receive data from the individual trials and perform pooled analyses, and its funding to perform pooled analyses is limited. Hence, while such analyses are deemed desirable, pooled data analyses will likely be performed by one of the trial sites, rather than the RCU.

A third challenge relates to trial monitoring. The NHLBI appointed one Protocol Review Committee to approve the independent protocols, and a single DSMB to then monitor them.

Monitoring three trials by a single DSMB has required additional efforts to present standardized, concise reports to the DSMB, and to conduct efficient and well-organized DSMB meetings. However, benefits of a common DSMB include in-depth understanding by its members of the common measures, eligibility criteria, and analytic plans and insights gained by evaluating three, related protocols, facilitated communication of lessons learned in monitoring one study to other studies, and conservation of data monitoring resources in clinical trials community.

CONCLUSION

The POWER Trials Collaborative Research Group is a case study of an alternative organizational model to conduct independent, yet coordinated trials. This paper has highlighted the characteristics of the Collaborative Research Group composed of three trials and one Resource Coordinating Unit, and discussed the currently known advantages and disadvantages of this hybrid model.

With additional NHLBI RFA's implementing this model, this model may have a more prominent role in future federally sponsored clinical trials. Given the substantial interest in comparative effectiveness research, the Collaborative Research Group model offers an opportunity to test different intervention strategies simultaneously. Nevertheless, the ultimate utility of this model will not be fully understood until after completion of the trials.

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Figure 1.
POWER Trials Collaborative Research Group Timeline

Table 1

Overview of the three trials in the POWER Trials Collaborative Research Group

	Be Fit, Be Well (Washington/Havard University)	POWER Hopkins (Johns Hopkins)	POWER-UP (University of Pennsylvania)
Target sample size	360 (~ 30% male; ~ 98% non-white)	390 (~ 35% male; ~ 45% non-white)	390 (~20% male; ~40% non-white)
Settings	3 community health centers in Boston area	6 primary care practices in Baltimore area	6 U Penn-affiliated primary care practices
Common inclusion criteria	BMI ≥ 30 –50 kg/m ² and weight ≤ 400 lbs; age ≥ 21 years; willingness to change diet, physical activity and weight. Diabetes mellitus, or prior CVD event > 6 months, or known stable CVD or peripheral vascular disease with PCP approval.		
Key site-specific inclusion criteria	High blood pressure on medication	Hypertension, dyslipidemia, or diabetes; demonstrated basic use of web and email; access to internet at least 4 days per week	At least 2 components of the metabolic syndrome
Common exclusion criteria	MI, Stroke or ASCVD procedure within 6 months; Serious medical condition likely to hinder accurate measurement of weight, or for which weight loss is contraindicated, or which would cause weight loss; Prior or planned bariatric surgery; Use of prescription weight loss medication or over-the-counter orlistat within 6 months; Chronic use of medications likely to cause weight gain or prevent weight loss; Intentional or unintentional weight loss within 6 months of enrollment ($\geq 5\%$ of body weight)		
Recruitment process	Review of medical records by research staff for potential participants. PCP referrals and participant self referral.	Direct referrals from PCP. Brochures and flyers in PCP offices. Mailings to potential patients with hypertension, dyslipidemia, diabetes, or obesity.	PCP referrals and participant self referral from brochures and posters in PCP office. Review of medical records by research staff for inclusion and exclusion criteria.
Treatment Groups			
Control	<i>Usual Care:</i> usual medical care provided by PCP, plus NHLBI's brochure	<i>Self-Directed:</i> Usual medical care provided by PCP plus list of weight loss website	<i>Usual Care:</i> receive NHLBI brochure during plus quarterly visits with their primary care provider (PCP).
Intervention 1	<i>Intervention:</i> Behavior change "prescription" and skills training via Internet or a combination of tailored print materials and an interactive voice response system	<i>Call-Center-Directed:</i> Phone calls with Healthways coach; interactive website; PCP reinforcement	<i>Brief Lifestyle Counseling:</i> usual medical care plus 26 brief counseling sessions with an auxiliary health care provider (e.g., a medical assistant).
Intervention 2	N/A	<i>In-Person Directed:</i> Individual and group meetings and phone calls with Hopkins interventionist; interactive website; PCP reinforcement	<i>Enhanced Brief Lifestyle Counseling:</i> Usual medical care plus 26 brief counseling sessions plus the choice of adjunctive meal replacements or pharmacotherapy (selected with PCP).
PCP role in intervention	Minimal; endorsement of study participation	Supportive role; advice to participate in interventions; review weight loss progress; re-engagement	Deliver PCP usual care intervention to all groups; counseling and monitoring
Primary outcome	Change in weight at 24 months		
Secondary outcomes	Reduction in blood pressure at 24m; dietary change; physical activity; medication adherence; quality of care.	Change in weight at 6 months; change in BMI, % weight, blood pressure, hypertension control, lipid levels, HOMA-IR, Framingham Risk Score at 6 and 24 months.	Change in weight, BMI, and % weight at 6 and 12 months; change in prevalence of metabolic syndrome at 6, 12, and 24 months; changes in: 1) eating and activity habits; 2) mood, quality of life,

	Be Fit, Be Well (Washington/Havard University)	POWER Hopkins (Johns Hopkins)	POWER-UP (University of Pennsylvania)
			and sexual function; 3) sleep quality; and 4) CVD risk factors and HOMA-IR.
Standardized measurements	Weight, height, and blood pressure. Annual measurement training and re-certification.		
Common questionnaires	Demographics, weight history; National Cancer Institute's fruit and vegetable screener; fat screener; EuroQoL for health outcomes; Paffenbarger physical activity questionnaire; Patient Health Questionnaire; 12-Item Short Form Health Survey; Pittsburgh Sleep Quality Index; patient costs; provider survey.		
Data collection mechanism	Computer-assisted data entry system	Internet-based data entry by participants or data collectors	Paper and pen
Collecting cost data	Monthly recall of time allocation by investigators, coordinators, research assistants, community health workers	Samples intervention staff in representative weeks to document time spent in interventions Physicians report of minutes in weight counseling.	Monthly recall of time allocation by physician/nurse, counselors, investigators, coordinators
Common analysis approaches	Power and sample size calculations based on common assumptions of minimal detectable difference, standard deviation, and longitudinal correlation. Developed common approach for primary data analytic plan.		
Common cost analysis	Apply standard labor rate at the national level in addition to local rate for the cost-analyses. Capture quality of life and medical costs from hospitalization, emergency room visit, and primary care visits.		
Common safety monitoring	Standardized reporting procedures and formats to document adverse events and unanticipated problems. Annual safety training sessions.		
Common Dissemination	Use RE-AIM framework. Potential audiences for dissemination: patients; health care provider; professional organizations; health care organizations; insurance companies; policy makers		

BMI: body mass index; CVD: cardiovascular disease; MI: myocardial infarction; ASCVD: arteriosclerotic cardiovascular disease; PCP: primary care provider; HOMA-IR: homeostatic model assessment - insulin resistance

Table 2

Comparison of the POWER Trials to traditional NIH-supported multi-center trials and single center trials

	Single Center Trials	Hybrid Model (e.g. POWER Trials)	Traditional Multi-center Trials	Research Network
Type of grant	Typically RO1 [†]	UO1 [§]	UO1 [§] or Contract [‡]	UO1 [§] , U54 [§] , or Contract [‡]
Protocol	One protocol	Separate protocols with distinct interventions but some common elements	One common protocol	Typically multiple protocols implemented simultaneously or sequentially
Sample size	Typically small or moderate size	Small or moderate size	Potential for very large size	Potential for large size
Coordinating functions	Not applicable	One coordination unit with mostly administrative functions	One Data Coordinating Center with administrative and data management and analysis functions	One Data Coordinating Center with administrative and data management and analysis functions
QA/QC	Individual site	Site-specific with input from other sites	Common procedures	Common procedures
Dissemination of principal findings	Independent	Independent with coordinated efforts	Centralized	Centralized
DSMB responsibility	Review and monitor one site.	Review multiple protocols. Monitor multiple sites	Review single protocol. Monitor multiple sites	Review single or multiple protocols. Monitor multiple sites.
Sponsor's role	Typically limited	Active role in some but not all aspects of designing and trial's monitoring progress	Heavily engaged in designing trial, setting common policies, and monitoring progress	Heavily engaged in designing trial, setting common policies, and monitoring progress
Cost to sponsor	Usually low or medium; support trial only	Medium to high; support trial sites and RCU coordination	High; support all sites and a data coordinating center for coordination and data analysis	Medium to high; support all sites and a data coordinating center for coordination and data analysis

[†]The NIH Research Project (R01) grant is an award made to support a discrete, specified, circumscribed project to be performed by the named investigator(s) in an area representing the investigator's specific interest and competencies, based on the mission of the NIH.

[§]The NIH U01 or U54 is a cooperative agreement award mechanism in which the Principal Investigator retains the primary responsibility and dominant role for planning, directing, and executing the proposed project. NIH staff (consisting of a Scientific Coordinator and Technical Advisory Group) will have substantial scientific and programmatic involvement during performance of the planned activity.

[‡]The NIH contract is an award instrument establishing a binding legal procurement relationship between NIH and a recipient obligating the latter to furnish a product or service defined in detail by NIH and binding the Institute to pay for it.