HealthPartners Riverside Clinic Recruitment Plan

Drs. Chadha, Margolis and the HealthPartners research team have extensive experience creating electronic recruitment database programs for large clinical trials such as ACCORD ((Action to Control Cardiovascular Risk in Diabetes,1N01HC095183-000) Study, AIM HIGH (AIM HIGH: Niacin Plus Statin to Prevent Vascular Events NCT00120289), the Journey for Control of Diabetes IDEA (Interactive Dialogue to Educate and Activate) Study, Hyperlink (1R01HL090965), and ASPREE (Aspirin to Reduce Events in the Elderly, U01AG029824). Using the process described below, HealthPartners has been one of the largest clinical sites in the US and Canada for many multi-site trials including ACCORD (305 subjects recruited), AIM HIGH (75 subjects recruited), IDEA (337 HP subjects recruited), Hyperlink (450 subjects recruited), ASPREE (181 subjects and still recruiting). Under Dr. Chadha's and Dr. Margolis' leadership, HealthPartners is among the largest sites for numerous other industry sponsored diabetes trials. The site coordinator, Shelly Cook, RN, was a member of the recruitment and adherence subcommittee for the AIM HIGH trial and HealthPartners Riverside was among the top recruitment sites for the trial overall.

The primary recruitment strategy used for D2d will be the same successful strategies used in previous clinical trials. The steps include developing the recruitment database program, weekly mailings of 150-200 letters, phone follow-up to non-responder patients, additional phone screening of interested eligible subjects prior to bringing them in for a screening visit. These steps are detailed below:

Maintenance of a Recruitment Database Program

HealthPartners members and patients identified through the electronic health record (EPIC Clarity) and Administrative Data Warehouse (ADW) who meet the primary eligibility requirements are populated in a recruitment database program that we have developed using a Microsoft ACCESS software. The recruitment database is refreshed as needed using the EPIC and ADW sources (e.g. monthly) to keep data such as A1c levels up to date and ensure that subjects within the recruitment database continue to meet the eligibility requirements (e.g. HbA1c 5.6-6.4, BMI >= 25, age, and current medication use).

Mailings

A query of the recruitment database is done periodically (e.g. weekly) to create a mailing list. The mail merge function is used to create letters of invitation for the selected patients. The primary recruitment methodology we use is to mail potentially eligible patients a letter of invitation along with a study brochure (assuming there is an approved brochure). The mailings are conducted efficiently using the HPRF Data Collection Center (DCC) located on the HPRF premises. The DCC is dedicated to efficient processes for mail, survey, and phone interviews related to research implementation.

The mailings are staggered weekly (e.g. 150-200 letters per week), so as to pace recruitment over the recruitment period. This staggered enrollment allows for an adjustment of letter volume on a weekly basis to deliver an even influx of participants and distribute the workload for staff over the recruitment and intervention period. Interested patients can either call a local number (a research assistant or coordinator located at the clinical research site) to learn more about the study or can return a form that we include with the invitational letter in a postage paid return envelope. Patients who are not interested can also return the form stating their lack of interest (opt-out) and can request not to be contacted again. Responders (including those who "opt out") are tracked in the recruitment database. Unless opted out, non-responders may receive a follow up phone call or second mailing if

necessary to stay on pace with recruitment goals. We have published data from the IDEA study demonstrating that a follow up phone call strategy can approximately double our recruitment yield from the mailed letters (but with added recruitment costs)

Phone follow up screening

Once a person has identified themselves as interested in the study, a research assistant verifies the information obtained from data sources and reviews the electronic health record to obtain additional information pertinent to the inclusion/exclusion criteria of the study. An IRB-approved process with a template will be used by screeners to verify all possible eligibility requirements prior to scheduling of a screening visit.

Screening visits

Screening visits are scheduled for patients who remain interested and eligible after the phone screening process.

Based on previous trials, recruitment efficiency using database and mailing methods (recruitment efficiency defined as the percent enrolled in the study out of the number of potentially eligible subjects mailed to) varies depending on the study, the funder, the risks identified in the consent, and the benefits of participating in the study (e.g. free medication and patient incentives). Our recruitment efficiencies have varied from 4.2 % (mailing method alone with no phone calls in the IDEA study) to 8.4% (mailing plus follow up phone calls IDEA study) to 10% (mailing methods ACCORD with relatively large patient incentives/free medications and care). Using a very conservative estimate of 4% efficiency, and using only the current population of patients (n=6635) with all criteria identified in our database (age >30, BMI >=25, no diabetes medications, and 5.8 < HbA1c < 6.5%), we could enroll 331 patients in this study. Another 128,383 patients were identified without A1c criteria (age >30, BMI >=25, no diabetes medication). We estimate that approximately 10% of these patients would meet pre-diabetes A1c eligibility requirements if screened, yielding a potential resource for an additional 12,000 eligible subjects within our care system. We also can access our HealthPartners insured members (non-patients) for mailings and we have identified an additional 35,816 members who are age > 30, no DM med claims, with diagnostic codes for obesity or overweight.

As demonstrated above, HPRF has a surplus of patients and members needed to enroll150 study participants over the 2 year recruitment period. We believe 300 enrolled subjects is a realistic commitment for our facility, independent of whether other sites in Minnesota are selected for D2d.

Site-specific Recruitment Strategy and Patient Population

Electronic Health Record (EPIC Clarity)

All medical care provided by HealthPartners-owned clinics and hospital is captured and maintained in an electronic health record (EHR) using Epic Systems, Inc., Madison, Wisconsin. Epic's main purpose is to support clinical care and to track billable treatments. For research and other reporting purposes, a subset of this data is extracted nightly into an Epic Systems database product named Clarity. Clarity includes pharmacy and laboratory data, vital signs, ICD, CPT, and other billing codes, and provider and patient identification. Data is fairly complete for race/ethnicity as this has been an area of attention for the care system in the last few years. Physician notes are obtained from a production server, Chronicles, which supports the EHR. To facilitate efficient chart review, we have developed a capability to extract specific notes based on patient ID and date range, and to text-search the contents of notes for combinations of words or phrases related to diagnoses and treatments.

Research Data Mart (RDM)

RDM is a subset of the ADW designed and constructed to allow efficient retrieval for standard types of research questions. The database is optimized for questions related to identification of patients with particular conditions based on various coding codes (e.g., ICD codes, pharmacy). This dataset allows a readily accessed archive of research data from the ADW, extending back to the mid- and early 1990's.

Estimated number of available participants

Total active patients: 376,917
Age > 30: 241,478
Age > 30 **and** BMI > 25: 144,678
Age > 30 **and** BMI >25 **and** no diabetes medications: 128,383
Age > 30 **and** BMI >25 **and** no diabetes medications **and** 5.8 < HbA1c <6.5%:6,635

Based on recent EHR data, the population is 77% white, 3% unknown or no answer, and 20% other racial groups. Minnesota has a growing minority and refugee population. We will initiate specially targeted mailings to minority patients, including telephone follow-up to assure adequate representation of minorities (at least 20%). We have used similar recruitment methods in other studies with excellent success in reaching recruitment goals in a timely fashion. These methods meet with our IRB's approval.